The Effects of Blood Glucose Levels on Cognitive Performance: A Review of the Literature

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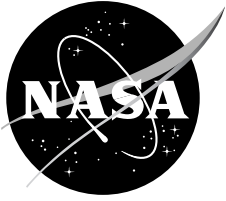
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INTRODUCTION

The purpose of this review paper is to discuss the research literature on the effects of blood glucose levels on executive and non-executive functions in humans. Non-executive functions are those involved in the basic processing of information (e.g., visual and auditory processing or motor skill). Executive functions involve higher order or more complex processing of information (e.g., reasoning, logic, planning, or problem solving). The aim of this review is to inform the development of a research project at NASA's Ames Research Center, investigating the effects of blood sugar levels on pilot performance. The review begins with a brief description of blood glucose, how it has been studied, previous syntheses of prior studies, and basic results regarding the role of blood glucose on cognitive functioning. The following sections describe work that investigated the effect of blood glucose on both non-executive and executive functions (e.g., sensory processing, psychomotor functioning, attention, vigilance, memory, language and communication, judgment and decision-making, and complex task performance). Within each section, summaries of the findings and challenges to the literature are included. Measurement conversions of blood glucose levels, blood glucose values (e.g., normal to abnormal levels), and associated symptoms are depicted in table 1. For consistency and clarity, all units of measurement of blood glucose values have been converted (from mmol/l) to mg/dl and rounded off. Similarly, use of descriptive qualifiers such as "mild," "moderate," and "severe" hypoglycemia are either used sparingly or are not included in study descriptions, due to a lack of consistency among researchers (e.g., different researchers label the same blood glucose level differently). Where qualifiers are used within the paper, blood glucose levels are reported. Table 2 provides references to the types of tests used to investigate blood glucose and cognitive performance. For more detailed descriptions of references within (and in addition to) this paper, an annotated bibliography is provided in the Appendix.

The literature describing research on blood glucose and cognition is large and diverse. While several important issues are evident within this body of literature (e.g., optimum glucose dosages and timing to measure peak performance) for the purposes of this review, these issues are only briefly discussed. Several moderator variables including individual differences and contextual variables related to the effects of blood glucose levels on performance (e.g., age, gender, time of day, familiarity with

the task and symptom awareness, expectancy effects, dose dependent effects, time dependent effects, task specific effects, rising and falling blood glucose levels, and speed and/or accuracy trade-offs) are addressed later in the paper. Some suggestions for future experimental methodologies are also made. This review does not include discussions on biochemistry (e.g., role of acetylcholine, epinephrine) or medical and nutritional perspectives (e.g., vitamins, supplements) concerning diagnosis or treatment of hypoglycemia (low blood sugar) because it is not within our scope or intent. We do not attempt to investigate the root causes of hypoglycemia or conditions associated with it (e.g., idiopathic reactive hypoglycemia or postprandial hypoglycemia), but rather are interested in describing the laboratory studies and findings that have investigated the effects of blood glucose levels on executive and non-executive functions.

WHAT IS BLOOD GLUCOSE?

Blood glucose, or blood sugar, is sugar in the bloodstream that easily passes the blood-brain barrier. The regulation of blood glucose involves the pancreas, liver, brain, and several hormones. Glucose is a simple sugar, which is an immediate source of energy for cells. Our brain uses a large amount of energy, and is dependent on blood glucose as its source of energy. The primary source of glucose is carbohydrates or starches and sugars, and consumption of these carbohydrates affects the rise and/or fall of blood glucose levels. Normal blood glucose levels in healthy (non-diabetic) adult individuals range from 70–110 mg/dl, and up to 140 mg/dl after meals. Consumption and digestion of all foods containing carbohydrates will raise blood glucose levels; however, some foods will raise levels at different rates than others. Because the brain cannot store glucose, it requires a continuous supply of glucose to function properly. Any shortage in this availability of glucose to the brain has adverse consequences for its functioning.

Reduced blood sugar level, or hypoglycemia, is "an abnormally low plasma glucose level that leads to symptoms of sympathetic nervous system stimulation or of central nervous system dysfunction" (Merck & Co., 2001). Hypoglycemia has been found to induce adrenergic symptoms such as nervousness and tremor as wells as central nervous system symptoms such as tiredness, confusion, and slowed mental function (Lincoln & Eaddy, 2001). Hypoglycemia occurs when glucose is released into the bloodstream more slowly than needed, when body glucose is used up too rapidly, or when excessive insulin is released into the bloodstream. The first signs and symptoms of low blood sugar can begin to occur below 70 mg/dl, although this varies from individual to individual. Hypoglycemia's effects on the central nervous system also include symptoms like deficiencies in coordination, headaches, blurred vision, anxiety, and dizziness (Field, 1989). Normal glucose regulation varies throughout the day. Circadian rhythms, time of day, and glucose tolerance have been reported to be associated with varied blood glucose levels. In some cases, performance has deteriorated only on certain tasks (e.g., sustained attention task) and glucose tolerance was worse in the afternoon, rather than in the morning.

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METHODOLOGICAL HISTORY

Investigations into blood sugar and its effects or associated conditions and diseases have largely been undertaken by those in the medical field. Early medical reports of blood sugar concentration and its effects began in the 1920s when symptoms similar to insulin-induced hypoglycemia (low blood sugar) were experienced in healthy individuals. A clinical condition termed "hyperinsulinism" by Harris (1924) was established in describing symptoms related to too much insulin in the bloodstream. Harris described a condition in which too much insulin enters the cell and results in a fall in blood sugar levels, or hypoglycemia. Whipple (1938) developed the Whipple's Triad to describe the triad of symptoms associated with hyperinsulinism. This triad includes specific symptoms (i.e., hunger, weakness), low concentrations of blood glucose at the same time, and reversal of these symptoms through the ingestion of sugar. This approach to diagnosing hypoglycemia is still used in the medical profession today in addition to the Glucose Tolerance Test (GTT) to determine how an individual's blood sugar level changes during fasting and after glucose administration. Throughout the years, numerous reports considered low blood sugar levels the source of various diseases, ailments, and even psychological disorders. Lack of a clear understanding of the effects of blood sugar levels, even in the medical profession, contributed to such reporting. This confusion rose to such epidemic proportions, that a special report was issued intended to address this mis-attribution of symptoms to hypoglycemia, clearly define hypoglycemia, and warn of the implications of over-diagnosis (American Diabetes Association, 1973). Over ten years later, Anderson and Lev-Ran (1985) raised this issue again, and after investigating 135 patients suspected of having hypoglycemia and finding only four cases in which patients were determined to be truly hypoglycemic, stressed the importance of using and interpreting the GTT accurately. Many dietary interventions and nutritional recommendations regarding blood glucose and its effects continue to be highly debated.

In experimental laboratory studies investigating the effects of blood glucose levels on performance of various tasks, researchers have relied on psychological tests and measures to assess the performance of individuals in compromised cognitive and physiological states. Some of these tests and measures have been described as "simple" and some have been described as "complex" or "cognitively demanding." This point requires further explanation. Through positron emission tomography (PET) scan evidence, Benton and Nabb (2003) describe how glucose metabolism in the brain is increased by increased mental activity. They describe an experiment in which a verbal task (associated with left hemisphere activity) depleted the metabolically active left hemisphere of glucose. In looking at the duration of a task, they state that it is often the later or more "complex tasks" that are affected (e.g., difficult but not easier trials on the Stroop and Porteus Maze tasks, choice rather than simple reaction times). While admitting the difficulty of defining such terms, Benton and Nabb assert that, "it is only the later stages of prolonged tasks that are susceptible to the provisions of glucose." According to Holmes, Koepke, and Thompson (1986), a Finger Tapping Task (FTT) and a letter recognition task were classified as "simple" tests, while a choice reaction time task was classified as a more "complex" test. They also found that more complex tasks rather than simple tasks were affected at low blood glucose levels. They based this task classification on the extent to which combined skills were required to perform it. However, it can be argued that a task might be viewed as "simple," but truly involve complex cognitive processes and may even be demanding. A clear categorization of task types (simple or complex) in relation to the specific processes or functions (executive or non-executive) is not the focus of this report. Such exploration would require a different approach and structure; therefore, this issue remains open for investigation. Despite the

obvious need for clear definitions and a standard use of labels within the literature (e.g., distinction between a "simple" versus a "complex" task or "mild" versus "moderate" hypoglycemia), it is clear that blood glucose levels affect performance on several tasks—regardless of how they are defined. This report is structured on that premise and on those processes that are affected. Clinical, cognitive, and neuropsychological tests that measure reaction time and accuracy enable researchers to determine what cognitive processes might be impaired, and to what extent these processes are affected. Typically, the procedure used in these experiments is to have participants, either insulin-dependent diabetics or healthy non-diabetics, fast overnight before participating in the experiment; alternatively, participants are induced to hypoglycemic or hyperglycemic (high blood sugar) states with a clamp technique that infuses insulin or dextrose into the bloodstream. Bischoff, Warzak, Maguire, and Corley (1992) provide a basic review of several studies on the acute and chronic effects of hypoglycemia (at blood glucose levels ranging from 35–60 mg/dl) on cognitive and psychomotor performance of adults and children, with and without diabetes. Essentially, the studies suggest that those who experience hypoglycemia exhibit performance impairments whether diabetes is present or not. In studies in which participants are not induced to hypoglycemic states but fast overnight, researchers provide a glucose drink or similar substance and/or a placebo and measure the effects on performance. To reduce the amount of variance or "noise" in experimental results, experimenters employ a double-blind repeated-measures design (each subject serving as their own control), use counterbalanced glucose (or saccharin or aspartamate as a placebo) drinks and validated standardized tests with accepted norms. They also obtain baseline blood glucose levels, fast participants overnight, and account for individual differences in glucose regulation. An important distinction is that, some studies focus on the positive effects of glucose ingestion, whereas others focus on the negative effects of glucose depletion.

Two studies (Manning, Hall, & Gold, 1990; Messier, Desrochers, & Gagnon, 1999) serve as prototypes of the methods typically used in this area. Manning et al. (1990) conducted an experiment to study memory and non-memory tasks in seventeen non-diabetic adults (62–84 years of age). They employed a repeated measures design using counterbalanced glucose drinks and tests. These standardized tests with accepted norms assessed memory (Selective Reminding Test, Logical Memory, Digit Span, Rey Osterreith Complex Figure, Ammon's Quick Test), attention (Letter Cancellation Test), and motor skill (Finger Oscillation Test). Participants arrived to the experiment after an overnight fast (9 hrs). After obtaining baseline blood glucose levels, levels were again measured fifteen minutes after beverage ingestion and every fifteen minutes thereafter (for the next hour and a half). Testing began ten minutes after ingestion of the beverage. Individual differences in glucose regulation were not a factor. They found that declarative, long-term memory (selective reminding test and logical memory) was enhanced after glucose ingestion (50 g) in older participants' performance, but short-term memory (digit span) and other processes (e.g., intelligence quotient (IQ test), attention (letter cancellation task), or motor functions (finger tapping task) were not affected. Messier et al. (1999) investigated impairments in young healthy adults caused by alterations in gluco-regulation, or the ability to properly utilize glucose. They sampled thirty-six college students using a double-blind repeated-measures design. Participants fasted overnight, ingested either a glucose or placebo beverage during two sessions, and were administered the tests ten minutes afterwards. Comparisons were made between those with good or poor gluco-regulation, and irrespective of gender, those with poor regulation had poorer word list recall performance than those with good regulation. This was found for both concrete and abstract words, and for immediate and delayed recalls. Benton and colleagues (1996) describe gluco-regulation as blood glucose levels that

fall markedly after administration of glucose and during a subsequent task (returning to baseline levels about two hours afterwards) reflecting better glucose tolerance and resulting in better performance on cognitive tests (similar to later predictions by Donohoe and Benton, 1999b). This is contrary to poor gluco-regulation where blood glucose levels remain raised after administration of glucose and while performing a task, reflecting the inability to move glucose from the blood and into the cells. For an extensive description of the types of tests used to investigate blood glucose and cognitive performance, see table 2. For studies investigating the effects of blood glucose levels on emotion and/or mood (which is not an area covered in this report) see: Benton (2002); Benton, Brett, & Brain (1987); Benton & Nabb (2003); Benton, Slater, & Donohoe (2001); Owens, Parker, & Benton (1997); Reid & Hammersley (1995); Smith, Kendrick, Maben, & Salmon (1994); Smith, Kendrick, & Maben (1992); and Taylor & Rachman (1988).

BASIC FINDINGS

Investigations into the effect of glucose on performance have been conducted in both animal and human models. Some experiments have explored the effect of glucose on learning in rats and mice, memory and mood in school children, attention, memory, and decision-making in college students, memory in adults and of those suffering from Alzheimer's Disease, and with drug interactions in enhancing memory. Interestingly, age-related decrements in human memory have been reversed by a glucose drink, and after glucose administration in animal studies. Aged mice performed as well as young mice in maze tests after glucose administration. Similar results have been found in aged versus young healthy participants, provided the task for young participants is "demanding" and "of appropriate duration." Researchers have also found that cognitive function is correlated with glucose regulation and have investigated the role of hormones and their interactions with glucose levels (Wenk, 1989). The glucose regulation of individuals is an important factor to be considered, independent of age and discrete populations. Young males with poor glucoregulation demonstrated equivalent performance on a memory task (recall of prose) to older men with good glucoregulation (Craft, Murphy, & Wemstrom, 1994).

Benton, Parker, and Donohoe (1996) provide a useful overall review of the effect of blood glucose on cognitive functioning, particularly with regard to issues relevant to non-diabetics. They discuss the widely accepted view that very low blood glucose levels (hypoglycemia) cause physical and psychological symptoms associated with a disruption of cognitive functioning. They emphasize that it is not only low blood glucose levels but also an individual's ability to tolerate blood glucose levels within a normal range that can affect performance. They also found that when participants entered experiments with higher initial blood glucose levels, they tended to recall more words from a list. The findings from the studies Benton and colleagues describe support the view that "cognitively demanding" situations deplete the brain of glucose, that those with higher rather than lower levels of blood glucose perform cognitive tasks more efficiently, and that individuals' good glucose tolerance (ability to effectively use glucose) is associated with better cognitive functioning.

The enhancing effects of glucose on memory (e.g., better retention, reduced-forgetting) have been reported well within normal blood glucose levels (Gold, 1995). This means that an individual does not have to be outside of the normal range of blood glucose levels to experience the benefits of a glucose provision. Messier and Gagnon (1996) have described the effect of glucose in both a periph-

eral (outside of the blood-brain barrier) and central manner, as well as its affects on disease (e.g., Alzheimer's). They report that increased glucose improves memory in several mammalian species and that ingestion of glucose improves declarative memory, while abnormal glucoregulation (e.g., Alzheimer's disease) is associated with memory impairment (see Korol & Gold, 1998, for interesting claims about broad enhancing effects of glucose ingestion).

Despite varied research approaches in the blood glucose literature, one finding has been reported clearly in numerous studies—blood glucose levels affect cognitive performance. Increased provisions of glucose in the bloodstream from a glucose drink or eating breakfast have been found to benefit participants' performance (e.g., Benton & Parker, 1998). On the other hand, decreased levels of glucose from participants fasting overnight and throughout an experiment and/or ingesting a placebo drink (that does not increase blood glucose levels) have been found to impair performance (e.g., Evans, Pernet, Lomas, Jones, & Amiel, 2000) (see table 2). With diminishing reserves and increased cognitive demands, individuals are susceptible to impaired performance (Benton et al., 1996). Low blood glucose levels either from fasting or from participants being induced to hypoglycemic levels have resulted in performance decrements (e.g., McAulay, Deary, Ferguson, & Frier, 2001). Tasks that involve both executive and non-executive functions have all been shown to be impaired at low blood glucose levels: declarative memory (immediate and delayed recall) assessed by word list recall (Craft et al., 1994; Benton et al., 2001), and spatial memory assessed by grid drawings (Benton & Parker, 1998; Benton & Sargent, 1992), decision-making and reaction time assessed by Jensen or Choice Reaction Time (CRT) tasks (Gold, MacLeod, Deary, & Frier, 1995; Owens & Benton, 1994), fine motor skill and divided attention assessed by a manual tracking tests (Schächinger, Cox, Linder, Brody, & Keller, 2003), verbal fluency assessed by word list generation (Scholey, Harper, & Kennedy, 2001), visual processing assessed by line length discrimination tasks (McCrimmon, Deary, Huntly, MacLeod, & Frier, 1996), auditory processing assessed by tests of basic auditory capabilities (TBAC) (McCrimmon, Deary, & Frier, 1997), selective attention assessed by the TBAC and CRT tests (McAulay et al., 2001; Evans et al., 2000), and sustained attention assessed by performing mental calculation tests (Schächinger et al., 2003). Increased reaction time and/or decreased accuracy have been observed on all of the tests used to assess these functions. Furthermore, higher functions (such as cognitive performance assessed by the Paced Auditory Serial Addition Task) are affected earlier than are lower functions (such as motor function assessed by a Finger Tapping Task) (Cox, Gonder-Frederick, Schroeder, Cryer, & Clarke, 1993). Low blood glucose levels have also negatively affected steering, braking, and speed control performance in driving simulator research (Cox, Gonder-Frederick, Kovatchev, Julian, & Clarke, 2000). These studies and these tasks are further examined later in this review.

CRITICAL FINDINGS IN THE LITERATURE

The importance of understanding the effects of low blood glucose levels on performance is evident given three main findings in the literature. First, individuals do not need to be hypoglycemic to experience symptoms of low blood sugar. Blood glucose levels could be low but well within a normal range, yet negatively affect memory performance (Benton & Owens, 1993; Donohoe & Benton, 1999b). Second, individuals may not immediately recognize the symptoms of low blood sugar. In a study by Evans, et al. (2000), awareness of hypoglycemic symptoms was delayed for up to twenty minutes after participants demonstrated obvious cognitive dysfunction. Third, individuals

need time to recover from low blood glucose levels. The rule of "15–15" treatment is used by diabetics for recovery of low blood glucose levels. When an individual realizes that she or he is becoming hypoglycemic, they are to treat themselves with fifteen grams of carbohydrates and wait fifteen minutes to recover. In a laboratory study of healthy individuals, Benton and Parker (1998) found that the negative effects of fasting (e.g., missing breakfast) on memory were nullified by the consumption of a 50 gram glucose drink, so that performance on a consonant trigram test significantly improved from trials 1–4 to trials 5–8. In a study by Holmes et al. (1986), reaction times did not return to normal until twenty to thirty minutes after euglycemia at 110 mg/dl. Comi (1993) describes literature to suggest that complete cognitive recovery may lag for thirty to forty-five minutes behind restoration to normal blood glucose levels.

The effects of low blood sugar level on cognitive processes may be most apparent when errors present risk. It is possible that individuals may be negatively affected by low blood glucose levels, may not be aware of this, and may not be able to respond in a timely manner. Individuals may not necessarily be hypoglycemic, but an individual's blood sugar level might drop from lack of food to a level where cognitive performance is negatively affected. Again, by the time the individual becomes aware of the impairment, their cognitive functions may have already been degraded for some time.

In the next chapter, experimental studies on the effects of blood glucose levels on sensory processing, psychomotor functioning, attention, vigilance, memory, language and communication, judgment and decision-making, and complex tasks are examined. One could argue that various forms of the tests used in blood glucose and performance research assess combinations of these basic functions and furthermore, that these basic functions may affect performance at higher levels of processing, whether they are intentionally tested or not. Clearly, several tasks described in this and subsequent sections involve more than assessment of a single function (e.g., visual processing). The task may involve or even require some level(s) of psychomotor functioning, attention, judgment and decision-making; therefore, such tasks may also be described in other sections of this report where relevant. However, a conservative approach is used – not every study related to each and every aspect of functioning is cited in each section. Effects of blood glucose levels on performance cannot be examined in an orthogonal manner – functions and tasks are largely interdependent. Determining whether a particular test described in a study assesses only one aspect of functioning (e.g., Trail Making B test to assess visual scanning), or whether the results from a particular test used in a study may extend to other categories of functioning (e.g., Trail Making B also involves aspects of attention, judgment and decision-making) is left to the reader's discretion.

THE EFFECT OF BLOOD GLUCOSE ON SENSORY PROCESSES

Initial performance effects from varying blood glucose levels may be seen in sensory processing abilities involving visual and auditory functioning. This section describes studies and results pertaining to these processes. Aspects of the tests used assess overall visual information processing, inspection time, visual change detection, contrast sensitivity, visual and visuo-motor tracking, visual discrimination, and visual selective attention. Some studies investigating reaction time to a visual stimulus are included in this section, but are also examined in the psychomotor section. The methods in which auditory processes have been studied, and what has been found using tests that assess

listening span performance, auditory selective attention, responses to an auditory stimulus measured by event-related brain potentials (P300 waveforms), and auditory memory and verbal learning are also described in a following section.

Visual Processing

Blood glucose levels have affected performance on tasks requiring visual processing. McCrimmon et al. (1996) investigated the effect of insulin-induced low blood glucose levels on visual functions and visual information processing in healthy, non-diabetic individuals (range 23–30 years of age). Using standard clinical vision tests, researchers investigated visual acuity, stereoscopic vision, and contrast sensitivity. Visual inspection time was assessed by differentiation of line length between two parallel vertical lines, where the participants' task was to detect the line of longer length. To assess visual change detection, participants had to attend to a wide stimulus field and detect the locus of discrete change in a large array of identical stimuli, essentially detecting an additional rectangle in an array of rectangles on a monitor. To assess visual movement detection, participants needed to detect movement of a triangle in a large array of triangles. Timing to detect and respond to these stimuli was measured. While McCrimmon and colleagues did not find visual acuity to be affected at an induced hypoglycemic level of 45 mg/dl, contrast sensitivity significantly deteriorated (as did performance on cognitive tests – Trail Making B test and Digit Symbol Coding). Hypoglycemia affected acuity of low, but not highly, contrasting symbols. Hypoglycemia impaired participants' ability to detect visual change and visual movement. Visual inspection time was longer during a hypoglycemic level of 45 mg/dl as compared to euglycemic (baseline) levels at 81 mg/dl. Whether the attentional field was broad (inspection time task) or narrow (visual change detection and visual movement detection tasks), both were significantly disrupted during hypoglycemia. Strachan, Deary, Ewing, Ferguson, Young, and Frier (2001) used a forced-choice discrimination task to assess inspection time and early visual information processing in healthy, non-diabetic individuals induced to hypoglycemic levels of 47 mg/dl. Similar to the visual inspection time task in the McCrimmon study, the task required participants, at their own pace, to correctly choose which of two parallel vertical lines were longer. Performance on this task deteriorated at this hypoglycemic level as compared to euglycemic (baseline) levels at 90 mg/dl. Lindgren, Eckert, Stenberg, and Agardh (1996) investigated event-related brain potentials looking at P300 amplitude and latency, in healthy, non-diabetic males induced to a hypoglycemic state of 45 mg/dl. A sub-group from this subject pool was used as a control group. The P300 component of event-related potentials is commonly used as an index of cognitive functioning. The amplitude of the P300 reflects attentional processes, while the latency reflects evaluation time. Lindgren and colleagues studied event-related potentials, during visual search tasks where participants were shown an array of rectangles and pressed a button when the target either appeared or did not appear. Two levels of this task were examined that involved either a parallel search or a serial search. These tasks were thought to require different levels of cognitive processing. They found that performance on serial search was significantly affected at hypoglycemia, showing decreased attentional processes. Parallel search latencies were generally longer in the hypoglycemic group, but did not vary significantly between sessions. Task accuracy was not affected by hypoglycemia.

Interestingly, level of awareness of hypoglycemic symptoms may be an indicator of the level of impairment of visual information processing that occurs at hypoglycemic levels. Gold, MacLeod, et al. (1995) investigated the effect of awareness (normal vs. impaired awareness) of hypoglycemia

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on performance in two groups of diabetic individuals. Participants were grouped according to history of impaired awareness or not and blind to the two conditions. One condition involved lowering participants' blood glucose levels to 45 mg/dl and maintaining it at that level for thirty minutes before returning it to normal levels at 81 mg/dl. The other condition involved maintaining blood glucose levels at 81 mg/dl throughout the testing sessions. The Rapid Visual Information Processing (RVIP) test was employed, whereby a series of numbers on a screen appear and the subject presses a button when three consecutive odd or even numbers appear. Correct answers, false positive answers, and reaction time were measured. Researchers found that a hypoglycemic level of 45 mg/dl significantly affected performance in both groups, with the patients with impaired awareness having a tendency to perform more poorly during hypoglycemia, and upon recovery from hypoglycemia remaining significantly impaired as compared to the normal awareness group. Those with a history of impaired awareness at hypoglycemic levels responded with more false positive answers than those with normal awareness. Both groups were significantly slower on RVIP reaction time performance at hypoglycemia than at euglycemia. Again, the impaired awareness group tended to be slower overall.

Reaction time performance to visual stimuli has been impaired at low blood glucose levels. Blackman, Towle, Lewis, Spire, and Polonsky (1990) used either an auditory or visual stimulus and recorded reaction time and P300 waveform to investigate performance in healthy, non-diabetic individuals induced to hypoglycemic levels (59 mg/dl then to 47 mg/dl). The visual component of the P300 waveform was measured while participants pressed a button in response to a red light-emitting diode (LED) centered on a screen. An additional task required participants to press a button in response to a red LED but not a green LED. Reaction times for these tasks were recorded. Hypoglycemia resulted in an increased latency in the P300 waveform at 47 mg/dl but not at 59 mg/dl. Blackman and colleagues interpreted the P300 results as reflecting the increased sensory and processing time associated with decision-making at low blood glucose levels. Hypoglycemia also increased simple reaction time to visual stimuli at 47 mg/dl. Visual and auditory event-related potentials were not significantly affected; however, reaction time was. Snorgaard, Lassen, Rosenfalck, and Binder (1991) found that reaction time to a visual stimulus deteriorated in suspected hypoglycemic patients at 50 mg/dl, and at 38 mg/dl in normal participants (control group). The task required participants to press a button when a red square appeared on a screen while they were reduced to hypoglycemic levels in a stepwise insulin-induced manner. Reaction time increased by fifty percent in both patients and normal participants. For normal participants, this impairment occurred between 115 and 155 minutes at insulin-induced levels, with a median blood glucose level of 38 mg/dl, and earlier for patients at 95 and 115 minutes, with a median blood glucose level of 53 mg/dl.

Similarly, low blood glucose levels have also negatively affected reaction time performance to a visual stimulus in diabetic individuals. As defined by Holmes et al. (1986), more "complex" rather than "simple" tasks appear to be affected by varying blood glucose levels, with performance on complex tasks (i.e., choice reaction time) being slowed. Holmes and colleagues were interested in the effects of varying blood glucose levels (hypoglycemia, euglycemia, and hyperglycemia) on complex or simple task performance in diabetic individuals (range 18–35 years of age). Male participants were induced to hypoglycemic levels (55 mg/dl) and performed either a simple Finger Tapping Task (FTT) or complex sensory motor tasks. Simple reaction time (one light presented, one key pressed), go/no-go reaction time (two lights presented, respond only to one light), and choice reaction time (two lights presented, either of two keys pressed) were measured. A letter recognition

task (participants view a letter for five seconds and later respond by finger tapping) assessed simple motor responding. This task was not affected at varying blood glucose levels. Even though simple reaction time to a visual stimulus was not affected, responses were increasingly slowed during hypoglycemia as the complexity of decision-making increased on the go/no-go and choice reaction time tasks. In a study by Maassen, Lingenfelser, Glück, Renn, Eggstein, and Jakober (1990), investigators were interested in the effects of different types of insulin on the performance of diabetic (18–27 years of age) and normal (21–25 years of age) participants at insulin-induced hypoglycemia ($M = 65$, 50, and 40 mg/dl). They used the Vienna Reaction Timer, to assess reaction time to a visual stimulus. The task required a subject to press a button as quickly as possible after a yellow light appeared. Results indicated that regardless of insulin or subject type, there was a significant increase in reaction time during hypoglycemia ($M = 40$ mg/dl) as compared with euglycemia ($M = 100$ mg/dl).

Visual scanning or tracking has shown somewhat mixed results in healthy and diabetic participants at hypoglycemic induced levels. Pramming, Thorsteinsson, Theilgaard, Pinner, and Binder (1986) recruited diabetic men and induced them to varying blood glucose concentrations (108, 54, 36, and 108 mg/dl) to assess cognitive functioning. The Trail Making B (TMB) test was used to assess attention, planning, and visual scanning. The TMB is a timed test and requires participants to connect letters with numbers in an alternating fashion. The researchers found that although scores fell on this test (and other measures) at 108 mg/dl to 54 mg/dl, the difference was not significant at this level. However, test score(s) fell significantly at 108 mg/dl to 36 mg/dl. They assert that performance on this task involves planning and control, which will suffer at about 54 mg/dl. Hoffman, Speelman, Hinnen, Conley, Guthrie, and Knapp (1989) found that performance of diabetic participants (22–35 years of age) induced to hypoglycemic levels of 50 mg/dl on a Pursuit Rotor Task (a subject tracks a dot rotating on a turntable with the stylus), and on the TMB test was significantly impaired as compared to euglycemic levels (100 mg/dl). Mean time on target during 1-minute intervals for the pursuit rotor task and time to complete the TMB test were affected, and reaction time was generally slower during hypoglycemia; however, further main effect evaluations for reaction time performance failed to reach significance. Conversely, Evans et al. (2000) used the TMB test to assess visual conceptual, and visuomotor tracking, in healthy male volunteers (26.8, ±3.6 years of age) induced to hypoglycemic levels at 48 mg/dl. While performance on other cognitive tests (i.e., Stroop) was impaired, the TMB test failed to show any deterioration. Evans and colleagues suspected that this was due to individual differences between participants' even at euglycemia.

Visual selective attention has been shown to be affected at low blood glucose levels. McAulay et al. (2001) investigated insulin-induced hypoglycemia on visual selective attention in healthy, non-diabetic volunteers using the Test of Everyday Attention (TEA). The TEA is the only test currently available to assess attention based on everyday materials, with high test-retest reliability and correlating significantly with existing attention measures. Two of the eight TEA subtests assess visual selective attention: Map Search (participants search for a symbol on a map of the Philadelphia area in two minutes – the number of symbols found within the first minute is compared with the final number of symbols found) and the Telephone Search (participants look for key symbols in a telephone directory). Performance on the Map Search test deteriorated at hypoglycemic levels of 47 mg/dl. During hypoglycemia versus euglycemia, the number of symbols found was lower, but this was not significant. In the Telephone Search test, no significant differences in the number of

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symbols located between euglycemia and hypoglycemia conditions were found. However, the time taken to complete the task increased during hypoglycemia. Accuracy was preserved at the expense of speed on this task – suggesting that either response speed is slower or that participants adopt a cautious approach to avoid errors. McAulay and colleagues conclude that at hypoglycemic levels of 47 mg/dl, a visual selective attention decrement had developed.

Visual discrimination performance at low blood glucose levels has shown mixed results. Low blood glucose levels have resulted in healthy participants showing performance impairments after fasting as compared to diabetics induced to hypoglycemic levels showing no effects. Holmes, Hayford, Gonzales, and Weydert (1983) maintained blood glucose at hypoglycemic (60 mg/dl), euglycemic (110 mg/dl), and hyperglycemic (300 mg/dl) levels in diabetic college students while assessing cognitive functioning. A Matching Familiar Figures Test (MFFT), where participants match a figure to a sample, was used to measure attention, but visual discrimination skill is also required. The Benton Visual Retention Test, where participants copy complex geometric designs, assessed visual spatial and visuomotor perception abilities. Holmes and colleagues did not find significant glucose-related effects for either of these types of tasks. However, sustained visual attention, where participants pressed a key as quickly as possible after a target light was presented, was negatively affected. Performance on attending and responding to a visual stimulus was slowed at blood glucose levels at 60 mg/dl and 300 mg/dl as compared with levels at 110 mg/dl. Performance at glucose levels at 300 mg/dl was significantly faster than at glucose levels at 60 mg/dl, although still slower than at levels at 110 mg/dl. Conversely, another study investigated performance using the MFFT in healthy non-diabetic children who either ate or did not eat breakfast. Using the MFFT to assess discrimination among similar visual stimuli, Pollitti, Cueto, and Jacoby (1998) found that the mean glucose concentrations were significantly different on the no breakfast day ($M = 77$ mg/dl) as compared to the breakfast day ($M = 80$ mg/dl). Performance on the MFFT task was negatively affected by blood glucose levels, in healthy children who had no breakfast as compared to those who consumed breakfast, as glucose levels dropped, the number of errors increased. In a second experiment, errors on the MFFT were significantly greater after participants did not eat breakfast than when they consumed breakfast. Fasting delayed performance on visual discrimination assessed by the MFFT – with children showing poor discrimination between meaningful versus irrelevant cues. Children were not induced to hypoglycemic levels, but fasted (in the no breakfast condition) and their performance was impaired on this task.

Challenges to Visual Processing Studies

The challenges to studies in this area include the type of tasks used and whether they are sensitive or complex enough to detect performance differences at varying blood glucose levels; the subject pool used (diabetics versus non-diabetic individuals); the differences in blood glucose levels (mg/dl) between experiments that used similar performance measures represent another challenge (i.e., TMB; see Pramming et al., 1986; Evans et al., 2000; Hoffman et al., 1989). Some visual tasks appear to be more sensitive to the effects of low blood glucose levels than others (e.g., visual contrast, visual movement, and inspection time; but not visual acuity of highly contrasting stimuli). What is unique about similar tasks that contribute to the conflicting results remains unclear at this point. For example, in the McAulay et al., study (2001), the tasks they used to assess visual selective attention were similar yet produced different results; hypoglycemia affected visual selective attention performance on a search for a symbol on a map task while a symbol search in a telephone

directory remained unaffected. Different subject types or varying blood glucose levels do not explain these differences within this experiment. One possibility suggested by Holmes et al. (1983), may explain the results found in the McAulay et al., study (2001). Holmes and colleagues (1983) speculated that they did not find visual drawings or matching figures tasks to be affected in their experiment because very quick (reaction time) responses are more susceptible to glucose-related impairments, rather than self-paced drawing or detailed visual perception. However, visual tasks requiring more intensive levels of processing (higher complexity) remain affected. The Blackman et al. (1990) and Lindgren et al. (1996) findings are similar. They employed similar methodologies and found corroborating evidence for the effects of low blood glucose level on reaction time. However, the difference in the Lindgren et al. (1996) study finding a significant effect on serial search, while the Blackman et al. (1990) study did not, may be attributed to task complexity. In the Blackman et al. study (1990), the task required participants to merely distinguish and respond or not to a red or green LED stimulus. On the other hand, the visual search task in the Lindgren et al. (1996) study required an increased level of processing on the serial search task that involved distinguishing among more features of a target. This task may be a more sensitive measure of intensive attentional processes. In the Strachan et al. (2001) and McCrimmon et al. (1996) studies, it is possible that performance at higher blood glucose levels would have been even more negatively affected if a time limit for the task were imposed.

Some assessments of performance on visual processing tasks at varying blood glucose levels have demonstrated mixed results in both non-diabetic and diabetic groups, and in some cases using the same test (Holmes et al., 1983; Pollitti et al., 1998). Sustained attention was affected at 60 mg/dl (Holmes et al., 1983) and reaction time was affected at 47 mg/dl (Blackman et al., 1990). This supports the notion that higher functions are affected earlier than are lower functions. However, the difficulty in investigating the effects on performance based on differing glucose levels on identical tasks remains (i.e., what blood glucose level is considered hypoglycemic). For example, in one study diabetic men were induced to hypoglycemic levels at 36 mg/dl and had impaired performance on the TMB test (Pramming et al., 1986), while in another study using diabetic participants who were induced to 48 mg/dl did not exhibit impaired performance on the TMB task (Evans et al., 2000). Experimenters may consider clarifying the definition of hypoglycemia to a specific and standardized blood glucose level.

Mixed results may also be due to the method in which participants are brought to low blood glucose levels (e.g., induced or fasting). In the Holmes et al. (1983) and Polliti et al. (1998) studies, the task was the same (MFFT) but the subject pool and blood glucose lowering technique varied. Polliti and colleagues recruited children who fasted as participants, while Holmes induced diabetic college students to hypoglycemic states. A significant effect on this task was found with the children, but not with the diabetic college students. Blood glucose levels of children in the no breakfast condition lowered as a result of fasting to 77 mg/dl, which is much higher than the college students induced to 59 mg/dl. This task may not have been difficult or sensitive enough for college students (e.g., ceiling effects) to clearly show effects of low (or high) blood glucose levels. However, a better explanation of the differences may be due not only to the glucose lowering technique (clearly, insulin-inducing techniques allow experimenters to exert more control over levels), but to age as a factor, with changes in glucose regulation over time.

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Interestingly, some visual processes are affected by low blood glucose level and these responses reflect different patterns of performance in both diabetics and healthy individuals (e.g., increased false positive answers in diabetics, and a speed-accuracy trade-off in healthy individuals). Level of hypoglycemic symptom awareness in diabetics was investigated and demonstrated performance effects (more aware, less impaired performance versus less aware, more impaired performance); this effect of symptom awareness on performance may also occur in healthy non-diabetics on other tasks (see driving performance in the Complex Task Performance section).

Summary of Findings of Visual Processing Studies

Hypoglycemic levels in non-diabetic healthy individuals do not appear to affect visual acuity, but do affect (low) contrast sensitivity and detection of visual change and movement at 45 mg/dl. Studies measuring performance on visual discrimination and visual scanning or tracking tasks have produced mixed results. Sustained visual attention, assessed by key pressing after a target appears, is negatively affected (slowed) at hypoglycemic levels at 60 mg/dl (Holmes et al., 1983). Inspection time and reaction time to visual stimuli increases at low blood glucose levels (McCrimmon et al., 1996; Blackman et al., 1990; Holmes et al., 1986; Maassen et al., 1990). The blood glucose range that appears to affect visual processing (including visual attention) tasks resides between 36–60 mg/dl (Pramming et al., 1986; Holmes et al., 1986).

Performance on (visual) reaction time tasks shows the clearest effects of varying blood glucose levels. Low blood glucose levels consistently show a reduction in the speed of reaction time performance on these tasks (Blackman et al., 1990; Snorgaard et al., 1991; Holmes et al., 1986; Maassen et al., 1990). Impaired performance on reaction time tasks to visual stimuli shows a type of response pattern that develops (increased false positive answers) at low blood glucose levels, but this may be limited to diabetic subjects (Gold, MacLeod, et al., 1995). However, patterns of speed-accuracy trade off responses in healthy individuals using different tests have also been demonstrated. Not only has a general slowing of performance been found with low blood glucose levels through various reaction time tasks, but also in tasks that involve more intensive processing, with a trend toward accuracy being preserved at the expense of speed (Lindgren et al., 1996; McAulay et al., 2001). Blackman and colleagues (1990) emphasize that hypoglycemia in their study did not appear to affect motor processes but did show a general slowing of the brain processes in decision-making. They reported that this deterioration can occur in healthy individuals between 47 and 59 mg/dl and detected a continuing cognitive lag in their participants after recovery time, lasting from forty-five and up to seventy-five minutes. Effects of blood glucose levels on decision-making and cognitive lag will be explored in later sections.

To summarize, certain visual functions (e.g., inspecting, attending and responding to visual stimuli) appear to be slowed at low blood glucose levels. Visual discrimination tasks may not be as affected, but impairments on reaction time tasks show a consistent effect. At low blood glucose levels, accuracy on visual processing tasks tend to be preserved at the expense of speed and whether this is due to individuals experiencing a general overall cognitive slowing or to adopting a more cautious approach to performing the task remains unclear.

Auditory Processing

Researchers have used the Test of Basic Auditory Capabilities, Listening Span Test, the Test of Everyday Attention, and event-related brain potentials in response to auditory stimuli to assess simple auditory processing, listening comprehension, and auditory selective attention. These tests assess auditory processes that range from simple sound discrimination to more complex memory and decision-making processes based on auditory information.

Blood glucose levels have affected performance of basic auditory processing in non-diabetic individuals. Using standardized auditory tests, McCrimmon et al. (1997) investigated the effect of hypoglycemia in healthy adults on auditory information processing. Using parts of the Test of Basic Auditory Capabilities (TBAC), the participant listens to pre-recorded auditory stimuli and identifies which of two stimuli following the initial stimuli is different from it, and discriminates the order in which the two tones occur. The parts assess simple auditory processing (pitch discrimination, single-tone loudness, single-tone duration), and auditory temporal processing (temporal order discrimination). At acute insulin-induced hypoglycemia (47 mg/dl), individuals' auditory temporal processing and single-tone loudness significantly deteriorated. However, determining duration of a tone, or pitch was not significantly affected. McCrimmon and colleagues assert that hypoglycemia slows down the process by which the brain gathers information through the auditory system, and that these low-level effects contribute to decline in high-level cognitive processes.

Blood glucose levels have also been shown to affect listening span performance in healthy individuals, whereas auditory digit span performance was not affected in diabetic individuals. Morris and Sarll (2001) used the Listening Span Test to assess listening span performance, a good predictor of listening comprehension, in non-diabetic students (M = 21.15 years of age) who fasted prior to the experiment and either received glucose or a placebo drink. The task required individuals to listen to statements and determine whether they were true or false (e.g., Tony Blair is a politician), and the second part required individuals to recall in serial order the last word in each statement that they heard. Listening span performance improved after a glucose drink, but not after a placebo (or saccharin drink) – where placebo group participants' glucose levels were measured and averaged at 83 mg/dl. An interesting point is that, the two groups did not significantly differ in blood glucose levels across the study; however, listening span performance significantly improved after a glucose drink but not after a saccharine drink. Conversely, Holmes et al. (1983) used an auditory memory task for digits (Digit supraspan), (diabetic individuals had twelve trials to repeat a series of nine digits), and the Rey auditory verbal learning task (individuals had five trials to correctly repeat fifteen words). No significant differences were found on either of these tasks at insulin-induced low blood glucose levels (60 mg/dl) as compared to euglycemia control (110 mg/dl) and hyperglycemia (300 mg/dl).

Blood glucose levels in healthy individuals have been shown to affect auditory selective attention. For example, McAulay et al. (2001) assessed aspects of working memory and attention as well as auditory selective attention in healthy volunteers using subtests from the Test of Everyday Attention (TEA), specifically Elevator Counting, Elevator Counting with Distraction and Elevator Counting With (direction) Reversal. The Elevator Counting task requires individuals to pretend that they are in an elevator with a broken floor indicator, and to listen for which floor they arrive on by counting the series of tones presented on an audiotape. For the distraction task, individuals counted based on the

same tones heard in the previous task, but were instructed to ignore a tone of higher distracting quality. In the (direction) reversal task, individuals were told to pretend that they were traveling up and down to different floors in an elevator, indicated by audio tones at a fixed speed, and to determine which floor they were on. They found that scores did not deteriorate during hypoglycemia on the elevator counting or the (direction) reversal task, but performance declined on the distraction task during hypoglycemia. A decline in the rate of auditory selective attention, as assessed by the Elevator Counting with Distraction task, was demonstrated in healthy individuals at 47 mg/dl.

Mixed results were found in performance on the auditory component of the P300 ERP, in healthy individuals at low blood glucose levels. Blackman et al. (1990) presented a 2-kilohertz (kHz) rare tone and a 1-kHz frequent tone to healthy volunteers at lowered blood glucose levels, and investigated event-related auditory brain potentials (P300 task), as described in the previous section. Blackman and colleagues found a significant increase in auditory P300 latency, claiming that these slowing effects on the brain's sensory and cognitive processing related to decision-making from auditory stimuli, at hypoglycemic levels of 47 mg/dl. Glucose was infused for forty-five minutes after the hypoglycemic episode to raise participants' blood glucose levels to baseline and then participants consumed the meal. At baseline, mean blood glucose levels for the hypoglycemic session were at 90 mg/dl (±0.72 mg/dl), and 88 mg/dl (±1.08 mg/dl) for the euglycemic session. After glucose administration, mean blood glucose levels for the hypoglycemic session were at 97 mg/dl (±0.36 mg/dl), and 92 mg/dl (±0.54 mg/dl) for the euglycemic session. After the high carbohydrate meal, mean blood glucose levels for the hypoglycemic session were at 137 mg/dl (±5.4 mg/dl), and 117 mg/dl (±3.6 mg/dl) for the euglycemic session. Auditory P300 remained significantly affected (slowed) after intravenous glucose administration, but returned to baseline after consumption of a high carbohydrate meal. They report that this may be due to a cognitive lag behind restoration of glucose levels. Using similar methods of investigating the effects of hypoglycemia on auditory performance, Lindgren et al. (1996) analyzed the auditory component of the P300 by presenting tone bursts at one of two frequencies: 2000 Hz and 500 Hz in random order. Individuals counted the infrequent, lower tones. No significant effects on performance during hypoglycemia at 45 mg/dl were found for the auditory P300.

Challenges to Auditory Processing Studies

Some of the challenges in this area include ceiling effects, the level of complexity of the task, sample size, and the complicated nature of the relationship between blood glucose levels and performance. McAulay and colleagues (2001) state that the ceiling effects found in the elevator-counting task may have contributed to a lack of significant findings. Lindgren and colleagues (1996) attributed the lack of finding significant results to the lack of complexity of the auditory task, as compared to the significant results from more complicated tasks (e.g., serial search) in their experiment. Similarly, Holmes and colleagues (1983) stated that the lack of findings on an auditory memory and an auditory learning task was due to the lack of task complexity. The task may have been too easy resulting in ceiling effects – number of words recalled averaged ninety-one percent, and individuals reached a ninety-three percent level of accuracy on recalling words on the last training trial, at any glucose level. Authors claimed that the word recall task was not a sensitive enough measure with these types of individuals, who were induced to low blood glucose levels at 59 mg/dl.

McCrimmon and colleagues (1997) believe that the small sample size affected the results in their study. Not inducing individuals to a low enough level of hypoglycemia to demonstrate an effect was also described. An interesting point the authors raise is that the TBAC measures short-term auditory storage, which was affected at hypoglycemic levels of 47 mg/dl in healthy individuals, and that this could in fact, affect another type of auditory sensory memory—or longer-term memory storage—of auditory information.

Two surprising findings are noted. First, in the Morris and Sarll (2001) study, blood glucose levels of individuals did not change significantly from initial levels to twenty minutes after glucose drink consumption. Despite this, performance significantly improved in the group that received the glucose drink but not in the group that received the placebo. The authors speculate that performance may have been affected by glucose secreted from the liver (glycogen) as a result of fasting. They emphasize that the idea that improvement occurs because blood glucose levels are elevated is actually a much more complicated relationship than is currently understood. Second, Blackman and colleagues (1990) describe further that the significant effects assessed by the P300 task for decision-making processes after intravenous administration of glucose were due to a cognitive lag occurring in individuals after being restored to normal levels. The complexity of the relationship between blood glucose and performance, including the delay in restoration of function after return to normal glucose levels, requires further investigation.

Summary of Findings of Auditory Processing Studies

Auditory processes have not been explored as much as visual processes (mainly 47 mg/dl for auditory vs. a wider range of blood glucose levels (38–59 mg/dl) for visual). Low blood glucose levels of individuals, induced to 47 mg/dl, impaired performance on auditory selective attention in tasks that required individuals to ignore tones of higher distracting qualities. Low blood glucose levels also affected auditory decision-making processes, deteriorated performance on discrimination of the order of tones when two tones were presented (however, this has shown mixed results) and single-tone loudness. A glucose drink (rather than a placebo drink) improved performance on a listening span task – this improvement occurred at glucose levels already well above hypoglycemic levels of 83–84 mg/dl, showing the benefits of added glucose rather than the adverse effect of hypo-glycemia. Given the tasks used, low blood glucose levels did not affect other auditory tasks (in some cases being described as "simpler" tasks, e.g., determining single-tone duration, and recalling aurally presented numeric information).

Some auditory processes are affected at low blood glucose levels. These affected processes may prove critical to more intensive auditory processes such as, long-term memory storage of auditory information or decision-making based on auditory information. Furthermore, impairments of simple tasks (e.g., single-tone loudness) may result in impairments at higher (or more complex) levels of audition, in addition to a possible cognitive lag in performance.

THE EFFECT OF BLOOD GLUCOSE ON PSYCHOMOTOR FUNCTION

Psychomotor performance has been investigated through tasks that may also tap motor skill and reaction time by using a variety of tasks including aiming or line tracing tasks, choice reaction time tests (CRT), basic (and variations of) finger tapping tasks (FTT), fine motor activity (or manual tracking), pursuit rotor, visuomotor tasks (i.e., Trail Making B test), hand-eye coordination tasks, and Jensen or Hick-type reaction time tasks. Reaction time performance effects can also be found in the attention (see Lobmann, Smid, Pottag, Wagner, Heinze, & Lehnert, 2000; Smith et al., 1992 studies) and sensory processing sections (see Strachan et al., 2001).

Reaction time performance has been affected in specific psychomotor tasks at low blood glucose levels, in both diabetic and non-diabetic individuals. Maassen et al. (1990) used a Number Connections Test (NCT), where participants connected circles as quickly as possible, and an Aiming Center Test (ACT), where participants positioned marks inside circles for a period of 60 seconds. A Line Tracing Test (LTT), where the participant drew a line between two parallel lines, and the Line Tracing Time Test (LTTT), where the time to complete the similar LTT task were also used. As described in the visual processing section, a Reaction Time Test (RTT) was also used where individuals pressed a button as quickly as possible after a light was presented. They found a significant increase in reaction time at hypoglycemia ($M = 40$ mg/dl) in diabetic and normal individuals only on the RTT task. However, other motor responses assessed by the NCT, ACT, LTT and LTTT were not affected at hypoglycemic levels. In addition to an Inspection Time task (IT), Strachan et al. (2001) used a Hick-type reaction time device that measured decision and movement time when participants lifted their finger off of a "home" button to press a stimulus light button on a panel. Strachan and colleagues (2001) also used the TMB test, and the Digit Symbol Substitution Test (DSST), where participants drew the symbol for a digit (using a key), the score was the number of correctly drawn symbols in 90 seconds. They found that decision and movement time performance of non-diabetic individuals induced to hypoglycemia (47 mg/dl) significantly deteriorated, as compared to performance at euglycemia (91 mg/dl). Performance also deteriorated on the DSST and TMB tests and the IT task at 47 mg/dl. Kerr, Macdonald, and Tattersall (1989) measured reaction time performance at 81 mg/dl (baseline) and twice at 63 mg/dl and 54 mg/dl in healthy individuals who pressed a switch in response to a target flashing light that appeared at variable intervals. The latency period was recorded. Finger tremor was also measured using an accelerometer for periods of 1 minute. Reaction time slowed during hypoglycemia when levels were lowered to 54 mg/dl. Tremor did not change significantly during euglycemia or hypoglycemia, when levels were lowered to 63 mg/dl. However, at 54 mg/dl, finger tremor increased significantly, and this was maintained at 54 mg/dl for over 60 minutes. Heller, Herbert, MacDonald, and Tattersall (1987) were interested in whether symptoms could warn individuals of upcoming neuroglycopenic episodes due to hypoglycemic levels. Using a serial four-choice reaction time test over a 5-minute period and an accelerometer for 1-minute periods, reaction time and finger tremor were measured. At 58 mg/dl reaction time was longer in all groups: normal, hypoglycemic aware, and hypoglycemic unaware individuals. Slower reaction times occurred at 45 mg/dl, but returned to baseline levels at 81 mg/dl. At 45 mg/dl, tremor readings increased in normal participants, but not in unaware diabetics.

Impaired performance has also been reported in more complex reaction time tasks in diabetics at low blood glucose levels. Holmes et al. (1986) failed to find significant effects in diabetic individuals on a simple finger tapping task (no decision-making, one light – one key), but did find effects on a

go/no-go reaction time task (two lights – one key) and on a complex choice reaction time task, where individuals respond by pressing one of two buttons when one of two lights were presented. Performance significantly slowed during hypoglycemia (55 mg/dl) as decision-making increased on the go/no-go and choice reaction time tasks. Simple reaction time performance was not affected at any of the glucose levels (55, 110, or 300 mg/dl). The results of these reaction time studies may be due to the brain's sensitivity to and utilization of glucose, which appears to be affected by task type and demand. An experiment by Rosenthal, Amiel, Yágüez, Bullmore, Hopkins, Evans et al. (2001) examined the areas of the brain and cognitive tasks affected during hypoglycemia in healthy participants using Functional Magnetic Resonance Imaging (fMRI) technique. The fMRI allowed Rosenthal and colleagues to detect changes in brain oxygenation during activation by a task. Performance deteriorated at hypoglycemic levels (45 mg/dl) on a four-choice reaction time task, where participants moved a joystick in the direction of an illuminated target (when one of four ovals on a screen were lit), and on a finger-tapping task. They found that acute hypoglycemia was found to be task- and region-specific. Different tasks showed different responses to hypoglycemia; four-choice but not simple choice performance was negatively affected.

An interesting finding is that a speed-accuracy trade off might occur on less complex reaction time tasks in diabetic individuals. A study by Driesen, Cox, Gonder-Frederick, and Clarke (1995) investigated the effect of hypoglycemia on reaction time (simple, choice, and complex) in insulin dependent diabetic (IDDM) participants using a computer equipped with Neurobehavioral Evaluation System (NES2) software. For the simple reaction time task (RT), participants pressed a button when they saw a block appear on the screen. For the choice-side task, participants pressed a button (indicating side by a right or left arrow) corresponding to the side of the screen where the block appeared. For the complex reaction time task, combined features of choice-side and choice-direction were employed. A box appeared with an arrow in it, and participants followed the directions of the words that appeared on the screen, either "side" or "direction," and pressed the appropriate key. For example, if a block appeared on the right side containing an arrow pointing left, and the preceding direction indicated "side," the right button would be pressed. "Side" indicated location of the block, and "direction" indicated direction of the arrow within the box. Time to complete these tasks, and errors were recorded. Participants were induced from blood glucose levels between 80–120 mg/dl, to blood glucose levels between 55–70 mg/dl, to blood glucose levels between 33–50 mg/dl, and returned to levels between 80–120 mg/dl on an experimental day. Comparisons showed that performance on all reaction time tasks significantly slowed during blood glucose levels between 33–50 mg/dl versus the 80–120 mg/dl (baseline) period. Performance errors increased on the complex RT task at blood glucose levels between 33–50 mg/dl, but no hypoglycemic effect was found for error scores for the choice RT task. A non-significant trend showed slowing at blood glucose levels between 55–70 mg/dl on every task. Hypoglycemia slowed performance on both simple and complex tasks. Speed was affected equally on simple and complex tasks. Although errors increased on complex tasks, accuracy on simpler tasks was preserved at blood glucose levels between 33–50 mg/dl.

Aspects of manual and pursuit tracking tasks have also been impaired at low blood glucose levels in diabetic and non-diabetic individuals. Schächinger et al. (2003) used a Choice Reaction Time Task (CRTT), where non-diabetic college students pressed the colored button that matched the color of the light that was flashed (red, blue, white, yellow, and green) as quickly as they could over a three-minute period. They also used a manual-tracking test, where the participant directed a pointer (small

cross) as close as they could to a target (white circle) orbiting on a screen in distorted ellipses at variable speeds over three minutes. Distance between the pointer and target were measured. CRTT reaction time and manual tracking performance scores showed significant impairment during hypoglycemia at 49 mg/dl. For the manual-tracking task, "distance" was significantly impaired. Fraser, Buck, and McKendry (1974) used non-diabetic individuals to investigate stress caused by hypoglycemia on psychomotor performance using the National Research Council (NRC) stressalyser, a subject-paced, step-input, pursuit-tracking task. Similar to an aircraft control yoke, individuals aligned the pointer with an illuminated light for a period of 200 miliseconds until the next light was illuminated. Insulin-induced participants' performance on this task produced two curves: one, an inverse-U where a marked deterioration was followed by recovery, and a continuous curve with no clear peaks or variability. Authors state that this continuous curve does not imply flat, and that some individuals showed deterioration, but that this was due more to fatigue than to glucose levels. Data were analyzed based on subgroups A (inverse-U curve) and B (continuous curve). Deterioration and variability were largely higher for group A than B. Increased movement time (execution) and reaction time (selection) occurred in individuals whose glucose levels and symptoms (i.e., observed and self-reported instances of sweating, tremor, drowsiness, headache) indicated hypoglycemia. Response execution (27% increase in movement time) accounted for more of the proportion of impairment than response selection (15% increase in reaction time), from trials 5 to 9 (18 total trials). Impaired tracking time appeared at very low blood glucose levels at 32 mg/dl or less. Error and overshoot rates (accuracy) did not significantly increase during hypoglycemia, and authors assert that this was due to individuals becoming more deliberate in their actions after recognizing their impairment.

Using the same test (e.g., Trail Making B) to assess either visuomotor or visual tracking, blood glucose levels were shown to affect performance in diabetics and non-diabetics. To assess visual tracking and visuomotor speed, Hoffman et al. (1989) used the TMB test and the pursuit rotor task, in which the diabetic participant's task was to track a dot rotating on a turntable with a stylus (the amount of time correctly positioned for five 1-min trials was measured). At hypoglycemia (50 mg/dl) as compared to euglycemia (100 mg/dl), pursuit rotor and TMB test performance was significantly impaired. Based on TMB test developers Reitan and Wolfson's categorization scores, twenty-five percent of the individuals indicated mild to serious impairment during the hypoglycemic condition. Simple motor speed and reaction time (to a visual stimulus) were also measured. The task was to press a key when a target light appeared; however, glucose levels did not affect performance on this task. Similarly, Stevens, McKane, Bell, Bell, King, and Hayes (1989) investigated psychomotor performance using a simple-reaction time test (auditory and visual), a finger-tapping test, and the TMB test in non-diabetics (range 18–27 years of age) by inducing them to a hypoglycemic state at 61 mg/dl. Only performance on the TMB test was significantly impaired. To assess visuomotor performance in healthy non-diabetic individuals (60–82 years of age), Kaplan, Greenwood, Winocur, and Wolever (2000) used the TMB test. Using either a glucose drink (50 grams) or high carbohydrate items (i.e., instant mashed potatoes, or barley), they found that there was no significant effect of food on TMB performance. There was an effect of time where performance on this task was better at 105 minutes than at 15 or 60 minutes. This suggests time-dependent effects, which will be discussed later. However, when participants' data were grouped based on β (beta) cell function (responsible for insulin secretion) performance on the TMB test was improved in individuals with poor β cell function. Blood glucose levels affected performance in individuals with impaired insulin secretion, but who were not necessarily diabetic.

Despite several significant findings using the TMB, Gold, Deary, MacLeod, Thomson, and Frier (1995) failed to find an effect of blood glucose levels on TMB performance. Gold and colleagues used five different cognitive tests in a testing battery to assess functioning and adaptation of non-diabetic individuals from hypoglycemia. The tests assessed information processing and were chosen because of their validity and usefulness in hypoglycemia research. A Choice Reaction Time Task was used in which participants held down a "home" button on a black box with four other response buttons on a panel until a response button illuminated and participants lifted their finger from the "home" button and pressed the lit button (decision and movement time were recorded). The Paced Auditory Serial Addition Task (PASAT) was also used. The PASAT requires participants to listen to a recording of single-digit numbers, at either a 2-second or 4-second interval rate, and add each new number to the previous and state the sum out loud as quickly and as accurately as possible. The task continues through 61-items over 150 seconds. The DSST, TMB test, and the Rapid Visual Information Processing (RVIP) test were also used. The RVIP test, a signal detection task, required participants to press a space bar after a target of three sequences of consecutive odd or even numbers appeared on a computer screen. Time to detect and respond accurately was recorded. Participants' ($M = 29.5$, ±4.3 years of age) blood glucose levels were controlled in three different conditions; condition A (participants were maintained at 81 mg/dl), condition B and C (participants were stabilized at 81 mg/dl for 30 minutes, lowered to 45 mg/dl for 60 minutes, and restored to 81 mg/dl for 30 minutes). Participants were given the cognitive test battery after 5 minutes at hypoglycemia (condition B) and after 40 minutes of hypoglycemia (condition C). Acute hypoglycemia resulted in significant deterioration in the CRTT (decision and movement time), PASAT (at both 2-s and 4-s intervals), DSST, and RVIP, but not for the TMB test. Performance ability did not differ between conditions B and C.

Several studies investigating performance of diabetic and non-diabetic individuals have not found significant effects of blood glucose levels on psychomotor performance when using hand-eye coordination or finger tapping tasks. Benton (1990) conducted an experiment that investigated the effect of increasing blood glucose levels in male and female college students on a computerized hand-eye coordination task. The task was to place a bat in front of (or hit) a moving ball on a computer screen where the speed of the ball could be adjusted. Participants fasted four hours prior to the experiment and either received a glucose drink (25 grams of glucose) or a placebo. During this task, participants also performed mental arithmetic (two digits had to be added) every 15s for 20 minutes – individuals were instructed to concentrate on this task more than on the bat and ball task. No significant differences related to a glucose or placebo drink on performance were found. Manning et al. (1990) investigated the effect of a glucose drink on memory and non-memory performance in older individuals (62–74 years of age). The Finger Oscillation Test required that individuals press down a lever attached to a counter as quickly as possible over a ten-second period. They found that motor performance of participants consuming a glucose drink (50 grams) was not significantly different compared to those consuming a saccharin-flavored placebo drink. Green, Taylor, Elliman, and Rhodes (2001) used college students (18–40 years of age) to study the expectancy effect of a glucose (50 grams) or placebo drink on performance. To assess cognitive functioning, they used a testing battery that included a two-finger tapping task. Time was recorded on how quickly individuals could alternately tap one of two keys on a keyboard. A glucose drink did not affect performance on this motor task. Cox, Gonder-Frederick, Schroeder, et al. (1993) used a Finger-Tapping Task (FTT) to assess pure motor function, where the participant presses a telegraph-like key as quickly as possible. Participants included diabetics ($M = 34$ years of age) and matched-controls at blood glucose levels

at 97, 47, 65, and 121 mg/dl. They found that only the cognitive test administered (Paced Serial Addition Task) was significantly affected at blood glucose levels at 47 mg/dl. As previously described in the visual processing section, simple motor speed and reaction time were assessed using a visually cued reaction timer, where individuals press a telegraph-style key as soon as they see a target light appear (Hoffman et al., 1989). Hoffman and colleagues (1989) found that reaction time performance on this task was slowed at hypoglycemia at 50 mg/dl, but failed to reach significance.

Other studies of psychomotor performance and blood glucose levels have found effects due to changing blood glucose levels (rising or falling), time of day effects, and cognitive lag. Owens and Benton (1994) used a Jensen-type device where eight lamps were arranged in a semicircle on a black panel. Flashing lights required participants to press the button in front of the corresponding flashing light as quickly as possible. Decision time (time to lift the finger from a home key) and movement time (time after leaving home key to appropriate button) were recorded. Simple reaction time was measured with only one light flashing (for 20 trials), while choice reaction time measured performance (over 20 trials) using 2, 4, and 8 lamps. Errors and out of normal range times were excluded from the analysis. Data were grouped based on those whose levels had fallen by 9 mg/dl and those whose levels increased by more than 18 mg/dl within a 15-minute period, on baseline glucose levels, and on constantly high or low levels during the testing. Decision times at each level of difficulty were not affected by type of drink (50 grams of glucose, or an aspartamate-acesulfame K placebo). However, changing blood glucose levels and time of day on the 8-lamp condition resulted in a significant effect. Those tested in the morning were faster if their levels were rising (more than 18 mg/dl) than those whose levels fell (less than 9 mg/dl). Similarly, those tested in the morning whose levels were rising were faster than those tested in the afternoon. Decision times were slower when participants experienced falls in blood glucose levels than those whose levels were rising. Falling levels were not associated with hypoglycemic conditions or symptoms (108 to 92 mg/dl). Movement time was unaffected by blood glucose level changes.

Similar to studies on effects of other functions, impairments at low blood glucose levels have shown lasting effects on reaction time tasks. Evans et al. (2000) used a 4-Choice Reaction Time task where healthy non-diabetic participants were presented with a computer screen separated into four quadrants onto which a target would appear randomly. Participants pressed a corresponding button to the location of the quadrant in which the target appeared. During the 5-minute task, speed and accuracy were recorded. Performance on the 4-Choice task significantly deteriorated at hypoglycemic levels (48 mg/dl). Furthermore, once restored to normal blood glucose levels (90 mg/dl), participants remained significantly impaired on this task for twenty minutes.

Challenges to Psychomotor Function Studies

The challenges to research in this area largely focus on the lack of task complexity, age as a factor, type of glucose administered, and levels or duration of low blood glucose. Hoffman et al. (1989) found decrements in performance on the pursuit rotor task, but not on a simple-reaction time task. They state that this effect of hypoglycemia on performance was not due merely to impairment in motor control, but affected more complex sensory and motor skills. Robust effects in studies using more complex tasks have been exhibited. In the Schächinger et al. (2003) study, the effect size for the manual tracking test and CRTT exhibited "large" effect sizes ($\delta = 1.07$ for tracking, $\delta = 1.83$ for CRTT). The CRTT appears to be more sensitive than the tracking task to the effects of induced low

blood glucose levels. Schächinger and colleagues report that the CRTT assesses not only sustained attention, but also executive motor function. With similar conclusions as in previous studies, simple motor tests were found to be less sensitive than cognitive tests. Driesen and colleagues (1995) report that errors increased on complex tasks but not on simpler tasks because of the testing apparatus employed. They state that simple tasks may be less affected by low blood glucose levels, and that future studies should exert more experimental control (e.g., matching control participants) and focus on residual performance deficits (e.g., after return to euglycemia). An understanding of this residual performance could assist in determining when diabetics could return to driving safely after a hypo-glycemic episode, for example.

Age was also described as a factor in results on psychomotor performance. Manning and colleagues (1990) suggest that glucose levels in older individuals affect selective declarative memory processes, rather than overall functioning (e.g., finger tapping, attention, or IQ). However, Kaplan and colleagues (2000) may not have found an effect on the TMB test because older participants in their experiment had reached their optimal performing capacities at baseline, and no further benefits could occur. When benefits did occur, they occurred in participants with poor glucose regulation. Age as it relates to changes in an individual's ability to effectively regulate blood glucose levels over time needs to be considered.

Type of glucose administered and level or duration of low blood glucose may also pose a challenge to research in this area. Benton (1990) used twenty-five grams of glucose in his experiment and failed to find an effect. It is possible that this dose may not have been enough to affect performance on this type of task (the typical glucose dose is 50 grams). Kaplan and colleagues (2000) suggest that carbohydrates may have a more profound effect in reversing certain performance deficits on certain tasks (e.g., difficult memory tasks), which will be more apparent in participants with poorer glucose regulation and mental capabilities. However, in the Owens and Benton study (1994), healthy non-diabetic participants did not fast prior to participating in their study, but followed their normal eating pattern. Participants' blood glucose levels were never low enough to reach a diagnosis of hypogly-cemic, yet the effects of a glucose drink significantly benefited performance. Stevens and colleagues (1989) reported a failure to find an effect on psychomotor tests due to the number of variables that can affect performance on these tests such as; age, sex, time of day, test strategy, and practice effects. They found fine motor coordination effects of low blood glucose levels on the TMB test but not on other tests, possibly due to the level of hypoglycemia being mild (blood glucose levels at 58 mg/dl) but not severe. Stevens and colleagues also describe how participants were tested once before the insulin-infusion, and once during the last thirty minutes of the clamp; they suggest that prolonging the hypoglycemia at 58 mg/dl may have resulted in significant effects on the tests.

Summary of Findings of Psychomotor Function Studies

Varying blood glucose levels affect psychomotor performance if the tests are of sufficient difficulty. In these studies, performance on the finger-tapping test did not produce significant effects at hypo-glycemic levels of 47 mg/dl in older, younger, diabetic or non-diabetic participants. Hand-eye coordination was also not affected when participants were fasting or given a drink consisting of 25 grams of glucose. However, reaction time performance on choice reaction time tasks was affected (decision and/or movement time being significantly slowed at hypoglycemic levels). Performance on pursuit or manual tracking and reaction time tasks (specifically, choice reaction time tasks) has

also been significantly impaired at low blood glucose levels. Reaction time performance has been affected at blood glucose levels ranging from 40–55 mg/dl. Other performance effects became apparent when investigating the performance of participants at rising and/or falling glucose levels, the duration of the hypoglycemic episode, and the residual impaired effects of hypoglycemia after participants were restored to normal glucose levels – which will be revisited later in the paper. Issues of task complexity and age as a factor were also evident.

Patterns of accuracy and speed appeared to depend on the type of task. Participants demonstrated fewer errors on "easier" tasks – that is, speed was affected equally on two CRT tasks (simple and complex), but errors increased with the more complex task. Participants did not exercise a speed accuracy trade-off where response time was slowed to reduce or prevent errors on this task. However, in a pursuit tracking task participants' response time for selection and execution increased while accuracy was not affected at low blood glucose levels. Patterns of performance on psychomotor tasks were similar to sensory processing task (e.g., visual processing) performance. On some psychomotor tests, participants demonstrated a speed-accuracy trade-off – accuracy was preserved at the expense of speed. Deterioration from the stress caused by hypoglycemia may have affected the quality of performance – affecting speed, but not necessarily accuracy (Fraser et al., 1974). In the Fraser et al. study, performance on a choice reaction time task showed that speed was preserved at the expense of accuracy. Furthermore, accuracy of performance wasn't affected until participants reported or showed signs of hypoglycemia on a pursuit-tracking task. It is possible that awareness of hypoglycemic symptoms could act as a mediator of performance. Perhaps awareness of symptoms could alert individuals to become more conscious of their actions and reduce impairments from hypoglycemia.

Performance on the Trail Making B (TMB) test produced somewhat mixed results, although largely showing impairments at low blood glucose levels. When impairments have occurred on this test, they occurred at blood glucose levels from 50–61 mg/dl. Interestingly, the TMB test is a validated test readily used in blood glucose literature as a sensitive measure of performance. Two studies listed here found no effect on performance on the TMB test at hypoglycemic levels; however, the participants' ages in one study ranged from 60–82 years, and in fact after further investigation, those with poor glucoregulation (poor ß cell function) did show impairments on this test. Overall, the TMB may not be a sensitive measure for this older population.

Typical physiological symptoms such as tremors or shaky hands can occur at low blood glucose levels or hypoglycemia. When glucose levels are low enough, this and other more subtle aspects (i.e., physiological) of psychomotor functioning may affect performance on tasks that require fine motor control, or tasks where input frequency is critical. This is also described in the next section. However, by the time psychomotor performance is affected, whether or not motor processes are in fact contributing to performance difficulty, it is likely that impairments in cognitive functioning have already occurred (Evans et al., 2000).

THE EFFECT OF BLOOD GLUCOSE ON ATTENTION

The effects of blood glucose levels on non-executive functions involving sensory processing (visual and auditory) have been clearly established (e.g., inspection time, visual change detection, contrast

sensitivity, simple auditory processing, listening comprehension). Their effects have also been demonstrated on psychomotor tasks (e.g., reaction time, fine motor activity, and hand-eye coordination). It is clear that there exists a continuum of degradation of performance on specific tasks at certain glucose levels. Executive functions (e.g., reasoning, planning, problem solving) are clearly affected by blood glucose levels on this continuum of degradation.

To assess various aspects of attention (e.g., visual, sustained, divided, and selective attention), studies have employed event-related brain potentials measures (ERPs), the Test of Everyday Attention (TEA), the Paced Auditory Serial Addition Task (PASAT), the Continuous Performance Task (CPT), the Rapid Information Processing Test (RIPT), the Trail Making A and B tests, Stroop (or Color-Word Interference) tests, the Hagen Central Incidental Test (HCIT), the Letter Cancellation Test and other variations of attention tests, which will be described further. In some cases, these tasks require either attending to and/or ignoring distracting stimuli.

Reaction time on a selective attention test in both diabetics and non-diabetics has been affected at low blood glucose levels. In attempting to determine the specific effects rather than overall global effects of hypoglycemia, Lobmann et al. (2000) used event-related brain potentials (ERPs) to investigate performance in diabetic and healthy matched controls. In this experiment, selective attention was assessed at different levels of blood glucose with a final hypoglycemic plateau of 47 mg/dl, which lasted for 30 minutes. Participants responded by key press with either their left or right hand (response selection) if a single letter of the correct color was presented (e.g., red letter D, right hand movement versus left-hand movement for letter L). ERPs of both selection negativity (SN), which indicates stimulus selection, and a lateralized readiness potential (LRP), which indicates response selection, were studied. Response time to relevant targets (target letters in the to-be-attended color), relevant non targets (in the to-be-attended color not requiring a response), irrelevant targets (target letters in the to-be-ignored color), and irrelevant non targets (non target letters in the to-be-ignored color) were recorded. Reaction time to the relevant targets, blinks, and eye movements were measured. Stimulus and response selection were analyzed separately in participants at both normal (99–112 mg/dl) and hypoglycemic levels. During hypoglycemia, reaction times increased by 27 seconds in the healthy group. Restoring glucose levels to normal reduced reaction times significantly in the diabetic group, but not the control group. Stimulus selection (SN) and response selection (LRP) were significantly delayed at hypoglycemia. Selection of a stimulus based on its color (SN) and selection of the motor response (LRP) based on letter shape were delayed in both groups at hypoglycemia. Response selection was still delayed in the healthy, but not diabetic, group after restoration to normal levels.

Although visual and auditory selective attention and visual attentional switching were affected in non-diabetics at low blood glucose levels, sustained attention was not affected. A speed accuracy trade-off was also demonstrated. McAulay et al. (2001) used the TEA to assess various aspects of attention (visual selective, sustained, and divided attention) in non-diabetic participants. Visual (e.g., Map Search, Telephone Search) and auditory (e.g., Elevator Counting, Elevator Counting with Distraction, and Elevator Counting with (direction) Reversal) attention tasks and results were described previously. The subtests of attention not previously described are the Visual Elevator, Telephone Search While Counting, and Lottery tasks. The Visual Elevator task assesses attentional switching. Participants are presented a series of pictures of elevator doors and arrows indicating an up or down direction and are to determine which floor they are on. The Telephone Search While

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Counting task assesses divided and sustained attention. For this test, participants search for key symbols in a telephone directory while simultaneously counting a series of tones on an audiotape. The Lottery task assesses sustained attention by having participants listen for their winning lottery number, a series of two letters followed by three numbers (e.g., BC152) over a ten-minute series, and write down the two letters preceding all lottery numbers ending in certain numbers (e.g., 77). As previously reported, there was significant deterioration in both visual and auditory selective attention. Furthermore, a significantly longer time was required to complete the visual elevator task (attentional switching) during hypoglycemia (47 mg/dl). Attentional flexibility deteriorated and the speed of information was delayed. Accuracy was preserved at the expense of speed on the Visual Elevator (and Telephone Search) task. However, sustained attention during either the lottery ticket or elevator counting was not affected during hypoglycemia.

Performance was impaired at low blood glucose levels when the Paced Auditory Serial Addition Task (PASAT) was used to assess sustained attention performance of non-diabetics. Errors of omission, as compared to errors of commission, were more evident at low blood glucose levels. To explore which tests would be most useful in detecting impairments from low blood glucose levels, Schächinger et al. (2003) used the PASAT, a Choice Reaction Time test (CRTT), and a manual tracking test to assess combinations of sustained attention, concentration, information processing speed, reaction time, spatial performance, eye-hand coordination, working memory, and strategic thinking. Performance on the PASAT was measured by the percentage of correct responses, omission errors, false responses, and verbal reaction time for correct responses (time did not differ from reaction time for false responses). Over a 3-minute period, the CRTT required participants to press a button, as quickly and accurately as possible, of the same color as a flashing target light. Mean reaction time for correct responses was recorded. The manual tracking test and results has been previously described. Using healthy non-diabetic college students, induced to hypoglycemic levels (49 mg/dl), they found that reaction time increased and accuracy decreased (increasing omission errors, and marginally, false responses) on the PASAT at hypoglycemia. During euglycemia and hypoglycemia, errors on the PASAT were largely omissions. Omission errors were more likely than false responses during euglycemia by 1.5 times; however, during hypoglycemia this ratio increased to 2.5 times. Reaction time on the CRTT was also significantly impaired.

In a similar but even less complex task than the PASAT, Pramming et al. (1986) used a test battery (including the TMB and Digit Span tests) at four different periods of glucose levels (108, 54, 36, and 108 mg/dl) to assess attention and short-term memory. During the Digit Span, a sub test from the Wechsler intelligence test, diabetic individuals listened and repeated digits in sequence that were read to them at 1-second intervals. From glucose levels 108 mg/dl to 54 mg/dl, all test scores (except for finger tapping) fell. However, only the Digit Span test resulted in significant deterioration in performance when levels were reduced from 108 mg/dl to 54 mg/dl. From 108 mg/dl to 36 mg/dl, all individual and overall test scores fell significantly (except for finger tapping which fell significantly from levels 54 to 36 mg/dl). Improvement in scores occurred when levels were increased from 36 mg/dl to 108 mg/dl.

Non-diabetic individuals exhibited faster reaction times from an administration of glucose, and slower reaction times from low blood glucose levels on tests of attention. Kanarek and Swinney (1990) investigated the effects of food and snack on cognitive performance in male college students in two experiments. They compared a confectionery product and a yogurt snack, to a caffeine-free

snack (e.g., low calorie soft drink), while assessing performance on arithmetic reasoning, reading, memory, and attention tasks. To assess attention, they used a continuous performance task (CPT) in which participants were presented with a sequence of 360 items (letters or numbers) and pressed a button when a consonant appeared after a trial when a number greater than 25 appeared. Participants pressed a button every time this situation occurred. Reaction time, correct detections and false alarms were calculated. Mean errors and reaction time were also measured. Participants were significantly faster after consuming a caloric snack than a low calorie soft drink. Similarly, in a second experiment, using similar methodology and cognitive tests, Kanarek and Swinney found that participants detected targets significantly faster and made marginally fewer errors after eating a caloric snack (fruit-flavored yogurt) than after consuming a diet soda drink. In a study by Owens and Benton (1994), the number of trials completed on an inspection time task in which participants pressed one of two keys to discriminate between two lines of different lengths, was used as a measure of attention. A computer generated the stimuli (vertical lines of lights) and exposure began at 500 ms and reduced to 250 ms after ten consecutive correct answers. Prior to this task, non-diabetic participants either ingested a glucose (50 grams) or placebo (aspartamate) drink. Inspection time was unaffected, but reaction (decision) time was faster on a Jensen-type device (participants, as quickly as possible, pressed a button in front of one of eight lamps that illuminated), when participants blood glucose levels were rising. To study the possible effect of blood glucose levels and behavior, Benton et al. (1987) investigated the effect of a glucose (25 grams of glucose) or placebo (diet soda with water only sweetened with saccharine) drink on children to measure the effect on attention and frustration in the afternoon. A sustained attention task required children to push a button when a light appeared and reaction time was measured. A computer game designed to measure the reaction to an increasingly difficult task was also used. They found that children who received the glucose drink had significantly faster reaction times and were more likely to concentrate during the trials; children who took the placebo were more likely to fidget, show signs of frustration, and more likely to talk.

Similarly, the reaction times of diabetic individuals to attention tasks decreased at low blood glucose. Holmes and colleagues (1983) induced individuals to hypoglycemia at 60 mg/dl, euglycemia (control group) at 110 mg/dl, and hyperglycemia at 300 mg/dl. They used the Matching Familiar Figures Test (MFFT) to assess visual discrimination and sustained attention. In this match-to-sample task, accuracy and latency (time elapse before responding) were measured. A Delayed Reaction Time task was used to assess sustained visual attention. Participants pressed a key as quickly as possible after a red target light appeared. Speed of responding was recorded. No effect of glucose level on the MFFT was found; however, reaction time performance was significantly faster at 300 mg/dl as compared to blood glucose levels at 60 mg/dl, but still slower than blood glucose levels at 110 mg/dl.

Low blood glucose levels affected performance on the TMB, which was used to assess divided attention in diabetics and non-diabetics. In healthy non-diabetic individuals induced to hypoglycemic levels of 47 mg/dl, McCrimmon et al. (1997) used the TMB test as a measure of divided attention and the Digit Symbol (DS) test. The DS test (a subtest of the Wechsler Adult Intelligence Scale – Revised) requires that participants use a coding key of numbers represented by symbols as a reference and are instructed to write down the correct symbol for each number (1–9) over a fixed time period. The time taken to complete the TMB test was significantly longer and the scores on the DS test were significantly lower during hypoglycemia than at normal glucose levels (90 mg/dl).

Hoffman et al. (1989) used the TMB to assess divided attention and the less demanding Trail Making A test. For this test, participants connect numbered dots (1–15) as quickly as possible. Diabetic individuals were induced to a high blood glucose level at 300 mg/dl, a normal blood glucose level at 100 mg/dl, and a hypoglycemic level at 50 mg/dl. Errors and time to complete the TMA and TMB were recorded. There was a significant effect of glucose on performance for the TMB test in that participants performed more poorly with hypoglycemic blood glucose levels at 50 mg/dl. Reaction time was generally slower, but further analysis showed no significant differences. The authors suggest that this was due to large individual differences.

Despite previous effects of blood glucose on TMB performance, Evans et al. (2000) did not reach similar conclusions. Evans and colleagues used the 4-Choice reaction time task as a test of attention where participants pressed a button when a target appeared on a screen and speed and accuracy were measured. Requiring selective attention, the Stroop test, where participants read either the word or the color of a word presented in a conflicting color, and the Trail Making B test were used. Non-diabetic individuals induced to a hypoglycemic state (48 mg/dl), showed significant deterioration in performance on the 4-Choice task and Stroop word and color-word subtests, but not the TMB test. After restoration to normal blood glucose levels (20 minutes after returning to normal levels at 90 mg/dl, ±0.36 mg/dl), performance on the 4-Choice reaction time task was still significantly impaired.

The benefits of glucose administration in non-diabetics may not be clear when increased errors result. To investigate effortful processing in younger and older adults after ingesting either a glucose (50 grams) or saccharin drink, Craft et al. (1994) used a Stroop Color-Word Interference Test. Error rate and response time were measured during each of three conditions. In the first condition, participants read as quickly as possible 100 color words on a sheet of paper. In the second condition, subject named the colors of 100 blocks presented in rows on a sheet of paper. In the third condition, participants named the color of the color-word that was printed in a discordant color (e.g., the word red was printed in green letters). They found that glucose administration decreased reaction time (participants were faster) but errors increased in the interference (discordant color) condition for all participants after a glucose drink. A reduction in time scores was found for the word reading to color naming and the color naming to the interference conditions after glucose ingestion. Conversely, more errors occurred during the interference condition than during color naming after glucose ingestion. More errors occurred in the interference condition compared with the word-reading and color-naming conditions. In another study, Flint and Turek (2003) used the Test of Variable Attention (TOVA), a Continuous Performance task (CPT) for 21.6 minutes in non-diabetic college students. During the TOVA task, participants pressed a button every time a square with a hole near the top appeared and refrained from pressing a button when a square with a hole near the bottom appeared. They investigated the effect of either an absolute dose (50 grams) or relative doses (10, 100, and 500 mg/kg) of glucose or a placebo (saccharin) drink on TOVA performance. After an eight-hour overnight fast, participants were assigned to one of the five groups and weighed, while the researcher mixed the appropriate beverage. A baseline blood glucose level was measured after which participants consumed the beverage and completed a practice version of the TOVA task. Fifteen minutes later, blood glucose levels were measured and participants began the actual TOVA task. After the task was over, blood glucose levels were again taken. Flint and Turek found that those in the 100 mg/kg group made significantly more errors of commission and omission than the other groups. Errors of commission occurred when participants incorrectly responded to the non

target stimulus, and errors of omission occurred when participants failed to respond to a target stimulus. The 100 mg/kg group also showed significantly greater post-commission response (number of responses following commission errors) time variability (milliseconds following a commission error and before a response to a target stimulus) than did the other groups.

Similarly, blood glucose and performance investigations from breakfast studies have produced mixed results. Pollitti et al. (1998) investigated attention, assessed by the Hagen Central Incidental Test (HCIT), of healthy children and nutritionally at-risk male children. This task taps into an attention component of the Matching Familiar Figures Test (MFFT), a visual discrimination task, which was also used in these experiments. As expected, scores were significantly higher (indicating impaired performance) on the HCIT task after individuals participated in a no breakfast condition than were scores after the breakfast condition. During this task, participants were presented with six cards sequentially, each with a picture of an animal and an object on it. Participants were then shown a single card with a picture of an animal on it, and asked to identify the serial position of the card in relation to the first presentation. Conversely, breakfast type did not affect performance on sustained attention tasks in the following Smith et al. (1994) study. Non-diabetic college students were assigned to a no-breakfast, cooked breakfast, or cereal/toast breakfast and completed a series of reaction time tasks and a repeated-digits vigilance task. Participants had to complete three 8-minute tests. A Variable Fore-period Simple Reaction Time Task required participants to press a key as soon as a square appeared in a box, and a Five-choice Serial Response Task requiring participants to press a key corresponding to the location where a square appeared in one of the five corresponding boxes. A Repeated-digits Vigilance Task, where digits appeared on a screen at a rate of 100 per minute was also used. For this task participants responded to repetitions of digits as quickly as possible. Hits, reaction time, and false alarms were recorded for each of these tasks. Only caffeine benefited performance, by decreasing reaction time on the simple reaction time task and improving performance on the Repeated-digits task, but breakfast type did not affect attentional performance.

Other (perhaps, less complex) measures of attention have also been used, but researchers failed to find any significant effects of glucose or blood glucose levels on performance. Manning et al. (1990) failed to find an effect of a glucose (50 grams) or placebo (saccharin) drink in older participants' performance on a Letter Cancellation Test, where participants mark specific letters from a large list of letters. Kaplan et al. (2000) used an attention task as a distracting task to prevent rehearsal during a break from a paragraph recall task, which required participants to watch a sitcom on a video tape and count the number of times a specific character's name or specific words were spoken, and the number of times doors opened and closed. The non-diabetic older participants ingested either a placebo or one of the three following treatments containing 50 grams of glucose; a glucose drink, instant mashed potatoes, or barley. No effects of food on attention were found. However, men with poor baselines on attention and all women performed better with barley consumption than the placebo. Howorka, Pumprla, Saletu, Anderer, Krieger, and Schabmann (2000) used the Grünberger alphabetical cross-out test to assess attention, concentration, and attention variability and found no significant differences between individuals with or without hypoglycemia awareness when investigating EEG patterns at blood glucose levels above 72 mg/dl.

An interesting finding is that changing blood glucose levels affected reaction time and sustained attention performance. Benton, Owens, and Parker (1994) were interested in the effects of blood glucose on attention in young adults. Using the Rapid Information Processing Task (RIPT), similar

to the RVIP task, participants either consumed two glucose drinks (50 grams immediately after baseline RIPT performance and 25 grams at 25 minutes later) or two placebo drinks. Individuals also completed a computerized version of the Stroop Task to assess attention (e.g., "red" printed in blue). Participants pressed one of four keys with the names of the colors used in the task. Response and time taken were measured (a congruent and incongruent task were also administered). No significant correlations between blood glucose and reaction times were found in those who had consumed a glucose drink; furthermore, glucose drinkers made significantly more errors on the RIPT task than placebo drinkers. However, young adults who consumed the placebo drink showed better performance in sustaining attention and quicker reaction times when blood glucose levels were higher at baseline, and if blood glucose levels were falling (between the first and second tests). Falling blood glucose levels indicated that the brain was using up the glucose. A negative correlation existed between higher blood glucose levels and initial blood glucose values, reflecting faster reaction time. Significant correlations and faster reactions were found between reaction time of those whose blood glucose levels were falling after baseline RIPT. The effect of changing blood glucose levels on performance is discussed later in the review.

Challenges to Attention Studies

Some of the challenges in attention and blood glucose level research include: individual differences or subject type, lack of methodological standardization, task complexity, physiological (symptom) interference, and patterns of errors. For instance, the Trail Making B test has been widely used to assess performance and blood glucose levels, including assessment of attention. Evans et al. (2000) suspect that they may not have found effects on the TMB (at hypoglycemic levels at 48 mg/dl in non-diabetics) due to large subject variability. However, Hoffman and colleagues (1989) found an effect on the TMB at 50 mg/dl in diabetics, but not for reaction time and suggested that this was due to individual differences. Regardless of these differences, subject variability should be a consideration for all tests. As previously suggested, perhaps older individuals' performance on certain tasks are at optimal states at baseline (and possibly only when blood glucose levels are increasing) and thus, no further benefits to performance can occur. Individual differences in non-diabetics and diabetics in relation to symptom awareness and how this awareness affects performance should also be considered. For example, selecting color-relevant stimuli, appropriate hand response, and reaction time were all delayed in both diabetic and non-diabetic participants induced to hypoglycemic levels. However, Lobmann and colleagues (2000) consider that color selection did not return to normal in healthy individuals after restoration of glucose levels because diabetic individuals are better able to cope with a hypoglycemic state, experiencing more frequent albeit less severe episodes. Even when tests are sensitive enough to detect differences, awareness of these impairments may not be obvious in cases where recognition of symptoms may help mediate decrements in performance. Hypoglycemic signs and symptoms may not be reliable indicators of deteriorating performance (Pramming et al., 1986). Pramming and colleagues reported that cerebral dysfunction occurred before symptoms appeared. They also noted that this dysfunction could occur at blood glucose levels around 54 mg/dl.

Other challenges include a lack of standardization on other variables (e.g., the nature and/or type of food or drink item, time of testing). In a review, Polliti and Matthews (1998) commented on the various methodologies employed and limitations on breakfast research and cautioned against the lack of standardization of research and the inability to make claims about the clear benefits of breakfast from current studies. Breakfast type in relation to macronutrients (protein, fat, and carbo-

hydrates) and even types of placebos used in these experiments need further investigation. Benton et al. (1987) stated that their results may reflect a negative reaction to the saccharine placebo rather than a positive reaction to glucose, or because of the age of the participants (i.e., children) that can vary significantly due to age-related development changes (e.g., glucose tolerance and aging), or due to the time of day or the tasks themselves. Kaplan et al. (2000) suggest that glucose may not be unique in producing cognitive enhancing effects as compared to food items containing similar amounts of carbohydrates, although differing in glycemic index (GI) levels (e.g., high-GI potato, low-GI barley). The benefits for attentional performance of a low-GI item such as barley, as compared to a placebo, is similar to Benton, Ruffin, Lassel, Nabb, Messaoudi, Vinoy, et al. (2003) findings of effects of a low-GI breakfast on memory performance. Kanarek and Swinney (1990) tested the performance of participants an hour after consumption of a snack, varying from previous studies which measured performance almost two hours after food intake, and suggest that similar supplements may improve performance on tasks requiring sustained attention – they state the need for further investigations on the time interval between food intake and measurement of performance.

Task complexity may also play a role on performance, with more or less processing involved in the task. Craft and colleagues (1994) reported that glucose affected complex memory (declarative) processes only. Letter cancellation, attention to details during sit-com scenarios, and Elevator Counting or Lottery tasks may not be task sensitive or demanding enough to detect differences at low blood glucose levels. Task complexity may explain the results found in the PASAT, which may be a more intensive task requiring mental calculations of single digits resulting in multiple digits, than the attention tasks used in the McAulay et al. (2001) study. Telephone Search While Counting involved searching for key symbols in a directory while counting tones on an audiotape, which may or may not have involved addition of multiple digit numbers. The effect of blood glucose levels on performance on mathematic calculations will be further examined in the section on memory. The PASAT test may be a more memory intensive task than the Telephone Search While Counting. However, only auditory processing is being used as a resource during the PASAT, while Telephone Search While Counting involved both visual and auditory processing. This too may have modified (or decreased) competition of attentional resources, allowing participants to "draw on" multiple resources. This consideration is based on Wickens' (1984) theory, which describes how processing stimuli in different modalities (auditory, visual) produces less attentional competition than processing within the same modality (auditory only).

An additional challenge is posed when physiological symptoms from low blood glucose levels may lead to situations where an individual's attention becomes divided (Smid, Trumper, Pottag, Wagner, Lobmann, & Scheich, 1997). Shakiness or hunger pangs may be distracting and add to demands during a task. Schächinger and colleagues (2003) used the PASAT and found that divided and sustained attention was impaired at low blood glucose levels. The PASAT was sensitive enough to detect impairments caused by hypoglycemia ($\sigma = 1.31$, "large" effect size), but another divided attention task (Telephone Search While Counting) did not produce a significant effect (McAulay et al., 2001). Schächinger and colleagues (2003) describe that inattention to stimuli and being overwhelmed resulted in increased reaction time and increases in omission errors on the PASAT. They suggest that distracting symptoms may have contributed to participants being overwhelmed on this task.

Types of errors on attention tests, like the PASAT, resulted predominantly in errors of omission (failing to respond) at hypoglycemic levels at 49 mg/dl and at normal blood glucose levels at 85 mg/dl (Schächinger et al., 2003). However, at blood glucose levels at 85 mg/dl omission errors were about 1.5 times more likely than false responses, but at blood glucose levels at 49 mg/dl this ratio increased to 2.5. Schächinger and colleagues (2003) reported that PASAT omission errors may have be due to participants' receiving inadequate glucose supplies such that they become so inattentive that they fail to notice stimuli, or are too overwhelmed to respond. Increased errors of commission (responding incorrectly) occurred on the CPT in participants at 100 mg/kg as compared to the saccharin group (Flint & Turek, 2003). Furthermore, impaired performance (on CRT and response selection) of healthy individuals remained, even after participants were restored to normal blood glucose levels at 85 mg/dl. Flint and Turek (2003) attribute errors of omission on the CPT task to inattention, and errors of commission to impulsivity, disinhibition, boredom, or fatigue. They suggest that 100 mg/kg of glucose is capable of producing increased commission errors. The cause of this apparent glucose-related impairment is unclear. They suggest that it's possible that increased proactive interference occurred (the processing of new information is disrupted by previously learned material) or that accelerated glucose uptake led to over-stimulation of areas responsible for memory consolidation. Blood glucose levels after 100 mg/kg of administered glucose showed an upward trend but did not rise significantly, contrary to other studies that have found significant increases in blood glucose levels after 50 grams of glucose. Interestingly, the 100 mg/kg condition was the only condition in which performance differences were shown. These errors of commission were apparently not due to an increased rise in blood glucose levels from 100 mg/kg, but did affect performance. Perhaps glucose interacted with other hormones that resulted in a change in performance. Morris and Sarll's (2001) assertion that the relationship between glucose and performance is more complex than currently understood is supported by this case.

Summary of Findings of Attention Studies

Blood glucose levels affect aspects of attention related to divided and selective attention, information processing, and decision-making. Tests used to assess sustained attention and visual attentional discrimination have produced mixed results. Studies investigating the effects of breakfast on performance may show selective effects of breakfast, rather than a clear overall benefit. The complex nature of the effect of blood glucose levels on performance is evident in this area. For example, increased errors were found on a Stroop task after a glucose administration versus placebo and differences in types of errors were demonstrated, possibly based on the task and blood glucose level (increased commission errors on a CPT task after a glucose administration of 100 mg/kg, and increased omission errors on the PASAT at a hypoglycemic level). Differences in whether accuracy was preserved at the expense of speed (participants may have been more inhibited), or whether speed was preserved at the expense of accuracy (participants may have been less inhibited) were shown. There were also impairments on attention tasks at low blood glucose levels that remained even after levels were restored to normal. Overall, performance on attentional tasks has been affected at blood glucose levels ranging from 36–59 mg/dl.

Blood glucose levels have affected speed of performance on attentional tasks. Reaction time is decreased (faster) when a glucose drink or similar snack is provided, while reaction time increases (slower) when participants fasted or were given a placebo. Reaction time increased at hypoglycemia

(47 mg/dl), which may be compounded when multiple tasks are presented. A glucose drink or similar snack benefited a sustained attention task and led to faster detection of targets.

Effects of both glucose administration and glucose depletion on speed versus accuracy performance on attention tasks have been demonstrated. Glucose administration has been found to negatively affect performance on some tasks requiring effortful attentional processing. However, on these tasks, when reaction time decreased, errors increased. This trade-off was evident with a Stroop performance task in that reaction times were faster while error rates increased after glucose administration as compared to saccharin administration (Craft et al., 1994). Individuals may or may not have been aware of their impairment and may not have maintained a more cautious approach. On the other hand, accuracy was preserved at the expense of speed in an attentional switching (Visual Elevator) and visual selective attention (Telephone Search) task, at blood glucose levels at 47 mg/dl as compared to blood glucose levels at 81 mg/dl. McAulay et al. (2001) suggested that either individuals were generally slower during hypoglycemia or that they adopted a more cautious approach in order to avoid errors during these tasks.

Many complex attention tasks relevant to everyday living have been impaired during hypoglycemia at 47 mg/dl. McAulay et al. (2001) described a subsystem of attention that they believe to be affected, including a selection system that responds to relevant stimuli and inhibiting irrelevant ones, a vigilance system that maintains readiness to respond in the absence of cues, and an orientation system responsible for moving and disengaging attention in space. In several studies, parts of this attention subsystem have shown that there are negative effects at lowered blood glucose levels and positive effects at elevated blood glucose levels (i.e., from a glucose drink, breakfast, or other glucose provision).

THE EFFECT OF BLOOD GLUCOSE ON VIGILANCE

The tests used to assess performance on attention tasks are similar to the types of tests used to assess vigilance, with a focus on assessing attention over time on tasks lasting from several minutes and up to an hour. Tasks such as monitoring sequences of digits on a computer screen, detecting target pips (or tones), rapid information processing, tracking tasks, a subtraction task, and reaction time during a vigilance task by evaluating electro-encephalograms (EEGS) have all been used to measure the effects of blood glucose on vigilance performance.

Increased glucose provisions have been shown to benefit digit-monitoring performance in non-diabetic individuals. In a study by Benton (1990), after having fasted four hours prior to the experiment, male students monitored digits (0–9) over a twenty-four minute period. Upon arrival, participants consumed either a glucose drink (25 grams) or a placebo (aspartamate), and began a vigilance task in which they pressed a button whenever certain numbers were presented. During this task, participants also added or subtracted single digits every 5 seconds as a distracter task. Performance on the digit-monitoring task was affected; participants performing simple calculations while monitoring digits produced significantly fewer errors if they had consumed glucose rather than a placebo drink.

However, the type of provision provided (e.g., drink, snack, breakfast-specific effects) during the experiment may (or may not) affect digit-monitoring performance. As previously described in the attention section, Smith et al. (1992) investigated the effects of breakfast and caffeine on performance in healthy college students. Using an eight-minute long Repeated Digits Vigilance Task, the participant was presented with three digit numbers on a screen and had to detect whether this combination of numbers was repeated by pressing a button as quickly as possible. Caffeine increased the number of hits and speed of responses, but there was no effect of breakfast in this task.

An interesting finding is that expectancy effects in non-diabetic individuals may affect performance on digit-monitoring tasks. To explore the effect of expectancy from a glucose drink on performance, Green et al. (2001) used the Bakan task, a six minute long test. For this task, participants (18–40 years of age) were presented with a stream of single digit numbers and pressed a response key as quickly as possible after they detected a sequence of either three even or three odd numbers. Individuals participated in five test sessions, with one session being an initial practice session. On two of these sessions a glucose drink (50 grams) was ingested, whereas on the other two a placebo drink (aspartamate) was used. Participants were correctly informed as to the content of their drink in one of each drink condition and misinformed in the other condition (i.e., told they received a placebo when they actually received glucose). Testing began thirty minutes after drink consumption and sessions lasted one hour. Correct hits were measured. Performance of healthy participants who were given the glucose drink improved on this task as compared to the control drink; however, this only occurred when they were told they would receive glucose and not when they were told they would receive aspartamate. When participants were informed that they were about to receive aspartamate, the content of the drink did not affect performance on this task. Participants made significantly more correct hits than in any other condition when they were informed that they would receive glucose and did. There were no effects of the drink type or expectancy on other measures used (Finger tapping, Recognition memory, and Verbal free-recall tasks). Although recognition memory times were faster in the glucose versus the placebo condition, the number of words correctly recognized was not significantly different across conditions. Based on these findings, Green and colleagues actually question research indicating that glucose benefits performance in non-diabetic and non food-deprived individuals.

In the following studies, reaction time and error rate have been shown to increase on vigilance tasks under conditions of low blood sugar. However, in one study performance on a reaction time but not a vigilance task was affected. These studies evaluated non-diabetics at hypoglycemic levels, at blood glucose levels after a glucose drink (or a placebo) was provided, and during changing blood glucose levels. Fruehwald-Schultes, Born, Kern, Peters, and Fehm (2000) were interested in how the effects of a previous hypoglycemic episode affected performance on a subsequent episode. Reaction time in healthy male participants was assessed during a vigilance task, using auditory-evoked brain potentials (AEBPs) that show different stages of the brain's processing of stimuli. For the task, participants detected target tones randomly interspersed among tones of lower frequencies and pressed a button as quickly as possible, while being induced to hypoglycemic levels (47 mg/dl). Reaction time performance to the target tones increased during hypoglycemia in both hypoglycemia groups. In determining whether performance was affected after a demanding (cognitive) task or non demanding (sitting quietly) task at declining blood glucose levels, Donohoe and Benton (1999b) used the Rapid Information Processing Task (RIPT). As a demanding vigilance and working memory task, the RIPT required participants to press a space bar every time three consecutive even or odd numbers

appeared over a ten-minute period. Following their normal breakfast (1243 ±277 kJ) and after ingesting either a glucose drink (50 grams) or a placebo, healthy participants completed the RIPT and a word list recall task. Those who had consumed the placebo made significantly more errors (incorrect responses) on the RIPT task at 2, 4 and 6 minutes than did glucose drinkers. There was a similar trend at 8 and 10 minutes. Differences on performance were also found on rising versus falling glucose levels, which will be discussed later. On the other hand, Donohoe and Benton (2000) investigated glucose tolerance of healthy college students and performance on cognitive tests to assess memory, reaction time, and vigilance. To assess vigilance, students completed a RIPT-type task. No effect of glucose levels on the vigilance test was found. Only reaction time was associated with glucose levels, during a task where participants pressed a button on a panel after hearing an auditory warning and a subsequent light was illuminated and decision and movement time were measured; that is, higher baseline glucose levels were associated with faster choice reaction times. Again, falling levels were further evaluated, and the faster the blood glucose levels fell while performing the test battery, the faster the decision times were.

Performance on tracking tasks in diabetic individuals has been shown to be impaired at low blood glucose levels. As previously described in the psychomotor section, Hoffman et al. (1989) used a pursuit-rotor tracking task (which also assesses vigilance), in diabetics at hypoglycemic levels (50 mg/dl). For this task, participants tracked a dot rotating on a turntable with a stylus. The correct position maintained by the stylus during a 1-minute period for five trials was measured. Significant performance decrements on this task occurred at hypoglycemic levels.

Concentration, an aspect of attention defined as undivided and focused, has been assessed using tests previously described. For example, Hoffman et al. (1989) used the TMB test and Howorka et al. (2000) used the Gruenberg alphabetical cross-out test to assess concentration. Howorka and colleagues (2000) did not find an effect, with participants' blood glucose levels above 72 mg/dl, while Hoffman and colleagues (1989) found that TMB performance was affected at hypoglycemic levels. In a study previously described, Schächinger et al. (2003) used the PASAT and Choice Reaction Time Test (CRTT) to assess various combinations of sustained attention, strategic thinking, information processing speed, reaction time, spatial performance, eye-hand coordination, working memory, and concentration and found robust negative (e.g., impaired performance) effects with blood glucose levels at 49 mg/dl on these tests.

Other tests have also been used to assess concentration. Pramming et al. (1986) used the Serial Sevens Subtraction task, in which participants counted backwards (from either one-hundred, ninety-nine, or ninety-eight) in sevens to assess concentration in diabetics induced to hypoglycemic levels. Number of errors and the time taken to complete the test were measured. Scores on this test fell significantly from 54 mg/dl to 36 mg/dl, and improved from 36 mg/dl to 108 mg/dl. Results are similar to those employing the TMB test used in this study as described in the attention section.

As seen in other tests measuring performance based on the effects of varying blood glucose levels, level of awareness of hypoglycemic symptoms remains evident in vigilance studies. Previous hypoglycemic episodes may also affect subsequent vigilance performance at hypoglycemic levels. In an evaluative study investigating the effect of recurrent hypoglycemia and awareness in diabetic individuals, Howorka, Heger, Schabmann, Anderer, Tribl, and Zeitlhofer (1996) used electroencephalograms (EEGs) to examine symptoms of hypoglycemia and vigilance performance of partici-

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pants with and without hypoglycemic awareness. They described vigilance as the behavior of watching for and responding to irregular critical signals under monotonous conditions (requiring sustained attention). In looking at various vigilance indices of the EEG at induced hypoglycemic levels below 40 mg/dl, they found that in hypoglycemic unaware participants as compared to a group of diabetic participants with good awareness, there was an immediate reduction in vigilance after even a slight lowering of blood glucose (from a target blood glucose level at 101 mg/dl, ±20 mg/dl to 63 mg/dl). Further lowering of levels resulted in increased decrements, with differences being more severe in those who were unaware of hypoglycemic symptoms than in those who were aware. Previous exposure to hypoglycemia may have contributed to this reduced vigilance in that cognitive deficits may be affected (lessen or increase) with previous exposure. In a later study, Howorka and colleagues (2000) used similar EEG evaluations and a similar patient group. They found significantly reduced vigilance at non-hypoglycemic levels (72–180 mg/dl) in diabetic participants with recurrent hypoglycemia versus a matched control group (non-diabetics) and a group without a history of such conditions.

Challenges to Vigilance Studies

Some of the challenges to studies in this area include the duration of the task (e.g., was the test long enough?), timing of testing (e.g., test at 20 or 30 minutes post-glucose consumption), controlling what participants eat (fasting or feeding) prior to the experiment, and other variables that may compound the effects on performance (e.g., symptoms causing additional distractions). The results in the Smith et al. (1992) study could be due to the task not being long enough; it was only an eight-minute task. However, the pursuit-rotor task, a one-minute task administered repeatedly, showed significant performance decrements at low blood glucose levels. Green et al. (2001) attributed their conflicting findings to the timing of the task; 30 minutes post-glucose ingestion, but not 20 minutes post consumption. Determining the appropriate time to test for effects differs among studies and therefore, requires further investigation and standardization. Additionally, controlling what participants eat prior to the experiment is essential. The main confound with the Donohoe and Benton (2000) study not finding an association with glucose levels on a vigilance task as compared to a similar previous studies task (Donohoe & Benton, 1999b) is that participants were allowed to eat breakfast prior to the task and the contents of these meals were not controlled. (Admittedly, the primary purpose of this experiment was to investigate performance in an evaluative manner; no glucose or placebo control conditions existed, only a glucose tolerance test (GTT) was given to the participants who were measured a week later on cognitive tests.)

Similarly, Howorka and colleagues (1996) describe the difficulty in interpreting their results due to confounding variables that include practice effects, patient cooperation, and more importantly, the distractions cause by the symptoms of hypoglycemia. This confound has been mentioned in the attention section, and remains relevant, regardless of task type. Blood glucose levels at 72–180 mg/dl did not appear to affect vigilance performance, but history of hypoglycemia did (Howorka et al., 2000). History of hypoglycemia and awareness of hypoglycemia are important issues to address in the population studied (e.g., diabetics), as they may be confounding variables on the effect of blood glucose levels on performance.

Summary of Findings of Vigilance Studies

A tracking task used to assess vigilance was a sensitive measure of the effects of glucose on performance, being a less complex task and of shorter duration than other vigilance tasks. Reaction time performance during vigilance tasks slowed at hypoglycemic levels or at glucose levels after a placebo (versus a glucose) drink. Hypoglycemic levels (47 mg/dl) or placebo conditions (without a glucose provision) resulted in decreased performance on reaction time measures when participants were tasked with detecting auditory (sounds) or visual (odd/even numbers) targets.

An administration of glucose enhanced performance on a digit-monitoring task while performing simple mathematical calculations. However, when the digit-monitoring task involved detecting sequences of even/odd numbers, mixed results were found. These results can be attributed to expectancy effects and/or breakfast type (either during or before the experiment). It is possible that these effects could occur regardless of the task presented and this possibility requires further examination. Evaluation of vigilance by electro-encephalograms (EEGs) provides interesting results for those who are hypoglycemia unaware and experience repeated hypoglycemic episodes.

THE EFFECT OF BLOOD GLUCOSE ON MEMORY

Investigation into memory processes and performance has garnered the majority of supporting evidence of the effects of blood glucose on cognition. A growing collection of studies demonstrates that an increased provision of glucose to the brain benefits memory performance. Furthermore, certain aspects of memory (e.g., declarative but not procedural memory) have been shown to be affected by varying blood glucose levels. Several different types of tests have been used to assess learning and memory such as word list recall, story recall (immediate and delayed), trigrams, stimuli recognition, list learning, digit span recall, and mathematical calculation.

Memory

Better recall of a word list has been found to be associated with increased blood glucose levels from a glucose drink in non-diabetic individuals. Word list recall is a method most commonly used in the blood glucose and cognitive performance literature to assess working memory. Benton and Owens (1993), for example, found that the number of words recalled correlated significantly with blood glucose levels from a 50 gram glucose (versus a placebo) drink in young healthy adult participants (males $M = 21.6$ years of age and females $M = 21.8$ years of age). Participants listened to a list of fifteen words, presented at a one word per second interval, after which a distracter task was completed to prevent rehearsal (writing down as many American states as they knew for 30 seconds), after which participants recalled as many words as they could at their own pace. Increasing blood glucose levels from the glucose drink were associated with participants remembering significantly more words from a word list, relative to participants whose blood glucose levels were falling from 113 mg/dl (±21 mg/dl) to 93 mg/dl (±24 mg/dl). Memory improved throughout various ranges of blood glucose levels from a glucose drink. In a second experiment by Benton and Owens (1993), blood glucose levels (after a 50 gram glucose drink at the beginning of the experiment and two top-up drinks of 25 grams at 45 and 75 minutes later) correlated significantly with the number of words recalled, but not with recall of a Wechsler story (i.e., participants listened to a story and then wrote

down as many details they could remember immediately and one hour later). They did not control whether participants ate a meal before the experiment, but report that in meal eaters, there was no significant difference in recall time between placebo and glucose drinkers. Interestingly, placebo drinkers did take significantly longer in recalling a word list if they ate a meal before the experiment. In a subsequent study, Benton, Owens, and Parker (1994) investigated the effects of blood glucose on memory and attention in non-diabetic young adults. To assess memory, the word list task required participants to listen to a tape recording of thirty nouns, and recall immediately for two minutes as many words as they could remember. Twenty minutes later, after the Rapid Information Processing Task, participants recalled the words again. They found increased blood glucose levels from a glucose drink (50 grams immediately and 25 grams 25 minutes later) versus placebo drinks (aspartamate) to be associated with better recall of a word list, a finding consistent with other reports.

As previously described, Donohoe and Benton (1999b) found that glucose drinkers were significantly faster and recalled more words than did those who consumed a placebo. Female undergraduate college students ate a normal breakfast and were provided with either a glucose drink (50 grams) or a placebo drink in a double-blind procedure. Baseline levels and measures were taken. Participants were then grouped into a demanding condition (completing RIPT cognitive task) or a non demanding condition (sitting quietly), each for a duration of 10 minutes. Twenty minutes later, a second sample was taken, a memory task was presented (a list of fifteen words was presented at one-second intervals on an audiotape and immediately afterwards participants wrote down as many words as they could remember). A distracter personality questionnaire was then given, and after ten minutes a delayed recall of word list was administered. The experiment lasted forty minutes. Glucose drinkers recalled more words and were significantly faster than those in the placebo group. Changing blood glucose levels were not a significant factor, except for those participants in the demanding condition (with the glucose drink) who showed better recall if their blood glucose levels were falling rather than rising. This issue will be discussed later.

A glucose drink did not benefit a verbal recall task, but recognition memory was affected in non-diabetic individuals. The Green et al. (2001) study used a Recognition Memory task in which participants were presented with two lists of twenty words and immediately thereafter were presented with a recognition set of forty words. Participants had to decide whether each of the forty words was present or not in the training list by pressing a key labeled "Present" or "Not Present." Number of correct recognitions and response times were recorded. A verbal free-recall task in which participants were presented with two lists of twenty words and given four minutes to recall as many words as possible from the list was also administered. A glucose drink (50 grams) as compared to a placebo (aspartamate) had no effect, nor was the expectancy effect evident, during the (immediate) verbal free-recall task. However, response times were faster in the Recognition task when participants were given glucose than when they received a placebo. Additionally, there was a marginally significant effect on recognition performance (responding faster) when participants were told they were receiving glucose rather than a placebo.

Varying blood glucose levels by the administration of a glucose drink also affected memory performance in non-diabetic older individuals. Manning et al. (1990) found that a glucose (50 grams) but not a placebo (saccharin) drink benefited performance in older participants (62–84 years of age) on long-term declarative memory processes but not for "non memory" processes. A Logical Mem-

ory Test, which is a modified version of the Wechsler Memory Scale, was used to assess memory. Participants listened to an audio tape of a passage and were asked to recall that passage, both immediately after hearing it and forty minutes later. A Selective Reminding Test in which a subject was read a list of words, asked to immediately recall the list, and then read the words missed from the original recall of the word list was also used. This procedure was repeated until all words were recalled. Performance on these memory tests was significantly enhanced after a glucose drink. In contrast, performance on other memory and "non memory" tests used to assess cognition (verbal intelligence), attention, and motor skill did not benefit significantly from a glucose drink.

Effects of Blood Glucose on Specific Memory Functions

Some discrepancies continue to exist regarding the specific memory functions that are affected by blood glucose. Working memory, spatial memory, and verbal declarative memory processes (rather than procedural memory processes) have all been shown to improve by increasing blood glucose levels using a glucose drink. Craft et al. (1994) investigated the effects of glucose on cognitive functioning while taking into account age and gender. They provided healthy participants (young adults $M = 20.8$ years of age and older adults $M = 68.5$ years of age), who had fasted overnight, with either a glucose drink (50 grams) or a saccharin-flavored drink. Cognitive testing began approximately fifteen minutes after the drink. Several measures were used to assess performance. To assess declarative memory, the Paragraph Recall was used in which participants listened to brief narratives and were then asked to recall as much of the information both immediately after and ten minutes later. A modified California Verbal Learning Test was also employed. Here, participants listened to a list of 16 words and were asked to recall as many items as possible. A second list was presented and participants were asked to recall it. After this interference trial, participants were then asked to recall items from the first list. The number of correct items was recorded. A Pattern Recall and Recognition Measure was also used. For this task, participants viewed a checkerboard pattern with four randomly blackened squares on a grid and studied the patterns for 10 seconds. The stimuli were removed and the subject reproduced the pattern on a black grid sheet. After the free recall, participants picked the 3 test patterns out of 12 checkerboard patterns (including 9 distracter patterns) and the number of correct items was recorded. Procedural memory was assessed via a Serial Reaction Time task, which was used to measure implicit motor memory. For this task, participants pressed a key corresponding to an asterisk that appeared on a screen. Once pressed, the asterisk would appear in another location on the screen. A pattern became evident as reaction time decreased across trails, showing motor learning without declarative (explicit) knowledge. Working memory was assessed through the PASAT. Word list generation measured verbal fluency, and the Stroop Color-Word Interference Test measured response inhibition, assessed by having participants read 100 color words (word reading) in the first condition. In the second condition participants named the colors of blocks on a piece of paper (color naming), and in the third condition, color names were printed in discordant colors (e.g., the word "blue" printed in the color green). Reading time and errors were recorded. The researchers determined that blood glucose levels most clearly affected declarative memory assessed by the Paragraph Recall task, and that a glucose drink did not affect measures of working memory, procedural memory, or verbal fluency, where participants generated word lists in 60 seconds (e.g., list as many words that start with the letter "G") and the number of correct responses was recorded. However, they did find that paragraph recall validated its usefulness as a sensitive measure by clearly showing the benefits on declarative memory from glucose administration, especially for younger and older men. Women (young and old) and older men with poor

recovery (determined by the degree to which blood glucose levels return to baseline after glucose administration) did not show significant differences with either the glucose or saccharin drink. Craft and colleagues (1994) suspect that older males (58–77 years of age) may be more susceptible to glucose effects on memory than younger men and older and younger women.

The effect of blood glucose on word list performance in non-diabetics has also been investigated in relation to breakfast consumption. An important point is that both the amount of material to be recalled (e.g., number of words to recall from a word list memory task) and the time taken to perform the memory task have been shown to be affected by glucose levels. For example, Benton and Parker (1998) compared the findings of three experiments involving young non-diabetic university students. They examined the role of increased blood glucose levels in improving memory through breakfast consumption. Spatial memory was assessed, by presenting participants with 16 drawings of objects and having them concentrate for 20 seconds on the position of each picture on the grid. They were then given a distracter task in which they wrote down as many U.S. states as they could remember in one minute. Afterwards, participants were asked to put the pictures in their original order on the grid. The latencies and number of errors were measured. Overall, they found that time to recall (but not number of errors) for both the word list recall (number of words and time elapsed before participants gave up were recorded), and a spatial memory task was significantly longer when participants were fasting than when they had eaten breakfast. Furthermore, participants who ate breakfast recalled more of a Wechsler story than those who fasted, but a glucose drink (50 grams) versus a placebo did not influence recall of the story. However, a glucose drink did nullify the effects of missing breakfast on the Brown-Petersen trigram task, which measures short-term memory and requires participants to remember a trigram of consonants (e.g., KSN) while counting backwards in threes, over various lengths of time.

In a subsequent paper, Martin and Benton (1999) further examined Benton and Parker's (1998) second experiment and investigated the effects of glucose level on a demanding working memory task, the Brown-Petersen task. In young healthy female students, fasting was associated with worse performance on this demanding task. A glucose drink improved memory performance of those who were fasting and nullified the effects of missing breakfast, but was of no further benefit to those who ate breakfast. An increase in blood glucose benefited memory performance regardless of whether one ate breakfast or not, but its impact was greater when breakfast had not been eaten. Benton and Sargent (1992) examined blood glucose level and its influence on two memory tasks in healthy male and female university students. Participants either fasted or were given a breakfast drink and were administered a word list recall and spatial memory task. Again, it was the time taken to complete the memory tasks rather than the number of errors that was associated with blood glucose levels. That is, those who had not received a breakfast drink were significantly slower on a spatial memory task and immediate recall of a list of words than were those who had a breakfast drink. For the spatial memory task, increased blood glucose levels significantly correlated with better performance. The higher the blood glucose level, the better the performance, but the correlation between blood glucose and the immediate word recall task failed to reach statistical significance.

Pollitti et al. (1998) conducted three experiments comparing male and female children (9–11 years of age) from the U.S., and nutritionally at-risk male children from Peru to investigate the effects of breakfast versus fasting on memory. Scanning memory speed assessed by the Sternberg Memory Search Test (SMST) was slower for those in the at-risk group who did not eat breakfast (after an

overnight and morning fast) than for those in the breakfast group. The SMST required participants to memorize one or more stimuli presented and to decide whether a new stimuli was present or absent. Response latencies were measured. The Hagen Central Incidental Test (HCIT) adds a memory component to the Matching Familiar Figures Test (MFFT) used to assess visual discrimination. During the HCIT, participants are presented with six cards with a drawing of an animal and an object on each. Once all cards have been presented, the participant is shown a single card with the picture of an animal only on it; the task was to determine the serial position of the animal based on the initial presentation. Participants were instructed to pay attention to only the animals. In experiments 1 and 2, recall time for incidental stimuli (objects) in the HCIT increased in the no breakfast (fasting) group. For the SMST task, recall was also delayed in the no breakfast group. For the HCIT task, fasting children were less able to discriminate between meaningful and irrelevant cues. The researchers were surprised to find that participants recalled the last central item in the series significantly better after the overnight and morning fast than after breakfast consumption. That is, items presented at the end of the to-be-remembered items (presented most recently) were better remembered than words presented in the middle or at the beginning (primacy effect) of the series. When glucose levels fell below the median, the recency effect was more likely to occur (in experiment 1, but not in experiment 2).

Breakfast studies (i.e., different breakfast types) have shown patterns of effects (e.g., fewer false alarms) in non-diabetic individuals' performance on memory tasks. In some cases, unexpected results were found. Smith et al. (1994) conducted two experiments to determine the effects of breakfast and caffeine on cognitive performance and mood in healthy male and female university students. Participants were assigned to different breakfast type groups: no-breakfast, cooked breakfast, or cereal/toast breakfast. In experiment 1, there was no effect of breakfast on a simple reaction time task, speed or accuracy on a Five-Choice Response Task, or a vigilance task. However, those who ate a cooked breakfast reported on a visual analog scale that they felt more contented, sociable, interested, and outward going than those in the other two groups. In experiment 2, participants who ate breakfast reported that they felt more quick-witted and proficient, and recalled significantly more words in a Free Recall Task than the no-breakfast group. For this task, participants were presented with a list of 20 words at 2-second intervals and afterwards had two minutes to write down as many of the words as they could remember. In a Recognition Memory Task, participants were presented with 40 words (20 target words plus 20 distracters) and had to decide whether each word had been presented in an original list or not. Breakfast eaters had significantly fewer false alarms than the no-breakfast group. High doses of caffeine improved performance on the sustained attention tasks, and increased blood pressure and mental alertness. Performance on both a Logical Reasoning Task and a Semantic Memory Task was improved by caffeine consumption but not by breakfast consumption. For the Semantic Memory Task, participants determined whether sentences about general knowledge were true or not (e.g., canaries have wings) with number of responses and accuracy being measured. For the Logical Reasoning Task, participants were shown statements of the order of letters A and B and had to decide whether certain statements were true or false (e.g., A follows B: BA). The researchers concluded that breakfast may improve cognitive performance, but that this effect may be task specific.

In an earlier study, Smith et al. (1992) recruited forty-eight university students and assigned participants to one of four groups: no breakfast with caffeine, no breakfast and no caffeine, breakfast with caffeine, and breakfast with no caffeine. A Free Recall Task, a Delayed Recognition Memory Task,

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a Semantic Processing Task, and a Logical Reasoning Task were administered. No effects of breakfast or caffeine were found in the Free Recall Task. A lower false alarm rate was found earlier in the morning (and pre-lunch) session in the breakfast group on the Recognition Memory Task. Caffeine improved speed and accuracy on the Semantic Memory Task, but no effects of breakfast were found. Logical reasoning was impaired (accuracy) in the breakfast group, but failed to reach significance.

Studies investigating memory of non-diabetic individuals through word recall performance based on different types of snacks, glycemic indices of foods, and food types have also been explored. Benton and colleagues (2001) investigated the possible benefits of a snack on mood and memory in female college students (M = 21 years, 3 months of age). Participants were grouped into one of six conditions: fasted throughout the experiment, no breakfast but a snack at 11:30 a.m., and combinations of 10 grams or 50 grams of corn flakes (carbohydrate) and a snack or not at 11:30 a.m. To assess memory, a list of 30 words was presented on a tape recorder, and participants immediately (and ten minutes later) recalled as many of the words as possible. A visual analogue scale was used to assess mood. Those who ate breakfast, and/or a snack reported being less hungry, as suspected. However, the blood glucose levels of those who fasted remained constant and only at 10:15 a.m. did the 10-gram breakfast produce significantly higher blood glucose levels than in those who had fasted. A snack after the 50-gram breakfast maintained blood glucose levels for another hour. Those who ate a snack reported better mood on every mood dimension, and the number of words recalled by snackers was significantly greater than for those who did not snack, but this effect was time-limited (occurred at 11:45 a.m. but not 12:30 p.m.). When recalling words from the word list there was no significant difference between those who ate breakfast and those who fasted; however, significantly less time was spent recalling words by those who had fasted. Those who ate breakfast spent more time recalling words, and Benton and colleagues speculate that this was due to increased motivation or better attitude rather than to decreased efficiency. A mid-morning snack resulted in better memory if a 10-gram breakfast was consumed, while the opposite occurred if an individual fasted or had a 50-gram breakfast.

In a subsequent study, Benton et al. (2003) investigated the delivery rate of a rapidly available glucose breakfast with a high glycemic index (quicker rise, shorter duration), versus a slowly available glucose (smaller rise, longer duration) breakfast with a low glycemic index on memory in healthy female undergraduates and Wistar rats. They found in the rats a significant effect of consumption of a slowly available glucose breakfast versus a rapidly available glucose breakfast on a learning task in which an operant condition test based on bright light aversion was assessed. The rats pressed one of two levers to either switch the light off for 30 seconds or have no light effect. In the young human participants, they also found a significant effect of consumption of a slowly available glucose breakfast versus a rapidly available glucose breakfast on verbal memory performance for word lists of abstract and concrete words, where participants wrote down as many words as they could recall immediately and again ten minutes later. Human memory was assessed at 30, 90, 150, and 210 minutes after breakfast. For participants, more of an effect was seen for abstract words (considered more difficult to remember) than concrete words. It was the low glycemic index breakfasts that improved memory on a word recall task of abstract and concrete words, especially for abstract words later in the morning (at 210 minutes). There were individual differences in the rate of return to normal blood glucose levels, but the type of food an individual consumes can determine this rate of rise and fall of blood glucose levels. Animal models showed similar findings; learning performance

of rats was significantly better after a slowly available glucose breakfast versus a rapidly available glucose breakfast three hours after consumption. Whether or not participants typically ate breakfast had no influence on the results.

To assess memory, Kaplan et al. (2000) employed a Word List Recall task, a test of short-term verbal declarative memory in which participants listened to three repetitions of an audiotape of words spoken at a one word per second interval, after which they immediately recalled as many words as they could remember and the number of words recalled was scored. A Paragraph Recall Task was also used to assess memory, where immediate and delayed (20 minutes) recall of a story with 25 ideas (or units) was scored. A nonverbal distracter task was administered during the delay period to prevent rehearsal. Overall, performance did not significantly differ after consumption of glucose (50 grams), potatoes, or barley as compared to a placebo. However, when poor baseline memory and poor β (beta) cell function were factored into the analyses, memory improvements (more for word list recall than paragraph recall) were seen in performance for glucose, potato, and barley as compared with the placebo. Furthermore, effects were more robust 15 minutes after ingestion of barley and potato, 60 minutes after glucose consumption, and more robust for delayed recall (long-term memory) than for immediate recall (short-term memory).

While blood glucose levels from administration of glucose (or a snack or breakfast) have been shown to enhance memory performance, low blood glucose levels resulted in impaired memory performance in non-diabetic individuals. A short-term memory task was used in the previously described Fruehwald-Schultes et al. (2000) study, where participants listened to 15 words from a word list containing 3 semantic word categories: neutral ("tree"), food-related ("eggs"), and emotional ("friend"), at a one-word-per-second interval after which participants recalled as many words as they could within one minute. Number of words correctly recalled was scored. Insulin-induced healthy participants with and without (control group) a recent previous hypoglycemic episode (for 2.5 hours the day prior to the experiment) exhibited deteriorated performance on this task at hypoglycemic levels (47 mg/dl). This effect also depended on the prior-hypoglycemic (non control group) experience; those in the prior-hypoglycemic group remembered on average 4 more words than participants in the control category.

Individual glucose regulation has also been explored and found to play a critical role in blood glucose and cognition studies, with quality of regulation being associated with performance. Donohoe and Benton (2000) investigated the ability to control blood glucose levels as a possible influence on memory and other aspects of cognition, using healthy young adult females ($M = 22$ years of age), who participated in two sessions. In the first session, after an overnight fast, a glucose tolerance test (GTT) was given. Participants remained quiet with no eating or drinking for 3.5 hours. In the second session, dietary restrictions were not enforced. Participants ate breakfast and completed cognitive tests such as a reaction time task, a vigilance task, and a word recall task where participants listened to a list of 30 words at 2-second intervals and immediately afterward wrote down as many words as they could recall, with a delayed recall test fifteen minutes later. The number of correctly recalled words was recorded. Performance on these tests was compared with glucose tolerance (session 1) and to blood glucose control during the tasks (session 2). Donohoe and Benton found that the brain is susceptible to fluctuations within a normal range (not necessarily hypoglycemic levels) and that the brain is susceptible to aspects of physiology (perhaps hormonal). The GTT data showed that the quicker blood glucose levels returned to baseline (reflecting the ability to regain baseline values)

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from nadir (the lowest blood glucose point), the better memory performance was. The faster the falling blood glucose levels, the quicker the decision time. The profile of good glucose tolerance was associated with enhanced performance on cognitive tasks.

Even in individuals with poor gluco-regulation, or the body's lack of ability to properly utilize glucose, the benefits of a glucose drink on memory remain. Messier et al. (1999), for example, classified individuals into those with or without good gluco-regulation. Participants served as their own controls, and had either a glucose (50 grams) or placebo (50 grams of saccharin) drink and completed a list-learning task. Participants were shown a list of words on a screen that they were told they needed to remember, after which they would write down on a sheet of paper as many words as they could remember. Word lists contained high imagery (e.g., stomach, star) and low imagery (e.g., theme, logic) words. High imagery words were recalled significantly better than low imagery words. They also found that those with poor gluco-regulation had poorer recall on the list-learning test than those with good gluco-regulation. However, even in those with poor gluco-regulation, a glucose drink versus a placebo eliminated the difference in performance between these groups on immediate and delayed recall of both concrete (high-imagery) and abstract (low-imagery) words.

Learning, as assessed by paired-associates learning and list-learning tasks, is another process that requires memory in which the effects of blood glucose levels have also been investigated in non-diabetic individuals. Lapp (1981) examined whether blood glucose levels above 130 mg/dl would facilitate learning and if recall would be superior for high imagery nouns in high school students. Participants were either assigned to a group with blood glucose levels below 80 mg/dl or above 130 mg/dl. Participants in the blood glucose level group above 130 mg/dl were provided a high carbohydrate food to maintain higher glucose levels. Lapp (1981) hypothesized that glucose levels above 130 mg/dl would enhance learning of both concrete and abstract levels of stimuli. Twelve low-imagery noun pairs (e.g., idea, honor) and twelve high-imagery noun pairs (e.g., elephant, volcano) were presented. On each paired-associates learning trial the pairs were presented at 4-second intervals, after which a bell signaled the beginning of the recall trial. The stimulus words, presented randomly, were read at 6-second intervals and participants wrote down their responses. Glucose levels significantly affected performance on both high- and low-imagery noun pairs. Lapp found that high-imagery nouns were more easily learned than low-imagery nouns and that memory for lists of high- and low-imagery words was greater when blood glucose levels were above 130 mg/dl than when they were below 80 mg/dl.

Memory performance has also been assessed using the Digit Span Task in diabetic and non-diabetic individuals, producing mixed results. Pramming et al. (1986) induced diabetics to hypoglycemic levels and used Story Recall to assess short-term memory, where participants listened to a narrative story with 18 units and immediately afterwards recalled as much of the story as possible. The number of units recalled was recorded. Scores on story recall deteriorated at these levels, but were not significant. The Digit Span was also used to assess working memory. Scores on the Digit Span subtest were significantly lower (as part of a total test score) with scores deteriorating between 108 mg/dl to 54 mg/dl and from 54 mg/dl to 36 mg/dl. However, Manning et al. (1990) found no effect of a glucose drink (50 grams) on the Digit Span task in older participants. Similarly, Holmes et al. (1983) employed word recall assessed by the Rey auditory verbal learning test (in which participants had five trials to correctly repeat fifteen words), but failed to find a significant effect.

That is, performance on this task was not affected at any blood glucose level (60, 110, or 300 mg/dl) in diabetic patients. Performance on the digit supraspan task, similar to Digit Span, was also not affected by varying blood glucose levels. However, Kanarek and Swinney (1990) studied the effect of food and snack on cognitive performance in male college students. In two experiments, they compared a high caloric confectionery product and a yogurt snack, to a low caloric snack (e.g., caffeine-free soda). To assess memory, they used the Forward and Backward Digit Span (subtests from the Wechsler Adult Intelligence Scale), in which participants listened to an audiotape of digit sequences from two digits and increasing to nine digits over eight sets. Participants repeated the digits in the same order as presented, and the mean of the longest set for the two sets of each set used were calculated. No significant differences were found for Forward Digit Span, but participants recalled significantly more digits during the Backward Digit Span after they consumed the caloric snack rather than the non caloric snack. In the second experiment, with similar procedures as the first, participants recalled significantly more digits during the Forward Digit Span when they consumed a yogurt snack than when they consumed a diet soda. Again, participants recalled significantly more digits during the Backward Digit Span after eating the caloric snack rather than the non caloric snack.

Working memory is required to complete tasks such as math calculation, and has been used to assess memory performance at varying blood glucose levels. The Serial Sevens Test (SST) has been commonly used to assess memory through math calculation performance at varying blood glucose levels. Scholey et al. (2001) used male and female volunteers (range 20–30 years of age) to investigate the effect of glucose (25 grams) versus a placebo drink on varying levels of cognitive demand and timing of task performance. They used a computerized Serial Sevens Task, in which participants subtracted 7 from a number between 800–999, and then subtracted 7 from the resulting number, and so on, by key-pressing the numbers in and continuing the task for 5 minutes. A control task, which requires less of a cognitive load, required participants to press a key four times after hearing a metronome tone at 20 beeps per minute, was also employed. The task lasted 5 minutes. A two-minute Word Retrieval Task, in which participants generated as many words as they could beginning with either the letter "S" or "A," and a Word Memory Task, in which participants studied a list of fifteen words for 5 minutes, and then recalled as many words as they could remember within 1 minute, were also used. The number of correctly recalled words was scored. Participants generated more responses on the Serial Sevens task in the glucose than in the placebo condition, but the number of errors between the conditions was not significantly different. No significant differences were found on Word Memory performance, but a strong trend for an increased number of responses during the Verbal Fluency Task was shown in the glucose but not the placebo condition. Similarly, Kennedy and Scholey (2000) used a Serial Sevens task that lasted for 2 minutes, and the number of correct and incorrect responses was recorded. A Serial Threes task was also administered, in which serial subtraction of threes was required. Participants performed a greater number of Serial Sevens subtractions in the glucose than the placebo condition. There was no effect of glucose on the Serial Threes task. There was no effect of glucose on the number of errors for either task.

Hale, Margen, and Rabak (1981) were interested in the effects of postprandial (post-meal) hypoglycemia on performance and used a Serial Sevens Test (SST), in which participants subtracted seven from a starting number until zero was reached every half hour, during a glucose tolerance test (GTT), to measure mental confusion and neuroglycopenic symptoms (e.g., mental confusion, fatigue, blurred vision, headache). They expected that the time required to complete the first

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15 subtractions would increase at hypoglycemic levels. Participants were grouped into two categories, those whose glucose levels fell to below 60 mg/dl, or those who remained above 60 mg/dl. Those whose lowest glucose levels fell to below 60 mg/dl experienced more regression (not steady improvement) in their SST performance than those whose levels remained above 60 mg/dl. Taylor and Rachman (1988) used a GTT and the Serial Sevens Test to investigate low blood glucose levels and impairments in cognitive functioning, mood, and symptoms. The time taken to complete the 14 subtractions on the SST was recorded. In order to prevent practice effects, participants were given two pre-trials on the SST before beginning the experiment. A typical steady pattern of improvement across trails was not found (suggesting impairments), but multiple comparisons did not reach significance. However, when participants were regrouped based on symptom scores, blood glucose nadirs (lowest blood glucose level point), and rate of blood sugar drop, those participants whose blood glucose level drops were between 36 and 73 mg per hour (high speed; low speed was between 21 and 35 mg per hour) took longer to do the SST at the nadir and half an hour after the nadir, than at one hour and half an hour before the nadir. Performance was also poorer at the nadir than at one hour after the nadir.

Solving word or multiplication problems has also been used to assess memory performance. In both experiments by Kanarek and Swinney (1990), participants' arithmetic reasoning was enhanced by a caloric snack versus a non caloric snack, whether or not participants had eaten or skipped lunch. Marginal effects of lunch on cognitive performance were found, and only reading times were significantly faster after participants had eaten lunch than when they skipped lunch. Scores on arithmetic word-problems, where participants listened to an audiotape and had to calculate the situations without pencil and paper, and had to state the answer, were recorded. Participants did marginally better on this task if they had eaten lunch than if they had not eaten lunch, and if given a confectionary product compared to a low calorie soft drink. More correctly solved problems resulted in these conditions than in any of the other conditions. However, in the second experiment, participants solved significantly more problems after consuming a caloric rather than a non caloric placebo but the lunch condition had no effect. When participants consumed a yogurt product, they solved problems significantly more rapidly than when they consumed a diet soda. Again, the lunch condition had no effect. Holmes et al. (1983) used mathematical computations, where participants completed simple math facts to measure speeded recall of rote or over-learned facts. Participants had one minute to complete the task, and the number of correctly recalled facts (including problems attempted) were recorded. There was a significant effect of glucose level on number of calculations correctly completed. Fewer problems were correctly completed at low blood glucose levels (60 mg/dl). There was no effect of number of correct problems completed to those attempted, so Holmes and colleagues (1983) asserted that participants must have worked more slowly at low blood glucose levels to maintain a relatively high level of accuracy ($M = 95.7\%$), as compared to participants at normal (110 mg/dl, $M = 95.8\%$ accuracy) and high (300 mg/dl, $M = 98.1\%$ accuracy) blood glucose levels. That is, participants correctly completed fewer math problems during hypoglycemia at 60 mg/dl because they attempted fewer math problems.

Performing two tasks simultaneously, with one of them being simple mathematical calculations has also been investigated. As previously described in the psychomotor and vigilance sections, in the Benton study (1990), performance on the digit-monitoring task was affected; participants performing simple calculations while monitoring numbers on a computer screen produced significantly fewer errors with a glucose versus a placebo drink. Performance on the coordination task in the second

experiment was unaffected by glucose, with participants producing more calculation errors (although this was not significant) than the simple calculations in the first experiment. Clearly, the level of difficulty and involvement of the task(s) will affect performance.

The PASAT has been used to assess cognitive functions (e.g., memory), in addition to aspects of attention and decision-making (see Attention and Decision-Making sections). Gold, MacLeod, et al. (1995) were interested in the effects of hypoglycemia in diabetics ($M = 37.4$ and 35.0 years of age of normal and impaired participants, respectively) who were either aware or not aware of their symptoms. Using several tests in the battery including the PASAT test, they found that when glucose levels were lowered to 45 mg/dl and maintained at that level for 30 minutes, irrespective of awareness, overall cognitive performance was significantly different than at 81 mg/dl. Not all of the tests were affected equally at the different testing time points. During hypoglycemia, PASAT performance significantly deteriorated. In another experiment by Gold, Deary, MacLeod, Thompson, et al. (1995), PASAT performance of healthy non-diabetic participants (29.5 years of age) significantly deteriorated at blood glucose levels of 45 mg/dl. Schächinger et al. (2003) found that reaction time increased and accuracy decreased on the PASAT during hypoglycemia (see Attention section).

An interesting finding is that awareness of hypoglycemic symptoms may affect performance assessed by mathematical calculations, although in this study not as one would expect. As previously described (see Vigilance section), to assess neuroglycopenia using a simple cognitive test in addition to several other measures, Howorka et al. (1996) evaluated EEGs while IDDM participants (with and without hypoglycemic awareness of symptoms) quickly multiplied two numbers (e.g., one digit by a two-digit number, 8 x 13 = ?) during insulin induced hypoglycemia (40 mg/dl, range 18–40 mg/dl). If participants were incorrect, they quickly multiplied a simpler problem (e.g., one-digit number by a one digit number, 6 x 7 = ?). They report that this inability to multiply two numbers occurred very suddenly in hypoglycemic aware patients; however, unaware patients did not show any impairment on this task, even at very low glucose levels.

Another interesting issue, discussed later in this review is that memory has been enhanced on memory tests, but these benefits may be dose dependent. Parsons and Gold (1992) recruited older participants (60–82 years of age) to investigate the dose dependent effects of glucose on memory. Cognitive testing began five minutes after administration of a particular glucose and saccharin mixed dosage (10, 25, or 50 grams of glucose) or a placebo (50.6 mg of saccharin but no glucose) drink on four separate sessions. Glucose levels were assessed prior to the experiment and at 15 and 50 minutes after drink consumption. Using the Logical Memory test, participants listened to an audiotape narrative and recalled as much of the passage as they could after a 5-minute delay, and again 40 minutes later. Scores on the logical memory test were significantly enhanced under the 25 grams of glucose condition, but not at higher or lower doses.

Despite support for the benefits of a glucose drink on memory processes, Azari (1991) failed to find an effect of a glucose drink (30 grams and 100 grams) on a word list recall task in young adults (19–25 years of age). On this task, 40 words were presented on a monitor and the participant wrote down as many words as they could remember. The number of correctly recalled words was recorded. A recognition test required participants to circle the word in a word pair that had just been presented (one noun from the test list and one distracter word). A power calculation was computed and despite the power to detect a medium effect, a beneficial effect of glucose on working memory

was not found. Similarly, in an experiment by Benton and Owens (1993), there was no significant relationship found between a glucose (50 grams) or placebo drink on performance on a spatial memory task. For this task, the participant was presented with 16 pictures of objects, which they studied for 30 seconds, after which they engaged in a counting backwards (distracter task to prevent rehearsal), and then arranged the pictures in the previous order with no time limit imposed.

Challenges to Memory Studies

Challenges include methodological differences such as the type of treatment administered (e.g., snack and/or breakfast type), participants' and experimenters' familiarity with the test or task, lack of standardization, time-related issues (e.g., duration of the task, optimum time to test perform-ance), and differences in glucose dosages.

A caloric drink affected Backward Digit Span recall, but not Forward Digit Span; and a yogurt snack (but not a non confectionary snack) affected both Forward and Backward Digit Span recall. Kanarek and Swinney (1990) argue that differences in results might be due to the protein (not merely carbo-hydrate) in the yogurt snack, which may have cancelled out the effects of a pure carbohydrate snack. Also, the Digit Backward Task is considered a more difficult task. The differences found in partici-pants in the Free Recall Task may be due to the type of glucose or breakfast being used as part of the treatment condition.

Specific effects of breakfast have been previously addressed and although breakfast studies have also contributed to significant results, they have raised further questions about memory processes. Pollitti et al. (1998) stated that they found no evidence of an association between glucose concentra-tion and memory function – only that an overnight and morning fast among children had adverse affects on memory and attentional processes. Benton and Parker (1998) suggested that eating breakfast benefits tasks that require retention of newly acquired information. Significant effects of breakfast were found on a Wechsler Story task, but a glucose drink had no effect. Interestingly, in their first experiment investigating spatial memory and word list recall, participants' blood glucose levels were not particularly low whether fasting or after eating breakfast and were never below 86 mg/dl. Donohoe and Benton (2000) state that the caveat to their study was that breakfast types were not recorded, and that different breakfast compositions might have different effects on glucose levels (e.g., higher carbohydrate meals equal higher blood glucose levels vs. combined carbohydrate and fat meal).

Experimenters' and/or participants' familiarity with the task are challenges to this line of research. To illustrate, participants' familiarity can be due to redundant cuing during a task and may also result in ceiling effects. In the Benton et al. (2001) study, breakfast did not clearly improve memory performance or mood, which conflicts with previous work. They point out the effects of experience and familiarity with cognitive tests that may offset the negative consequences usually associated with missing breakfast. Similarly, Holmes et al. (1986) found that reading comprehension was not affected by either low (at 60 mg/dl) or high (at 300 mg/dl) blood glucose levels and attributed this to the nature of multiple redundant informational cues in a story recall task.

Scholey and colleagues (2001) suggest that ceiling effects may have occurred on the Word Memory Task as a result of over-learning of the material prior to testing. Kanarek and Swinney (1990)

attributed their differing word problem results to experimenters being more familiar with the task during the second experiment, and that in the first experiment the results were marginal and almost reached significance – and might have been significant given experimenters experience with administering the tasks in the first experiment.

Lack of standardization in the reporting of the research may also be significant problems in this area. For example, in the Hale et al. (1981) study, no clear description of the population group was provided other than "patients" from a medical center. The specifics of the subject group were not explicitly described, such as the age range of the participants and whether participants were diabetic or non-diabetic. This information as well as providing calculated effects sizes is not only critical in determining how large these effects may be, but also in determining which aspects of a methodology or treatment may or may not truly be contributing to these effects on performance. Howorka et al. (1996) did not attempt to provide an explanation as to why they failed to find a math calculation performance impairment in those who were hypoglycemic unaware, even though their study primarily focused on vigilance performance being more affected in hypoglycemic unaware than aware subject, whereas Smith et al. (1992) were unclear as to the effects of breakfast being associated with impaired performance and suggested the need for future studies.

Researchers have investigated and addressed the potential confounds of glucose dosages and time-related issues. Performance on the Digit Span test has been negatively affected at hypoglycemic levels at 54 mg/dl, but not at 60 mg/dl. Despite overwhelming evidence to suggest that 50 grams of glucose enhances performance on various functions, Azari (1991) stated that it was unlikely in his experiment that using 50 grams of glucose (instead of 30 grams or 100 grams) would have resulted in different results. Scholey and colleagues (2001) used 25 grams and not 50 grams typically used in experiments, and attribute their lack of significant findings to this dosage. Kanarek and Swinney (1990) describe other effects, such as the fact that participants knew what they were consuming in their experiment (additionally, the effects of aspartamate versus saccharin being used as part of the control drink for a placebo condition needs further exploration). Time factors may also contribute to effects. Kanarek and Swinney suggest that testing should be conducted at several time points after food consumption. This issue has been argued previously, and there continues to be a lack of consensus in determining the optimal time of testing for effects. Additionally, limiting the participants' time on the tasks may result in more sensitive measures of performance (e.g., spatial memory task). Taylor and Rachman (1988) raised some important methodological issues such as refraining from evaluating participants' performance only at specified, or researcher expected time periods, such as the nadir only, since participants' reports of symptoms occurred after the nadir and not during the nadir. Similarly, they investigated the rate of the fall in blood glucose levels, expecting that the greater falls in levels would show the larger negative effect. Indeed, a high rate (high-speed) rather than a low rate (low-speed) of blood glucose drop affected SST performance.

While in some cases investigators failed to explain their findings adequately or provide rationale for their present research, useful avenues for potential research areas were described in others. Kennedy and Scholey (2000) were interested in heart rate, and suggested that participants in their study may have viewed the task as complex, which increased participants' heart rates, and in turn resulted in an increase in blood glucose delivery and utilization. From further analyses in one study, participants who ingested a placebo drink took significantly more time in recalling a word list if they had eaten breakfast before entering the experiment (Benton & Owens, 1993). Does this truly reflect better

motivation to complete the task as has been suggested? Do fewer false alarms in a Recognition Memory Task mean that participants are being more cautious in their responses? Donohoe and Benton (2000) suggest separating physiology from psychological measures because questions remain about what exactly leads to enhanced performance. Is it due to re-uptake associated with a decline in blood glucose, to an increased metabolic rate, or induced by increased motivation which leads to enhanced performance? Questions regarding participants' motivation, expectations, and patterns of performance (i.e., accuracy-speed trade off) continue to be explored.

Summary of Findings of Memory Studies

Several studies have shown that glucose provisions, either by a drink or carbohydrate snack and/or breakfast can significantly enhance memory performance. Amount of material recalled and speed of performance on memory tests have been shown to be positively correlated with blood glucose levels. Similarly, recognition and recall times have been shown to increase with a glucose drink (but not a placebo drink) and/or breakfast provisions (but not by fasting or missing breakfast). Enhanced performance on working, declarative, and spatial memory tasks have been demonstrated with increased glucose levels, while memory performance assessed by Wechsler Story Recall, Digit Span, and Free Recall show minimal or mixed results. Accuracy appears to continue to be preserved at the expense of speed (e.g., performance on a spatial memory task following a breakfast drink). Individual glucoregulation plays a critical role, yet the benefits of a glucose provision remain even in those individuals with poor glucoregulation. Performance on list-learning tasks has also shown benefits from a glucose provision. Consistent with other tasks and processes, effects on memory may be dose-dependent.

Memory performance assessed by mathematical calculation or problem solving tasks appears to show similar patterns as word list recall tasks. The amount of mathematical material that participants were able to solve correlated with their glucose levels and/or provisions. For example, an increased glucose level or provision (e.g., caloric versus non caloric or placebo drink) increased the number of calculations an individual completed. Likewise, fewer problems were completed when participants' blood glucose levels were low. Performance on an auditory serial addition task was impaired at low blood glucose levels of 45 mg/dl. The accuracy versus speed trade-off was not as clear. In one study, accuracy appeared to be preserved at the expense of speed in calculating simple math facts (Holmes et al., 1983); however, there was no effect on the number of errors, or no "speed-accuracy trade-off" demonstrated in another study – glucose did not affect the number of subtractions and/or the number of errors on an SST (Kennedy & Scholey, 2000).

Effects of blood glucose levels on specific memory processes require further investigation. Explicit (rather than implicit) declarative memory processes have been shown to benefit from increased glucose levels. Craft and colleagues (1994) asserted that declarative memory processes, and not other processes, were affected by a glucose drink and determined that paragraph recall was a useful and sensitive measure to investigate the effect of a glucose drink on these memory processes. They found mixed results on two other tests used to assess declarative memory, the Pattern-Recognition Recall task which they stated failed to reach significance due to ceiling effects, and the Stroop Color-Word Interference Task in which a glucose drink quickened responses but increased errors. In another study by Polliti, Cueto, and Jacoby (1998), children performed better on memory of the last central item in a series after having fasted overnight, than did children who consumed breakfast.

Unfortunately, they did not speculate as to why this occurred. Messier and Gagnon (1996) describe a general effect of glucose on encoding in animal studies. However in humans, does the effect of glucose occur at encoding or retrieval? This, too, remains unclear. Manning and colleagues (1990) speculate that a glucose drink may benefit different aspects of declarative memory, as the Logical Memory Test involves contextual memory while the Selective Reminding Test involves non contextual memory recall. Differences in performance on the Free Recall Task also occurred. Participants' performance was either enhanced or showed no effect after consumption of either a glucose or breakfast provision.

Research on the effects of blood glucose levels on memory has provided the most substantial evidence of the benefits of glucose administration on performance. Although blood glucose levels have been shown to affect memory, many questions, (e.g., why some memory processes are affected and others are not and when these effects occur), remain unanswered.

THE EFFECT OF BLOOD GLUCOSE ON LANGUAGE AND COMMUNICATION

Few studies have been conducted in this area, but verbal fluency (assessed in terms of word generation) and reading speed and/or comprehension tests have been used to assess language and communication performance after participants consumed either a glucose provision or not, or were induced to hypoglycemic levels.

Blood glucose levels from a glucose drink have affected verbal fluency performance in non-diabetic individuals. In healthy college students who had consumed breakfast, Donohoe and Benton (1999a) used the Controlled Oral Word Association test, (participants named as many words as possible within one minute, beginning with a letter of the alphabet—letters C, F, and L before the drink and letters P, R, W, after the drink, were used), and found a significant effect of a 50-gram glucose drink on performance. Those who had consumed a glucose drink rather than a placebo (aspartamate and saccharin) generated significantly more words 25 minutes after the drink. Kennedy and Scholey (2000) employed a 2-minute word retrieval task (verbal fluency) in which participants generated as many words as they could starting with the letter "T". While also assessing information stored in long-term memory, verbal fluency is also described in this section based on the type of task (i.e., a language task) participants engaged in during the experiment. A glucose drink (25 grams) resulted in a trend towards improved word retrieval. Further analyses of pre-task levels and changes in blood glucose levels during the task(s) (i.e., difference between the second and third glucose measurements) showed significant correlations. Word retrieval performance was significantly affected at pre-task glucose levels, but only for the placebo condition (saccharine drink). Scholey et al. (2001) used the same word retrieval task as in a previous experiment, except participants generated as many words as they could beginning with the letter "S" or "A." There was a strong trend in terms of the number of responses elicited in the glucose condition (e.g., improved performance on Word Retrieval task) as compared to the placebo condition. Likewise, low blood glucose levels have been shown to adversely affect performance on this task. Mitrakou, Ryan, Veneman, Mokan, Jenssen, Kiss, et al. (1991) employed a Verbal Fluency task, with responses being limited to 60 seconds. Performance on this task, as well as on several other tests, deteriorated significantly during a final insulin-induced blood glucose plateau of 43 mg/dl ($\pm$1 mg/dl).

In one study, however, as described in a previous section (see Effect of Blood Glucose on Specific Memory Functions section), Craft et al. (1994) employed a Verbal Fluency Task in which participants generated as many words beginning with a particular letter (e.g., the letter "G") within 60 seconds, but failed to find an effect of a glucose drink on performance. Craft and colleagues assert that there are very specific effects of glucose on improving participants' abilities to perform complex tasks. While the Verbal Fluency Task was considered a measure of declarative memory, perhaps the task was not sensitive enough. For example, when looking at age and type of drink on performance, older participants did not perform significantly different on this task than younger participants.

Reading comprehension has also been assessed at varying blood glucose levels, with minimal effects. However, consumption of lunch or ingestion of a caloric drink did increase reading speed of non-diabetic individuals. Holmes and colleagues (1983) used the Nelson Denny Reading Test, a test for grades 10 through 16, where participants read three passages of graded difficulty and answered four multiple-choice questions. A total of eight minutes was allotted for administration of the test, and comprehension was scored based on the number of questions answered correctly. Comprehension was not impaired at either of the abnormal (at 300 mg/dl or 60 mg/dl) blood glucose levels. Kanarek and Swinney (1990) evaluated reading speed using three sixteen-line "vague" stories that participants read on a display screen. Participants read the story (sufficiently well to understand) presented on the screen as quickly as possible and pressed a button after reading a line of the story, which then showed the next line of the story. A computer recorded the time from the initial presentation until the button was pressed for that line. Consumption of lunch or not and a caloric or non-caloric snack, were varied and did not affect the average reading times of the story in experiment 1; however, in experiment 2, when participants had consumed lunch, they read each line of the story significantly faster than when they did not consume lunch. Similarly, after receiving a subsequent caloric fruit-flavored yogurt as a snack (versus a non caloric diet soft drink as a snack), participants read significantly more rapidly.

Challenges to Language and Communication Studies

Currently, the challenges include appropriate glucose dosage, experimenter effects, and multiple redundant cues (e.g., context, semantics) in reading. Given the appropriate glucose dosage (only 25 grams in this experiment) and if task parameters were slightly modified, Scholey and colleagues (2001) assert that there is a trend toward enhanced performance on these tasks despite their limited findings. As previously mentioned, Kanarek and Swinney (1990) argue that experimenter familiarity with test administration contributed to the performance difference from experiment 1 to 2. Kennedy and Scholey (2000) describe their unexpected results of finding performance being affected only in the absence of a glucose load (placebo) and argue that this may be driven by other possible physiological and neurobiological mechanisms.

Summary of Findings of Language and Communication Studies

Research investigating the effect of blood glucose on language and communication is limited. It is possible that the ability to retrieve information from long-term storage, based on verbal fluency tasks, may be enhanced by glucose provisions. Trends exist such that an enhanced provision of glucose led to improved performance on word generation tasks, while low blood glucose provisions

impaired performance. In one study (Kanarek & Swinney, 1990), reading speed was enhanced after a caloric snack (or eating lunch); however, in the tests used so far, reading comprehension has not been affected. More research in this area is still needed.

THE EFFECT OF BLOOD GLUCOSE ON DECISION-MAKING

Decision-making processes have been assessed using tests that measure reaction time. Thus, the studies previously described and examined in the psychomotor and attention section should be referred to (see also Blackman et al., 1990 in the Sensory Processing section); however, decision-making also involves processes associated with planning, reasoning, mental flexibility, and ideational fluency, which are discussed in turn below.

Decision-Making

Choice reaction time tasks and discrimination tasks have been used to assess decision-making processes. In insulin-induced diabetic participants, Holmes et al. (1986) employed a simple Finger Tapping Task (FTT) and a Letter Recognition Task, comparing them to a more complex choice reaction time task (Go/No-Go RT, Choice RT). Holmes and colleagues concluded that with blood glucose levels at 55 mg/dl, more complex decision-making skills (rather than simpler mechanisms) are disrupted. In the Pollitti et al. (1998) study, nutritionally at-risk (well- and under-nourished boys from Peru) children demonstrated shorter decision times on a Stimulus Discrimination Test (SDT) on the day they ate breakfast than on the day they fasted. Children not at-risk nutritionally (well-nourished boys and girls from the United States) were quicker on the SDT after the no-breakfast condition than after the breakfast condition.

Planning

Researchers have used the TMB to assess planning ability of participants at varying blood glucose levels, and the PASAT to assess strategic thinking. As previously described (see Visual Processing, Psychomotor Function, and Attention sections), Hoffman et al. (1989) employed the TMB test as a method of assessing planning ability. Time to complete the task and number of errors were recorded. Performance was significantly poorer (slower) at hypoglycemia (50 mg/dl) than at euglycemia (100 mg/dl) or at hyperglycemia (300 mg/dl) in diabetic individuals (range 22–35 years of age). Pramming et al. (1986) also used the TMB test as part of a test battery to assess planning ability at four different periods of glucose levels (108, 54, 36, and 108 mg/dl) and found that during blood glucose level period 108 mg/dl to 54 mg/dl, test battery scores fell. In the blood glucose level period 108 mg/dl to 36 mg/dl, all diabetic participants' individual and overall test scores fell significantly. Improvement in scores occurred when levels were increased from 36 mg/dl to 108 mg/dl. As previously described, Schächinger et al. (2003) recruited healthy non-diabetic college students and employed the PASAT, an adaptive Five-Choice Reaction Time Test (CRTT), and a manual tracking test to assess various aspects that included strategic thinking. Again, CRTT reaction time and manual tracking performance scores showed significant impairment during hypoglycemia (49 mg/dl). For the manual-tracking task, "distance" was significantly impaired. At hypoglycemia,

reaction time increased and accuracy decreased (increasing omission errors, and marginally, false responses) on the PASAT. Errors on the PASAT were mostly omissions, and during hypoglycemia errors increased by a factor of 2.5.

Reasoning

Contrary to several studies that have found that blood glucose levels affect performance, reasoning abilities do not appear to support this body of evidence. Abstract, associative, logical, and arithmetic reasoning have been assessed using tests in which participants are required to evaluate conditional statements. With the exception of arithmetic reasoning, blood glucose levels did not affect performance in several of these studies. Benton and Parker (1998) employed the Graduate and Managerial Assessment Test of Abstract Reasoning, described as a matrix-type design for those with above-average intelligence. Participants were grouped into the following categories: 1) ate breakfast and consumed a glucose drink; 2) ate breakfast and consumed a placebo drink (aspartamate); 3) fasted and consumed a glucose drink; and 4) fasted and consumed a placebo drink. No significant effect of a glucose drink (50 grams), breakfast consumption, or interaction was found on abstract reasoning in college students. Associative reasoning was assessed using the Nelson Denny Reading Test in which participants read passages of graded difficulty and answered multiple-choice questions after each paragraph (Holmes et al., 1983). Performance was not affected on this task at varying blood glucose levels (60, 110, and 300 mg/dl). Donohoe and Benton (1999a) assessed logical reasoning using the Baddeley Logical Reasoning Task. Participants respond "true" or "false" to statements such as; if M is smaller than C tick "false." No tick was made if the conditional statement did not correctly describe the two letters. Incorrect solutions were subtracted from correct solutions, and the test lasted for 5 minutes. Participants consumed either a glucose drink or a placebo (aspartamate and saccharin), after eating their normal breakfast. After 20 minutes, blood glucose levels were measured and participants completed a test battery including the reasoning task. Results indicated that the type of drink did not affect the Logical Reasoning Task. Changing blood levels also did not affect performance. Smith et al. (1992) employed the Baddeley Logical Reasoning test in which participants were presented with statements about the order of letters (e.g., A follows B: BA), and had to decide and indicate by pressing a button as to whether it was a true or a false statement. Participants completed as many of these statements as they could within 3 minutes. Participants who were given breakfast actually performed the Logical Reasoning test significantly less accurately ($M = 89.4\%$ correct) than those who were in the no-breakfast group ($M = 93.9\%$ correct, $p < 0.05$). Contrary to the above studies, arithmetic reasoning was assessed and was shown to be enhanced (e.g., participants solved more problems) after eating lunch compared to those who had not eaten lunch, and after consuming a confectionary product compared to those who had consumed a low caloric soft drink (Kanarek & Swinney, 1990).

Mental Flexibility and Tracking

Researchers have employed the TMB test and the Stroop test and subtests to assess mental tracking and flexibility. For example, Hoffman et al. (1989) assessed mental flexibility using the TMB test, which requires the participant to alternate between connecting letters (A–L) and numbers (1–13) as quickly as possible. Again, at hypoglycemia (50 mg/dl), performance on this test was significantly impaired compared to normal glucose levels (100 mg/dl). Similarly, Evans et al. (2000) used a test battery including the TMB, a Four-Choice Reaction Time task, and the Stroop Word and Color-

Word subtests. The Stroop tests assess mental tracking, as well as other functions like selective attention. As previously described, performance on the TMB was not affected at hypoglycemia (48 mg/dl), primarily due to the large variability in performance even at euglycemia; however, performance on the Stroop and Color-Word subtests significantly deteriorated at hypoglycemia (48 mg/dl).

Ideational Fluency

Similar to verbal fluency tasks, within a battery of several neuropsychological tests, Pramming et al. (1986) employed a Categorization Test to assess ideational fluency. For this task, participants wrote down as many items of a specific category as possible within one minute. The number of relevant items was scored. Participants were insulin-infused to four periods of varying glucose levels and were administered a cognitive test battery. Between blood glucose level periods 108 mg/dl to 36 mg/dl and 54 mg/dl to 36 mg/dl, scores on this test fell. Scores improved between blood glucose level periods 36 mg/dl to 108 mg/dl, and there were no significant differences in scores at pre- and post- periods at 108 mg/dl.

Challenges to Decision-Making Studies

Some of the challenges in this area include only evaluating performance at specific points (in the Holmes et al. study,1986, for example). Evaluating rising and/or falling blood glucose levels may provide a clearer picture of the effects of blood glucose levels on performance by pinpointing when processes are involved and at what point tasks are affected. It may also help to show how the brain is using glucose and what occurs during the task as blood glucose levels change. Smith et al. (1994) argue that their findings demonstrate that the effect of breakfast on performance is dependent on the type of task the subject carries out; breakfast enhanced performance on memory tasks (i.e., free recall, delayed recognition) but not on other memory or reasoning tasks (i.e., semantic memory, logical reasoning). Again, breakfast-specific effects require further investigation.

Summary of Findings of Decision-Making Studies

Certain aspects of decision-making processes (e.g., planning, arithmetic reasoning, mental tracking, ideational fluency) appear to be affected at varying glucose levels. Planning performance was significantly affected at low blood glucose levels, resulting in slower performance and test score deterioration. Only arithmetic reasoning performance was affected, with consumption of lunch (rather than not eating lunch) resulting in participants solving more arithmetic problems. Mental flexibility was impaired and mental tracking performance, assessed by the Stroop task, significantly deteriorated at hypoglycemia. Hoffman et al. (1989) suggested that poor performance on the TMB indicated a cortical component of neuroglycopenia, which was responsible for this impairment. Ideational fluency performance was also affected, with scores on this task falling at hypoglycemic levels. Conversely, reasoning processes were largely unaffected and, in one study, eating breakfast resulted in more impaired performance than not eating breakfast. Consumption of breakfast did not affect abstract reasoning, hypoglycemic levels did not affect associative reasoning, and a glucose (or a placebo) drink did not affect logical reasoning.

A four-step model of decision-making processes for diabetics has been developed (see Kovatchev, Cox, Gonder-Frederick, Schlundt, & Clarke, 1998) and may also be referred to for healthy individuals' decision-making processes at low blood glucose levels. The process involves the evaluation of an individual's own Internal Condition (e.g., blood glucose level), Perception (e.g., symptoms and difficulties), Appraisal (e.g, estimation of blood glucose level), and Decision (e.g., treatment or not, continue to drive or not). The model accounts for several probabilistic outcomes, not one predetermined path (e.g., one may be aware of one's symptoms, but may not accurately evaluate their blood glucose level) and incorporates the idea that several other factors (e.g., personality) are at play. From this model, the authors offer several good points. Because hypoglycemia can occur with no clearly perceived symptoms, and individuals in their experiment made the decision to drive at impaired levels (also supported by studies in the next section), Kovatchev and colleagues assert that individuals need to learn to recognize these symptoms and apply good judgment and risk assessment skills to guide good decision-making.

THE EFFECT OF BLOOD GLUCOSE ON COMPLEX TASK PERFORMANCE

Several studies have described the effect of blood glucose levels on simple or complex tasks by employing reaction time tasks, either Simple Reaction Time (SRT) tasks or complex or Choice Reaction Time Tasks (CRTT). In this section, a complex task is defined as a task involving several cognitive processes (e.g., attention, memory, and psychomotor performance) being engaged simultaneously. Driving performance is one such task and has been used to measure performance of individuals at varying blood glucose levels. It requires multiple processes, such as, motor control and coordination, concentration, vigilance, and attention to visual stimuli.

Blood glucose levels have been shown to affect the driving performance of diabetic individuals. Cox, Gonder-Frederick, and Clarke (1993) investigated whether hypoglycemia affected driving performance and were interested in determining which driving tasks might be affected and at what level(s) this might occur. They were also interested in whether or not individuals recognized this possible impairment, and how quickly individuals recovered from this impairment. Male and female diabetics ($M = 35.9$, ±14.2 years of age) were blind to their blood glucose read-outs and to control and experimental conditions. During the control condition, patients were kept at euglycemia levels (blood glucose levels at $M = 113$, ±16 mg/dl) throughout the session. During the experimental condition, patients were kept at euglycemia levels, then insulin-induced to hypoglycemic levels at 65 mg/dl, and then to hypoglycemic levels at 47 mg/dl, and finally returned to euglycemia. Due to the difficulty in maintaining a consistent low level of blood glucose in individuals, each patient drove the simulator for four minutes at a time, four times a day, for two consecutive days. The Atari Driving Simulator, a realistic driving simulator, incorporated life-size features of driving equipment (i.e., wheel, pedals), eight simulated versions of a three-mile driving course, a continuously updating graphic screen with high resolution, auditory, visual, and kinesthetic feedback, and simulator tracking of 112 driving variables. A driving performance score was based on two parameters: steering control characterized as swerving, spinning (yaw), time across the midline, and time off-road, and speed control characterized as smoothness (foot pressure on brake pedal), smoothness of acceleration, speeding, and very slow driving. During the experimental day, patients at levels of hypoglycemia at 47 mg/dl swerved more, and spent more time over the midline and off-road, as compared with the control day. Upon restoration to euglycemia levels, no significant driving decrements occurred.

Very slow driving was the only speed control variable found to be significant (< 30% of the posted speed limits) during hypoglycemic levels at 47 mg/dl. Thirty-five percent of patients showed decrements in performance at levels of hypoglycemia at 47 mg/dl and of those, forty-four percent did not anticipate the decrements and stated that they would be willing to continue driving under such conditions. Driving performance appeared to be unaffected until blood glucose levels resided between 47 and 65 mg/dl. Cox, Gonder-Frederick and Clarke (1993) suggest that this behavior involved a "compensatory strategy" when participants believed that they were impaired.

Under similar conditions as the previous experiment, driving impairments were found but at lower hypoglycemic blood glucose levels. Cox et al. (2000) investigated the effects of insulin-induced progressive hypoglycemia on driving simulator performance in male and female diabetics ($M = 35.3, \pm7.1$ years of age). Blood glucose levels were maintained between 101 and 149 mg/dl for the first hour, then progressively lowered to 40 mg/dl (euglycemia always preceded hypoglycemia), and glucose sampling occurred every five minutes. Participants were blind to levels and to the condition. Using the Atari Driving Simulator (see Cox, Gonder-Frederick, and Clarke, 1993 study), participants drove a 16-mile course over thirty minutes. Driving performance variables included steering control, braking control, and speed control. All driving parameters (e.g., driving off-road, high and low speed, inappropriate braking, swerving) were significantly impaired during some level of hypoglycemia. At hypoglycemia, participants were most likely to drive across the midline, speed, and use the brakes more on the open road. Failing to stop at stop signs and more crashes at sudden stops occurred during the last fifteen minutes of hypoglycemia, compared to euglycemia levels. While those who demonstrated significant impairments were more likely to take some form of corrective action (e.g., taking a provided glucose drink, or pulling off of the road when they thought their blood glucose levels were too low), forty-three percent of the participants (or 6 of the 14) did not. The more aware and alert participants were of the need to treat themselves, the more likely they were to do so. To assess their level of awareness, at each 5-minute blood glucose sampling, participants rated to what extent they could tell by their symptoms that their blood sugar was low. However, while participants may be aware of their symptoms, they often do not take corrective actions, and if they do, they often wait too long before taking this action (after blood glucose fell below 50 mg/dl). Driving impairments became evident at hypoglycemic levels between 61–72 mg/dl.

Conversely, in another simulated driving investigation, no effect of blood glucose level was found in driving performance. In this study (Hoffman et al.,1989), male and female diabetic patients (29.3, ±1.2 years of age) performed various sensory, motor, and cognitive tests, including driving an automobile simulator. Performance was assessed at controlled, or insulin infused, blood glucose levels at hypoglycemia (50 mg/dl), euglycemia (100 mg/dl), and hyperglycemia (300 mg/dl) levels. Three simulated driving scenarios were presented to participants who were required to adjust speed (through braking and acceleration) and direction (through steering) to avoid hazards. Speed and steering control, signaling ability, and braking pattern were assessed. Variability existed among individuals, with poorer performance for signaling, braking and acceleration (speed) for several participants during hypoglycemia, but this was not significant. Further analyses of the variability did not find either duration of disease, or the average blood glucose levels of participants for the past 2–3 months (HbA1c test) to have affected performance.

Challenges to Complex Task Studies

Some challenges to driving simulator performance research include issues involving sample size, the complexity, novelty, and duration of the task, and application to real-life situations. In the Hoffman et al. (1989) study, scheduling problems resulted in fewer participants (10 out of 18) completing this task during the experiment thereby increasing type-2 error. The level of complexity of the task was not equivalent to an actual driving situation, reducing the amount of attention required. For example, a limited visual field (a screen) was employed instead of the normal 360-degree field of view. Participants had several years of driving experience, and performance on this highly familiar task may be less affected by varying glucose levels than performance on a novel task. To illustrate, Hoffman and colleagues (1989) found significant effects of low blood glucose on other tasks involving vigilance and concentration during this experiment, but did not find this for driving performance. In the Cox, Gonder-Frederick, and Clarke (1993) study, driving performance was assessed at very short intervals of four minutes. They suggest that blood glucose levels at 65 mg/dl (±6 mg/dl) may affect driving trials if these trials were longer, and that the 4-minute task was probably not long enough to detect the effect. The limitation guiding research in the Cox et al. (2000) study, as authors described, was a lack of external validity; simulated driving may not reflect real-world driving demands.

What is not addressed in simulator studies is the use of diabetic individuals as participants and insulin-inducing techniques. The blood glucose levels that impair driving performance were slightly low, but not necessarily at hypoglycemic levels (72 mg/dl). Furthermore, individuals do not need to be hypoglycemic to experience symptoms of hypoglycemia; healthy non-diabetic individuals may demonstrate similar performance decrements from less invasive blood level control methods. Several previous studies have shown that individuals in fasted states (from not eating and/or receiving placebo drinks), and not necessarily induced to low blood glucose levels, to have sensory, psychomotor, attention, and memory difficulties. A better understanding of the effects of low blood glucose levels on healthy individuals (rather than diabetics only) performing everyday tasks, and recruiting healthy participants who fast overnight and remain fasted throughout the experiment (rather than being insulin-induced) may be beneficial.

Summary of Findings of Complex Task Studies

Low blood glucose levels have been shown to negatively affect performance in driving simulator research (Cox, Gonder-Frederick, & Clarke, 1993; Cox et al., 2000). Additionally, the research indicated that participants were not necessarily aware of their driving impairments. Basic driving skills such as steering, speed control, and braking performance variables have been found to be significantly impaired at hypoglycemic levels, ranging from 72 to 47 mg/dl (Cox, Gonder-Frederick, & Clarke, 1993; Cox et al., 2000). Compensatory strategies (e.g., very slow driving) at low blood glucose levels may reflect a speed-accuracy trade-off similar to performance found on cognitive tests (e.g., Trail Making B test, visual search tests).

The conflicting findings from both Cox studies and the Hoffman's study may not necessarily be attributed to subject type (both groups were diabetics). And, although both groups were induced to hypoglycemic levels using insulin, variations in blood glucose level techniques may have contributed to differences. The low blood glucose levels at which individuals were assessed varied among

studies by a range of 4–9 mg/dl (hypoglycemia at 45 mg/dl (Cox, Gonder-Frederick, & Clarke, 1993); 40 mg/dl (Cox et al., 2000); and 49 mg/dl (Hoffman et al., 1989). It is possible that in the Hoffman study participants were not induced to a low enough blood glucose level to detect this performance impairment. These differences could also be related to the sensitivity of the equipment used to detect these effects. The Cox studies used a driving simulator that provided auditory, kines-thetic, and visual feedback, while the microcomputer driven simulator in Hoffman's study did not, providing only visual scenarios. The technology used in Hoffman's study (not closed-course driving scenarios) may have differed from the simulator equipment and scenarios used over ten years later in the Cox studies (closed-loop/course). Hoffman and colleagues clearly state that their data was not sufficient to reach any conclusions about the driving performance of diabetics. Additionally, in the Cox studies, the driving parameters assessed may have been more clearly defined prior to the experiment (but not necessarily more demanding), more inclusive in the behaviors being assessed (112 driving variables), and more thoroughly investigated, with driving performance being the primary focus of the experiment. Under the assumption that increased age may increase exposure and experience to driving, those participants in the Cox studies presumably had more years of driving experience (35.9, ±14 and 35.3, ±7.1 years of age) than Hoffman's (29.3, ±1.2 years of age), which may mediate or reduce chances of impaired performance. While driving experience was not measured, if this assumption is true, then finding impairments in a group with presumably more experience would increase the validity of blood glucose effects on performance. This idea of famili-arity of task will be discussed in the next section.

MODERATOR VARIABLES AND EFFECTS OF BLOOD GLUCOSE ON PERFORMANCE

Several variables were considered during the investigation of performance effects within the experiments. These include individual differences, such as participants' age, gender, IQ, glucose-regulation, and contextual variables such as caffeine consumption, fatigue, and time of day. Researchers investigating blood glucose levels and performance have also raised the following issues: participants' familiarity with the task, expectancy effects, dose-dependent effects, time-dependent effects, and task specific effects.

Variables Affecting Performance

Individual Differences
Glucose has been shown to affect performance on several types of tasks within several types of population groups, including children, young adults, middle-age adults, and older individuals. One study suggests that older men (range 58–77 years of age) may be more susceptible to the effects of glucose on performance (e.g., memory) than younger men and younger or older women (Craft, et al., 1994). In this same study, women showed less sensitivity to a glucose administration effects on memory performance than men. Other researchers have investigated the effects of blood glucose levels on memory in college students (e.g., benefit of a snack on memory). Benton and Owens (1993) state that previous work in this area has not found gender differences in responses to similar blood glucose manipulations used in their experiment. Likewise, whether individuals regularly ate breakfast or not was insignificant (Smith, et al., 1992; 1994), and memory following a glucose provision improved irrespective of breakfast consumption (Benton et al., 2001; Benton & Sargent,

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1992). The effect of intelligence has also been explored with researchers finding that those with higher intelligence quotients (IQs) were more affected by deteriorating blood glucose levels versus those with average IQs (Gold, Deary, MacLeod, & Frier, 1995). In a study of pre-tested diabetic individuals (27–35 years of age), Deary, Langan, Graham, Hepburn & Frier (1992) investigated IQ and cognitive functioning on recurrent hypoglycemia. They found that the severity of the hypoglycemic episode correlated with pre-morbid IQ and current IQ; repeated episodes negatively affected performance (i.e., post-morbid IQ scores lower).

Contextual Variables

Many factors must be considered when investigating blood glucose and performance. Alcohol can decrease blood glucose levels by inhibiting the production or release of blood glucose from the liver, known as alcohol-induced hypoglycemia (or AIH). Exercise can also decrease blood glucose levels with effects lasting up to 48 hours. Likewise, several factors can increase blood glucose levels. Stress caused by pain, surgery, intense heat/cold, illness (since the body reacts defensively causing glucose levels to increase), or lack of sleep can increase blood glucose levels. There is limited data on stress and blood glucose levels, but the effects of adrenaline (as a result of stress) can raise levels.

Certain types of medications (e.g., diuretics, steroids, antibiotics), mega-doses of vitamins (not normally consumed by the majority of the population), stimulants that may change the manner in which the body metabolizes carbohydrates (e.g., coffee, black tea), and nicotine (which affects cardiovascular and kidney functions of the individual) can have varying effects on blood glucose (personal communication, C. Zaveson, March, 10, 2003). Caffeine clearly affects performance on cognitive tests, especially with regard to attention and vigilance (Smith, et al., 1992; 1994), and in some cases combinations of glucose and caffeine drinks have been related to improved performance on cognitive tests (Scholey & Kennedy, 2004).

Circadian rhythm may also affect blood glucose levels. As noted previously, normal glucose regulation varies across a twenty-four hour period, and glucose tolerance decreases from morning to midnight (Van Cauter, Polonsky, & Sheen, 1997). Performance and mood can be affected by glucose tolerance, which may be worse later in the day rather than earlier in the day; performance on sustained attention tasks was more affected in the early afternoon compared with late morning (Dye, Lluch, & Blundell, 2000). Blood glucose levels and time of day affected psychomotor performance in non-diabetic individuals (Owens & Benton, 1994). Glucose Tolerance Tests (GTT) have shown that non-diabetic individuals can have higher blood glucose levels in afternoon and evening tests, than when the test is performed in the morning. A phenomenon called "afternoon diabetes" describes the increased potential of false-positive diagnosis of diabetes in the afternoon, as compared with the morning. Alternatively, the time of day, rather than the individual's circadian rhythm, may also have an effect, known as the "dawn phenomenon," which describes how blood glucose levels are commonly higher in the morning in both diabetics and non-diabetics. Because of these differences, it has been suggested that the GTT be administered to individuals several times and at different times of the day. In a study that investigated the role of circadian rhythm and blood glucose levels, participants' response to a breakfast of corn flakes was considered at different times of the circadian cycle (Benton et al., 2001). Glucose tolerance was found to be poorer later in the day. Benton and colleagues (2001) suggest that interpretations of the effect of blood glucose levels from a morning snack on performance later in the day should be made with caution.

Investigating time of day effects has shown that the size and composition of a meal (e.g., macronutrients such as proteins, fats, and carbohydrates) may also be an issue. Meals with increased carbohydrates are less well tolerated later in the day; fatigue changes as the day progresses and meal tolerance may also vary (Owens, Macdonald, Benton, Sytnik, Tucker, & Folkard, 1996). Smid et al. (1997) interpreted results from this experiment as not being due to fatigue, because of the differences between response production and stimulus-selection; fatigue should show an equal effect on selection and response processes. Body mass is another factor that may play a role in blood glucose levels. Being overweight will increase an individual's chances of becoming diabetic and insulin-resistant; however, a healthy two hundred-pound man and a healthy one hundred and fifty-pound man would have similar blood glucose curves, and they metabolize glucose in a similar manner. Blood glucose levels are affected more by the health of an individual than by body mass, within a reasonable weight range (S. Duff, personal communication, October 28, 2003).

Familiarity with the Task and Symptom Awareness

Participants' familiarity with the task and awareness of symptoms may mitigate performance decrements. The effects of low blood glucose levels may not be detected with highly learned tasks, tapping procedural memory processes, or tasks that are biased by rehearsal or redundant cuing. Awareness of the symptoms of low blood glucose levels may also reduce negative effects. For example, on some tasks participants were more cautious in their responses, slowing performance but maintaining accuracy. Cox, Gonder-Frederick, and Clarke (1993) stated that in their experiment, some participants could recognize being impaired, and that it could take those participants longer to demonstrate hypoglycemic impairments. If participants are aware of their symptoms of hypoglycemia, it is possible that performance decrements lessen. However, as previously described (see Psychomotor section), Kerr et al. (1989) found that prolonging hypoglycemia in participants caused a decrease in the symptom score, meaning that participants "did not feel hypoglycemic." This lack of awareness occurred simultaneously with improved reaction time. To explain how reaction times improved, they describe how the brain may have used alternate sources of energy or that cerebral blood flow may have increased. Further, they suggest that cerebral adaptation can occur during prolonged hypoglycemia with blood glucose levels at 54 mg/dl.

Even though familiarity with the task may mitigate decrements, performance on a complex task such as driving, where participants have several years of driving experience, was negatively affected at low blood glucose levels. Participants were often not aware of their impairments, resulting in continuing the task while impaired, and they failed to treat themselves even when provided with a glucose drink. These studies demonstrate that despite familiarity with certain tasks, performance may still be negatively affected at low blood glucose levels.

Expectancy Effects

Few studies have explored the effect of participants' expectations on performance. Furthermore, is the effect of expectations general to all tasks or, are there specific tasks that are more sensitive to these effects? Green and colleagues (2001) described that there appears to be some expectancy for the positive effects of glucose on performance. Kvavilashvili and Ellis (1999) (as cited in Green et al., 2001) describe an interesting effect of "reverse placebo effects" where participants in a placebo group actually exerted less effort due to believing that their performance will be enhanced automati-

cally. As previously examined in the Green study, when participants were told that they received an aspartame drink, the content of the drink exerted no effect on performance of this task. No effects were found for immediate verbal recall or finger tapping tasks. Response times were faster for the recognition memory task when participants were given glucose than when they were not, and marginal effects of expectancy (quicker responses) were shown when participants were told they received glucose, but didn't. No relationship existed for changing glucose levels and cognition or mood. Green and colleagues challenge findings on the enhancing effects of glucose on cognition in healthy, non food deprived populations. The effect of expecting glucose on performance requires further investigation. Determining participants' expectations of the influence of glucose prior to testing may explain underlying effects on performance that have more to do with expectations than with glucose itself.

Dose Dependent Effects

An optimal glucose dosage to enhance performance during cognitively demanding tasks is yet to be determined. However, based on both human and animal studies, optimal memory performance resides within the range of 150–180 mg/dl, typically from ingesting 50 grams of glucose (Benton et al., 1996). Animal studies have described glucose levels for optimal memory storage as ranging from 150–175 mg/dl (Parsons & Gold, 1992). In a review of the role of blood glucose and cognition, Gold (1995) reported that the optimal dose-response curves for memory were those that produce concentrations near 160 mg/dl. Parsons and Gold (1992) further described an inverted U-dose response curve, which illustrated that low (10 grams) and high (50 grams) blood glucose dosages either failed to have an effect, or in fact impaired memory performance, while intermediate doses (25 grams) of glucose benefited (recall test) performance.

Azari (1991) failed to find an effect on memory performance using three different dosages of glucose (0, 30, and 100 grams), claiming that this finding would not differ with different dosages; however, this was the only study found in a vast body of literature reporting such results. Another study reported the unexpected result that a moderate dose of glucose (100 mg/kg) actually reduces impulsivity on a continuous performance task (Flint & Turek, 2003). To determine whether and how test administrators (psychiatrists, etc.) should impose dietary restrictions (fasting) before testing, Flint and Turek (2003) investigated the effect of different doses of glucose (10, 100, and 500 mg/kg, or 50 g) or a saccharin placebo on a continuous performance test called the test of variables of attention (TOVA) in healthy college students ($N = 67$). Five hundred mg/kg and 50 grams of glucose raised blood glucose levels significantly as compared to the 10 mg/kg, 100 mg/kg, and placebo groups. Not finding that 100 mg/kg of glucose resulted in increased blood glucose levels is contrary to other findings that 100 mg/kg doses are comparable to increases produced by 50 g of glucose when tested 15 minutes after ingestion. The 100 mg/kg group was the only group that showed significant changes in behavior (with increased commission errors, post-commission responses, and post-commission response time variability) as compared to the saccharin group. Commission errors were described as errors of impulsivity or disinhibition. Flint and Turek described an upright U-dose-response curve for commission-related responses – that a moderate dose of glucose (100 mg/kg) impaired performance while smaller and larger doses had no significant effect. For dose-dependent results, they report that 50 grams of glucose (in adults) and 25 grams (in children) are sufficient to improve performance and that 50 grams in humans and 100 mg/kg in humans and animals improves memory. They suggest that others have described a possible effect of increased

proactive interference or accelerated glucose uptake (which may over-stimulate the mechanisms for memory consolidation), and suggest that the lack of a correlation between attention and blood glucose dose was possibly due to insufficient time to record the gluco-regulatory response. A conservative interpretation of their findings was recommended for their failure to find a significant effect. Variability was high among the groups and may have resulted in the lack of statistical power to detect group differences.

While 50 grams of glucose in a glucose drink has been consistently shown to affect performance, 25 grams of glucose has also been shown to increase cognitive performance (Kennedy & Scholey, 2000). Parsons and Gold (1992) failed to find an effect on memory in older participants using 50 grams of glucose, but did find an effect with 25 grams of glucose on a Logical Memory test. While the reported ranges of blood glucose levels have been similar (150–180 mg/dl), a uniform or specific dose of glucose to administer when evaluating performance (50 grams versus 25 grams) is yet to be set. Parsons and Gold (1992) suggested that the discrepancy of not finding an effect on memory from 50 grams of glucose was due to differences in basal glucose levels of their participants (125 mg/dl) as compared to previous experiments (e.g., 90 mg/dl). Furthermore, differences in blood glucose regulation of individuals from past experiments (e.g., 160 mg/dl after 50 grams of glucose) to the current study (225 mg/dl after 50 grams of glucose) existed. It may be possible that participants with higher basal rates and/or better glucose regulation (from a smaller dose (25 grams) versus a higher dose (50 grams)) were more efficient in utilizing glucose. Participants with good (efficient) blood glucose regulation may benefit more, exhibiting better performance on memory tests than individuals with lower basal blood glucose levels and poor glucose regulation. Clearly, baseline glucose levels and glucose regulation play critical roles in determining optimum glucose dosages.

Time Dependent Effects

Similar to dose dependent effects, determination of the optimum timing for testing has not been established. Typically, studies allow twenty minutes to pass post-glucose consumption prior to testing. However, some researchers have argued that participants' levels are still rising and that the cognitive load imposed would be more clear if measurement occurred during falling levels; therefore some studies have waited up to forty-five minutes to test participants and still found significant effects on performance (e.g., Scholey et al., 2001). Some researchers report that two hours post-consumption is the peak time to test for mood effects, but that cognitive performance effects may not follow the same time course (e.g., Dye et al., 2000).

The effect of blood glucose on functions such as memory appears to be time related. In the Benton et al. (2003) study on verbal memory performance of young adults, the slowly-available glucose breakfast was associated with better memory throughout the morning, with the greatest difference at 210 minutes. Learning performance of adult rats was significantly better 3 hours after a slowly-available glucose feeding than rapidly available glucose. This line of research raises questions as to the types of carbohydrates associated with significant benefits to performance, specifically glycemic index ratings of the food, drinks, or snacks. Investigations into carbohydrates and whether they result in a smaller rise in blood glucose levels (low glycemic index) for a longer duration, or a quicker rise in blood glucose levels (high glycemic index) for a shorter duration are necessary.

Perhaps the best method for dealing with the uncertainty of timing for peak effects, suggested by Kanarek and Swinney (1990), is that testing should be conducted at several time points after consumption.

A review by Rogers and Lloyd (1994) references over a dozen experiments that investigated the effects of a glucose drink on performance. They report that performance effects occurred within one hour or sooner after the drink was consumed (in fasted and non fasted individuals), but found that these effects were largely not significant. They assert that no clear pattern or relationship between glucose and enhanced performance exists "per se," and that the impairments that can occur at hypoglycemic levels would not be expected to occur in normal healthy individuals. Under most circumstances, Rogers and Lloyd (1994) state that improvement in performance following a glucose drink or eating a meal or snack is unlikely to be due to glucose supply to the brain as it does not reliably predict performance. However, Donohoe and Benton's (1999b) findings conflict with Roger and Lloyd's research, showing that during conditions of increased demands (i.e., Rapid Information Processing Task, Word List) immediately following glucose ingestion (glucose drink), a fall in blood glucose level benefits performance (in glucose drinkers significantly faster, and they recalled more words). They describe the ability to predict performance by investigating the benefits that occur during falling levels of blood glucose, following a demanding task. Rising and falling blood glucose levels are discussed in the Changing Blood Glucose Levels section.

Task Specific Effects

The benefits of glucose administration on performance appear to be somewhat task specific (e.g., demand of the task, rather than the domain of the task). Studies have demonstrated that performance on tasks that are more demanding and complex deplete the brain of blood glucose more than simple tasks (Benton et al., 1996). It follows that performance on more complex tasks involving intensive processing and/or those that include distracting stimuli of longer duration may be more affected by varying blood glucose levels.

Rosenthal et al. (2001) reported that acute hypoglycemia was found to be task specific and that this was brain region-specific. Different tasks showed different responses to hypoglycemia; four-choice but not simple-choice performance was negatively affected. Donohoe and Benton (1999a) investigated the impact of blood glucose on non memory tasks and found that an increased supply of glucose benefited performance on more demanding tasks. Holmes and colleagues (1986) investigated blood glucose levels and the varying degrees of difficulty (simple versus choice) of a reaction time task. They found that it was the performance on more complex reaction timed tasks (choice reaction time) that was impaired while performance on the simple tasks, FTT and Letter Recognition Task remained relatively unaffected by varying blood glucose levels (at 55, 110 and 300 mg/dl). Similarly, higher functions of cognitive performance have been affected earlier than lower functions or motor performance (Cox, Gonder-Frederick, Schroeder, et al., 1993). Cox and colleagues failed to demonstrate impairment on a Finger Tapping Task, which measures pure motor function, at low blood glucose levels (47 mg/dl), in contrast to impairment that was found on the more cognitively intense PASAT test.

Furthermore, there may be task-specific effects of macronutrients (e.g., protein, carbohydrates, and fats) on performance. Dye et al. (2000) provide an in-depth review of the issue of macronutrients and mental performance. They report the different cognitive processes (e.g., memory, attention, reaction time, vigilance, etc.) that macronutrients may operate on might be task-specific. They present findings that describe how carbohydrate meals lead to slower reaction times and impaired attention, while high protein meals lead to distraction and slower memory scanning. Similarly, in studies investigating pure macronutrients, carbohydrates were found to improve memory but impair attention, reaction time, and peripheral processing depending on several factors. Dye and colleagues (2000) emphasize the need for further research in this area of macronutrients and their influence on the brain.

Changing Blood Glucose Levels & Speed-Accuracy Trade-off

Examination of other areas has been helpful in determining whether glucose utilization increases with heart rate (Kennedy & Scholey, 2000), and what the implications are for performance. However, two interesting areas of research involve investigations into rising versus falling blood glucose levels during testing and evaluating the speed-accuracy trade-off demonstrated on specific tests, possibly providing useful insight and clarifying the role of glucose on performance. For example, investigations of changing levels can show what is happening to blood glucose levels during a task, which may help in linking blood glucose levels to performance (perhaps enabling researchers to make performance predictions), and evaluation of the speed-accuracy trade-off that occurs may indicate what is being compromised during different tasks.

Changing (Rising and Falling) Blood Glucose Levels

Rising glucose levels have been shown to contribute to improved performance. For example, several studies have demonstrated the benefits for cognitive performance (e.g., memory) from increasing blood glucose levels (e.g., glucose drink). In a study by Benton and Owens (1993), participants whose blood glucose levels were increasing remembered significantly more words than those whose blood glucose levels were falling. Faster decision time performance has also been demonstrated when blood glucose levels were rising compared to when they were falling (Owens & Benton, 1994). Owens and Benton (1994) found that the decision times of participants with blood glucose levels in the range of 72–90 mg/dl and those with levels over 90 mg/dl still benefited (were faster) from further increases (from a 50 gram glucose drink). Participants who experienced increases (94 to 114 mg/dl) in blood glucose levels were faster than those who were falling (108 to 92 mg/dl). Additionally, higher baseline levels of blood glucose upon arrival to an experiment have been associated with better memory (Benton & Owens, 1993).

Other findings have suggested that performance (e.g., memory) was improved only when glucose levels were falling. These falling levels are possibly due to the brain's efficient utilization of glucose. On the other hand, poor glucose tolerance occurs when an individual's blood glucose levels remain high and fall slowly after consumption of a provision (e.g., glucose drink or snack). It is thought that in this situation glucose is not moving from the bloodstream and into cellular tissues. Kennedy and Scholey (2000) investigated the relationship among blood glucose levels, heart rate, and cognitive performance in healthy college students. One of their hypotheses proposed a relationship that may exist between the change in blood glucose level (rise or fall) and task performance.

They found that the total number of subtractions on the Serial Sevens and Serial Threes tasks correlated positively with the magnitude of fall in glucose levels. However, word retrieval performance did not appear to be related to fall in blood glucose levels. The researchers also found that performance on the most demanding task (i.e., Serial Sevens) was significantly affected by glucose administration and described how some cognitive processes may be "fuel limited." Benton and colleagues (1994) found that falling blood glucose levels from either a glucose or a placebo drink were associated with less forgetting on word list recall. Additionally, falling levels were associated with faster reaction times on the RIPT task in participants administered the placebo drink. Martin and Benton (1999) also found that for those taking a glucose drink, after an initial rise, rapidly falling levels of blood glucose were associated with better memory.

Further examination of blood glucose levels has led to a theory proposed by Donohoe and Benton (1999b) that focuses on falling blood glucose levels as an indicator of enhanced performance. They claim that immediately following a glucose drink, falling blood glucose levels (rather than rising) after a cognitively demanding task predicts improved performance. Declining blood glucose levels have been associated with enhanced memory but only when individuals are subjected to cognitively demanding tasks. Donohoe and Benton state that the difficulty resides in finding tasks that are sufficiently demanding and complex. Perhaps the performance required increased blood glucose level consumption and thus leading to falling levels. Those who were able to utilize more blood glucose, or more efficiently, were able to perform better, but also showed a greater decline in blood glucose level.

Performance appears to be modified by the changes in blood glucose levels throughout a task. Upon consumption of a glucose provision, initial rises in blood glucose levels benefit performance; however, continued rising levels possibly reflect impaired glucose tolerance. Once levels peak and blood glucose levels begin to drop, the rate and timing at which this occurs may affect performance. Evaluating performance during these periods has shown that falling levels correlate with performance on demanding tasks.

The discrepancies among studies investigating rising versus falling levels may be associated with the task type. Individuals' glucose tolerance, task type, and timing of testing remain important considerations to investigating the effects of changing blood glucose levels.

Speed-Accuracy Trade-off

On some tasks, participants slowed their performance and maintained accuracy, while on other tasks participants maintained speed while compromising accuracy. It is difficult to determine whether participants were cognizant of their approach. Were participants being more cautious or merely slowed overall? Were participants over-stimulated and/or disinhibited?

Across several studies, increased time but not necessarily decreased accuracy was observed in certain tasks such as choice reaction time, and math calculations (Bischoff et al., 1992). Accuracy of performance was preserved at the expense of speed, resulting in less math calculations completed without decreasing accuracy (Holmes et al., 1983). Similarly, in attention tasks (e.g., Telephone Search, Visual Elevator) accuracy was again preserved at the expense of speed (McAulay et al., 2001).

There were few situations in which speed was preserved at the expense of accuracy (e.g., CRTT task), which may relate to proactive interference (e.g., where participants forgot to adhere to specific requirements of one task over another) or were not provided with specific directions (e.g., "do this as quickly as possible"). The time limits imposed, the motivation of participants, and the requirements and difficulty of the task may affect the trade-offs that occur.

These issues can be addressed when designing experiments to investigate blood glucose and performance (see Recommendations for Future Studies section). Methodologies can be improved so that questions such as participants' motivation might be more clearly addressed. It would be useful to determine when participants trade off speed for accuracy, and whether participants are aware of this or not. Studies can explore whether and how individuals are compensating on their tasks at low blood glucose levels (e.g., from a lack of food).

EXECUTIVE SUMMARY OF EXECUTIVE AND NON-EXECUTIVE FUNCTIONS STUDIES

We have reviewed here multiple studies examining the effects of blood glucose levels on executive and non-executive functions; sensory processing, psychomotor functioning, attention, vigilance, memory, language and communication, judgment and decision-making, and complex task performance. We discussed challenges to research in each area, in some cases reiterating similar methodological concerns such as task complexity, duration, and glucose dosage. And we also suggested further avenues to explore such as speed-accuracy trade-off and rising versus falling glucose levels.

Sensory Processing

Certain visual functions were affected at low blood glucose levels (e.g., low contrast sensitivity, detection of visual change and movement), especially reaction time (e.g., inspecting, attending and responding) to visual stimuli (McCrimmon et al., 1996; Blackman et al., 1990; Snorgaard et al., 1991). Accuracy appeared to be preserved at the expense of speed on the visual tasks used (Lindgren et al., 1996; McAulay et al., 2001). Task complexity was an issue; a lack of significant findings may be due to the task being too simple (e.g., basic versus more complex serial search tasks). It appears that performance on visual tasks requiring more involved processing are adversely affected at low blood glucose levels. Ability to perform auditory tasks that require ignoring distracting stimuli, discrimination of tone order, single-tone loudness, and decision-making based on auditory processes have been likewise impaired at low blood glucose levels (McCrimmon et al., 1997). Similarly, a glucose provision benefited listening span performance (Morris & Sarll, 2001). Impairments of earlier basic auditory processes (i.e., single-tone loudness judgments) may increase at later and more intensive processing stages such as long-term memory storage. Some challenges to research in this area include small sample size and ceiling effects.

Psychomotor Functioning

Complex psychomotor functions were adversely affected at low blood glucose levels; reaction time performance on choice reaction time tasks was significantly slower (Holmes et al., 1986). A speed-accuracy trade-off was demonstrated, but appeared linked to the task (e.g., participants slowed performance on a pursuit tracking task, but not on a choice reaction time task; see Fraser et al., 1974;

Driesen et al., 1995). Challenging factors include performance as a function of age (e.g., with older participants at optimal blood glucose levels performing at baseline), task complexity, level of hypoglycemia not being severe enough, and task duration.

Attention

Aspects of attention (e.g., divided and selective attention, and attentional processes involved in information processing and decision-making) were affected at low blood glucose levels: Speed of performance on attentional tasks was reduced (i.e., participants were quicker) with a glucose provision and likewise increased (i.e., participants were slower) when blood glucose levels were low (Lobmann et al., 2000; Kanarek & Swinney, 1990). Patterns of performance on attention tasks measuring reaction time and error were found. Participants preserved accuracy at the expense of speed (e.g., on subtests from the Test of Everyday Attention, see McAulay et al., 2001)) or preserved speed at the expense of accuracy (e.g., on the Stroop task, see Craft et al., 1994). Furthermore, increased errors of omission were found on the PASAT (Schächinger et al., 2003), while increased errors of commission were found on the CPT task (Flint & Turek, 2003). Subject type, task complexity, and a standard methodology (e.g., glucose, food, or placebo type, and time of testing) were found to be challenging factors. Distracting effects (e.g., shakiness or hunger from low blood sugar) were also raised as potential contributors to impaired performance. The effects of fatigue were examined in one study, which found differing effects of fatigue on stimulus selection and response production (Smid et al., 1997).

Vigilance

Reaction time performance during vigilance tasks, detection of auditory or visual tones, and a tracking task was significantly slowed at low blood glucose levels (Fruehwald-Schultes et al., 2000; Hoffman et al., 1989). Conversely, a glucose dosage benefited performance on a digit-monitoring task when performing simple mathematical calculations (Benton, 1990). Task duration (e.g., is a 1-min versus a 10-min task long enough?), timing of testing for effects, pre-experimental controls (e.g., fasting or feeding prior to experiment?), effects of expectancy of glucose on performance (Green et al., 2001), history and awareness of hypoglycemia (Howorka et al., 2000), and symptoms associated with potential distractions to performance (Howorka et al., 1996) were some of the challenges to vigilance performance studies.

Memory

Memory performance was significantly enhanced by a glucose provision (Benton & Parker, 1998; Martin & Benton, 1999; Benton et al., 2001; Pollitti et al., 1998). Quantity of material recalled and speed of recall have been affected at varying glucose levels – with benefits from a provision of glucose, and impairments from fasting or a placebo (Benton & Parker, 1998; Benton & Sargent, 1992). Performance on mathematical tests showed similar patterns (Kennedy & Scholey, 2000). The speed-accuracy trade-off was not as clear in mathematical tests (Scholey et al., 2001; Holmes et al., 1983). Accuracy of simple math facts was preserved at the expense of speed, but not on the number of subtractions or the number of errors on a serial sevens test. Other effects of glucose on memory

processes (e.g., implicit, explicit, encoding, retrieval) require further investigation. Challenges due to duration of the task, familiarity with the task, breakfast type, glucose dosage, timing of testing, and standardization of methodology (e.g., subject types, age) were described.

Language and Communication

In contrast to the vast literature on blood glucose and memory, language and communication studies are limited. Trends demonstrated the benefits of a glucose provision on verbal fluency tasks and reading speed, with impaired performance at low blood glucose levels (Donohoe & Benton, 1999a; Kennedy & Scholey, 2000; Scholey et al., 2001; Mitrakou et al., 1991). On the other hand, reading comprehension was not affected by varying blood glucose levels (Holmes et al., 1983). Glucose dosage, cuing in reading tasks, and experimenter effects may have affected performance of participants in these experiments.

Judgment and Decision-Making

Similar to attention studies, aspects of decision-making and its processes were affected at varying glucose levels. Planning performance was slower, and mental flexibility and tracking were impaired at low blood glucose levels (Hoffman et al., 1989; Pramming et al., 1986; Schächinger et al., 2003). Only arithmetic reasoning benefited (more problems solved) from increased glucose provisions (Kanarek & Swinney, 1990). Abstract and logical reasoning were not enhanced by a provision, and associative reasoning was not affected at low blood glucose levels (Benton & Parker 1998). Type of task, type of provision (e.g., glucose or snack), and timing for testing were challenges to studies.

Complex Task Performance

Low blood glucose levels significantly impaired complex task performance, assessed by driving simulation (Cox et al., 1993). Steering, speed control, and braking were negatively affected at low blood glucose levels. Accuracy of performance was preserved at the expense of speed on these tasks, with very slow driving being demonstrated. As described in several other studies, participants were not always aware of their impairments (Cox et al., 2000). The complexity, novelty, duration of the task, and lack of standard methodology (e.g., sample size) were challenges to these findings.

CONCLUDING REMARKS

Glucose levels affect several domains of functioning assessed by performance on various tasks. Decreased provisions of glucose in the bloodstream impair performance, while increased levels benefit performance. Which mechanisms are involved (e.g., hormones, regulatory systems) remains largely unknown. Research clearly supports the notion that hypoglycemia significantly compromises performance, resulting in longer response times and lower scores on cognitive tests. Similarly, injections of blood glucose into localized areas of the brain in rats have demonstrated beneficial effects on memory and learning while glucose drinks administered to fasting human participants have benefited performance on various measures (even in those with impaired glucose regulation). Significant impairments in cognitive performance tasks have been found not only in Insulin-Dependent Diabetes Mellitus (IDDM) participants, but also in healthy adults when their blood

glucose levels were even moderately altered. More importantly, individuals do not need to be hypoglycemic to experience symptoms of hypoglycemia. They may not necessarily recognize their symptoms and may experience a cognitive lag leading to impairment for some time after returning to normal glucose levels.

Challenges to blood glucose and performance research include participants' familiarity with the task, expectations of a glucose provision, dose- and time-dependent effects with the focus largely on the task type and level of complexity used to measure performance. The nature of the task (e.g., redundant cuing in a reading task) and the sensitivity or complexity of the task (i.e., possible ceiling effects) also remain as challenges to researchers. Varying task demands, duration, glucose-dosages, timing of testing, and treatment types (e.g., specific breakfast effects, 25 or 50 grams of glucose) are necessary to further understand the processes involved, but more standardized approaches are also required. Researchers may have the opportunity to learn more about the role of glucose on performance by evaluations of rising and falling blood glucose levels, and also the speed-accuracy trade-offs that occur during certain tasks and under certain conditions.

A significant challenge to the study of this domain involves terminology (e.g., units, labels, qualifiers), which has been addressed in the past (Gastineau, 1983). It is difficult to draw conclusions across studies when researchers report different units of measure for blood glucose levels (mg/dl vs. mmol/l), use different labels for blood glucose levels (what counts as "normal," or how low is "low"?), or qualify hypoglycemic states (e.g., "mild" or "moderate") inconsistently. It often seems that these terms are not necessarily based on any standardized blood glucose levels, but on their effects (e.g., "mild" levels are those that result in mild effects). Such definitions are very problematic given the wide range of effects, and the large individual differences that exist in the broad population. Furthermore, task descriptions such as "simple," "complex," "demanding," and "appropriate" also pose considerable challenges to this area of study; they lack clear definition and consistency in use among researchers. Thus, the field will do well to settle on shared accepted definitions, consistent labels, and standardized units.

RECOMMENDATIONS FOR FUTURE STUDIES

Based on the challenges described by researchers evaluating performance using various measures, several recommendations can be made for improved methodologies in studies of blood glucose level and performance:

Pre-experiment:
- Employ within-subject design when possible (based on intra-individual variability)
- Determine appropriate time to test for effects
- Control length of fast prior to experiment (and snacks, meals, breakfast consumption patterns and compositions)
- Account and/or control for moderating variables (e.g., caffeine, exercise, etc.)
- Assess participant's history and awareness of hypoglycemia

- Consider effects of fatigue (e.g., add fatigue assessments to testing battery)
- Consider placebo choice (e.g., effects of saccharine versus aspartamate to determine whether results are due to negative effects of saccharine rather than benefits of a glucose drink)
- Account for the effects of various glucose dosages and/or macronutrients to be used (e.g., glycemic index, carbohydrate to protein ratio)

During experiment:

- Control for timing of testing (ideally evaluating performance at several time points)
- Control for the duration of the task (employing similar tests of varying durations)
- Control for the complexity of the tasks (use validated tests for measurement, operationally define complex versus simple tasks, and vary task demands)
- Limit the participants' time on the task to create more sensitive measures (e.g., spatial memory task)
- Measure all participants at the same time of day (not am or pm between group comparisons) or counterbalance this variable (equal number of am and pm participants)
- Assess physiological (and mood) symptoms (to assess effects on performance with and without symptoms acting as distracters)
- Continuously monitor blood glucose levels (to be able to evaluate performance at rising and falling levels, and ability to identify optimal time to test for peak effects)
- Determine glucose regulation and tolerance of participants (e.g., HB1AC test for glucose regulation)
- Account for practice effects (determine baseline levels)
- Measure participants' expectations of glucose on performance, motivation, and confidence levels
- Monitor experimenters' biases (keep blind to conditions)
- Monitor experimenter effects (familiarity with task administration)

Post-experiment:
- Evaluate time of day effects
- Evaluate dose-dependent effects
- Analyze rising and falling glucose levels
- Report use of standard units and labels
- Report effect size(s)

Few studies, if any, incorporated features such that they were specifically designed to investigate the effects of blood glucose levels on performance of healthy non-diabetic individuals at normal levels (not induced to hypoglycemic states), and engaged in normal every day tasks. This is a major gap that research has not clearly addressed. To illustrate, in driving studies, participants have typically

been diabetics who are induced to hypoglycemic levels in a driving simulator or have been healthy participants induced to hypoglycemic levels. Under these conditions, it is difficult to determine how these studies can establish normative data and generalize results to the general population.

Given what has been demonstrated in the literature, it is not a question of "if" glucose levels affect performance, but "when" and "how" they affect performance. Performance decrements may be mitigated because tasks are not necessarily mutually exclusive, and individuals may rely on several different cognitive processes in order to complete a task successfully. Likewise, decrements to one area of functioning (e.g., auditory information processing) may affect other functions and processes (e.g., long-term memory storage) as well. It would not be surprising to find impaired performance when multiple tasks are presented to either diabetic or non-diabetic populations at compromised blood glucose levels. Individuals might experience their attention to distracting stimuli, mathematical calculation performance, ability to (and rate of) recall of certain information, and even basic driving skills to be affected at varying glucose levels as a result of fasting, and/or situations similar to hypoglycemic or experimental conditions. These individuals do not necessarily have to be diabetic to experience impairments from low blood glucose levels, and may not be able to reasonably respond to time-critical demands. Such impairments may result in costly and/or dangerous situations.

Blood glucose levels affect performance. As evidenced in this review, varying blood glucose levels (whether through fasting, receiving a placebo or insulin-inducing techniques) affected performance of individuals on tasks that assessed several executive and non-executive functions: sensory, psychomotor, attention, vigilance, learning and memory, language and communication, judgment and decision-making, and complex task performance. While many questions remain unanswered, these effects may best be understood as a continuum of degradation (from optimum to severely impaired performance). Establishing a unified approach and standardized methodology and terminology, determining appropriate levels and sensitivity of measurements, and accounting for the many factors that also affect performance are critical to understanding the role of glucose in performance, and where the affected cognitive processes reside along that continuum.

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TABLE 1. CONVERSION OF BLOOD GLUCOSE VALUES AND ASSOCIATED SYMPTOMS

mmol/l levels	mg/dl levels	Range of possible symptoms
2.0	36	Extremely low levels may result in: loss of coordination, slurred speech, feeling cold, paralysis of extremities or face, involuntary muscle contractions, seizures, unconsciousness, coma
2.1	37.8	
2.2	39.6	
2.3	41.4	
2.4	43.2	
2.5	45	
2.6	46.8	Moderately low levels may result in: tiredness, slowed mental function, confusion, muscle weakness, blurred or double vision, mood changes (giddiness or anger), dizziness, headache, bizarre behavior, numbness or tingling
2.7	48.6	
2.8	50.4	
2.9	52.2	
3.0	54	
3.1	55.8	
3.2	57.6	
3.3	59.4	In diabetics, an adrenaline release occurs that may result in: anxiety, nervousness, hunger, rapid heartbeat, tremor, nausea, paleness or flushing, sweating, chest pain or tightness
3.4	61.2	
3.5	63	
3.6	64.8	
3.7	66.6	
3.8	68.4	Slightly low, first symptoms of lethargy, etc.
3.9	70.2	
4.0	72	
4.1	73.8	
4.2	75.6	
4.3	77.4	
4.4	79.2	
4.5	81	
4.6	82.8	
4.7	84.6	
4.8	86.4	
4.9	88.2	
5.0	90	Normal blood glucose in people who do not have diabetes upon waking 70–110 mg/dl, after meals 70–140 mg/dl
5.1	91.8	
5.2	93.6	
5.3	95.4	
5.4	97.2	
5.5	99	
5.6	100.8	
5.7	102.6	
5.8	104.4	
5.9	106.2	
6.0	108	

Source: http://diabetes.niddk.nih.gov/dm/pubs/hypoglycemia/index.htm; Lincoln & Eaddy (2001)

TABLE 2. TESTS USED TO INVESTIGATE BLOOD GLUCOSE AND COGNITIVE PERFORMANCE

Type of Test & Description	Cognitive process assessed	General Findings	Reference
Ammon's Quick Test – subject chooses from four pictures which matches a series of words	Verbal intelligence	Performance was comparable under the control (no glucose) and treatment (10g glucose, 25g glucose, & 50g glucose) conditions. Glucose did not alter performance on this test.	Parsons & Gold,1992, $N = 10$ (older participants), fasting Manning, Hall, & Gold, 1990, $N = 17$ (older participants), fasting
Baddeley Logical Reasoning Task – series of if/then conditional statements, "true" or "false"	Logical reasoning	Lack of a relationship between blood glucose and this test may be due to it being a non-memory task and non-demanding task.	Donohoe & Benton, 1999a; $N = 67$
Block design test – set of modeled or printed two-dimensional geometric patterns that examinee replicates using two-color cubes	Perceptual organization	A glucose drink did not affect performance on this task, but the difficult rather than the easy trials of this task were susceptible to blood glucose – faster if consumed glucose drink.	Donohoe & Benton, 1999a; $N = 69$
Brown-Peterson – 40 consonant-syllable trigrams, subject to remember a trigram while counting backwards, in threes, percentage correctly recalled recorded	Short term memory; Information processing	Fasting was associated with poorer performance. The percentage of trigrams correctly recalled was higher in the second rather than in the first block of trials. A glucose drink improved the memory of those who had fasted, although it did not influence those who had eaten breakfast. In those who had fasted, the glucose drink resulted in memory comparable to those who had consumed breakfast. Those with higher levels of blood glucose upon arrival in the laboratory had better memories. In those taking a glucose drink, after an initial rise, rapidly falling levels of blood glucose were associated with better memory. Recall improved throughout the task if the subject had eaten breakfast rather than fasted. Performance of the participants who had fasted but consumed a glucose drink was similar to those who ate breakfast.	Martin & Benton, 1999; $N = 80$, fasting Benton & Parker, 1998; $N = 33$, fasting (Exp 1), $N = 80$ (Exp 2*), $N = 137$ (Exp 3)
Categorizational test – write down as many items of a specific category as possible in one minute, scored by relevant items	Ideational fluency	Score (part of test total score) deteriorated between periods from 108 mg/dl–54 mg/dl and 54 mg/dl–36 mg/dl, but not significantly.	Pramming, Thornsteinsson, Theilgaard, Pinner, & Binder, 1986; $N = 22$ IDDM, clamp
Color-word (interference) subtest – identify color of ink, 2 min period 112 words presented, time taken and number of correct responses recorded	Selective attention, Mental tracking, Color vision, Ability to inhibit conflicting inputs	Impaired immediately at onset of hypoglycemia; significant deterioration (at 47 mg/dl); score indistinguishable from EU after 20 min of recover from HYPO.	Evans, Pernet, Lomas, Jones, & Amiel, 2000; $N = 8$, clamp
Controlled Oral Word Association test – name as many words as possible, beginning with a given letter of the alphabet, within 1 min, score sum of all acceptable words	Verbal fluency, Supervisory attentional system	The consumption of a glucose containing drink resulted in faster performance. Participants who had taken a glucose drink generated significantly more words, 25 min after the drink, than placebo drinkers.	Donohoe & Benton, 1999a; $N = 69$

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Type of Test & Description	Cognitive process assessed	General Findings	Reference
Word list generation	Verbal fluency	No main effects or interactions observed, and while the older partici-pants performed similarly to younger participants, performance was unaf-fected by glucose administration.	Craft, Murphy, & Wemstrom, 1994; $N = 59$ (young/older), fasting
Generate as many words beginning with "T"	Access to and retrieval of information in long term storage (Halpern, 1992)	Trend towards enhanced performance in the glucose (25 g) condition.	Kennedy & Scholey, 2000; $N = 20$, fasting
Digit Span (WAIS subtest, Wechsler) – series of orally presented number sequences that examinee repeats verbatim for forward and in reverse	Working memory, distracti-bility, auditory concentra-tion, attention span	Score significantly lower (part of test total score); test result deteriorated sig-nificantly between periods 108 mg/dl to 54 mg/dl, and from 54 mg/dl to 36 mg/dl.	Pramming et al., 1986; $N = 22$ IDDM, clamp
	Short-term memory	Digit Backward shows age-related defi-cit, but did not show a glucose effect. Authors suggest that this was due to Digit Span tapping fluid IQ and atten-tion than memory.	Manning, Hall, & Gold, 1990, $N = 17$ (older participants), fasting
Digit Span, Trail B, Serial 7s, Tapping, Categories	Various faculties	All subtest scores, except tapping, significantly lower between euglycemia and severe hypoglycemia	Pramming et al., 1986; $N = 16$
Digit Supraspan (digit span)	Mental mathematics	Slow RT during both hypo and hyper-glycemic conditions, rate of response during math computation was slowed during hypoglycemia, accuracy was unimpaired	Holmes, Hayford, Gonzales, & Weydert, 1983; $N = 12$ w/IDDM
Digit Symbol Coding (or Digit Symbol Substitution) – Wechsler Adult Intelligence Scale subtest – series of numbers, each is paired with own hieroglyphic-like symbol, using a key the examinee writes the symbol corresponding to its number	Cognitive processing speed, Persistence in the face of a boring task, Clerical speed, Distractibility, Working under time pressure, Visual-motor dexterity, Rote/School learning, Visual scanning/ processing, Visual-motor integration	Scores achieved significantly lower.	McCrimmon, Deary, Huntly, MacLeod, & Frier, 1996; $N = 20$ non-diabetics, clamp
		Significant disruption in brain function-ing, during hypoglycemia (47 mg/dl) when compared with euglycaemia, times significantly longer.	McCrimmon, Deary, & Frier, 1997; $N = 20$ non-diabetics, clamp
		Acute hypoglycemia induced a signify-cant deterioration in cognitive function.	Gold, Deary, MacLeod, & Thomson, 1995; $N = 24$ non-diabetic, clamp
		Significantly affected by hypoglycemia.	Gold, MacLeod, Deary, Frier, 1995; $N = 20$ IDDM
		Acute hypoglycemia induced significant deterioration, changes in performance similar between high/low IQ.	Gold, Deary, MacLeod, & Frier, 1995; $N = 24$, non-diabetic
Driving Simulator – Atari Research Driving Simulator – realistic, inter-active, fixed platform simulator that generates accurate and sensitive driving performance data (auditory/ kinesthetic feedback), simulate driving demands typical to grade 2 highway, 16-mile course, 30 min to traverse, records data 4x/sec, generates 9 driving performance variables	Steering – standard deviation steering (swerving), off-road, risk midline; Braking – inappropriate braking, missed stops, collisions; Speed control – low speed, high speed, standard devia-tion speed	During all three hypo ranges, driving significantly impaired – off-road driving (driving across the midline), driving fast, applying brakes more on the open road, failed to stop at stop signs, crashed more at sudden stops, speed limit changes, detours at stop signs intersec-tions, encroaching fixed objects, nego-tiating oncoming and cross traffic affected; corrective action (glucose drink) not occur until blood glucose was < 50 mg/dl; impairment at mild hypo (61–72 mg/dl).	Cox, Gonder-Frederick, Kovatchev, Julian, & Clarke, 2000; $N = 37$, IDDM

Type of Test & Description	Cognitive process assessed	General Findings	Reference
M-8000A Driver Simulator system – subject respond in simulator to three video scenarios, adjusting speed using break and accelerator, and turning steering wheel to avoid hazards, errors automatically calculated via computer		Signaling, braking, and acceleration (speed) performance was poorer for participants during hypoglycemia (50 mg/dl), but failed to reach signifi-cance. Considerable variability in performance during hypoglycemia. Authors suggest possibly lack of enough sample size, task complexity since simulator not require same level of divided attention skills, limited field of vision, and evidence to suggest that selective attention and concentration may be less affected by glucose levels if task is familiar or over-learned. Suggest using closed-course driving situation.	Hoffman, Speelman, Hinnen, Conley, Guthrie, & Knapp, 1989; $N = 18$ w/IDDM, clamp
Embedded Figures – 35 embedded figures, each multiple choice, find smaller figure embedded in larger/ complex figures	Perceptual Flexibility	Lack of a relationship between blood glucose and this test may be due to it being a non-memory task and non-demanding task.	Donohoe & Benton, 1999a; $N = 67$
Event-related brain potential	Reaction time	RT and P300 significantly slowed only at 47 mg/dl. Sensory and motor processes unaffected.	Blackman, Towle, Lewis, Spire, & Polonsky, 1990; $N = 19$
Finger Oscillation Test (Reitan & Wolfson, 1985) – participants press down lever attached to a counter as quickly as possible over ten second period	Motor function	Glucose did not alter performance.	Manning, Hall, & Gold, 1990, $N = 17$ (older participants), fasting
Finger Tapping Task – press a telegraph-like key as rapidly as possible	Pure motor function	Failed to demonstrate impairment at nadir (47 mg/dl) unlike cognitive task (PASAT versions).	Cox, Gonder-Frederick, Schroeder, Cryer, & Clarke, 1993; $N = 10$ IDDM
		Score significantly lower (part of test total score); test result deteriorated significantly between periods 108 mg/dl to 54 mg/dl, and from 54 mg/dl to 36 mg/dl.	Pramming et al., 1986; $N = 22$ IDDM, clamp
	Simple motor function	Not affected by blood glucose alter-ations (at 55, 110, or 300 mg/dl)	Holmes, Koepke, & Thompson, 1986; $N = 25$ IDDM men, clamp
Graduate and Managerial Assessment Test of Abstract Reasoning – matrix type design	Abstract Reasoning	Abstract reasoning was not affected by a glucose drink, breakfast consumption, or interaction of these variables.	Benton & Parker, 1998; $N = 33$, fasting (Exp 1), $N = 80$ (Exp 2), $N = 137$ (Exp 3*)
Jensen-type RT device, black panel w/eight lamps, one of eight flashed, press button	Decision-making; Simple/ Choice Reaction Time	Speed of processing is faster when availability of glucose to brain is increased; change in blood glucose critical since not induced to hypo levels; participants experiencing falls in blood glucose had slower decision times than those who were rising (2 groups: blood glucose fell by more than 9 mg/dl vs. blood glucose increase of more than 18 mg/dl.	Owens & Benton, 1994; $N = 96$, no dietary restrictions
P300 wave (latency), event related potential – depressing handheld button to red LED but not green LED	Visual/Auditory Decision-making; Reaction Time (motor)	Reaction time to stimulus slowed; cognitive dysfunction between 59–47 mg/dl. Motor processes not affected.	Blackman et al., 1990; $N = 19$, clamp

Type of Test & Description	Cognitive process assessed	General Findings	Reference
Hick Reaction Time Task: black box w/eight response buttons, either simple or choice reaction time, Jensen-type RT device	Decision/Movement time, assess different degrees of response uncertainty	Repeated hypoglycemic episodes results in significant increase in number of false responses	Deary, Langan, Graham, Hepburn, & Frier, 1992; $N = 85$
		Deterioration in both groups, significant deleterious effect of hypoglycemia on performance of movement time in both groups	Gold, Deary, MacLeod, & Frier, 1995; $N = 24$
Neurobehavioral Evaluation System – push a button when see a 2x2 block appear on screen (simple); block on left or right side of screen, press button to side where block appeared (choice); words "side" or "direction" flashed on screen, box with arrow on either right or left side, subject follows directions given by words (complex)	Simple, choice, and complex reaction time tasks	Trend toward slowing at mild hypo levels (55–70 mg/dl) on every task but not significant; hypo affected speed equally (slowed speed) on complex and simple tasks, but at moderate (45 mg/dl) participants increased errors on complex but maintained accuracy on simpler ones; moderate levels significantly increases reaction time	Driesen, Cox, Gonder-Frederick, & Clarke, 1995; $N = 25$ w/IDDM
Four Choice Reaction Time (CRT) – device measures both decision and movement time, black box, sloped top, one of response buttons is lit, timer begins when finger lifted and stopped when button is pressed	Attention, Motor speed of reaction, Discrimination	Impaired immediately at onset of hypo-glycemia; significant deterioration (at 47 mg/dl); reaction time still significantly impaired 20 min after bg levels recovered to euglycemia	Evans et al., 2000; $N = 8$, clamp
	Decision time and movement	Significant deleterious effect of acute hypoglycemia on performance	Gold, Deary, MacLeod, & Thomson, 1995; $N = 24$ non-diabetic
Choice Reaction Time Test (CRTT) – lasted 3 min, press a button of same color as one of the five which flashed, random sequence, test difficulty adjusted to achieve a false response rate, scored by mean reaction time and inter-stimulus interval (ISI)	Psychomotor function, sustained attention and executive motor function	Hypoglycemia (49 mg/dl) significantly impaired CRTT and measure of ISI. CRTT showed high long-term test-retest reliability. Large effect size, Cohen = 1.83, authors suggest greater sensitivity than PASAT or manual tracking task.	Schächinger, Cox, Linder, Brody, & Keller, 2003, $N = 17$ healthy male students, fast and clamp
Cued reaction timer – press telegraph-style key as soon as target light comes on, 25 trials at each glucose level, reaction time recorded	Simple motor speed and reaction time	Reaction times generally slower during hypoglycemia, much variability in performance, and overall effect did not reach statistical significance.	Hoffman, Speelman, Hinnen, Conley, Guthrie, & Knapp, 1989; $N = 18$ w/IDDM, clamp
Panel with 8 lamps, 1,2,4 or 8 lamps illuminate, time taken to raise finger is decision time, pressing the button is the movement time	Reaction and movement time	A higher baseline blood glucose level was associated with faster choice reaction times and lower intra-individual variability. The faster the falling of blood glucose the quicker the decision times.	Donohoe & Benton, 2000; $N = 46$ female undergraduates, fasting GTT
Letter Cancellation Test (Lezak, 1983)	Attention	Glucose did not alter performance.	Manning, Hall, & Gold, 1990, $N = 17$ (older participants), fasting
Lines of different lengths, triangles in array or moves	Visual	Marked deterioration in speed of visual information processing (inspection time, detect change, detect movement) and contrast sensitivity; but not significant deterioration of visual acuity, affects early stages of visual info. (speed, ability, and sensitivity affected).	McCrimmon et al., 1996; $N = 20$ non-diabetic, 47 mg/dl
		Increased reaction time.	Snorgaard, Lassen, Rosenfalck, & Binder, 1991; $N = 18$

Type of Test & Description	Cognitive process assessed	General Findings	Reference
Discriminate between two lines of different lengths, press keys to which line longest, self-paced, computer calculates inspection time and reaction times	Inspection time task, rate of information processing	Inspection time unaffected by glucose drinks and blood glucose levels; none to hypo levels, rather, change in bg critical factor; increasing glucose levels beneficial when performing demanding tasks.	Owens & Benton, 1994; $N = 96$, no dietary restrictions enforced
Manual tracking test – participants direct a pointer (small cross) as close as possible to a target, white circle, orbiting at variable speed on a screen, test was 3 min long with only 2 min analyzed, scored is based on recorded distance between target and pointer	Fine motor function, attention, coordination	The response measure "distance" was significantly impaired by hypoglycemia. Test showed high long-term test-retest reliability and large effect size, Cohen = 1.07.	Schächinger, Cox, Linder, Brody, & Keller, 2003; $N = 17$ healthy male students, fast and clamp
Modified California Verbal Learning Test – listens to list of 16 items from four semantic categories as to recall in any order. Procedure repeated two more times. Subjects then heard second list and asked to recall list (interference task). After, participants asked to recall items from first list. Free recall and recognition measured after 15-min delay. Number correct is recorded for short-delay recall, long-delay recall, and for recognition trial	Declarative memory by verbal learning	Main effects observed for all groups, reflecting better performance of the younger participants with a glucose provision. No interactions for immediate recall of the list or for short- and long-delay recall.	Craft, Murphy, & Wemstrom, 1994; $N = 59$ (young/older), fasting
Monitoring numbers – 24 minute digit monitoring task, as they appeared on a screen of a microcomputer – scores reflect times subject failed to respond to a target stimulus and Television computer game – ball and bat – adjust speed of ball, angle – while complete mental arithmetic	Fine motor control, hand-eye coordination task and arithmetic	Increasing blood glucose improved performance on non-demanding task (Exp1), simple calculations produced fewer errors, while monitoring single digits (25 g glucose); but more demanding arithmetic calculations produced more errors while continuously responding to quickly moving and unpredictable object – but no effect of glucose (Exp2).	Benton, 1990; fast 4 hours prior
Paragraph Recall – listen to brief narratives with 25 bits of information, recall as much after and 10 min later	Immediate and delay of declarative memory recall	Older men with good recovery (or degree to which blood glucose levels return to baseline following glucose administration is related to glucose effects on performance) performed significantly better in glucose condition than in saccharin condition. Older men with poor recovery and older women with good or poor recovery showed no significant differences between glycemic conditions. Younger men with poor recovery showed significantly improved scores for both immediate and delayed recall in glucose condition vs. saccharin; while performance of younger men with good recovery deteriorated with glucose administration. Younger women with good or poor recovery did not show any significant differences in recall between conditions. No significant sex differences in saccharin conditions, which suggests that both men and women had comparable memory performance at baseline.	Craft, Murphy, & Wemstrom, 1994; $N = 59$ (young/older), fasting

Type of Test & Description	Cognitive process assessed	General Findings	Reference
PASAT – audio tape and perform mental additions, sequence of numbers 1–9, add first number to second, give answer, second to third and so on for 61 numbers (Scores are highly correlated with WAIS LNS); 4 sec task moderately correlated w/memory performance, 2 sec task w/speed of information processing	Attention, Information processing speed, Concentration	Significantly affected performance w/deterioration in scores during hypoglycemia.	Gold, MacLeod, Deary, & Frier, 1995; $N = 20$
		Significant effect of hypoglycemia in both groups, but not between groups, although average IQ s deteriorated significantly less than higher IQ s during hypo in 4-sec task.	Gold, Deary, MacLeod, & Frier, 1995; $N = 24$
		Performance decay related to absolute bg level at nadir (47 mg/dl); cognitive tasks more sensitive to neuroglycopenia than motor tasks; the greater the hypo during nadir the greater the decrement in performance; the poorer the initial performance the greater the decay during moderate hypoglycemia.	Cox, Gonder-Frederick, Schroeder, Cryer, & Clarke, 1993; $N = 10$ IDDM
	Working memory	Fewer correct responses for older group versus younger group, but performance was unaffected by glucose administration.	Craft, Murphy, & Wemstrom, 1994; $N = 59$ (young/older), fasting
PASAT scored by percentage correct, omission errors, and false responses, and verbal RT for correct responses	Sustained and divided attention, concentration, working memory, and speed of information processing (Diehr et al., 1998)	Hypoglycemia increased reaction time and decreased accuracy by increasing omissions and false responses (intermediate-large effect size, Cohen = 1.31). In both hypoglycemic and normal conditions, errors on this test were due to omissions, but during normal glucose levels omissions are 1.5x more likely than false responses, but during hypoglycemia this ratio increases to about 2.5x. First time verbal reaction time for PASAT during hypoglycemia.	Schächinger, Cox, Linder, Brody, & Keller, 2003, $N = 17$ healthy male students, fast and clamp
Pattern Recall and Recognition – view checkerboard patterns, 3x3 grid, study for 10 sec., stimuli removed and asked to reproduce patter. Process repeated two more times. Free recall after a 10-min delay, then subject told to pick 3 test patterns from an array. Three scores constructed: number correct for first three trials, for delayed recall, and for recognition trial	Declarative memory by pattern recall and recognition	Possible ceiling effects for delayed recall and recognition – difficult to determine meaningful analyses of these data. Significant main effects for age group: higher scores for the younger participants in both glucose and saccharin conditions. For younger men and women and older women, poor and good recovery groups performed similarly. However, older men with poor recovery had better scores than older men with good recovery.	Craft, Murphy, & Wemstrom, 1994; $N = 59$ (young/older), fasting
Porteus Maze – mazes for those aged 7–14 and for adults, complete series of mazes at own pace	Supervisory attentional system	The consumption of a glucose containing drink resulted in faster performance. It was difficult rather than easy mazes that were influenced. After taking a glucose drink, poor performance was associated with blood glucose that remained at higher levels.	Donohoe & Benton, 1999a; $N = 69$
Ravens Progressive Matrices	General Fluid Intelligence	Intelligence scores did not deteriorate during hypoglycemia; fluid intelligence was preserved.	McAulay et al., 2001; $N = 20$ non-diabetics, clamp
Rey Osterreith Complex Figure (Osterreith, 1944) – copy a complex design and then asked to draw the design from memory	Memory for figure design	Glucose did not enhance memory for figure design. Authors suggest due to test's poor reliability.	Manning, Hall, & Gold, 1990, $N = 17$ (older participants), fasting

Type of Test & Description	Cognitive process assessed	General Findings	Reference
Rapid Information Processing Task (RIPT) and/or Rapid Visual Information Processing – computer generated series of digits on blk/wht screen, press space bar when detect sequences of three consecutive odd or even digits – number of sequences correctly detected, time taken to respond and number of errors are recorded (hits – signal detection efficiency vs. misses – response bias or threshold)	Information processing speed, Sustained Attention	Reaction times were faster both during the baseline period and after a glucose drink if the blood glucose values were high.	Benton, Owens, & Parker, 1994; $N = 70$ (Exp 1), $N = 50$ (Exp 2), fasting
		Frequency of severe hypo correlated significantly w/RVIP miss, but not with hits or RT.	Deary et al., 1992; $N = 85$
		There was no significant difference in RVIP false alarms or reaction time. Hypoglycemia did not have an effect on performance in this test.	Gold, Deary, MacLeod, & Thomson, 1995; $N = 24$ non-diabetics
		Significantly affected performance in this test in both groups (normal hypo awareness vs. impaired), more false positives than normal patients, patients in both groups became significantly slower during hypoglycemia.	Gold, MacLeod, Deary, & Frier, 1995; $N = 20$
		Significant deterioration, no difference between groups (high vs. low IQ) for hits; average IQ more false-positives during hypo, average IQ less cautious during hypo, sign difference between performance between groups during hypoglycemia.	Gold, Deary, MacLeod, & Frier, 1995; $N = 24$
		Demand condition (RIPT) significantly slower than no-demand (sitting) which may be a speed-accuracy trade-off; placebo (no glucose) drinkers made significantly more errors at 2 and 6 min (trend at 8 and 10 min); participants whose blood glucose levels falling during demand condition made significantly fewer errors, than those whose levels were rising.	Donohoe & Benton, 1999b; $N = 188$
Pursuit rotor – track a dot rotating on a turntable with a stylus, amount of time correctly positioned stylus calculated for five 1-min trials	Vigilance and motor control	Participants showed significantly greater performance decrements in tracking when hypoglycemic than on a simple reaction time task. Performance was significantly difference from those at euglycemia (100 mg/dl) and hyperglycemia (300 mg/dl), with performance poorest at hypoglycemia. Authors also suggest some reversible decrements in cognitive functioning at levels of 50 mg/dl, especially during novel tasks requiring concentration and decision-making.	Hoffman, Speelman, Hinnen, Conley, Guthrie, & Knapp, 1989; $N = 18$ w/IDDM, clamp
Single digits on computer screen, press space bar every time detected sequences of three consecutive odd/even digits, eight sequences presented every minute, task performed for 5 min, number of sequences correctly identified are reported	Vigilance	Those with higher peak of blood glucose (zenith) levels performed worse on this task.	Donohoe & Benton, 2000; $N = 46$ female undergraduates, fasting GTT

Type of Test & Description	Cognitive process assessed	General Findings	Reference
Selective Reminding Test (SRT) (Buschke & Fuld, 1974 as modified by Levin, Benton, & Grossman, 1982) – read list of twelve words, repeat as many as can remember, next read only words from list not recall, then asked again to recall as many words as possible from entire list – procedure repeated until all words recalled, scored long-term storage/retrieval = total number of words recalled on trials words not presented, short-term retrieval = percentage of words recalled immediately following presentation	Declarative memory, short-term retrieval memory and long-term storage and retrieval memory – taps recall of non-contextual verbal information	Long-term word memory was significantly enhanced after glucose ingestion (50 g) versus saccharin, but not short-term memory.	Manning, Hall, & Gold, 1990, $N = 17$ (older participants), fasting
Serial Sevens – subtract 7 from a starting number then again and so on until reach zero, each SST begun, different starting numbers to prevent memorization and change order of presentation, scored for length of time to complete first 15 subtractions (can be computerized)	Mental confusion (neuro-glycopenic symptom)	Participants whose bg levels fell below 60mg/dl experienced significantly more regression in SST performance than participants who remained above 60 mg/dl.	Hale et al., 1981; $N = 67$
		Performance deteriorated at glucose nadir; impairment greater in participants who showed rapid decreases in blood glucose than for participants who showed slow decreases.	Taylor & Rachman, 1988; $N = 35$
Serial Sevens & SS control task		Significant effect of glucose on performance, generated significantly more responses when in glucose vs. placebo condition, glucose condition associated with fewer errors vs. placebo condition which rules out "speed-accuracy trade-off" on this measure.	Scholey, Harper, & Kennedy, 2001; $N = 20$
		Score (part of test total score) deteriorated between periods from 108 mg/dl–54 mg/dl and 54 mg/dl–36 mg/dl, but not significantly.	Pramming et al., 1986; $N = 22$ IDDM, clamp
Serial Threes (subtraction of threes) & Serial Sevens – more demanding than Serial Threes & control STs, SSs tasks		Significant main effect of glucose on Serial Sevens tasks – participants give greater number of subtractions in glucose condition than placebo; no effect of glucose on number of subtractions for Serial Threes; no effect on number of errors for either task.	Kennedy & Scholey, 2000; $N = 20$, fasting
Serial Reaction Time Task – computer screen task to press key that corresponded to location of asterisk that appeared on screen, block trials: some randomly generated and some followed a repeating sequence. Mean reaction time measured – participants unaware of pattern yet reaction times decrease, and demonstrates motor learning without declarative, explicit knowledge of pattern	Procedural implicit motor memory	Glucose administration did not affect performance for any subject group.	Craft, Murphy, & Wemstrom, 1994; $N = 59$ (young/older), fasting
Spatial Memory – 16 drawings of objects on grid, 20s concentrate on image, no rehearsing so write down US states, then, place pictures in original position, time takes/errors recorded	Spatial memory	Performance correlated significantly with blood glucose concentrations. Time taken was significantly greater when participants fasted than when they ate breakfast.	Benton & Parker, 1998; $N = 33$, fasting (Exp 1*), $N = 80$ (Exp 2), $N = 137$ (Exp 3)

Type of Test & Description	Cognitive process assessed	General Findings	Reference
		No relationship found between blood glucose and performance on a test of spatial memory (16 colored pictures of objects on cards in 4x4 arrangement, presented for 30s, rehearsal prevented, arrange into previous positions, time taken/correctly placed items recorded)	Benton & Owens, 1993; N = 153 (word list), N = 96 (spatial) (Exp 1), N = 53 (Exp 2)
		Time taken significantly slower when fasting vs. a drink; significant negative correlations between level of blood glucose and time taken (rather than, number of errors); the higher the blood glucose the better the performance; first time association between relatively small differences in levels of blood glucose by normal dietary means and memory performance.	Benton & Sargent, 1992; N = 33, fasting
Story recall – connected narrative consisting of 18 units is read slowly and immediately afterwards the subject is asked to recall as much as possible, score is number of units recalled	Short-term memory	Score (part of test total score) deteriorated between periods from 108 mg/dl–54 mg/dl and 54 mg/dl–36 mg/dl, but not significantly.	Pramming et al., 1986; N = 22 IDDM, clamp
Stroop – names of colors red, green, yellow, blue presented (can be computerized) as congruent/incongruent – presented then disappear, press one of four keys which color, response/time taken recorded	Sustained Attention	Ability to perform the most cognitively demanding sub-test was selectively enhanced if blood glucose values were increasing prior to starting the test.	Benton, Owens, & Parker, 1994; N = 70 (Exp 1), N = 50 (Exp 2), fasting
(Stroop, 1935). Task included three conditions: read 100 color words, name 100 color blocks, color-word interference. Score total reading time and errors recorded	Selective attention, Mental tracking	Impaired immediately at onset of hypoglycemia; significant deterioration (at 47 mg/dl); score indistinguishable from EU after 20 min of recovery from HYPO.	Evans et al., 2000; N = 8, clamp
	Requires effortful, on-line processing (Perret, 1974)	Similar glycemic effects for all subject groups, with faster response times and more errors in the interference condition following glucose administration, so glucose appeared to quicken response time and increase errors during interference condition for young/older and males/females.	Craft, Murphy, & Wemstrom, 1994; N = 59 (young/older), fasting
Tapping, Letter Recognition, RT (choice), RT (simple)	Reaction time	Performance during choice reaction time was increased during hypoglycemia	Holmes et al., 1986; N = 24
Test of Basic Auditory Capabilities (TBAC) – tests recorded on audiotape, similar/different sounds, used extensively in auditory research, 22 tests into 8 subtests, major dimensions of auditory capability, 3 primary = simple discrimination, temporal processing, speed perception; score provides overall speed/efficiency of auditory information processing	Auditory	Significant deterioration in auditory temporal processing, sound discrimination; slows speed of information processing; disrupts short auditory storage during hypo., standard measures of general cog function significantly affected at blood glucose levels of 47 mg/dl.	McCrimmon et al., 1997; N = 20

Type of Test & Description	Cognitive process assessed	General Findings	Reference
Test of Everyday Attention (TEA) – broad-based measure, only test of attention based on everyday materials, 8 subtests: 1. Map Search 2. Elevator Counting 3. Elevator Counting with Distraction 4. Visual Elevator 5. Elevator Counting With Reversal 6. Telephone Search 7. Telephone Search While Counting 8. Lottery	Attention: (1) Visual selective attention, (2) Sustained attention, (3) Auditory Selective Attention, (4) Attentional Switching, (5) Auditory Selective Attention, (6) Visual Selective Attention, (7) Divided/Sustained Attention, (8) Sustained Attention	Significant deterioration in both visual and auditory selective attention; attentional flexibility deteriorated and speed of information was delayed; sustained attention did not deteriorate during hypoglycemia; accuracy was preserved at expense of speed on Test 4 and 6 – either speed is slower during hypo or individuals possibly adopt more cautious approach to avoid errors.	McAulay, Deary, Ferguson, & Frier, 2001; $N = 20$ non-diabetics, clamp
Trail Making A (less demanding than TMB) – connect series of numbered dots 1–25 as quickly as possible, score is time to complete task	TMA – simple visual search task requiring number recognition and motor speed. TMB – sensory motor and higher-cortical functioning, divided attention, letter and number recognition, concentration, visual scanning, motor speed, planning ability, mental flexibility (Corrigan & Hinkeldey, 1987)	Trail Making A did not result in significant main effects for glucose levels. Trail Making B performance was significantly poorer during hypoglycemia (50 mg/dl) than euglycemia (100 mg/dl) or hyperglycemia (300 mg/dl).	Hoffman, Speelman, Hinnen, Conley, Guthrie, & Knapp, 1989; $N = 18$ w/IDDM, clamp
Trail Making B – connect the circles, alternating series between letters (A–L) and numbers (1–13) as quickly as possible	Cognitive processing speed, Concentration, Visual motor dexterity, Ability to shift sets, Visual processing and visual-motor integration/tracking, divided attention task	Significantly longer time to complete test.	McCrimmon et al., 1996; $N = 20$
		Time taken to complete longer during hypoglycemia when compared with euglycaemia at 47 mg/dl.	McCrimmon et al., 1997; $N = 20$
		Performance ability did not differ when induced to acute hypoglycemia.	Gold, Deary, MacLeod, & Thomson, 1995; $N = 24$ non-diabetic
		Significant change in performance at certain time points in all participants.	Gold, MacLeod, Deary, & Frier, 1995; $N = 20$
		No significant difference between groups or effect of hypoglycemia overall.	Gold, Deary, MacLeod, & Frier, 1995; $N = 24$
		Failed to show any deterioration, largely because of large variability in performance at euglycemia.	Evans et al., 2000; $N = 8$, clamp
		Score (part of test total score) deteriorated between periods from 108 mg/dl– 54 mg/dl and 54 mg/dl–36 mg/dl, but not significantly.	Pramming et al., 1986; $N = 22$ IDDM, clamp
Water Jars task – series of arithmetic problems, 3 water jars, adding/subtracting volumes, establish "set", can use "set" to solve "critical" problems, examinees write out solution	Influence by set	Higher levels of (baseline) blood glucose on arrival at the laboratory were associated with better performance – solved critical problems significantly faster than those with lower blood glucose levels.	Donohoe & Benton, 1999a; fasting, 72–144 mg/dl, $N = 67$
Wechsler story – tester read story aloud, give participants 2 min to write down as much as they could recall	Working Memory	Recall of story was not significantly correlated with blood glucose levels.	Benton & Owens, 1993; $N = 153$ (word list), $N = 96$ (spatial) (Exp 1), $N = 53$ (Exp 2)

Type of Test & Description	Cognitive process assessed	General Findings	Reference
		Those who ate breakfast recalled more of the story and those who fasted; a glucose drink did not influence recall of the story.	Benton & Parker, 1998; $N = 33$, fasting (Exp 1), $N = 80$ (Exp 2), $N = 137$ (Exp 3*)
Modified version of Wechsler story – listen to audio-taped passage and recall in written form, following a 5 min delay, participants also asked to recall a second time at end of testing, 40 minutes after presentation of passage and 55 min after glucose ingestion	Logical memory	Significant enhancement found at 5 min test and 40 min test under 25 g glucose condition but not at higher or lower doses (10g glucose, 25 g glucose, & 50 g glucose). 10g resulted in non-significant increase in scores at both time points, but 50 g dose led to scores near saccharin condition (0g glucose). Blood glucose levels that are optimal for memory storage appear to be approximately 150–175 mg/dl in both rats and humans. 50 g ineffective in experiment and authors suggest that may be due to higher basal glucose level than prior experiments – due to differences in blood glucose regulation (shifted dose-response curve), that blood glucose levels reached after 50 g were higher in this experiment (225 mg/dl) than in previous (175 mg/dl). Evidence to suggest that participants with higher basal blood glucose levels may perform better on logical memory test than do participants with low basal levels.	Parsons & Gold, 1992, $N = 10$ (older participants), fasting
Modified version (same as above)	Contextual verbal information – long term, declarative memory	Performance at both recall times was significantly enhanced after glucose ingestion.	Manning, Hall, & Gold (1990), $N = 17$ (older participants), fasting
Word list recall – presented using tape recorder, recall as many words immediately, then after delay of 10 min, distracter task personality questionnaire used	Immediate and delay recall	Memory not influenced by eating breakfast; however, 20 but not 60 min after snack, more words were recalled; those who ate breakfast spent longer time trying to recall words – eating breakfast associated possibly with better motivation; better memory associated lower bg levels, that is, findings support that better glucose tolerance associated with better memory; except those who only ate 50 g carbohydrate breakfast and 10g carbohydrate w/a snack where higher blood glucose levels associated with better memory; blood glucose levels who fasted remained constant, 10g breakfast only higher than fasting at 1015 h, snack after 50 g maintained enhanced blood glucose levels for another hour.	Benton, Slater, & Donohoe, 2001; $N = 150$, fasting
30 nouns presented at one word every 2 sec using a tape recorded, each word 6 letters and two syllables high in imagery, concreteness, and frequency of use, immediately after presentation of list, write down and delayed was 15 minutes later, number of correctly recalled reported		The speed which blood glucose recovered from the lowest blood glucose value (nadir) was associated with memory (from a 3.5 hr GTT test with 50 g of glucose). The quicker blood glucose returned from nadir to baseline (fasting blood glucose) values, the better was memory. Possible confound is not control for type of breakfast.	Donohoe & Benton, 2000; $N = 46$ female undergraduates, fasting GTT

Type of Test & Description	Cognitive process assessed	General Findings	Reference
Word list recall – 249 nouns of A and AA frequency (Thorndike & Lorge, 1944), 3 different lists of 40 words each for 3 experimental conditions, another three sets of words served as distracter words – write as many words on sheet of paper as recalled from 40 seen on monitor, recognition test 40 pairs of words on sheet to circle word in pair that was presented, number of words correctly recognized analyzed	Memory	Glucose ingestion elevated levels, but had no effect on memory performance (3 different glucose solutions: 0g glucose, 30g, & 100g). Power analysis performed and sample size was sufficiently large to result in 80% probability of detecting a medium treatment effect at .05. No memory enhancement effect for glucose in young, healthy normal adults.	Azari, 1991; $N = 18$ males, fasting
Word recall – recall a list of words	Working memory	Number of words recalled correlated significantly with blood glucose levels (50 g glucose drink); blood glucose levels increasing remembered significantly more words than those whose levels were falling; glucose induced improvement in memory occurred throughout range of blood glucose levels.	Benton & Owens, 1993; $N = 153$ (word list), $N = 96$ (spatial) (Exp 1), $N = 53$ (Exp 2)
	Declarative memory (consciously recalled/ declared verbally)	Blood glucose associated with better recall of list.	Benton, Owens, & Parker, 1994; $N = 70$ (Exp 1), $N = 50$ (Exp 2), fasting
		Time taken to recall significantly greater when fast versus breakfast.	Benton & Parker, 1998; fasting, $N = 33$ (Exp 1*), $N = 80$ (Exp 2), $N = 137$ (Exp 3)
	List learning of high imagery words versus low imagery words	Poorer recall if subject had poor glucose regulation – for both concrete (high imagery) and abstract (low imagery words) for immediate and delayed recall; but glucose ingestion (50 g) eliminated this difference.	Messier, Desrochers, & Gagnon, 1999; $N = 36$
Two lists of 15 words, task to allowed 5 min to study list, write down as many of the words from the list within 1 min, task number of correctly recalled words	Word memory	No significant difference between placebo and glucose condition (25 g glucose); may be reciprocal relationship between task performance and falling blood glucose levels. Task involves retrieval of recently (not past) over-learned material – authors suggest maybe cognitive demand than domain of task that is susceptible.	Scholey, Harper, & Kennedy, 2001; $N = 20$, fasting
		Performance quicker when breakfast taken than fasting; but taking breakfast not influence number of errors; correlations between performance on test of immediate recall and blood g failed to reach statistical significance; time taken not number of errors associated with blood glucose levels.	Benton & Sargent, 1992; $N = 33$, fasting
	High- and low-imagery word recall	High-imagery nouns more easily learned than low-imagery nouns – high blood glucose levels showed significantly superior recall in both high- and low-imagery pairs; controlled for diurnal variations and sleep patterns; optimal condition for learning paired associates while blood glucose greater than 130mg/100cc and when high-imagery nouns presented.	Lapp, 1981; $N = 36$

Type of Test & Description	Cognitive process assessed	General Findings	Reference
	Immediate and delayed recall	Glucose drinkers significantly faster than placebo drinkers and recalled more words (50 g glucose drink); time taken for recall not significantly influenced by changing (rising/falling) bg levels or level of demand (sit vs. RIPT) for glucose or placebo drinkers.	Donohoe & Benton, 1999b; $N = 188$
	Abstract and concrete word recall	Significant effect on type of breakfast, consumption of high SAG (slowly available glucose) associated with better memory throughout the morning, greatest difference at 210 min after, more for abstract words than concrete / Learning performance of adult rats significantly better 3 hr after a high SAG rather than high RAG (rapidly available glucose) breakfast.	Benton, Ruffin, Lassel, Nabb, Messaoudi, Vinoy, et al., 2003; $N = 106$ fasting females, $N = 48$ Wistar rats
Word Retrieval – easy form of task, ask to generate (out loud) as many words w/either letter "S" or letter "A"	Verbal fluency, access to and retrieval of information stored in long-term memory	Increased number of responses in glucose condition (25 g) vs. placebo (30 mg of saccharin).	Scholey, Harper, & Kennedy, 2001; $N = 20$, fasting

APPENDIX: ANNOTATED BIBLIOGRAPHY

American Diabetes Association, the Endocrine Society, & the American Medical Association (1973). Special report: Statement on hypoglycemia. *Diabetes*, *22*, 137.
This one-page special report describes the mis-attribution of symptoms to hypoglycemia. Defines hypoglycemia as "low blood sugar." The author(s) warn of over-diagnosis of hypoglycemia, and describe the many cause of hypoglycemia. Also, describes adrenal insufficiency – that hypoglycemia is a symptom of this.

Anderson, R. W., & Lev-Ran, A. (1985). Hypoglycemia: The standard and the fiction. *Psychosomatics, 26*(1), 38–47.
The authors (one a medical doctor, the other a Ph.D.) describe the danger in over- and mis-diagnosing individuals with hypoglycemia. They stress the importance of using and interpreting the GTT accurately. Of 135 patients suspected of having hypoglycemia, only 4 were found in the clinic, using appropriate assessment tools, to be true functional hypoglycemics. They warn of the dangers of disregarding the criteria for correct diagnosis.

Azari, N. P. (1991). Effects of glucose on memory processes in young adults. *Psychopharmacology, 105*, 521–524.
This investigation by Azari found no effect of glucose thirty minutes post-glucose consumption (three doses: 0, 30, 100 g) on word list recall and recognition with male university students as participants (N = 18, 19–25 years of age). Azari also conducted a power calculation that showed that an effect should have been found, if one existed. Blood samples were drawn at regular intervals, but no effect of glucose on memory performance was found. Glucose measures did not correlate with memory test scores (number of words correctly recalled or recognized). These results contradict the hypothesis that glucose enhances (memory) performance in young, healthy non-diabetic adults. Azari criticizes the vast findings on blood glucose and memory – he discusses the lack of glucose dosage standardization.

Barrilla, J. (1999, Dec). Get a grip on glucose. *Better Nutrition*. Retrieved January, 26, 2003, from http://www.findarticles.com/cf 0/mOFKA/12 61/59535041/print.jhtml
This non-peer-reviewed article, describes type I and type II diabetes in layman's terms. Barilla describes how insulin is the main blood-controlling hormone that is needed by our bodies to help convert the foods we eat into energy. Insulin is released when we eat, so that the cells can take in the sugar, or store it for use later. When too much insulin is released, it results in low blood sugar, or hypoglycemia. Barilla describes Type I diabetes, where the body cannot make insulin—it has to use stored fat as fuel—a toxic compound called ketone bodies are generated. Type II diabetes, non-insulin-dependent diabetes, is a metabolic disorder from the body's inability to make enough or not use insulin properly. Insulin resistance is when the pancreas makes too much insulin and the cells develop a resistance to it. Type II is much more common. It's nearly epidemic due to obesity and sedentary lifestyles. He states how supplements are described to help maintain good blood sugar control: alpha-lipoic acid (specialized supplement), B vitamins (vitamin), Chromium (mineral), Magnesium (mineral), Good fats: omega-3 fatty acids (fish oil, polyunsaturated fatty acids) (food components), and Gymnema sylvestre (herbs). The symptoms of diabetes include: frequent urina-tion, unusual thirst, extreme hunger, recurring skin/gum/bladder infections, blurred vision, unusual

weight loss, cuts/bruises that are slow to heal, extreme fatigue, tingling/numbness in the hands/feet, and/or irritability.

Benton, D. (1990). The impact of increasing blood glucose on psychological functioning. *Biological Psychology, 30*, 13–19.

From the Department of Psychology at University College at Swansea, Benton conducted two experiments that investigated the effect of increasing blood glucose levels on a digit monitoring task and a computerized hand-eye coordination task. College student participants fasted four hours prior to experiment 1 ($N = 20$, males only), and 25 grams of glucose (or a placebo) was used in both experiments. Experiment 2 included male and female students ($N = 40$). In experiment 1, performance on the digit-monitoring task was affected; participants performing simple calculations while monitoring numbers on a computer screen produced significantly fewer errors by consuming a glucose versus a placebo drink. In experiment 2, participants performed a hand-eye coordination task in which they watched a computer screen and turned a knob to place an electronic bat in front of the path of an electronic ball (level of difficulty was adjusted to "high" – fast ball and 40 degree angle). While performing this task, participants also performed mental arithmetic every 15s for 20 minutes. They were told to focus on the arithmetic task, since it was the more important task. Performance on the coordination task in experiment 2 was unaffected by glucose, with participants producing more calculation errors (although this was not significant). This study challenges the notion that blood glucose levels affect more complex tasks than simpler tasks – the digit monitoring while performing basic calculations task was viewed as a simpler task than the hand-eye coordination and arithmetic task. The author suggests varying task demands and duration in future studies.

Benton, D. (2002). Carbohydrate ingestion, blood glucose and mood. *Neuroscience and Biobehavioral Reviews, 26*, 293–308.

This is a review by David Benton, from the University of Wales that provides an overall description of blood glucose, carbohydrates, hypoglycemia, and mood. Better mood is associated with eating breakfast rather than fasting – this has clear support. He cautions the anecdotal claims that sugar effects increased subjective energy; when evidence tends to support the contrary, that carbohydrate intake actually increases arousal. He describes the role of blood glucose in preventing the decline in mood while individuals perform demanding tasks. Benton suggests using proteins/fats/ carbohydrates to diagnose reactive hypoglycemia that would reflect reactions to more normal (realistic) diets of humans. Irritability and aggression in individuals, not described as hypoglycemic, were shown in studies by Donohoe and Benton (1999, "Blood glucose control and aggressive in females"). Studies with children and young adults showed that glucose reduced the effects of frustration and irritability when participants were engaged in a frustrating computer games/tasks. Quickly falling blood glucose levels have been associated with aggression (author describes the Quolla Indians in Peru and their tendency towards high sugar consumption and violent culture; and studies with undergraduate students). Benton describes the Wurtman proposal that "carbohydrate intake increases the synthesis of serotonin in the brain…and that the rate of serotonin synthesis was normally controlled by food intake and that individuals eat high carbohydrate foods not only for their taste, but for the psycho-pharmacological effects" (e.g., PMS, SAD). Simply stated, they eat food rich in carbohydrates to enhance their mood (relieve depression). Good evidence has shown that a meal almost exclusively made up of carbohydrates will raise tryptophan levels (but as little as 5% of protein will prevent this increased provision); however, even if tryptophan increases it does not necessarily increase release of serotonin. In another section, Benton describes womens' cravings during the menstrual cycle and

determines that it is not necessarily a craving only for high carbohydrate foods, but increases in appetite, metabolic rate, and caloric intake including foods high in both fat and carbohydrate. He also describes several studies that found that diets higher in carbohydrate are associated with better mood. He cites a study by Castro (1987) that found that a higher intake of carbohydrate was associated with feeling more energetic. He describes the optimal combination of fat and sugar for humans is 24.5% fat, 7.6% sugar (chocolate is close to hedonic ideal). A section on chocolate cravings and how this craving is associated with those who are bored, anxious, or poor mood (mostly poor mood) – Benton suggests that it is not only the receptor sites that are affected by chocolate consumption, but also taste and mouth-feel of chocolate. Benton continues to discuss the association between negative mood and increased intake of high carbohydrate/high fat foods – eating palatable foods to increase endorphins. Benton describes stress in relation to eating and compares the behaviors of restrained versus emotional eaters. The author describes how much of a rarity hypoglycemia is and states that it is unlikely that a normal individual will regularly, if ever, consume large amounts of sugar on an empty stomach and then wait for 3 hours without eating again. However, this may be the very issue of concern for certain populations – there may be more evidence of change of blood glucose concentrations in healthy participants in everyday life. He also describes his snack experiment with the larger breakfast causing poorer mood later in the morning, with the effect being reversed by eating a snack. Benton describes Thayer's (1987) study where individuals ate a candy snack that increased energy after 20 min, but the feeling of energy declined after 1–2 hours; carbohydrate intake is associated with feeling less energetic about 2 hours afterwards. Determining the optimal timing of a mood measurement in future research studies is critical.

Benton, D., Brett, V., Brain, P. F. (1987). Glucose improves attention and reaction to frustration in children. *Biological Psychology, 24*, **95–100.**
The authors, researchers from the University College in Swansea investigated the effect of glucose or a placebo on children to measure the effect on attention and frustration in the afternoon (after lunch). The sustaining attention task involved the children pushing a button when a light appeared (measuring reaction time), while the frustration test involved having the child place a bat in front of an electronic ball during the computer game. Researchers could adjust the speed of the ball – aim was to measure the reaction to the difficult task. Behavior on the task was grouped into 4 categories: quietly concentrating, fidgeting, signs of frustration, and talking. These are all clearly defined categories (article contains more descriptions of behaviors). Children who received the glucose had significantly faster reaction times. Children who took the glucose drink were more likely to concentrate during the trials, while children who took the placebo were more likely to fidget, show signs of frustration, and more likely to talk. Blood glucose levels weren't measured in this study. The authors suggest that the results may reflect a negative reaction to saccharine than a positive reaction to glucose, and that it may be due to ages of children (especially the many developmental changes that occur during age-related critical changes), the tasks and time of day may also be factors.

Benton, D., & Nabb, S. (2003). Carbohydrate, memory, and mood. *Nutrition Reviews, 61*(5), **S61–S67.**
Authors from the Department of Psychology, University of Wales Swansea, UK, provide a brief but useful overall review of glucose and the brain, carbohydrates, and mood. They describe how the brain relies on a continuous supply of glucose to function, which can be depleted in a matter of minutes (small reserves). The energy requirement of the brain is disproportionately large and is responsible for 20% of the body's energy consumption yet, accounts for only 2% of the body's

weight. The question of whether the brain is well supplied with glucose remains debatable. Glucose goes to the parts of the brain that are required to perform a particular task – increased mental activity results in increased metabolism of glucose. The supply and demand for glucose (glucose benefits tasks that are cognitively demanding—later not earlier stages of a task, more difficult trials not simple) and the effect of glucose on memory (raising glucose supply is associated with increased amounts of acetylcholine—which benefits memory) is reviewed. They describe the relationship between acetylcholine and glucose, suggesting that rising glucose levels release acetylcholine from the hippocampus, an area responsible for memory. Benton and Nabb assert that the mechanism by which an increased supply of glucose enhances memory is poorly understood – again, is it the system or substrate itself or the regulation of the system? Despite this lack of clarity, they point to robust effects found in certain populations and the necessity to investigate meal type (or glycemic load) and individual glucose tolerance. A discussion on carbohydrates and meal type is given – does an association exist between patterns of meals and/or glycemic load on memory? Authors describe studies finding memory performance two hours after breakfast correlating with glucose levels. One study found that the content of the carbohydrate, and not the glucose levels, affected older participants performance on a memory task. The effect of carbohydrate on mood is also investigated; findings revealed an association between mood and carbohydrate based on a cumulative effect (over several days) and not around the time of eating – in one study, the more carbohydrate consumed the happier participants reported they were in the morning. Timing after consumption to test the effect of carbohydrate on mood is addressed. Increased energy was reported after 15, 30, or 60 minutes, but decreased energy was reported after two hours. Authors describe a two-stage effect: short-term increase followed by a longer-term fall. Changing levels (rising/falling) effect on mood is explored. They emphasize that the mechanism(s) involved, by which increased glucose levels enhance memory, remain unclear and poorly understood, but that good glucose tolerance (blood glucose levels fall rapidly, following a rise after a glucose drink) results in better mood and memory. Authors consider investigating meal scheduling and effects of snacks as useful lines of future research.

Benton, D., & Owens, D. S. (1993). Blood glucose and human memory. *Psychopharmacology, 113*, 83–88.
Researchers from the University College in Swansea, UK conducted two experiments and found an association between blood glucose and word recall in young healthy adults ($N = 153$, equal numbers of males and females). Those whose blood glucose levels were increasing remembered significantly more words than those whose blood glucose levels were falling. No spatial memory support was found. In a second experiment, the number of words recalled from a word list correlated significantly with blood glucose levels but not with recall of a Wechsler story. They didn't control whether participants ate breakfast or not prior to the experiment, but this was not significant except in the placebo condition – where participants took more time in recalling words if they ate a meal before the experiment. Fifty grams of glucose was used in one of two conditions. Testing began fifteen minutes after either a glucose or placebo drink. First the memory test was given then the spatial memory test. Blood glucose levels were determined again either 15 min or 30 min later. Two groups were formed based on the change from the first to the second blood glucose measurement: those whose levels had fallen by more than 9 mg/dl and those whose levels increased by more than 18 mg/dl. Increasing or decreasing blood glucose levels did not affect recall time. Data illustrated that the glucose-induced improvement in memory occurred throughout the range of blood glucose levels.

Benton, D., Owens, D. S., & Parker, P. Y. (1994). Blood glucose influences memory and attention in young adults. *Neuropsychologia, 32*(5), 595–607.

Researchers from University College, Swansea, UK conducted two experiments to study the influence of blood glucose on memory and attention. In experiment 1, female students ($N = 70$) consumed two glucose drinks (50 grams; 25 grams respectively) or two placebo drinks after which their performance on a Rapid Information Processing Task (RIPT) and word list recall task was assessed. No dietary restrictions were enforced. For experiment 2, procedures and drinks were the same as experiment 1, but to assess attention, the Stroop task was used in male college students ($N = 50$). An association was found between glucose levels and speed of performance on two attentional tasks. Rising and falling levels during tasks are discussed. Falling blood glucose levels prior to hearing the word list was associated with better immediate recall. Participants in the placebo group with a higher initial level of glucose were associated with faster reaction times. Consistent with conclusions of other reports, blood glucose levels were associated with better recall of a word list, better performance in two tasks requiring sustained attention and quicker reaction times. In this study, the association with blood glucose levels (rising/falling) rather than the glucose drink itself was significant.

Benton, D., & Parker, P. (1998). Breakfast, blood glucose, and cognition. *American Journal of Clinical Nutrition, 67*(suppl), 772S–778S.

This article compares the findings of three studies that explored the role of increased blood glucose in improving memory function for participants who ate breakfast. An initial improvement in memory function for these participants was found to correlate with blood glucose concentrations. In subsequent studies, morning fasting was found to adversely affect the ability to recall a word list and a story read aloud, as well as, recalling items while counting backwards. Failure to eat breakfast did not affect performance on an intelligence test. It was concluded that breakfast consumption preferentially influences tasks requiring aspects of memory. In the case of both word list recall and memory while counting backwards, the decline in performance associated with not eating breakfast was reversed by the consumption of a glucose-supplemented drink. Although a morning fast also affected the ability to recall a story read aloud, the glucose drink did not reverse this decline. It appears that breakfast consumption influences cognition via several mechanisms, including an increase in blood glucose.

Benton, D., Parker, P. Y., & Donohoe, R. T. (1996). The supply of glucose to the brain and cognitive functioning. *Journal of Biosocial Science, 28*(4), 463–479.

The authors, researchers from the University in Swansea, UK provide a really useful overall review of the effect of blood glucose on cognitive functioning. The paper includes sections on young adults, older adults, those suffering with Alzheimer's disease, glucose tolerance (the difference in rate of fall/rise of non-diabetics vs. diabetics), cites and describes studies investigating several issues that are relevant to non-diabetics. Key points to remember from this article are how they describe that it is not necessarily low blood glucose levels but an individuals ability to tolerate blood glucose levels within a normal range that can affect performance. They describe how blood glucose levels which rapidly fall reflect better glucose tolerance and result in better performance on cognitive tests. They also describe how when participants have entered experiments with higher initial blood glucose levels; they remembered more. This paper is useful for reference of several relevant studies (included in this bibliography) investigating critical issues in blood glucose literature. It also discusses the prevailing assumption that normal range levels of blood glucose do not influence intellectual functioning, in spite of the widely accepted view that very low blood glucose (hypoglycemia)

causes physical and psychological symptoms associated with a disruption of cognitive functioning. The neural metabolic rate and cognitive functioning of young adults and older adults are examined. The increasing evidence of an association between the ability to control blood glucose and cognitive functioning was more easily demonstrated among the older participants, but can also be demonstrated in young healthy adults. The findings from these studies support the view that cognitively demanding situations can locally deplete the brain of glucose, that a greater fall of blood glucose is associated with better cognitive functioning, and that those with higher levels of blood glucose perform cognitive tasks more efficiently.

Benton, D., Ruffin, M., Lassel, T., Nabb, S., Messaoudi, M., Vinoy, S., Desor, D., & Lang, V. (2003). The delivery rate of dietary carbohydrates affects cognitive performance in both rats and humans. *Psychopharmacology, 166*, 86–90.
The university professor from Swansea, David Benton and colleagues from Biology, Physiology, and Nutrition laboratories in France investigated the delivery rate of a rapidly available glucose breakfast with a high glycemic index (quicker rise, shorter duration), versus a slowly available glucose (smaller rise, longer duration) breakfast with a low glycemic index and these effects on memory in healthy female undergraduate students ($N = 106$) and Wistar rats ($N = 48$). Benton found that it was the low glycemic index breakfasts that improved memory on a word recall task of abstract and concrete words, especially later in the morning (at 210 min) for abstract words. There are individual differences in the rate of return, but the type of food an individual consumes can determine this rate of rise and fall of blood glucose levels. Animal models showed similar findings; learning performance of rats was significantly better after a slowly available breakfast versus a rapid available breakfast three hours after consumption. Whether or not participants normally ate breakfast or not had no influence on the results.

Benton, D., & Sargent, J. (1992). Breakfast, blood glucose and memory. *Biological Psychology, 33*, 207–210.
Researchers from University College of Swansea, UK investigated blood glucose and memory performance in healthy college students ($N = 33$, males and females). The participants fasted prior to the experiment, and upon arrival were either starved or provided with a breakfast drink. Memory tests were given two hours later. Performance on the spatial memory test and word list recall (immediate recall) test was quicker when breakfast was given, than for those who starved. Significant negative correlations were found for the spatial memory task between the level of blood glucose and the time taken and number of errors; that is, the higher the level of blood glucose the better the performance. The correlations between performance on the test of immediate recall and blood glucose failed to reach statistical significance. The author comments on the relatively small differences in blood glucose levels, from a normal diet, that influenced memory performance.

Benton, D., Slater, O., & Donohoe, R. T. (2001). The influence of breakfast and a snack on psychological functioning. *Physiology & Behavior, 74*, 559–571.
Researchers from University College of Swansea, UK, investigate the possible benefits of a snack on mood and memory in college students ($N = 150$, females only). They cite that previous work in this area has not found gender differences in responses to similar blood glucose manipulations used in this experiment. Likewise, whether individuals regularly ate breakfast or not was insignificant, and memory improved regardless. Participants were grouped into one of six conditions: fasted throughout the experiment, no breakfast but a snack at 11:30 a.m., and combinations of 10 g or 50 g of corn

flakes and a snack or not at 11:30 a.m. A word list was used to assess memory and a visual analogue scale was used to assess mood. Those who ate breakfast, and/or a snack reported being less hungry, as suspected. However the blood glucose levels of those who fasted remained constant; and only at 10:15 a.m. did the 10 g breakfast produce significantly higher blood glucose levels than those who had fasted. A snack after the 50 g breakfast maintained blood glucose levels for another hour. Those who ate a snack reported better mood on every mood dimension, and the number of words recalled by snackers was significantly greater than those who did not snack, but this effect was time-limited (at 11:45 a.m. but not 12:30 p.m.). Those who ate breakfast took longer to recall words, suggesting possibly better motivation. Interestingly, breakfast did not improve memory performance or mood, which conflicts with previous work. Authors suggest this may have been due to methodological differences, like familiarity with testing procedures that may have affected mood scores. Their study supports the possibility that a snack improves mood, but may depend on the contents of the previous meal. A mid-morning snack resulted in better memory if a 10 g breakfast was consumed, while the opposite occurred if an individual fasted or had a 50 g breakfast. They point out that the effects of experience and familiarity with cognitive tests may affect the negative consequences usually associated with missing breakfast.

Betteridge, D. J. (1987). Reactive hypoglycemia. *British Medical Journal, 295*, 286–7.
Short paper cautioning against the misdiagnosis of reactive hypoglycemia. Advocates determination of Whipple's triad rather than glucose tolerance tests.

Bischoff, L. G., Warzak, W. J., Maguire, K. B., & Corley, K. P. (1992). Acute and chronic effects of hypoglycemia on cognitive and psychomotor performance. *Nebraska Medical Journal, 77*(9), 253–262.
The authors, researchers from the University of Nebraska (Medical Center) and Meyer Rehabilitation Institute (Children's Hospital) provide a basic review of several studies on the acute and chronic effects of hypoglycemia on cognitive and psychomotor performance of adults and children, with and without diabetes. The paper is useful in creating a table references to about 20 studies that have used cognitive tests including the TMB, DSS, and Digit Span. The table includes categories: participants, number, and age, duration of IDDM, age of onset, dependent variables, independent variables, and major findings. Basically, the studies they cite suggest that those with and without diabetes who experience hypoglycemia (through insulin-induced experiments) exhibit performance impairments. Increased time, but not necessarily decreased accuracy has been shown in tasks such as choice reaction time, math calculations, and naming skills. They describe the two lines of investigation: the short-term insulin-induced hypoglycemia and the chronic effects of repeated hypoglycemia (due to one of several factors). Key points authors describe and cite include: performance declines prior to awareness (Stevens et al., 1989), recovery time lag (Blackman et al., 1990), non-IDDM participants exhibit slower response time in hypoglycemic conditions (Herold, 1985), slower reaction times in hypoglycemic and hyperglycemic conditions (Holmes, Hayford, Gonzales, & Weydert, 1983a), slower performance on cognitive flexibility and verbal fluency at hypoglycemia versus euglycemia or hyperglycemia, but accuracy was not affected (Holmes, Koepke, Thompson, Gyves, & Weydert, 1984), and blood glucose on visual-motor performance increased response time on reaction time tasks but no difference in error rate was found (Holmes et al., 1986 – simple vs. complex). The paper describes studies investigating early onset of diabetes (EOD) and frequent and/or severe hypoglycemic episodes. Authors bring up the issue of difficulty of comparing studies due to inequivalent measures and across young versus older diabetic participants. Other factors such as poor school

attendance may account for decreased performance of children with IDDM. Authors list key points to improve patient care. One point they raise is the need for further research on effects of hypoglycemia on specific aspect of cognitive performance and recovery time (still needs to be fully explored).

Blackman, J., Towle, V., Lewis, G., Spire, J., & Polonsky, K. (1990). Hypoglycemic thresholds for cognitive dysfunction in humans. *Diabetes, 39*, 828–835.
Researchers from the Departments of Medicine and Neurology at the University of Chicago investigated the brain functions affected by hypoglycemia using an event related P300 brain potential (ERP) measure in healthy men and women ($N = 19$) induced to hypoglycemic levels as they completed decision-making reaction time tasks. They claim that the threshold for cognitive dysfunction occurred between 59 mg/dl and 47 mg/dl. Visual and auditory ERPs were not significantly affected; however, reaction time was. Increased reaction time was exhibited during hypoglycemic sessions. No significant interaction was found between sensory modalities and glucose levels, using another event related potential measure, the P140. Authors emphasize that hypoglycemia in this instance did not appear to affect motor processes but a general slowing of the brain processes in decision making. Hypoglycemia led to reports of palpitations, difficulty thinking and concentrating (two cases of blurred vision), but symptoms disappeared when levels returned to baseline. High carbohydrate meals were provided to restore participants to normal levels. Recovery from hypoglycemic levels lagged, patients did not recovery immediately after elevating glucose levels. Authors suggest that even after mild hypoglycemia, a period of at least 45–75 min may be necessary before adequate cognitive functioning returns.

Booth, D. (1994). *The psychology of nutrition.* **London: Taylor and Francis.**
The basic elements of the chapters of the book present the following: a cognitive theory of food and drink, how a cognitive approach to appetite can provide information about the development of eating habits, and food preferences and control of food intake in infancy and childhood and throughout adulthood. It also addresses the ways in which the body might influence the mind to affect decisions about eating and drinking from a psychological viewpoint, cultural constraints on and diversification of food and drink are considered in terms of cognitive processes involved, the psychology of customers' uses of food and drink is considered from the point of view of improving the quality of match between what food businesses provide and what their customers use food and drinks for; and the heart and the diet (the psychology of healthy eating). It discusses the cognitive psychology of uses of food that are conventionally regarded as appropriate to people who are overweight; and finally, placement of the psychological science among the several different sciences and professions that deal with food, nutrition and eating behavior.

Comi, R. J. (1993). Approach to acute hypoglycemia. *Endocrinology and Metabolism Clinics of North America, 22*(2), 247–261.
The paper written by medical doctor Richard Comi, from the Department of Medicine at Dartmouth, NH and geared toward the diagnosing physician describes how hypoglycemia is a common clinical disorder with a large number of possible causes. The article reviews the definition of hypoglycemia, symptoms of hypoglycemia that are similar to any state of physiological stress, reactive hypoglycemia and hypoglycemia not only in adults, but children. Comi describes how hypoglycemic states are usually due to medication, fasting, or postprandial (post-meal or reactive hypoglycemia).

Cooper, H. (1998). Synthesizing research: A guide for literature reviews (3rd ed.). Thousand Oaks: Sage Publications.
A book, within the Applied Social Research Methods Series, which covers the stages of research syntheses, with chapters on the following: the problem formulation state, the literature search state, the date evaluation state, data analysis stage, the interpretation and presentation stage, and general issues.

Cox, D., Cryer, P., Gonder-Frederick, L., Clarke, W., Antoun, B. (1993). Perceived symptoms in the recognition of hypoglycemia. *Diabetes Care, 16*(2), 519–527.
Researchers from Washington University, MI and University of Virginia Health Sciences Center investigate recognition and reporting of hypoglycemic symptoms in diabetic individuals in survey study ($N = 41$), experimental-field study ($N = 36$), and experimental laboratory study ($N = 42$) type methods. They propose a four-step model that takes into account modifiers that can enhance and interfere with the recognition of hypoglycemia. Individuals completed surveys that required them to list symptoms that they felt indicated hypoglycemia. After completing survey data, individuals used hand-held computers to record symptoms and blood glucose values (hit/false alarm approach – hypoglycemic symptom to blood glucose correlation). For the laboratory study, individuals reported symptoms and blood was drawn every 10 minutes, with a constant insulin infusion over 120 minutes. They found that the most frequently reported symptoms associated with low blood glucose levels are: difficulty concentrating, trembling, uncoordinated, pounding heart, slowed thinking, nervous/tense and sweaty. Three of the top 5 symptoms are neuroglycopenic: difficulty concentrating, uncoordinated, slowed thinking. The number of hypoglycemic symptoms correlated significantly with the individual's ability to recognize hypoglycemia, although this did not ensure recognition. Authors emphasize that all four steps of their model are necessary: physical reaction (CNS dysfunction, counter-regulation), physical consequences (adrenegeric symptoms, neuroglycopenic symptoms), symptom detection (detected or not detected), and symptom interpretation (accurately or inaccurately interpreted), and that hypoglycemia awareness is on a continuum. Discussion includes the role of attention including distraction and the role of activity level (e.g., sitting at desk reduces awareness of uncoordination), and the utility of field-study method of assessing "hit" and "false" alarms. Also, authors also state that symptoms can be misattributed (e.g. irritability due to schedule pressure rather than low blood sugar).

Cox, D., Gonder-Frederick, L, & Clarke, W. (1993). Driving decrements in type I diabetes during moderate hypoglycemia. *Diabetes, 42*, 239–243.
Researchers from the University of Virginia Health Sciences Center investigated the effect of insulin-induced hypoglycemia individuals ($N = 25$, males and females) at mild (65 mg/dl) and moderate levels (47 mg/dl) on performance in a driving simulator. Patients were blind to the two conditions: control (entire session at euglycemia) or experimental (euglycemia, to mild levels, then to moderate levels, and return to euglycemia), sequence, and nature of target levels. Four times a day, for four minutes at a time, participants drove the simulator over two consecutive days, after fasting overnight. To minimize practice effects, participants drove the simulator for 30 minutes the evening before the study. Driving performance was assessed by steering and speed control. They found that only moderate (47 mg/dl) levels of hypoglycemia disrupted driving performance negatively, primarily affecting steering (swerving, spinning – car's yaw, time across the midline, time spent off the road). For speed control, driving more slowly at moderate levels was also found to be

significant. Almost half of these affected individuals (44%) stated they would be willing to drive under these impaired conditions. Somewhere between 65 and 47 mg/dl performance was disrupted.

Cox, D. J., Gonder-Frederick, L. A., Kovatchev, B. P., Julian, D. M., & Clarke, W. L. (2000). Progressive hypoglycemia's impact on driving simulation performance. *Diabetes Care, 23*(2), **163–170.**
Researchers from the University of Virginia Health System, VA investigated the effect of progressive hypoglycemia (72–61 mg/dl, 59–50 mg/dl, and <50 mg/dl) in diabetic individuals ($N = 37$, males and females) on performance during a simulator-driving task. Participants were infused with insulin at a rate of 18 mg/dl every five minutes to bring individuals from 101–149 mg/dl down to 40 mg/dl. Every 5 minutes, levels were sampled and participants rated their symptoms on a seven-point scale – jittery, tense, pounding heart, trembling, sweating. After practicing in the simulator, they drove it for 30 minutes. Feedback from the simulator was provided visually, aurally, and kinesthetically. During hypoglycemia participants more often drove across the midline, speeded, and used the brakes more on the open road. During some levels of hypoglycemia, all driving parameters were significantly impaired, at some point. Failing to stop at stop signs and more crashes at sudden stops occurred during the last 15 minutes of hypoglycemia. Forty three percent of impaired individuals do not take corrective action (e.g., a provided glucose drink, or pulling off the road) – patients are not likely or wait too long before treating themselves. Authors report that small sample size and realism or external validity (simulator to actual driving) may attribute to findings.

Cox, D., Gonder-Frederick, L., Schroeder, D., Cryer, P., & Clarke, W. (1993). Disruptive effects of acute hypoglycemia on speed of cognitive and motor performance. *Diabetes Care, 16*(10), 1391–3.**
Researchers, including medical doctors from the University of Virginia, Health Sciences Center and the Washington University School of Medicine, Missouri investigated the effect of hypoglycemia on cognitive and motor performance of diabetic individuals ($N = 10$, males and females). Ten healthy control participants were used but remained at normal blood glucose levels. Using the Finger Tapping Task to assess motor function and the Paced Auditory Serial Addition Task to assess cognitive function. Only cognitive task performance was impaired at 47 mg/dl, and not motor task performance. Individual differences were not influenced by gender, age, education, or hormone release (e.g., epinephrine), but on the cognitive task the lower the glucose level at hypoglycemia – the worse the performance; and the poorer the initial performance – the greater the impairment at moderate hypoglycemic levels. Authors suggest that cognitive skills are more easily disrupted than motor skills.

Craft, S., Murphy, C., & Wemstrom, J. (1994). Glucose effects on complex memory and nonmemory tasks: The influence of age, sex, and glucoregulatory response. *Psychobiology, 22*(2), 95–105.**
This article investigates the effects of glucose administration on complex memory and non memory functions in younger and older men and women. Participants were twenty-seven non-diabetic young adults (aged 19–28) and 32 older adults (aged 58–77), who fasted overnight and consumed a glucose drink (50 g dextrose) or a placebo on two separate sessions. A blood sample (using the One Touch blood sampler) was taken prior to ingesting the beverages and at 15, 30, 45, and 60 minutes. Declarative memory was assessed by paragraph recall, a modified CA Verbal Learning Test, and a pattern recall and recognition task. Procedural memory was measured using a reaction time task to

measure implicit motor memory (asterisk appears in patterned location that subject does not know). Working memory was assessed using the Paced Serial Addition Test, and verbal fluency was measured through word-list generation. To measure response inhibition the Stroop color-word interference test was used. The effect of glucose was primarily restricted to declarative memory; this was independent of complexity. Investigation suggests that older adults (aged 58–77) are more susceptible to glucose's effects than younger men and older/younger women. Sex differences raised inconsistent results (no sex differences/or women show less sensitivity to glucose administration). Glucose administration did not affect difficult/sensitive measures of working memory, procedural memory, and verbal fluency.

Cryer, P., Fisher, J., & Shamoon, H. (1994). Hypoglycemia. *Diabetes Care, 17*(7), 734–55.
Investigators from the Washington University School of Medicine, Missouri, the University of Tennessee, Tennessee, and the Albert Einstein College of Medicine, New York, provide a comprehensive technical review on hypoglycemia. The review discusses diagnosis using Whipple's triad: symptoms compatible with hypoglycemia, a low plasma glucose concentration, and relief of symptoms after the glucose level is raised. It describes the Diabetes Control and Complications Trail (DCCT), where data on the frequency of severe symptoms was collected in diabetics. Research is cited that has determined that the brain is reliant on a continuous supply of glucose. Individuals are encouraged to learn to recognize the symptoms of hypoglycemia that are relevant to them and that the first symptoms are those of neuroglycopenia that means that often it is too late for patients to treat themselves. It describes how most episodes can be treated with a carbohydrate-containing drink or snack, and that the smaller the treatment-dose the more transient the relief of symptoms. Since effective glycemic control ameliorates problems, more research in this area is required (especially for reducing long-term complications). It is suggested that the goal would be for individuals to maintain higher than optimal glucose levels, rather than euglycemia – at least initially. It also provides discussion on symptoms, treatment, management and prevention of and defenses against hypoglycemia in IDDM and NIDDM individuals.

Cummings, J. L. C. (1996). Assessment: Neuropsychological testing of adults. Considerations for neurologists. Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. *Neurology, 47*(2), 592–599.
This special report through the American Academy of Neurology provides an overview of the types of tests and caveats in using such tests (e.g., validity, sensitivity, gender differences, etc.) to assess brain diseases and impairments. It is a useful reference that describes the types of tests typically used to assess functioning. A table shows the types of tests used to assess particular domains; for example, that Digit span is used to assess the neuropsychological domain of attention and the Trails B test is used to assess executive function.

Deary, I. J., Langan, S. J., Graham, K. S., Hepburn, D., & Frier, B. M. (1992). Recurrent severe hypoglycemia, intelligence, and speed of information processing. *Intelligence, 16*, 337–359.
From the University of Edinburgh and Royal Infirmary of Edinburgh, researchers evaluated data from previous work to investigate the effects of recurrent severe hypoglycemia on performance (e.g., IQ, reaction time, memory, and rapid visual information processing) in diabetic participants ($N = 85$) – specifically the biological-environmental effects on intelligence. The Wechsler Adult Intelligence Scale – Revised, the National Adult Reading Test, Rapid Visual Information Processing

test, the Hick Reaction Time Task, and the Sternberg Memory Scanning Test were used. Recurrent episodes had a negative effect on reaction time and a lowered response-threshold effect (i.e., more false positives on RVIP task). A significant association was found – with a reduction in IQ being associated with frequent severe hypoglycemic episodes.

Donohoe, R. T., & Benton, D. (1999a). Cognitive functioning is susceptible to the level of blood glucose. *Psychopharmacology, 145*, 378–385.
Researchers from the University of Swansea, UK, conducted two experiments that investigated the impact of blood glucose on non memory tasks and the extent to which individuals are influenced by set (assessed by the Water Jars tasks) and perceptual flexibility (assessed by Embedded Figures task) and higher level processing (assessed by a test of logical reasoning). In both experiments
(Exp 1: $N = 67$; Exp 2: $N = 69$), using female college students only, participants were allowed to eat their normal breakfast. Baseline measures were taken, participants consumed either a glucose or placebo drink, and after 20 minutes, blood glucose levels were measured again. A final blood glucose level was then determined about 50 min after taking the drink. Testing occurred between 0900 and 1300 hours. In experiment 1, there was a significant main effect of baseline blood glucose – participants solved Water Jars critical problems faster than those with lower baseline blood glucose levels. However, Logical Reasoning and Embedded Figures tasks were not affected at baseline blood glucose levels. In experiment 2, performance on Block Design was not affected by a glucose drink (50 g). However, consumption of a glucose drink, as compared to a placebo drink, resulted in faster performance on the Porteus Maze task (assesses supervisory attentional system) and greater Verbal Fluency (assesses supervisory attentional system). Glucose drinkers generated significantly more words on the Verbal Fluency task after the glucose drink than after the placebo drink. A fall in blood glucose after a glucose drink was associated with faster performance on the Block Design and Porteus Maze tasks (this was thought to reflect better glucose tolerance). In the present study, it was the difficult rather than easy tasks and trials that were influenced and susceptible to blood glucose. An increased supply of glucose appears to benefit more demanding tasks.

Donohoe, R., & Benton, D. (1999b). Declining blood glucose levels after a cognitively demanding task predict subsequent memory. *Nutritional Neuroscience, 2*, 413–424.
Researchers investigate the question of why falling blood glucose levels are beneficial in some situations, whereas rising levels benefit others. Female undergraduate college students ($N = 180$) ate a normal breakfast and were provided either a 50 gram glucose drink or a placebo drink (double-blind procedure). Baseline measures were taken. They were then grouped into a demand condition (completing cognitive tasks) or a non-demanding condition, where they just sat quietly. The Rapid Information Processing Task (RIPT) was used to assess working memory – individuals press a space bar for odd/even digits. Individuals performed the RIPT for 10 min while the control group sat quietly. Twenty minutes later, a second blood glucose level sample was taken, a memory task was presented, a distracter personality questionnaire was given, and then a delayed recall of word list was given. The experiment lasted 40 minutes. In looking at the effect of the drink, glucose drinkers recalled more words and were significantly faster than those in the placebo group. Baseline levels did not affect number of words recalled or time taken for recall. Changing blood glucose levels were not significant except for those participants in the demand condition (with glucose drink) who had better recall if their blood glucose levels were falling rather than rising. Performance on the RIPT task was similar; fewer errors were made when levels were falling during performance than those whose levels were rising. Placebo drinkers made more errors on the vigilance task than glucose

drinkers. The study describes the ability to predict performance. Researchers suggest that during conditions of increased demand and increased glucose supply, the ability to utilize blood glucose can predict performance. Their findings led them to further hypothesize that declining blood glucose levels are associated with enhanced memory but only when individuals are doing cognitively demanding tasks. The difficulty, authors suggest, is finding demanding and complex enough tasks. It is reiterated that falling blood glucose levels reflect the uptake of glucose by the brain, and authors comment that cognitive demand can induce levels of circulating glucose and that if there's a neuronal demand, one may only be restricted by the supply of glucose as fuel.

Donohoe, R., & Benton, D. (2000). Glucose tolerance predicts performance on tests of memory and cognition. *Physiology & Behavior, 71***, 395–401.**
Authors from the University of Swansea, UK, investigate the ability to control blood glucose levels and it's possible influence on memory and other aspects of cognition, using healthy young adult females ($N = 46$), who participated in two sessions. On the first session, after an overnight fast, a glucose tolerance test (GTT) was given. Participants remained quiet with no eating or drinking for 3.5 hours. On the second session, dietary restrictions were not enforced (ate breakfast) and participants completed cognitive tests (word recall—immediate and delayed, reaction time task, and vigilance task—monitoring odd/even numerical sequences). Performance on these tests was compared with glucose tolerance (session 1) and to blood glucose control during the tasks (session 2). They found that the brain is susceptible to fluctuations—within a normal range (not necessarily hypoglycemic levels)—and that the brain is susceptible to aspects of physiology (perhaps hormonal). GTT data showed that the quicker blood glucose levels returned to baseline (ability to regain baseline values) from nadir (the lowest blood glucose point) the better memory performance was. The faster the falling blood glucose levels the quicker the decision time. The profile of good glucose tolerance was associated with enhanced performance on cognitive tasks. Some caveats to this study state how breakfast type was not recorded, and that different breakfast compositions can have different effects on glucose levels (e.g., higher carbohydrate meal = higher blood glucose levels vs. combined carbohydrate and fat meal). Authors suggest separating physiology from psychological measures because questions remain on what leads to enhanced performance. Is it due to re-uptake that is associated with a decline in blood glucose or is it due to an increased metabolic rate, induced by increased motivation that leads to enhanced performance. The mechanism(s) and/or mediating factors remain to be explored.

Driesen, N., Cox, D., Gonder-Frederick, L., & Clarke, W. (1995). Reaction time impairment in insulin-dependent diabetes: Task complexity, blood glucose levels, and individual differences. *Neuropsychology***, 9(2), 246–254.**
Researchers from the University of Memphis and University of Virginia Health Sciences Center, investigated the effect of hypoglycemia on reaction time (simple, choice, and complex) in insulin dependent diabetic (IDDM) participants ($N = 25$, males and females). Participants were induced from euglycemia (80–120 mg/dl) to mild (55–70 mg/dl), to moderate (33–50 mg/dl) blood glucose levels and returned to euglycemia on an experimental day. A control day where no glucose deprivation occurred was part of the experiment. A table of references of eleven papers on the effects of blood glucose on simple reaction time is provided. Comparisons showed that performance on all reaction time tasks significantly slowed during the moderate versus the baseline (euglycemic) period. There were increased performance errors on the complex RT task at moderate hypoglycemia, but no effect was found for hypoglycemic effect on error scores for the choice RT task. No signifi-

cant differences were found between men and women in hypoglycemic sensitivity (measured by residual scores). A non-significant trend showed slowing at mild hypoglycemia on every task. Hypoglycemia slowed performance on both simple and complex tasks. However, while speed was affected equally on simple and complex tasks – at moderate hypoglycemia increased errors resulted on complex tasks but accuracy on simpler tasks was preserved. This was attributed to the testing apparatus employed. Authors found that hypoglycemia increases reaction time, that simple tasks may be less affected, and suggest that future studies exert more experimental control (matching control participants) and focus on residual performance deficits (after return to euglycemia).

Dye, L., Lluch, A., & Blundell, J. (2000). Macronutrients and mental performance. *Nutrition Research, 16*(10), 1021–1034.
The authors, researchers from the University of Leeds, UK, review the literature on the effects of macronutrients (e.g., protein, fat, carbohydrates and combinations of these types of nutrients) on mental performance. They describe the theoretical basis for glucose studies – with research establishing the beneficial action of glucose on performance. They provide a good basis of the overall findings of hypoglycemia (good glucose tolerance is defined as the ability to transport glucose from the bloodstream to the brain), blood glucose research (individual responses, men more affected than women, higher IQ's more impaired than lower IQ's – but this may depend on task type), and criticisms and suggestions for methodologies (lack in details about food compositions, need appropriate task difficulty/demand, determine if effect is task specific or a net effect). A table of the functions assessed by cognitive tests is provided, as well as tables to references of studies investigating effects of different dietary components on performance (e.g., carbohydrate and fat manipulations). A discussion of mitigating factors such as alcohol, circadian rhythms, type of tasks – specifically cognitive demand, populations used, and habitual diet is provided.

Evans, M. L., Pernet, A., Lomas, J., Jones, J., & Amiel, S. A. (2000). Delay in onset of awareness of acute hypoglycemia and of restoration of cognitive performance during recovery. *Diabetes Care, 23*(7), 893–898.
Researchers from the Yale University School of Medicine, Connecticut, and from the GKT School of Medicine, London, UK, investigated the speed of and recovery from acute hypoglycemia (48 ±0.36 mg/dl) in healthy male participants ($N = 8$). Participants were induced to hypoglycemic levels on one of two sessions (experimental and control). Using a test battery to assess cognitive performance (Stroop, Trail Making B, 4-Choice reaction time), performance did not change during euglycemia; however, during hypoglycemia performance on the 4-choice reaction time task, and Stroop and color-word sub-test was significantly impaired. No significant effect of hypoglycemia on performance on the TMB test was found. Authors suggest this was due to the large variability found in performance during the practice trails at euglycemia. Performance differed on test type after individuals were returned to normal levels. Stroop and color-word performance returned to euglycemia performance levels after restoration from hypoglycemia; however, 4-choice reaction time remained significantly impaired twenty minutes after blood glucose levels had recovered. Using sensitive measures, they found that individuals become impaired immediately after reaching significant hypoglycemia – and suggest that this twenty-minute lag time may be even longer than their results suggest. After the onset of hypoglycemia nadir (lowest blood glucose level point) and after detectable cognitive dysfunction, symptom generation was delayed. By the time individuals realized their impairment (symptom awareness), their cognitive functions were affected for some time. While neuroglycopenic symptoms diminished once individuals were returned to euglycemic levels – total

symptom recovery took up to twenty minutes to be restored (some brain functions continued to be impaired).

Feskanich, D., Buzzard, M., Welch, B., Asp, E., Dieleman, L., Chong, K., & Bartsch, G. (1988). Comparison of a computerized and a manual method of food coding for nutrient intake studies. *Journal of the American Dietetic Association*, *88*(10), 1263–7.

Researchers from the University of Minnesota, MN, compared performance of data entry (processing) time on the Dietary Data Collection (DDC) microcomputer with manual methods. The microcomputer design, simplicity, flexibility, standardization, and efficiency are described. Using a phase I version of the DDC microcomputer, five coders (including 1 trainee coder) entered food data over thirty-two days. The average processing time was shorter using the DDC system than when coders used the manual coding system. For three of the four codes, these times were significantly less for DDC than manual coding. The coding time of the trainee was similar to the expert coders using the DDC system; however, trainee-coding time was greater than expert coders using the manual system. These findings support further development of the system for detailed food descriptions and nutrient calculations (e.g., food source, processing method, special dietary preparations, ingredients, etc.), to be used for research in human nutrition research.

Field, J. B. (1989). Hypoglycemia: Definition, clinical presentations, classification, and laboratory tests. *Endocrinology and Metabolism Clinics of North America, 18*(1), 27–43.

A professor of medicine at Rutherford provides an in-depth description from a medical perspective of what is hypoglycemia, the symptoms of hypoglycemia, physiological changes and responses to hypoglycemia, and methods of classification (Field recommends extending the glucose tolerance test to 6 hours).

Flint, R. W., & Turek, C. (2003). Glucose effects on a continuous performance test of attention in adults. *Behavioural Brain Research, 142*, 217–228.

The authors from the College of Saint Rose in Albany, NY, investigated the effect of different doses of glucose (10, 100, and 500 mg/kg, or 50 g) or a saccharin placebo on a continuous performance test called the test of variables of attention (TOVA) in healthy college students ($N = 67$, males and females). The 100 mg/kg group was the only group that showed significant changes in behavior (increased commission errors, post-commission responses, and post-commission response time variability) compared to the saccharin group. Commission errors were described as errors of impulsivity or dis-inhibition. Researchers describe how demanding tasks deplete the brain of glucose more than less demanding tasks. Glucoregulation is key to the benefits of glucose on performance. They contribute some of their lack of findings to their subject pool – "young adults are less prone to glucoregulatory instability" and by excluding those with hypo- or hyperglycemia. For dose-dependent results, the authors describe how 50 g (in adults) and 25 g (in children) are sufficient to improve performance, and that 50 g in humans and 100 mg/kg in humans and animals of glucose improves memory. However, they describe how, in some studies, glucose has shown impairments in comparison to saccharin in young adults (they cite Craft et al., 1994 study). They state that the cause of this is not clear, but suggest that others have described a possible effect of increased proactive interference or accelerated glucose uptake (which may over-stimulate the mechanisms for memory consolidation). They describe an upright U-dose-response curve for commission-related responses – that a moderate dose of glucose (100 mg/kg) impaired performance while smaller/larger doses had no significant effect. They suggest that a lack of finding a correlation between attention and blood

glucose dose was possibly due to a lack of sufficient time to record the gluco-regulatory response. They recommend a conservative interpretation for their failure to find a significant effect and state that variability was high among the groups and that their study may lack the statistical power to detect group differences. One of their main purposes was to determine if/how test administrators (psychiatrists, etc.) should impose dietary restrictions (fasting) before testing. Conflicting results are found between this study the Holmes et al. (1983) study.

Foster, D., & Rubenstein, A. (1983). Hypoglycemia, insulinoma, and other hormone-secreting tumors of the pancreas. In Petersdorf, R. G., Adams, R. D., Braunwald, E., Isselbacher, K. J., Martin, J. B., & Wilson, J. D. (Eds.), *Harrison's Principles of Internal Medicine* **(10th ed). McGraw-Hill: New York.**
The chapter is from a well-regarded medical text on hypoglycemia. It discusses symptoms, classification, treatment, and causes of hypoglycemia (e.g., alcohol).

Foster-Powell, K., & Miller, J. B. (1995). International tables of glycemic index. *American Journal of Clinical Nutrition*, *62*, **871S–93S.**
The authors, researchers from the Department of Biochemistry, University of Sydney, Australia, provide a table of several foods tested to create a glycemic index table. This ranking of foods, based upon the blood glucose response compared with a reference food, has been demonstrated to be reproducible, which is especially important for use with dietary management of diabetics. The table provides all published data on the glycemic index (GI) of individual foods, with the study number and subject-type tested. Differences in cooking and processing markedly affect the GI – although when wide variation exists there may not be a clear explanation. Low-GI foods have been found to increase endurance time and provide higher concentrations of fuels towards the end of an exercise session; conversely, high-GI foods lead to faster replenishment. Insulin responses are associated with the rank order of the glycemic responses.

Franz, M., Horton, E., Bantle, J., Beebe, C., Brunzell, J., Coulston, A., Henry, R., Hoog-werf, B. J., & Stacpoole, P. W. (1994). Nutrition principles for the management of diabetes and related complications. *Diabetes Care, 17*(5), **490–518.**
The article provides a comprehensive review of the literature concerning the nutritional management of diabetes. It includes specific considerations regarding proteins, carbohydrates, sweeteners, fiber, sodium, alcohol, micronutrients, exercise, and obesity among others. This article could be a useful reference in investigations regarding aspartamate and sucrose effects.

Fraser, B. A., Buck, L., & McKendry, J. B. R. (1974). Psychomotor performance during insulin-induced hypoglycemia. *CMA Journal, 110*, **513–518.**
Funded by the Traffic Injury Research Foundation of Canada, researchers investigated the effect of hypoglycemia on performance (participants were either injected with insulin (test condition) or saline (placebo condition)) using a pursuit-tracking task (similar to flying) after participants fasted overnight. Signs of hypoglycemia such as sweating and tremor were seen at blood glucose levels at 32 mg/dl, and symptoms of hypoglycemia such as headache, drowsiness, numbness, blurred vision, and hunger were reported at 37 mg/dl. Impairments in tracking performance were found (speed but not accuracy was affected) at hypoglycemic levels.

Fruehwald-Schultes, B., Born, J., Kern, W., Peters, A., & Fehm, H. L. (2000). Adaptation of cognitive function to hypoglycemia in healthy men. *Diabetes Care, 23*(8), 1059–1066.
Researchers from the Medical University Luebeck, Germany, investigated the effect of a prior (and subsequent) induced hypoglycemic episode on performance in healthy participants performing various cognitive tasks – a control group who did not experience a prior-hypoglycemic episode was used for comparison. After an overnight fast, thirty participants were induced to 74, 65, 56, and 47 mg/dl blood glucose levels over a 6-hr period. At each hypoglycemic level, cognitive tests were administered. Fifteen of the participants received an antecedent hypoglycemic clamp at 56 mg/dl on the preceding testing day, while the remaining fifteen did not (control group). Evaluations of reaction time (during a vigilance task), memory (e.g., word list), mood, and auditory-evoked brain potentials (AEBPs) were made. AEBPs assessed the different stages of processing and reaction time during an auditory vigilance task. The task required that participants detect target tones (i.e., press a button as quickly as possible when s/he recognized a target) that were randomly presented among tones of varying pitches and intervals. In both groups, cognitive performance deteriorated during hypoglycemia (e.g., reaction time to target tones increased (AEBPs), short-term recall deteriorated). A prior hypoglycemic episode was also found to affect (i.e., benefit) performance when a subsequent episode was experienced. Participants in the prior-hypoglycemic episode group suffered performance decrements, but less than those the control group. Despite the deterioration in both groups, in the prior-hypoglycemic group, more words were recalled on average, reaction time to target tones was less prolonged, and affects on brain processing were less pronounced at hypoglycemia than in the control group.

Gastineau, C. F. (1983). Is reactive hypoglycemia a clinical entity? *Mayo Clinic Proceedings, 58*, 545–549.
An editorial piece by a medical doctor, in the Division of Endocrinology/Metabolism and Internal Medicine, describes the causes and symptoms of hypoglycemia, asserts the difficulty in diagnosis of hypoglycemia (variability in accuracy of techniques), and the lack of standardized terminology used in the field to describe such conditions. He defines hypoglycemia (low concentration of blood glucose) and reactive hypoglycemia (when a few hours after oral glucose or a meal, blood glucose levels are lower than pre-consumption), and claims that reactive hypoglycemia cannot be diagnosed through a glucose tolerance test. The author states that while ingestion of sugars restores an individual's levels to normal; neurologic symptoms may be delayed. Higher mental processes seem to require more time to return to fully functioning levels, after normal blood glucose levels have been reached. Gastineau challenges patients' self-reports and poor understanding of symptoms and diagnosis of the notion of reactive hypoglycemia.

Gold, P. (1991). An Integrated Memory Regulation System: From Blood to Brain. In R. C. A. Frederickson, J. L. McGaugh, & D. L. Felton (Eds.), *Peripheral signaling of the brain: Role in neural-immune interactions, learning and memory* **(pp. 391–420). Toronto: Hogrefe and Huber.**
This book chapter provides in depth discussion of the formation of memories in relation to the systems and hormones involved (e.g., epinephrine) and how glucose acts on functions in young and old participants, and in animal studies. Age-related effects on memory, and glucose regulation are also described.

Gold, P. E. (1995). Role of glucose in regulating the brain and cognition. *American Journal of Clinical Nutrition, 61*(suppl.), 987S–95S.

Gold describes several of his and his colleagues' studies on the effects of glucose and other hormones in rats, and older individuals. He cites that studies have investigated memory formation enhancements or impairments by treatments administered shortly after an experience, and how hormones regulate memory formation (similar to descriptions by Korol and Gold, 1998) – released when animals are trained in a memory task. The author provides an example of stress-related hormones (epinephrine) that might modulate your memory of an event (e.g., car collision in parking lot better reminder of where your car is parked). Gold reports epinephrine's role in rats' foot shock avoidance training – epinephrine injection mimicks effects of an intense shock (than a less intense shock) in showing enhanced memory. He describes the action of epinephrine of releasing glucose stores into circulation (glucose may mimic effects of epinephrine on memory), and how post-training injections of glucose in rats enhanced memory performance immediately, but not later (time-dependent effects). Gold refers to the 2 brain injection sites where glucose effects on learning and memory: the amygdala and the hippocampus (area for learning and memory of spatial tasks). Other neurotransmitters may be involved when glucose metabolizes (through pyruvate) – may be the mechanism in which glucose regulates brain function. The author suggests further investigation into the role of acetylcholine in glucose's effect on learning and memory and asserts that glucose interacts at most with a limited set of neurotransmitters. Gold refers to age-related impairment rats studies, which have shown that performance declines in aged rats occur at shorter intervals (forget quicker) than declines in young rats; however, this train-test interval varies with the task – it could be due to either impairment of the substrate for learning and memory (e.g., loss of specific neurons) or due to a loss of regulators of memory storage (e.g., hormonal and neurotransmitter changes). Studies of aged rats versus young rats (looking at rapid forgetting) showed that injections of epinephrine after training results in aged rats performance mirroring young rats performance. Glucose injections before training benefited aged mice performance; aged mice performed as well as young rats (both epinephrine and glucose ameliorated age-related deficits in learning and memory in rats). Gold describes his experiments with older participants that showed that a glucose drink had an effect only on verbal declarative memory (contextual narrative prose not non-contextual word list). In older participants, explicit memory was affected by glucose but not attention, motor speed, or overall IQ; whereas, implicit memory involves separate memory stores and is less sensitive to glucose. The author describes the inverted-U dose-response curve that optimal doses for memory are those that produce concentrations near 160 mg/dl (Gold cites Parsons & Gold, 1992 study) – and how it enhances memory in humans when administered shortly after training (Gold cites Manning, Parsons, & Gold, 1992 study). He cites glucose research with Alzheimer's patients and how it benefits a broader range of cognition than in healthy participants.

Gold, A. E., Deary, I. J., MacLeod, K. M., & Frier, B. M. (1995). The effect of IQ level on the degree of cognitive deterioration experienced during acute hypoglycemia in normal humans. *Intelligence, 20*, 267–290.

Researchers from the Royal Infirmary and University of Edinburgh, Scotland, examined the influence of IQ on cognitive performance during acute hypoglycemia with non-diabetic adults ($N = 24$, males and females). Based on similar studies investigating alcohol's effects on higher IQ versus lower IQ participants, investigators hypothesized that hypoglycemic blood glucose levels (45 mg/dl) would affect lower IQ participants more negatively than higher IQ participants. Participants were divided into high and average IQ groups according to the Alice Heim 4 test and the National Adult

Reading Test. Cognitive function was assessed on four separate occasions, at least two weeks apart, during controlled euglycemia (81 mg/dl, condition A) or hypoglycemic sessions (conditions B and C) by the Four Choice Reaction Time test (CRT), Paced Auditory Serial Addition Test (PASAT), Rapid Visual Information Processing (RVIP), Digit Symbol Substitution Task (DST) and Trail-Making B (TMB) tests. In all of the tests, significant baseline differences existed between the groups, with the exception of CRT decision and movement times. A significant effect of hypoglycemia on PASAT performance was seen in the high IQ group, with significant deterioration in performance, but this was not evident in the low IQ group. Average IQ group showed significantly better scores during hypoglycemia compared to baseline scores than did the high IQ group. Hypoglycemia affected both groups during the CRT test, but only reached significance for movement. A significant negative effect of hypoglycemia on performance of movement time was seen in both condition B and C. There were no significant changes in performance during hypoglycemia between groups for the DSST, but performance did deteriorate in both groups. Hypoglycemia did not affect performance on the TMB test. Hypoglycemia did not affect RVIP hits in either condition B or C. However, there was a trend for IQ to have an effect on false alarm performance on the RVIP. There were significant differences in performance between the groups during hypoglycemia. Average IQ groups made more false-positive (less cautious) responses during hypoglycemia in both condition B and C. Authors describe the tendency for high IQ participants to be more cautious than average IQ participants during hypoglycemia. Suggestions for the contrary findings are that perhaps high IQ participants have little additional capacity (supply of glucose is maximized already) or perhaps high IQ participants utilize different neuronal pathways to perform the same tasks than average IQ participants. Level of mental efficiency may be the discriminating factor between high IQ (very efficient) and low IQ (less efficient) performance. Authors also emphasize the practicality and utility of hyperinsulinemic glucose clamp technique.

Gold, A. E., Deary, I. J., MacLeod, K. M., Thomson, K. J., & Frier, B. M. (1995). Cognitive function during insulin-induced hypoglycemia in humans: short-term cerebral adaptation does not occur. *Psychopharmacology, 119*, 325–333.
Researchers from the Department of Diabetes, Edinburgh and the University of Edinburgh, UK investigated the nature and degree of impairments of, and possible adaptation to, hypoglycemia on cognitive functions. Healthy non-diabetic participants ($N = 24$, males and females) were recruited for three different experimental sessions; euglycemia control condition (blood glucose levels at 81 mg/dl throughout condition A), induced "early" hypoglycemia (45 mg/dl with subsequent cognitive testing after 5 minutes of hypoglycemia, condition B), and induced "late hypoglycemia" (45 mg/dl with subsequent cognitive testing after 40 minutes of hypoglycemia, condition C) separated by at least two weeks apart. Tests were used to assess cognition (Paced Auditory Serial Addition Test (PASAT), Four Choice Reaction Time (CRT), Digit Symbol Substitution (DSST), Trail Making B test, and Rapid Visual Information Processing (RVIP) test), blood pressure and heart rate were monitored, and a symptom questionnaire was used. All tests showed cognitive deterioration (including differential effects on individual tests) except for the Trail-Making B test. At baseline, there were no significant differences among the three conditions for any cognitive test variable. Performance improved throughout the study on the DSST in condition A; however, performance deteriorated during hypoglycemia on the DSST test, no adaptation occurred (no significant difference between conditions B and C), and participants' recovery period scores were not significantly different from baseline scores. During hypoglycemia for both conditions B and C, there was a significant deterioration of performance on both the 4-s test and 2-test of the PASAT. There was no improvement on

PASAT performance at continued hypoglycemia. For the CRT test, performance did not change during the euglycemia control condition, although deteriorations were observed both in decision time and movement time during hypoglycemia (conditions B and C), which returned towards baseline values during the recovery period. Comparisons confirmed a significant deleterious effect of hypoglycemia on performance (A versus B versus C, $p = .01$, A versus B, $p = .03$, A versus C, $p = .01$; and on movement time: A versus B versus C, $p = .01$, A versus B, $p = .002$, A versus C, $p = .004$). The time of testing after onset of hypoglycemia (condition B versus condition C) did not affect decision time performance. After prolonged hypoglycemia (condition C), there was a trend for the movement time to be slower than in condition B ($p = .03$) – movement time deteriorated increasingly with prolonged hypoglycemia. Performance did not differ significantly from baseline during recovery. For the RVIP test, there was no significant difference in false alarms observed during any of the conditions. Authors suggest that hypoglycemia did not have an effect on performance on this test. In condition A, a slight improvement in performance was found with a slight deterioration in performance in condition C, but no change in condition B. No significant difference was found between the conditions, nor was there any effect of hypoglycemia or any difference between conditions B and C. While the difference in increased mood scores progressed from 30 to 60 minutes, this was not significant. A lack of a significant deterioration on false alarm response on the RVIP task (viewed as response caution), illustrates how accuracy tends to be preserved at the expense of speed during this stress. Authors suggest that if cerebral adaptation (baseline functioning during continuous hypoglycemia) does occur, it may depend on the degree (may need to exceed "moderate" level) of hypoglycemia and is more likely to be seen after a period of 60 minutes of continuous hypoglycemia. In this study, cerebral adaptation did not occur after 60 minutes of continuous moderate levels (45 mg/dl) of hypoglycemia.

Gold, A. E., MacLeod, K., Deary, I. J., & Frier, B. (1995). Hypoglycemia-induced cognitive dysfunction in diabetes mellitus: Effect of hypoglycemia unawareness. *Physiology and Behavior, 58*(3), 501–511.

Researchers from the Department of Diabetes, Scotland, UK and Department of Psychology, University of Edinburgh, Scotland, investigated the effect of hypoglycemia (45 mg/dl) unawareness in insulin-dependent diabetics ($N = 20$) using hyperinsulinemic glucose clamp technique and validated cognitive tests to assess performance. A control group, based on normal hypoglycemia awareness, was formed for comparison against an impaired hypoglycemia awareness group. Individuals participated in two sessions (euglycemia-hypoglycemia-euglycemia versus a maintained euglycemia session), separated by at least 2 weeks. They found that for overall cognitive performance, tests batteries demonstrated a significant difference in performance between the hypoglycemia study and the euglycemia control study (study effect $p = .001$, study by time interaction $p = .008$), illustrating a detrimental effect of hypoglycemia on overall cognitive performance. A significant difference in performance in the different cognitive tests was also observed across time in the two different studies (Test by Study by Time interaction, $p = .009$), suggesting that not all of the tests were affected equally by the changes in blood glucose at all time points. For the Trail Making B test, a significant change in performance at certain time points in all participants (study by time interaction, $p < .001$) was found. For the PASAT, hypoglycemic levels significantly affected performance during these tests, with deterioration in scores during hypoglycemia (study and study by time interactions, $p < .001$). The Digit Symbol Substitution task was also significantly affected by hypoglycemia (study effect $p = .03$; study by time effect $p < .001$). For the Rapid Visual Information Processing task, hypoglycemia significantly affected performance on this test in both groups (study

by time interaction $p = .004$). Participants with impaired awareness at hypoglycemic levels created more false positives than normal patients throughout the study (awareness effect $p = .007$, awareness by study by time interaction $p = .04$). For RVIP reaction times, participants in both groups became significantly slower during hypoglycemia (study effect and study by time interaction $p < .001$). Those with impaired awareness were more negatively affected (e.g., took longer to recovery full cognition) than those with normal awareness. Authors describe the global, rather than specific, effects of impaired hypoglycemia awareness.

Goldfine, I., Ryan, W., & Schwartz, T. (1969). The effect of glucola, diet cola, and water ingestion on blood glucose and plasma insulin. In *Proceeding of the Society for experimental Biology and Medicine*, *131*(2), Academic Press: New York.**
Researchers from the Department of Medicine, Presbyterian-St. Luke's Hospital, and the University of Illinois, Chicago, IL, investigated the effect of a sweet tasting substance on blood glucose and insulin levels. Using healthy adults ($N = 4$, males), participants were fasted overnight, and participated in three sessions either, receiving Glucola (107g of glucose), diet cola (30g saccharin), or water. At 5 minutes, insulin levels rose over 300% and to over 500% at 30 min, with Glucola ingestion. No significant rises in insulin occurred from either the diet cola or water.

Gonder-Frederick, L. A., Cox, D. J., Driesen, N. R., Ryan, C. M., & Clarke, W. L. (1994). Individual differences in neurobehavioral disruption during mild and moderate hypoglycemia in adults with IDDM. *Diabetes, 43* (1407–1412).**
Researchers from the University of Virginia investigated the effect of hypoglycemia in diabetic individuals and found that performance on various cognitive and motor tasks were negatively affected at both mild (3.6 mg/dl) and moderate (2.6 mg/dl) levels of hypoglycemia. Timed tasks included "easy" and "difficult" versions of the following; writing name and address, coin flipping (flipping either a large or small coin), serial subtractions (mentally subtracting either by 3 or 7), twos and sevens (where the participant had to locate and mark these digits in rows of letters or digits) and the trail making B (participants sequentially connect numbers and letters going from 1 to A then 2 to B and so on). Number of errors was scored for coin flipping (number of drops) and serial subtractions. Verbal fluency was scored based on the number of correct responses. Important points to note were performance impairment differences among individuals in performance (ranging from < 47 mg/dl to > 65 mg/dl) and also the differences in the rate of return to normal functioning—some remained impaired—authors suggest some individuals may be more susceptible to these effects (e.g., participants with a history of unconsciousness due to hypoglycemia showed more deterioration than participants with no such history).

Green, M. W., Taylor, M. A., Elliman, N. A., & Rhodes, O. (2001). Placebo expectancy effects in the relationship between glucose and cognition. *British Journal of Nutrition, 86*, 173–179.**
Researchers from the Institute of Food Research, Berkshire, UK, and the Department of Human Nutrition, London, UK, investigated the effect of expectancy of glucose on cognitive performance. College students ($N = 26$, male and females) abstained from food, glucose or sucrose drinks, and exercise 8 hours prior to the experiment, and entered into one of four conditions; either expecting glucose or a placebo (aspartame) and either receiving glucose (50 g) or a placebo. Cognitive (e.g., finger tapping task, recognition memory (word list recognition), verbal free-recall, and Bakan task (3 consecutive odd/even number recognition) and mood measures (visual analog) were administered. Participants made significantly more correct "hits" on the Bakan task, than in any other

condition when they were told they received glucose and actually received it. Authors state this was also the case for those in the aspartame condition who were told they received glucose. When participants were told they received aspartame drink, the content of the drink exerted no effect on performance of this task. This indicates that there might be some level of expectancy, based on the nature of the drink, underlying performance. No relevant effects were found for finger tapping or immediate verbal recall or finger tapping tasks, which is contrary to a number of studies that have found significant improvement on verbal recall. Response times were faster for the recognition memory task when participants were given glucose than when they were not, and marginal effects of expectancy (quicker responses) were shown when participants were told they received glucose. Correlational analyses showed no relationship for changing glucose levels and task performance or mood. This suggests that any improvements on the Bakan task were not completely due to the glucose content of the drink. Green and colleagues challenge findings on glucose's enhancing effects on cognition, in healthy non food deprived populations. Authors also describe an interesting effect, found in research by Kvavilashvili & Ellis (1999) of "reverse placebo effects" where participants in a positive placebo group exert less effort due to believing that their performance will be enhanced automatically.

Gross, M. D. (1985). Reactive hypoglycemia: Overlooked or overdiagnosed? *Psychosomatics, 26*(2), 110–113.
Medical doctor and professor of Psychiatry at the University of Illinois College of Medicine, Chicago, investigated psychiatric patients ($N = 72$, males and females) to determine if their symptoms would suggest a diagnosis of reactive hypoglycemia. Referred patients were given a five-hour glucose tolerance test (GTT). The criteria to determine a relationship between hypoglycemia and psychiatric symptoms were such that: the psychiatric symptoms occur during GTT at blood glucose level's lowest point, symptoms coincide with expectations (e.g., skipping a meal, high-carbohydrate meal), and symptoms are relieved by low-carbohydrate caffeine-free diet. No relationship existed between the hypoglycemia and the psychiatric symptoms. Patients believed they were hypoglycemic – when the presenting symptoms were in fact related to effective treatments used for psychiatric disorders and/or psychological problems. In many of the cases, psychotherapy or medications (e.g., antidepressants) reduced symptoms without respect to diet. Authors suggest that when patients have symptoms of hypoglycemia, it may in fact not be reactive hypoglycemia, but an emotional disturbance. They suggest that psychiatrists need to rule out a medical or neurological disorder like, reactive hypoglycemia before linking these symptoms to a psychiatric disorder.

Hale, F., Margen, S., & Rabak, D. (1981). Postprandial hypoglycemia and "psychological" symptoms. *Biological Psychiatry, 17*(1), 125–130.
Researchers from the Department of Family Medicine in Maryland, the School of Public Health at University of California, Berkeley, California, and the Department of Family Practice, Malcolm Grow USAF Medical Center, Maryland were interested in the misdiagnosis of postprandial hypoglycemia due to psychological symptoms being present at the same time. Using patients ($N = 67$) from the medical center, 5-hr glucose tolerance tests were given while mental confusion was assessed every half-hour using the Serial Sevens Test (SST). An index score was calculated (time of lowest blood glucose value subtracted from best previous time score) – to reflect the magnitude and direction of change (i.e., regression or steady improvement). For the SST, participants whose glucose nadir fell below 60 mg/dl experienced more regression in performance on the SST than participants whose nadir remained above 60 mg/dl. A Mann-Whitney test found this observed difference to

be significant ($p = .0002$). Authors conclude that mental confusion and symptoms of neuroglyco-penia (rather than the previous assumption of only adrenergic symptoms) can occur with postpran-dial hypoglycemia. The paper also provides a table of the adrenergic and neuroglycopenic symptoms associated with hypoglycemia.

Heller, S. R., Herbert, M., MacDonald, I. A., & Tattersall, R. B. (1987, August). Influence of sympathetic nervous system on hypoglycemic warning symptoms. *The Lancet*, 359–363.
Researchers from the Department of Medicine and Behavioral Sciences, and Nottingham University Medical School investigated the effect of insulin-induced hypoglycemia in both diabetic and non-diabetic individuals to assess physiological changes, symptom awareness, and performance (reaction time). They found that reaction time was longer in all groups at 58 mg/dl, remained prolonged at 45 mg/dl, and returned to normal at 81 mg/dl. Awareness of symptoms is briefly discussed.

Hoffman, R. G., Speelman, D. J., Hinnen, D. A., Conley, K. L., Guthrie, R. A., & Knapp, R. K. (1989). Changes in cortical functioning with acute hypoglycemia and hyperglycemia in Type I diabetes. *Diabetes Care, 12*(3), 193–197.
Researchers, from the University of Minnesota, University of Kansas, and Wichita State University in collaboration with several medical centers and organizations, investigated the effect of varying levels (hypoglycemia at 50 mg/dl, normoglycemia at 100 mg/dl, and hyperglycemia at 300 mg/dl) of blood glucose on performance in diabetic individuals. To assess reaction time, participants pressed a key as soon as a target light came on. Vigilance and motor control were assessed by a pursuit rotor task, where the participant tracks a dot rotating on a turntable with a stylus. Sensory motor functions and attention were assessed by the trail making A and B tests. Driving performance was also evalu-ated. Performance on several tasks (pursuit rotor and trail making B test) was negatively affected at hypoglycemic levels (50 mg/dl) as compared to normoglycemic levels. Performance (signaling, braking and acceleration) in the driving simulator was poorer for several participants during hypo-glycemia but did not reach significance. Visual reaction time was not affected by varying blood glucose levels. Hoffman and colleagues refer to work suggesting that over-learned tasks may be less affected at varying blood glucose levels (cited: Holmes, C.S., Koepke, K.M., Thompson, R.G., Gyves, P.W., & Weydert, J.A., 1984).

Holmes, C., Hayford, J., Gonzalez, J., & Weydert, J. (1983). A survey of cognitive of function-ing at different glucose levels in diabetic persons. *Diabetes Care, 6*(2), 180–185.
Researchers recruited diabetic individuals ($N = 12$), students from the University of Iowa, to investi-gate performance on several measures such as; digit supraspan, auditory verbal learning, the match-ing familiar figures test (MFFT), delayed reaction time, the Benton visual retention test, the Nelson Denny reading test, and mathematical computation to assess memory, attention, visual spatial, and academic tasks at induced varying glucose levels (hypoglycemia at 60, euglycemia at 110, and hyperglycemia at 300 mg/dl). Visual reaction time was slowed at altered blood glucose levels as compared to euglycemic levels. Reaction time performance (slowed) and mathematical calculations (time required to solve problems was slowed) were also affected at abnormal (hypoglycemic) levels. Fewer mathematic problems were solved correctly at low blood glucose levels than at euglycemic and hyperglycemic blood glucose levels. Participants correctly completed few math problems because they attempted few problems during hypoglycemia. Researchers suggest that participants must have worked slower at low blood glucose levels to main relatively high accuracy ($M = 95.7\%$),

as compared to normal ($M = 95.8\%$ accuracy) and high ($M = 98.1\%$ accuracy) blood glucose levels. Reading comprehension was not affected at varying blood glucose levels.

Holmes, C., Koepke, K. M., & Thompson, R. G. (1986). Simple versus complex performance impairments at three blood glucose levels. *Psychoneuroendocrinology, 11*(3), 353–357.
Investigators from the University of Iowa used diabetic individuals ($N = 24$) to examine if simpler or more complex tasks were affected at varying blood glucose levels (55, 110, and 300 mg/dl). Simple tasks (i.e., finger tapping task) were not affected, but more complex tasks (Go/No-Go RT, Choice RT) were negatively affected at hypoglycemic levels.

Howorka, K., Heger, G., Schabmann, A., Anderer, P., Tribl, G., & Zeitlhofer, J. (1996). Severe hypoglycaemia unawareness is associated with an early decrease in vigilance during hypogly-caemia. *Psychoneuroendocrinology, 21*(3), 295–312.
Researchers from the University of Vienna, Austria, evaluated diabetic individuals using electro-encephalography (EEG) at induced-hypoglycemic levels. Difference in vigilance was found in those with symptom awareness of hypoglycemia as compared to those who were unaware. Neuroglyco-penia was evaluated by having patients multiply two numbers. A scoring of 0–3 was recorded with a 0 =, correct answer within 15s, 1 = correct answer but subject needs longer than 15s for correct result, 2 = wrong answer but subject can multiply a one-digit by one-digit number, and 3 = subject is unable to multiply one-digit by a one-digit number. After lowering of glucose values, vigilance performance was impaired. The authors operationally define vigilance and address a critical issue of the distractions that occur due to symptoms; they suggest that performance may improve if these distracting symptoms disappear.

Howorka, K., Pumprla, J., Saletu, B., Anderer, P., Krieger, M., & Schabmann, A. (2000). Decrease of vigilance assessed by EEG-mapping in type I diabetic patients with history of recurrent severe hypoglycaemia. *Psychoneuroendocrinology, 25*(1), 85–105.
Researchers from various departments of the University of Vienna investigated recurrent severe hypoglycemia in diabetic (and non-diabetic controls) through neurophysiological evaluations of EEGs, neuropsychological tests (e.g., alphabetical cross-out test, fine motor activity), motivational measures, and other mood measures. The implications for this study (that repeated episodes signifi-cantly reduced vigilance as compared to controls) are mostly relevant for symptom unaware partici-pants who experience recurring severe hypoglycemic episodes. They state that their testing battery may not have been able to detect clinically significant differences.

Kanarek, R., & Swinney, D. (1990). Effects of food snacks on cognitive performance in male college students. *Appetite, 14*, 15–27.
Authors, from the University of Tufts, investigated the effects of food snacks on cognitive perform-ance in college-aged men in two experiments. They compared a high calorie confectionery product (Exp 1) and a high calorie yogurt snack (Exp 2) to a low calorie snack (lemon-lime diet soda without caffeine). Four cognitive tests were used; digit span recall, arithmetic reasoning, reading, and attention (continuous performance task) in both experiments. Performance on these tests at high caloric vs. low caloric snacks was compared. Cognition was tested 1-hr post-snack. Researchers found that participants recalled significantly more digits on the digit span test and responded signifi-cantly faster in the attention task when they consumed the confectionary product (Exp 1) and yogurt snack (Exp 2) than when they consumed the diet soda. In experiment 2, participants also solved

significantly more arithmetic problems in significantly less time after the yogurt snack than after the diet soda.

Kaplan, R. J., Greenwood, C. E., Winocur, G., & Wolever, T. (2000). Cognitive performance is associated with glucose regulation in healthy elderly persons and can be enhanced with glucose and dietary carbohydrates. *American Journal of Clinical Nutrition, 72*, 825–836.

In collaboration with several organizations, researchers from the University of Toronto and Trent University, Canada, recruited healthy individuals to participate in four sessions after an overnight fast and enter into one of the following conditions: consuming 50 grams of carbohydrate in a drink, instant mashed potatoes, barley, or a saccharin drink (placebo condition). Performance on tests of memory, attention, visuomotor, and attention were administered after baseline glucose level measures and then after consumption of provisions. The tests included the following three verbal memory tasks; immediate word list recall and immediate and 20-minute delayed paragraph recall. First, participants were tested on an immediate recall of a word list, then immediately after this test were tested on paragraph recall, and after a 20-minute delay were tested on recall of the same paragraph. During the delay period (20-minute period in between tests), participants completed a nonverbal distracter tasks (trail making B test and an attention tasks, where participants attended to aspects of a television program). Glucose levels were measured at 15, 60, and 105 minutes after initial consumption. Overall performance after consumption did not differ significantly from the placebo, but additional analyses suggest some benefits to performance. Baseline score and ß cell function (indicates insulin resistance) correlated with improved performance on both immediate and delayed paragraph recall for all three carbohydrates as compared to the placebo. Poor (low) ß cell function correlated with improvement on the trail making B test, but not on the attention task. Time-dependent effects were demonstrated (e.g., significant effect of time, performance at 105 minutes was better than at 15 minutes on trail making B test performance). Researchers suggest that carbohydrates may improve performance on difficult tasks and in participants with poor glucose regulation (poor ß cell function) but may have less of an effect on easy tasks and in participants with good glucose regulation.

Kennedy, D., & Scholey, A. (2000). Glucose administration, heart rate and cognitive performance: Effects of increasing mental effort. *Psychopharmacology, 149, 63–71.*

Researchers examined several hypotheses regarding glucose administration on cognitive performance and heart rate during three tasks of differing mental demand (i.e., Serial Threes, Serial Sevens, and Word Retrieval), based on the assumption that demanding tasks are associated with elevated heart rate that may serve as a mechanism to increase delivery of glucose to active brain sites. Fasting male and female college students (n = 20) came for two sessions at 24 hours apart, for 50-minute sessions. Twenty-five grams of glucose was used in one of two conditions (glucose or placebo), as a within- participants design. Heart rates were significantly higher in the glucose than in the placebo condition. A significant main effect of glucose on performance only on the Serial 7s task was found, which was rated as the most mentally demanding and elicited the highest heart rate. Participants performed significantly more subtractions on this task during the glucose than placebo condition. There was no effect of glucose on the Serial Threes for number of subtractions or number of errors. Authors state that this rules out the possibility that those in the glucose condition were exhibiting a "speed-accuracy" trade-off. Word retrieval performance was unaffected. No other studies, so far, have examined the interaction between glucose and heart rate during cognitive processing. Authors describes how the brain (or particular tasks) may be "fuel limited", that acetylcholine may play a

role like insulin and memory, and the relationship between physiology and cognitive efficiency – that is, one's physiological efficiency (resting heart rate and glucose utilization during tasks) can predict cognitive performance.

Kerr, D., MacDonald, I. A., & Tattersall, R. B. (1989). Adaptation to mild hypoglycemia in normal subjects despite sustained increases in counter-regulatory hormones. *Diabetologia, 32*(4), 249–254.

From the Department of Medicine and Physiology at University Hospital, Nottingham, UK, researchers studied healthy individuals who were induced to varying glucose levels (81, 63, 54 mg/dl) for varying durations. They focused on the effects of awareness of hypoglycemic symptoms on performance in non-diabetic individuals. Participants were assigned to one of two conditions: euglycemia at 81 mg/dl for the duration of the experiment, or after 30 minutes at 81 mg/dl being reduced to 63 mg/dl for 60 minutes, and then 54 mg/dl for another 60 minutes. Awareness of symptoms was assessed by asking participants if they felt that their blood glucose levels was low. Participants also rated symptoms (e.g., trembling, blurred vision) on a 4-point scale (e.g., absent, mild, moderate, or severe). Physiological measures (e.g., heart rate, blood pressure), hormone analysis, and reaction time (where participants press a switch in response to a flashing light and latency is recorded) were also evaluated. The majority of impairing effects (e.g., tremor, blurred vision, etc.) were demonstrated at 54 mg/dl. An improvement in reaction time performance (paralleled by a decrease in symptom score) at hypoglycemia was thought to be due to cerebral adaptation, where the brain uses alternative fuels or glucose availability is increased by blood flow. This study showed that even non-diabetic individuals experience effects at low blood glucose levels.

Korol, D. L., & Gold, P. E. (1998). Glucose, memory, and aging. *American Journal of Clinical Nutrition, 67*(suppl)*,* 764S–771S.

These authors provide an overall view of the effects of glucose administration (and possible effects of hormones – epinephrine & also heart rate) on memory and attentional processes, and state that the efficacy of glucose as a cognitive enhancer is far broader than previously thought (in populations such as healthy young adults, healthy older adults, and individuals with severe cognitive problems). They describe the memory enhancing qualities of hormones (e.g., triggered by highly emotional events). Epinephrine is one hormone that has been studied and linked to memory modulation. They also describe how glucose affects young, middle-aged, and old rodents; specifically how glucose improves learning and memory performance of older rodents in a maze task such that their performance is equivalent to performance of young rodents. They describe how the cognitive deficits in aged people may either be a problem of a diminished regulatory mechanism in addition to a loss of a storage mechanism. Korol and Gold describe their experiment with older participants versus young college students on the Wechsler Memory Scale, a paired word associated test, and memory of a prose passage, digit-span (forward/backward – immediate recall), and a test of visual memory for geometric figures. They found that only the older participants had better performance after consuming 50 g of glucose than the placebo saccharin on the prose passage. Korol and Gold also describe studies by Manning et al. (1990; 1997) that investigated older participants and other tests of verbal memory following a glucose dose. They suggest that glucose enhanced specific classes of memory. In Manning's studies, glucose improved memory for contextual verbal information from a paragraph (immediately, 40 minutes later, and 24 hours later) and from a word list – but failed to improve IQ scores, performance on short-term memory, attention, or motor function. Korol and Gold also describe how the optimal dose for memory enhancing occurs when blood glucose concentrations are

at 160 mg/dl (they refer to studies by Parsons & Gold, 1992; Manning et al., 1992). For young adult participants, research on glucose effects has been inconsistent. It's been suggested that this is due to the lack of increased difficulty of the tests used (ceiling effects). However, Korol and Gold used more difficult versions of the same types of tests in young men and women participants and found that glucose significantly enhanced performance on both immediate and delayed recall of a narrative prose passage. They note that it is important to adjust task difficulty across cognitive domains (of verbal contextual memory, verbal non contextual memory and attention). They describe past studies where glucose peaked at different times for younger versus older participants. That is, glucose peaked (from 50 g glucose dose) on average 45 minutes after consumption, while other studies show peaking within 10–30 min of consumption of a beverage. Glucose regulation was different for the younger group. They describe a study (Craft et al., 1994) where performance on recall of a prose passage was similar between young males with poor gluco-regulation and older men with good gluco-regulation. Authors also describe how glucose injections in rats were not effective in increasing acetylcholine output when rats were merely sitting in their cages – they suggest that participants need tasks of sufficient difficulty in order for cognitive-enhancing effects of glucose to be observed.

Kovatchev, B., Cox, D., Gonder-Frederick, L., Schlundt, D., & Clarke, W. (1998). Stochastic model of self-regulation decision making exemplified by decisions concerning hypoglycemia. *Health Psychology, 17*(3), 277–284.
This article describes a model or process of decision-making (including risk) during hypoglycemia and the processes involved in treating or not treating hypoglycemia (w/IDDM participants). Some key points are that hypoglycemia can occur with no perceived symptoms and that participants still made decisions to drive at impaired levels – authors suggest a need to teach patients good judgment and risk assessment skills to guide decision-making process. In their experiment, they suggest that perhaps patients' decision making was affected by the amount of feedback they were given – however, such information does not necessarily enhance accuracy or influence critical behavior (they refer to studies by Cox et al., 1991; Cox, et al., 1994). The authors re-examined their data and found that no learning effect occurred. They suggest the usefulness of their model can be used individually to assess decision-making processes and focus on the weak areas for improvement.

Lapp, J. E. (1981). Effects of glycemic alterations and noun imagery on the learning of paired associates. *Journal of Learning Disabilities, 14*, 35–38.
From McGill University, Canada, Lapp investigated whether glucose levels would affect performance on paired-associate (list) learning. Participants (11th grade students, $N = 36$) were assigned to either a low blood glucose condition (no food consumed, blood glucose levels less than 80mg/100cc) or to the high blood glucose condition, where participants ate a standard preparatory GTT diet containing 300 grams of carbohydrates – testing was carried out over several days to reduce diurnal variations and differential sleeping patterns across participants. Blood samples were drawn and those with readings of 130mg/100cc of blood remained in the data analysis for the high blood glucose condition. High-imagery nouns were more easily learned than low-imagery nouns. Both high-imagery and low-imagery noun pairs were significantly affected by glucose levels ($p < .001$). High blood glucose levels (more than 130 mg/100cc) resulted in significantly superior performance (higher recall) for both high- and low-imagery word pairs. Lapp suggests that poor performance by the low blood glucose group could have been due to hunger or distraction rather than any cerebral changes.

Lincoln, T.A., & Eaddy, J.A. (2001). *Beating the blood sugar blues*. **American Diabetes Association.**
The authors, both medical doctors, published a book by the American Diabetic Association to inform the general public about hypoglycemia, understanding blood sugar levels and what affects levels (e.g., alcohol, exercise), and functioning in daily life (e.g., traveling, hypoglycemia awareness, driving, etc.).

Lindgren, M., Eckert, B., Stenberg, G., & Agardh, C. (1996). Restitution of neurophysiological functions, performance, and subjective symptoms after moderate insulin-induced hypogly-caemia in non-diabetic men. *Diabetic Medicine, 13*(3), 218–225.
Researchers from Lund University, Sweden, recruited healthy male participants ($N = 16$) and induced them to hypoglycemic levels to assess EEG recordings, serial subtractions, symptom ratings, and event-related brain potentials (visual and auditory). Two levels of a visual search task were examined which involved either a parallel search – the target was black the distracters were white, or a serial search – the target was black and horizontal and the distracters had one or none of these features. These tasks were thought to require different levels of cognitive processing. Perform-ance on specific tasks (e.g., serial search task but on an auditory P300 component) was significantly affected at hypoglycemia. Decreased attentional processes (reflected in P300 amplitude) and increased evaluation times (reflected in P300 latency) were found during hypoglycemia at 45 mg/dl (± 7 mg/dl). Authors describe the potentially distracting effects of hypoglycemia, which may have resulted in participants' performance (i.e., missing low-intensity targets, but not high-intensity targets).

Lobmann, R., Smid, H. G. O. M., Pottag, G., Wagner, K., Heinze, H. J., & Lehnert, H. (2000). Impairment and recovery of elementary cognitive function induced by hypoglycemia in type-1 diabetic patients and healthy controls. *The Journal of Clinical Endocrinology and Metabolism, 85*(8), 2758–2766.
Researchers, from the Departments of Endocrinology and Metabolism and Neurology at Magdeburg University Medical School, Germany, recruited healthy ($n = 12$) and diabetic ($n = 12$) participants and induced them to hypoglycemic levels (plateau at 47 mg/dl lasting 30 minutes) to investigate reaction time performance and aspects of attention by evaluating event-related brain potentials and administering a cognitive task (selective attention task). The cognitive task required participants to press a button with either their left or right hand in response to letters (e.g., targets in the correct color, irrelevant non-targets) presented on a screen. Differences in stimulus selection and response selection were found at hypoglycemic levels. Overall, reaction time increased at hypoglycemic levels, but the overall difference in reaction time between the groups was not significant. Across groups, restoring euglycemia resulted in significantly shorter reaction times. However, after restora-tion to euglycemia (108 mg/dl, range 99–112 mg/dl), color selection but not response and reaction time, returned to baseline levels in healthy participants. Authors suggest that perhaps type-1 indi-viduals are better able to cope with hypoglycemic states.

Maassen, M. M., Lingenfelser, T., Glück, H., Renn, W., Eggstein, M., & Jakober, B. (1990). Cognitive and psychomotor function during hypoglycemia: A comparison between porcine and human insulin. *Neuropsychobiology, 24*, 30–36.
Researchers from the University of Tübingen, FRG, investigated different types of insulin (animal and human derived) and their effects on performance during hypoglycemia. Healthy and diabetic

participants were recruited ($N = 16$), and had their blood glucose levels reduced and evaluated at $M = 65$, 50, and 40 mg/dl. Participants completed neuropsychological tests (e.g., line tracing, reaction time). Researchers found that performance on visual reaction time was impaired during hypoglycemia. Deterioration was more apparent under porcine insulin (animal derived) than human derived insulin (at hypoglycemia and euglycemia) – reaction time performance in both groups significantly increased at hypoglycemia as compared to euglycemia (at 100 mg/dl). No significant effects on performance on the simple motor tests occurred at hypoglycemia in the psychomotor test battery.

Manning, C., Hall, J., & Gold, P. (1990). Glucose effects on memory and other neuropsychological tests in elderly humans. *Psychological Science, 1*(5), 307–311.
The authors from the University of Virginia conducted an experiment to study the effect of blood glucose levels on memory and non memory tasks in healthy older (62–84 years of age) participants ($N = 17$). Memory was assessed using a Selective Reminding Test, Logical Memory, Digit Span, and the Rey Osterreith Complex figure test. A Selective Reminding Test was used where a word list, of twelve words, was read and the subject was asked to repeat as many words as they could remember. Words that weren't recalled were then re-read and the subject was asked to repeat the entire word list again. This was repeated until all twelve words were repeated or 12 trials were completed. Scoring was based on the total number of words recalled when the words weren't presented (long-term storage), and the percentage of words immediately recalled (short-term retrieval). Logical memory was assessed using a modified version of the Wechsler Memory Scale, where a narrative passage was read and after five minutes participants recalled the passage. Forty minutes later, a second recall of this passage was recorded. Digit Span required participants to recall digits forward and backwards. The Rey Osterreith Complex Figures required participants to copy complex designs and then to draw them from memory. Cognition was assessed using the Ammon's Quick Test, where the participants were required to choose the picture that best matched a series of words from a set of four pictures. Attention was assessed using the Letter Cancellation Test, where the participants marked designated letter from a larger set of letters. Motor skill was assessed using the Finger Oscillation Test, where subjects pressed a lever attached to a counter as quickly as possible for ten seconds, with five trials per hand. Only declarative memory performance was enhanced (Logical Memory Test and Long-Term Word Memory on the Selective Reminding Test) in older participants but not other memory or other processes (Digit Span, Complex Figure, IQ test, Letter Cancellation Task, or Finger Oscillation). Glucose regulation may be an issue (i.e., brain glucose utilization may be different in aged versus young animals). Authors report that a debate exists as to whether glucose enhancement happens at storage or retrieval. The article describes the role of epinephrine on memory, and is useful for its experimental design methodology.

Martin, P. Y., & Benton, D. (1999). The influence of a glucose drink on a demanding working memory task. *Physiology & Behavior, 67*(1), 69–74.
Researchers from the University of Wales (Swansea, UK), found that in healthy young females, fasting was associated with poor performance on the Brown-Petersen task (a test of memory using recall of trigrams, e.g., QCN or KSF). No dietary restrictions were enforced, and participants had fasted or eaten their normal breakfast. On the basis of a meal record, and standard portion sizes, the energy content of the breakfast was calculated from food tables. In the majority of cases breakfast consisted of breakfast cereal and milk and/or toasted bread with butter or margarine and preserve. Four groups of participants were compared, those who had: 1) eaten breakfast and consumed a drink

that contained 50 g glucose, n = 28; 2) eaten breakfast and consumed a placebo drink, n = 25; 3) fasted and consumed a drink containing 50 g glucose, n = 12; and 4) fasted and consumed a placebo drink, n = 15. Participants gave their written informed consent, and their blood glucose was measured for the first time. Randomly and under a double-blind procedure the participants consumed either a glucose or placebo drink. The participants sat quietly for 20 min and after a second blood glucose measure, testing began. Testing lasted for 30–35 min, after which blood glucose was measured for a third time. Testing took place in the morning. A glucose drink improved memory, but did not influence those who ate breakfast. Those who took a placebo recalled less trigrams than participants in other groups. A drink containing glucose nullified the negative effects of missing breakfast, but a glucose drink did not further benefit those who ate breakfast.

McAulay, V., Deary, I., Ferguson, S., & Frier, B. (2001). Acute hypoglycemia in humans causes attentional dysfunction while nonverbal intelligence is preserved. *Diabetes Care, 24*(10), **1745–1750.**
Researchers from the University of Edinburgh, UK recruited healthy participants ($N = 20$) and induced them to euglycemic (at 81 mg/dl) and hypoglycemic (at 47 mg/dl) levels to investigate performance on cognitive tests. The Test of Everyday Attention (e.g., Map Search, Elevator Counting, Telephone Search) was used to measures various aspects of attention, and the Raven's Progressive Matrices (RPM) was used to test to assess fluid intelligence. The RPM task requires participants to identify the parts missing in diagrammatic puzzles. Researchers found that visual selective attention was significantly impaired, auditory selective attention declined, sustained attention was not affected, longer response time to complete the attentional switching task, and the divided attention task was not affected during hypoglycemia. No significant differences were found between conditions for the RPM test. They describe that many everyday complex attention tasks are likely to be impaired during moderate levels of hypoglycemia (at 47 mg/dl) in non-diabetic individuals.

McCrimmon, R., Deary, I., & Frier, B. (1997). Auditory information processing during acute insulin-induced hypoglycemia in non-diabetic human subjects. *Neuropsychologia, 35*(12), **1547–1553.**
Researchers from the University of Edinburgh, Scotland, UK investigated the effect of hypoglycemia at 47 mg/dl (as compared to the control condition with euglycemic levels at 90 mg/dl) on auditory processing in non-diabetic participants ($N = 20$) using auditory information processing tests (the Test of Basic Auditory Capabilities, TBAC) and cognitive tests (Trail Making B tests and the Digit Symbol Substitution test). Participants undertook three laboratory sessions; the initial visit was to familiarize individuals with the experiment, and during the subsequent visits half of the participants were induced to hypoglycemia for one hour and then returned to euglycemia, and the other half underwent the reverse (euglycemia then hypoglycemia). The TBAC contains eight sub tests to assess auditory capabilities such as pitch discrimination, tone loudness and duration). At hypoglycemia, auditory temporal processing and one of the three simple auditory processing tasks (temporal order discrimination) was significantly impaired. Authors describe the possibility of impairment of high-level cognitive abilities due to impairment of lower level (basic) auditory processes.

McCrimmon, R., Deary, I., Huntly, B., MacLeod, K., & Frier, B. (1996). Visual information processing during controlled hypoglycemia in humans. *Brain, 119*, **1277–1287.**
Researchers from the University of Edinburgh, UK investigated the effect of induced hypoglycemia, at 45 mg/dl as compared to euglycemia at blood glucose levels at 81 mg/dl, on visual processing in

healthy participants ($N = 20$). Individuals participated in three separate sessions (one session was a familiarization session), each at least two weeks apart. Symptoms questionnaires, psychometric tests (Trail Making B and Digit Symbol Substitution), and visual tests such as; visual acuity, stereoscopic vision (judging distances through binocular vision), contrast sensitivity (gratings of black dots on a white background giving the impression of grey lines with white spaces between them – the participants task is to discriminate between on two pages that contain the gratings), and visual information processing were administered. Scores were lower and times were longer on the cognitive tests, visual acuity was not affected, contrast sensitivity was significantly affected, inspection time and detecting visual change and movement were significantly impaired at hypoglycemia. Authors describe the negative implications on performance of stimuli that either is presented under shortened time conditions or degraded by lowering the contrast of the visual stimuli.

Merck & Co. (2001, January 31). *Hypoglycemia* **(Electronic Version). The Merck Manual: Home Edition. Retrieved January 31, 2001 from http://www.merck.com/pubs/mmanual_home/sec13/148.html.**
An on-line version of the medical reference book created by Merck & Co., that provides medical information in basic terminology to aid physicians and those without a medical background. This section on hypoglycemia describes the basics of low blood sugar, its causes, symptoms, and treatment.

Messier, C., Desrochers, A., & Gagnon, M. (1999). Effect of glucose, glucose regulation, and word imagery value on human memory. *Behavioral Neuroscience, 113*(3), 431–438.
This study followed a double-blind repeated measures design in which each participant ($N = 36$) was tested under both conditions of glucose and saccharin and served as his or her own control. Half of the participants received the glucose solution on their first visit and the other half drank the saccharin solution. The procedure of the second visit was the same as the first except that alternate lists and alternate drinks were used. Body mass index was recorded. Glucometer used to verify that blood glucose was between 72 to 108 mg/dl and verify the fasting status. Tests were performed before each session to ensure that the glucometer was accurate. The participants then ingested 240ml of a lemon-flavored beverage that contained either 50 g glucose or 50.6 mg saccharin. To make the taste of the two solutions comparable, 4 mg saccharin was added to the glucose drink. All participants were instructed not to eat or drink (except water) after midnight preceding each early morning test session. Participants given lists of individual words on a computer screen (high and low imagery words) that they would be required to recall. List learning started immediately after the blood glucose test (that was performed 10 minutes after drinking the glucose or saccharin solution). Participants were categorized within each gender as having poor or good glucoregulation. A recovery index was computed for each participant by subtracting baseline blood glucose levels from levels obtained 60 min later. A median split was then performed; all participants whose values were above the median were categorized as having poor glucoregulation and all participants with values below the median split were categorized as having good glucoregulation. This procedure was performed separately for each gender. Planned comparisons revealed that participants categorized as having poor regulation (irrespective of gender) had a poorer recall performance than participants with good regulation. This difference was observed for both concrete (high-imagery) and abstract (low-imagery) words for the immediate and delayed recalls. This poorer recall performance in participants with poor regulation was absent when these participants were tested after drinking a glucose solution. Participants characterized as having poor glucose regulation remembered fewer words during

recall than did participants with good glucoregulation, but glucose ingestion eliminated this difference. The study supports the hypothesis that poor glucoregulation is associated with reduced memory performance (even in young healthy participants) and that the ingestion of glucose can improve memory in those participants. Considering that impaired glucoregulation is an important risk factor for reduced cognitive performance in older adults, it may be important to study the development of less efficient memory performance found in younger adults and to assess its significance for cognitive performance later in life.

Messier, C., & Gagnon, M. (1996). Glucose regulation and cognitive functions: Relation to Alzheimer's diseases and diabetes. *Behavioural Brain Research, 75,* **1–11.**
Researchers from the University of Ottawa and Institute of Mental Health Research, Canada, describes studies investigating the role of glucose and impairments from Alzheimer's Disease. Authors describe the mechanisms of glucose concentrations, the role of acetylcholine, dopamine, and opiates on memory. Studies have shown the beneficial effects of glucose on those with Alzheimer's at mild but not necessarily later stages of the disease. The article also describes how glucose improves declarative memory processes and that 100 mg/dl is referred to as the optimal blood glucose level, with young and older participants showing glucose memory improvement at 140 mg/dl. Does glucose affect performance at encoding or retrieval? This remains unclear. Several conclusions are made: that glucose ingestion improves declarative memory and altered glucoregulation is associated with memory impairment, and the status of glucoregulation moderates the benefits on declarative memory in those with Alzheimer's Disease.

Mitrakou, A., Ryan, C., Veneman, T., Mokan, M., Jenssen, T., Kiss, I., Durrant, J., Cryer, P., & Gerich, J. (1991). Hierarchy of glycemic thresholds for counterregulatory hormone secretion, symptoms, and cerebral dysfunction. *American Journal of Physiology, 260,* **67–74.**
Researchers from the University of Pittsburgh, PA and Washington University School of Medicine, MO in collaboration with departments of medicine investigated hormone secretion (counterregulatory response), symptoms, and cognitive functions to determine thresholds of impairment in healthy volunteers induced to hypoglycemic levels (90, 78, 66, 54, 42 mg/dl). Cognitive functions were assessed using the Trail Making A and B tests, verbal fluency test, Stroop test, simple and choice reaction time tasks, digit vigilance, digit span, and verbal memory tests. Significant interactions were found for all but two cognitive tests (forward digit span and TMA test) at hypoglycemic levels. A hierarchy of responses occurred – a regulatory response or hormone release (around 70 mg/dl), autonomic warning symptoms (around 60 mg/dl), and onset of cognitive deterioration (around 50 mg/dl) do not occur at the same concentrations of blood glucose.

Morris, N., & Sarll, P. (2001). Drinking glucose improves listening span in students who miss breakfast. *Educational Research, 43*(2), **201–207.**
Researchers from the University of Wolverhampton, WV were interested in the effects of a glucose drink on listening span performance. Using Daneman and Carpenter's Listening Span test, non-diabetic students (*N* = 80) either consumed a glucose drink (50 grams) or a placebo (saccharin) drink and were then administered the test. Interestingly, blood glucose levels did not change (glucose group blood glucose at 84 mg/dl as compared to the placebo group at 83 mg/dl, 20 minutes post-drink consumption); however, listening span performance significantly improved (about a half sentence increase) after a glucose drink, but not after a placebo drink.

Owens, D. S., & Benton, D. (1994). The impact of raising blood glucose on reaction times. *Neuropsychobiology, 30*, 106–113.

Under the conclusion that speed of processing is faster when the availability of glucose to the brain is increased, researchers from the University of Swansea, hypothesized that the speed of reaction times might be facilitated by increasing blood glucose levels, in male and female college students (*N* = 96). Randomly, and under double-blind procedures, participants were placed in a glucose or a placebo drink condition. No dietary restrictions were enforced (i.e., fasting), but participants were classified according to changes in their levels from the first to second blood glucose measure (those whose levels had fallen by more than 9 mg/dl and those who increased by more than 18 mg/dl). Further classification by levels remaining constantly high or low during the testing was done. Rising versus falling levels and time of day (morning and afternoon) effect were examined. For the self-paced inspection time task, which assesses the rate at which information can be taken into brain for processing, participants were required to discriminate between two lines of different length. Participants pressed keys corresponding to which line was longest, and the computer calculated inspection time, and reaction times. Blood glucose levels were slightly higher in the afternoon than in the morning, at the start of the experiment; at the end of the experiment, levels were also higher in the afternoon than in the morning. For the inspection time variables, participants were classified according to the change in their blood glucose levels from the first to the second blood glucose measure, as inspection time was measured immediately after the second determination. For the measures of reaction time, subject classification was based on the change from the second to the third blood glucose measure, as the task was completed between these two measures. Two groups were formed: those whose blood glucose level had fallen by more than 9 mg/dl and those who had experienced an increase of more than 18 mg/dl. Participants who did not fall within these limits were excluded from the analysis. Owens and Benton found that simple reaction, movement time, and inspection times were unaffected by a glucose drink. However, monitoring of 8 lamps was sensitive to blood glucose levels. When researchers evaluated increasing and decreasing levels in the morning and afternoon on the 8-choice decision time, they found that participants had faster decision times if their levels were rising rather than falling. Inspection of the means indicated that participants experiencing falls in blood glucose had slower decision times than those who were rising. Significant gender differences were found on movement time and level of difficulty; males were faster than females. Interestingly, participants following their normal eating pattern and levels were within the normal range yet, their information processing performance was affected. The change in glucose levels was indicated as the critical factor as none of the participants experienced blood glucose levels low enough to diagnose hypoglycemia (40 mg/dl). Authors suggest that glucose can influence information processing under frequently occurring physiological conditions, and increasing glucose levels proved to be beneficial when performing demanding tasks.

Owens, D. S., Macdonald, I., Benton, D., Sytnik, N., Tucker, P., & Folkard, S. (1996). A Preliminary investigation into individual differences in the circadian variation of meal tolerance: Effects on mood and hunger. *Chronobiology International, 13*(6), 435–447.

Researchers from the University of Wales, UK were interested in the effects of blood glucose levels and circadian rhythms by investigating its effects on meal tolerance and on mood. Healthy female students (range 19–20 years of age) lived in a confined residence hall for 31 days with normal time of day cues during a "constant routine" period. Later, participants lived on a 27-hr day schedule – which caused a "forced-desynchrony" with 18 hours of wakefulness with 9 hours of sleep for 19 days, ending with a second period of a 26-hour "constant routine" day. Blood glucose level rates

of recovery and return to baseline varied at different times of day. Associations between participants' meal tolerance and feelings of calmness were described. Countermeasures for shift-workers and suggestions of varying dietary regimes to maintain performance and mood were suggested.

Owens, D., Parker, P., & Benton, D. (1997). Blood glucose and subjective energy following cognitive demand. *Physiology & Behavior, 62*(3), 471–478.
The authors from the University of Wales conducted three experiments to investigate the effect of glucose during a cognitive demanding and/or frustrating task (from earlier experiments with children) on mood in college students. It is interesting to note, that participants were grouped in the first experiment according to changes in blood glucose levels (greatest rises or falls within a normal range grouped) from a 50-g drink, not based of type of drink consumed. In experiment 1 (effect of glucose on mood in a frustrating situation), investigators were interested in changing blood glucose levels before testing and during testing ($N = 96$, male and female). Lower mood was reported on a 30-item mood questionnaire, if levels were falling while completing the task. Changes in blood glucose levels prior to completing the task did not influence mood. In experiment 2 (effect of raising blood glucose levels on mood during the Stroop-task), investigators were interested in whether falls in levels would result in lower mood as in experiment 1 ($N = 50$, males only). Participants received 50 g glucose or placebo then, 20 minutes later, received another 25 g glucose or placebo. Falling levels during the task resulted in reports of lower energy. Changes in levels prior to the task did not affect mood. In experiment 3 (effect of glucose on mood on a rapid information processing task, RIPT), Owens and colleagues expected to find similar results as in the two previous experiments, if not a larger effect, using the RIPT, a more demanding attentional task ($N = 70$, females only). Contrary to the two previous experiments, it was rising blood glucose levels during the task that was associated with falling subjective energy. Falling blood glucose levels prior to testing resulted in falls in energy while completing the task. In this study, no dietary restrictions (e.g., fasting) were enforced. Tension did not increase when levels fell in all three experiments. Stress can increase blood glucose levels. Authors suggest that high blood glucose levels may reflect the release of glucose (a consequence of stress) and not an inefficient glucose uptake.

Parsons, M. W., & Gold, P. E. (1992). Glucose enhancement of memory in elderly humans: An inverted-U dose-response curve. *Neurobiology of Aging, 13*, 401–404.
Researchers from the University of Virginia investigated the dose-response curve for glucose in older participants (range 60–82 years of age) using various cognitive tests (of verbal intelligence and logical memory). Using a within-subjects counterbalanced design, participants entered into one of four conditions of varying levels of glucose and/or saccharin drinks for four weeks. Logical memory performance was enhanced by glucose. They describe that the optimal glucose dose for memory is 180 mg/dl, and that blood glucose levels that are optimal for memory storage ranges from 150–175 mg/dl. Basal blood glucose differences do affect performance. Age-related memory impairments may be ameliorated by a provision of glucose.

Pollitti, E., Cueto, S., & Jacoby, E. R. (1998). Fasting and cognition in well- and undernourished schoolchildren: A review of three experimental studies. *American Journal of Clinical Nutrition, 67*(suppl), 779S–784S.
The authors conducted three experiments using male and female children from the US (Exp 1 and 2) and male children from Peru (Exp 3) to investigate the effect of breakfast (BR) or not (placebo, NBR) on memory and attention. The tests used were the Matching Familiar Figures Test (MFFT,

discriminate similar visual stimuli) and the Hagen Central Incidental Test (assesses visual stimuli and memory through determination of serial position of pictures on cards). A verbal intelligence test was also used (Picture Vocabulary Test for Exp 1 and 2; but the Slossum Intelligence Scale for Exp 3). Performance on the MFFT was negatively associated with a change in the number of errors – as glucose levels dropped, the number of errors increased. During experiment 1, on the Hagen Test, recall (for recall of animals, not for objects) was significantly better after the overnight and breakfast fast (NBR) than after breakfast (BR, 2238.4 calories) consumption. For experiment 2, error performance on the Matching Test was significantly greater after no breakfast than after breakfast (1874.4 calories). For experiment 3, simple reaction time was adversely affected by not eating breakfast for the at-risk (or nutritionally at-risk poor Peruvian families); their scanning memory speed was slower than the breakfast group. At-risk participants performance on a matching task for geometric stimulus was also affected – decision time was shorter on the day they ate breakfast than on the day they fasted. A couple of contrary findings involve performance of participants in experiment 3, participants without nutritional risk were quicker after NBR than BR on the matching geometric stimuli. Also, participants in experiment 1 showed a higher recency effect after NBR than after BR. Researchers found that attentional processes were affected by glucose. Specifically, that matching task performance was better at BR than NBR, fasting delayed performance on tasks involving selection of visual information (poor discrimination between meaningful vs. irrelevant cues). Experiment 3 showed that nutritionally at-risk children were more vulnerable to the adverse effects of fasting than well-nourished children.

Pollitti, E., & Matthews, R. (1998). Breakfast and cognition: an integrative summary. *American Journal of Clinical Nutrition, 67*(suppl.), 804S–813S.
Researchers review the breakfast literature and critically evaluate the methodologies used and conclusion reached. Tables are provided that describe several studies used to test the effects of breakfast omissions and glucose provision on cognitive performance. Authors address the challenges in the research (e.g., age, long-term breakfast studies).

Pramming, S., Thorsteinsson, B., Theilgaard, A., Pinner, E., & Binder, C. (1986). Cognitive function during hypoglycaemia in type I diabetes mellitus. *British Medical Journal (Clin Res Ed), 292*, 647–650.
Researchers from State University and Steno Memorial hospitals in Denmark induced diabetic individuals ($N = 16$) to varying blood glucose concentrations at four periods (period A at 108 mg/dl, period B at 54 mg/dl, period C at 36 mg/dl, and period D at 108 mg/dl) and assessed effects on functions using neuropsychological tests (e.g., Digit span, tapping, letter cancellation, categorizational test, story recall, serial sevens subtraction, and the trail making B test). Researchers found that only digit span deteriorated significantly between periods A and B, and between periods A and C all single test scores fell (except for the tapping test). Symptom scores were recorded and no significant changes in total symptoms scores were found during the four periods – meaning that symptoms failed to be indicators of impaired performance. Performance was affected at around 54 mg/dl on certain tasks (trail making and subtraction tests), which (as authors claim) is not usually considered hypoglycemic.

Reid, M., & Hammersley, R. (1995). Effects of carbohydrate intake on subsequent food intake and mood state. *Physiology & Behavior, 58*(3), 421–427.

Researchers from the Behavioral Sciences Group at the University of Glasgow were interested in the effects of a carbohydrate-rich drink (or a placebo, or water) on hunger and mood in healthy college students ($N = 60$). Using the Profile of Mood States (where participants were asked to rate their mood), students were tested after fasting overnight and immediately after consumption of a beverage (and at 30 and 60 minutes later). A food diary was also given to participants. They found that sucrose delayed subsequent eating. Two interesting points are that participants were allowed to leave the testing area after the second POMS administration (a potential confound if participants consumed food) and that behaviors shown in the laboratory may limit results (with participants possibly deviating from their normal eating patterns). Researchers suggest examination of food effects in a natural environment.

Rogers, P. J., & Lloyd, H. M. (1994). Nutrition and mental performance. *Proceedings of the Nutrition Society, 53*, 443–456.

Researchers from the Consumer Sciences Department of the Institute of Food Research, Reading, UK, provide a review of studies investigating the effects of meals (protein to carbohydrate proportion and effect on tryptophan release) and an overall discussion of the effect of glucose on mood and performance. Discussions also include research on the effect of alcohol and caffeine on mood and performance. Authors address the methodological challenges of studying effects of caffeine, for example, whether results are due to beneficial effects, or to deleterious effects, or a combination of both. Interesting differences in performance are noted in studies of caffeine where participants are deprived for 24 hours prior to an experiment versus one week. The beneficial effects of caffeine are discussed (e.g., increased vigilance by reducing the "post-lunch dip" effect). Authors challenge the results of breakfast findings – stating that a lack of supportive evidence exists to suggest the adverse effects of missing breakfast. Authors describe the effect on behavior via adaptation to foods over the short- and long-term. The paper describes thirteen experiments that have investigated the effect of glucose on performance, which clearly show the effect on performance occurring within one hour of consumption. No clear pattern on performance or task type affected was evident. Authors state that under normal circumstances, it is unlikely for healthy individuals to be affected by hypoglycemia levels sufficient to cause an effect. Authors challenge the notion that glucose levels affect performance. They suggest the need for clear and specific hypotheses to investigate and measure performance effects, that studies address meals or snacks at other times of the day, and increase discussions of unaffected areas of performance.

Rosenthal, M., Amiel, S. A., Yágüez, L., Bullmore, E., Hopkins, D., Evans, M., Pernet, A., Reid, H., Giampietro, V., Andrew, C. M., Suckling, J., Simmons, A., & Williams, S. C. R. (2001). The effect of acute hypoglycemia on brain function and activation. *Diabetes, 50*, 1618–1626.

Researchers from the Department of Medicine at Guy's, King's, and St. Thomas' Schools of Medicine, the Institute of Psychiatry at King's College, and Maudsley Hospital in London, UK examined the areas of the brain and cognitive tasks affected during induced hypoglycemia (45 mg/dl) as compared to euglycemic levels (90 mg/dl) in healthy participants ($N = 8$, male and female) using fMRI (Functional Magnetic Resonance Imaging) and Finger Tapping (FT), Simple Reaction Time (SRT), and Four-Choice Reaction Time (4CRT) tasks. Participants abstained from caffeine for three days prior to the experiment, and arrived fasted overnight for two different sessions (prolonged

euglycemia or euglycemia followed by hypoglycemia). Sessions were three weeks apart. Brain areas affected during each task at normal blood glucose levels were similarly affected during low blood glucose levels. However, levels of brain activation for each task differed at hypoglycemia. Performance on finger tapping and four-choice reaction time tasks deteriorated at hypoglycemic levels. Researchers found acute hypoglycemia to be task and region specific. Different tasks showed different responses to hypoglycemia; four-choice but not simple choice performance deteriorated significantly.

Schächinger, H., Cox, D., Linder, L., Brody, S., & Keller, U. (2003). Cognitive and psychomotor function in hypoglycemia: Response error patterns and retest reliability. *Pharmacology, Biochemistry, and Behavior, 75,* **915–920.**
Researchers from the University Hospital at Basel, Switzerland, University of Virginia, VA, and University of Tübingen, Germany were interested in the types of measures that would be the most reliable indicators of impairments from hypoglycemia and more closely examined performance patterns on these tests. Healthy students ($N = 17$) participated in two separate sessions (either induced to hypoglycemia at blood glucose levels at 49 mg/dl in one session, or experiencing euglycemia at 85 mg/dl throughout in another session), and completed a Paced Auditory Serial Addition Task, Choice Reaction Time Task, and a manual-tracking task. At hypoglycemia, they found an increase in RT and decreased PASAT accuracy (with increased omissions). Tracking "distance" was significantly impaired at hypoglycemia. Relatively "large" effect sizes were calculated for all of the tests, and high test-retest reliability was also found.

Scholey, A., Harper, S., & Kennedy, D. (2001). Cognitive demand and blood glucose. *Physiology & Behavior, 73*(4), **585–592.**
The researchers from the University of Northumbria, UK, investigated the effect of 25 grams (they cite their earlier work in finding this a suitable dosage to enhance performance on memory and non-memory tasks) of glucose on various cognitive measures (i.e., computerized serial sevens, word retrieval (a verbal fluency task), and word memory) of varying demanding levels, in healthy college students ($N = 20$, male and female). Regarding the procedure, they felt that testing 20 minutes after drink consumption, glucose levels would still be rising; therefore, the effects on levels would be more evident if glucose-to-task interval was 45 minutes. Generation of responses for the Serial Sevens task was affected by glucose level, significantly more responses were generated in the glucose than the placebo condition; and while statistically insignificant, the glucose condition was associated with fewer errors on this task. There was a trend for increased number of responses for the verbal fluency task in the glucose versus the placebo condition, possibly showing the effect of glucose on long-term memory (involving retrieval of past-learned information). No significant difference existed between the placebo and glucose condition on word memory performance, involving retrieval of recently over-learned information. It was suggested that this was due to the dosage (25 grams not 50 grams) and to the discrepant findings for small effects of glucose affecting verbal recall performance in young adults versus a larger effect in older participants. Authors state that these findings lend support to the notion that more cognitively demanding tasks are more affected by glucose levels. They speculate that cognitive demand may also result in a raise of glucose metabolism, which then facilitates performance on the task – this ties into heart rate and glucose research by Kennedy & Scholey (2000). Scholey and colleagues also suggest that it is the cognitive demand, rather than the domain that is susceptible to glucose enhancement as seen in the contrasting findings between the word retrieval and word memory tasks.

Scholey, A. B., & Kennedy, D. O. (2004). Cognitive and physiological effects of an "energy drink": An evaluation of the whole drink and of glucose, caffeine and herbal flavouring fractions. *Psychopharmacology, 176*, 320–330.

From Northumbria University, researchers investigated the effect of various combinations of glucose and/or caffeine in healthy participants ($N = 20$) during six separate sessions (7-days apart) and measured performance using a computerized cognitive assessment battery. The battery included tests such as; word recall, simple reaction time, digit vigilance, choice reaction time, etc.). Mood was also assessed using a visual analog scale and the Profile of Mood States. They found that performance was affected by glucose and caffeine (e.g., "energy drink") on some tasks (quality of memory), while performance on others was not significant (digit symbol substitution). Benefits largely appeared to be the result of consumption of a glucose and caffeine drink (subtraction task) without significant effects on mood. Further research on this approach is suggested.

Smid, H., Trumper, B., Pottag, G., Wagner, K., Lobmann, R., & Scheich, H. (1997). Differentiation of hypoglycemia induced cognitive impairments: An electrophysiological approach. *Brain, 120*, 1041–1056.

Researchers from the Otto-von-Guericke University in Germany and Federal Institute of Neurobiology, Germany evaluated amplitude and latencies of event-related brain potentials to investigate the effects of hypoglycemia on measures of attention, response choice, and reaction time. Inducing healthy volunteers ($N = 24$) to hypoglycemic levels at 48 mg/dl, they found that performance on a selective attention (stimulus-selection/response-choice) task was impaired (increased reaction times and error frequencies) as compared to euglycemic levels at 110 mg/dl. The task required participants to respond with their right hand to one set of criteria of stimuli, or target letters (e.g., letter G) on a computer screen, and with their left hand to another grouping of stimuli (e.g., letter N), but only if these letters were in the relevant color (e.g., red) as opposed to the irrelevant color (e.g., green). Differences were found in stimulus-selection process and response-selection. Hypoglycemia delayed both stimulus selection and the motor-response selection. Response-selection performance did not return immediately upon restoration to normal levels, but stimulus-selection did. Authors address the increase in symptoms that may create a divided attention situation, and the difference between hypoglycemia and fatigue – that it's not a universal impairment, but exerts specific effects (e.g., difficulty with response-selection, but not stimulus-selection).

Smith, A. P., Kendrick, A. M., & Maben, A. L. (1992). Effects of breakfast and caffeine on performance and mood in the late morning and after lunch. *Neuropsychobiology, 26*, 198–204.

Researchers from the University of Wales, UK investigated the effect of either: no breakfast with caffeine (4 mg), no breakfast with no caffeine, breakfast with no caffeine, and breakfast with caffeine in healthy participants ($N = 48$) on performance and mood (18-item bi-polar visual analog scale). Effects of caffeine were found, but breakfast consumption did not affect sustained attention (digit vigilance task), memory (free recall, semantic memory test), or logical reasoning. Eating breakfast had no effect on performance of a sustained attention task either early morning or after lunch. Authors suggest that the effects of breakfast on a free recall task (memory task) are restricted to a few hours after the meal. Effects on mood were time-dependent (varied according to the time of testing. Specifically, prior to lunch participants with breakfast felt more tense and proficient – but after lunch effect was reversed with the no-breakfast group feeling more proficient and energetic). This also varied with the type of breakfast consumed. Key points to note were that: 4 mg caffeine produced changes in mood – but is this a realistic dose(?) and general effects of caffeine and break-

fast were consistent across sexes. Authors describe how protein consumption leads to increased distractibility, and carbohydrate consumption leads to decreased reaction to stimuli.

Smith, A., Kendrick, A., Maben, A., & Salmon, J. (1994). Effects of breakfast and caffeine on cognitive performance, mood and cardiovascular functioning. *Appetite, 22*, **39–55.**
Researchers from the University of Wales, UK conducted two experiments using healthy participants to investigate breakfast types with mood and cognitive performance. In experiment 1, participants ($N = 48$) either: ate no-breakfast, a cooked breakfast, or a cereal/toast breakfast, and were either given decaffeinated coffee or caffeinated coffee with 4 mg/kg of caffeine in it. They found that participants' mood two hours later was affected by breakfast type, with those consuming a cooked breakfast being more content, interested, sociable and outward-going than the no breakfast and cereal/toast group. Breakfast type did not affect performance on simple reaction time, five-choice serial response, or repeated-digits vigilance tasks. In experiment 2, participants ($N = 48$) entered into similar conditions except that the cereal breakfast condition was dropped and performance measures were different. Performance on the memory tasks was affected by breakfast type. Participants given breakfast recalled significantly more words than those in the no-breakfast condition. Breakfast eaters made fewer false alarms than those in the no-breakfast condition. Mood changes and effects of caffeine were described. Performance on sustained attention tasks was improved by caffeine. Increasing the supply of glucose to the brain by breakfast consumption and the selective effects of breakfasts require further investigation. The suggestion that an occasional omission of breakfast is more deleterious than constant omission is raised.

Snorgaard, O., Lassen, L. H., Rosenfalck, A. M., & Binder, C. (1991). Glycaemic thresholds for hypoglycaemic symptoms, impairment of cognitive function, and release of counterregulatory hormones in subjects with functional hypoglycaemia. *Journal of Internal Medicine, 229*, **343–350.**
Researchers from the Steno Memorial Hospital, Denmark investigated the effects of induced-hypoglycemia (stepwise from 63, to 54 and finally to 36 mg/dl) in a healthy (control, n = 9) and a functional food-relieved hypoglycemic (patient, n = 9) group on performance using a visual reaction time test, neuropsychological tests (Digit Span, Letter Cancellation, and Trail Making A and B tests), and evaluation of symptoms and hormones. Participants abstained from alcohol for 36 hours and fasted overnight, prior to the experiment. Differences in performance between the groups were found. Reaction time increased in all participants during the hypoglycemic clamp, but glucose levels and timing of deterioration were different (e.g., between 95–115 minutes at median glucose level 52 mg/dl in the patient group, and between 115–155 minutes at median glucose level 38 mg/dl in the control group). While deterioration was more evident in the patient group, deterioration of performance scores in both groups occurred on the digit span and letter cancellation tests, and the time to complete the trail making tests increased (but not for the control group, where time remained unchanged on the trail making tests). Functional hypoglycemics showed a higher threshold for detecting signs and symptoms of hypoglycemia (47–50 mg/dl) as compared to controls (7–14 mg/dl lower). Authors state that hypoglycemic symptoms exist in every day life, despite normal blood glucose levels.

Stevens, A. B., McKane, W. R., Bell, P. M., Bell, P., King, D. J., & Hayes, J. R. (1989). Psycho-motor performance and counterregulatory responses during mild hypoglycemia in healthy volunteers. *Diabetes Care, 12*(1), 12–17.
Researchers from the Queen's University of Belfast, UK investigated the effect of insulin-induced hypoglycemia at 61 mg/dl as compared to euglycemic levels at 88 mg/dl on psychomotor perform-ance, in healthy participants ($N = 12$). Performance was measured, on two separate sessions 3 to 7 days apart, using tests such as; the Trail making test, choice reaction time, critical flicker-fusion threshold, and digit symbol substitution. Hypoglycemic symptoms were also assessed by question-naire at 0, 10, 30, 50 and 90 minutes. Participants were asked to sleep their normal hours the night before, abstain from alcohol for 2 days before, and to avoid smoking on the morning of the experi-ment. Participants were familiarized with the tests to reduce practice effects. Baseline psychomotor measures were taken before the clamp and then again between 60–95 minutes. At 50 and 90 min-utes, total symptom scores were significantly higher during hypoglycemia than at euglycemia (but no difference in scores were found at 10 and 30 minutes). Only the trail making and digit symbol substitution tests showed significant impairment during hypoglycemia.

Strachan, M. W. J., Deary, I. J., Ewing, F. M. E., Ferguson, S. S. C., Young, M. J., & Frier, B. M. (2001). Acute hypoglycemia impairs the functioning of the central but not periph-eral nervous system. *Physiology & Behavior, 72*, 83–92.
Researchers from the Royal Infirmary of Edinburgh and University of Edinburgh, UK were inter-ested in the effect of insulin-induced hypoglycemia on the peripheral and central nervous system. Healthy individuals ($N = 8$) participated in three sessions (a familiarization session, a hypoglycemic condition at 47 mg/dl, and a euglycemic condition at 90 mg/dl), separated by at least two weeks. Tests of cognitive ability (Digit symbol task, Trail making B test) and information processing (speed of information processing, reaction time, and inspection time) were administered. A self-rating hypoglycemic scale was also administered. Autonomic and neuroglycopenic symptom scores were significantly affected at hypoglycemia. Performance on the digit symbol and trail-making B test significantly deteriorated during hypoglycemia. Performance on the "difficult" rather than the "easy" subset of the speed of information processing test was slowed at acute hypoglycemia; however, number of errors was not affected. Performance also deteriorated on the inspection time task, and on the four choice reaction time task. They only induced participants to 47 mg/dl concentrations because subject experienced increased physical discomfort – and it was not necessary (or ethical) to subject participants to further discomfort. With participants acting as their own control, sample size provided 80% power to detect a 0.75 S.D. change in median nerve conduction velocities – the peripheral nervous system was not affected in the same manner by glucose (to hypoglycemic levels) as the central nervous system.

Taylor, L. A., & Rachman, S. J. (1988). The effects of blood sugar level changes on cognitive function, affective state, and somatic symptoms. *Journal of Behavioral Medicine, 11*(3), 279–291.
The authors from the University of British Columbia, Canada, investigated the hypothesis that lowered blood glucose levels are associated with impaired performance, adverse emotional changes, and somatic symptoms. They also hypothesized that these effects are greater the lower the glucose nadir (the lowest level of blood sugar achieved after the ingestion of glucose), the more rapid the decrease in blood glucose levels (or speed of fall in blood sugar between the peak and nadir), and the higher the hypoglycemic index score (the decrease in blood glucose during the 90 minutes before

nadir). Their subject pool included men and women ($N = 35$) between 21 and 66 years of age, who believed or suspected that they had hypoglycemia. Participants fasted overnight, and then participated in a Glucose Tolerance Test (GTT, using 75 grams of glucose solution). Participants reported greater mood disturbances and more bodily symptoms at low blood glucose levels (these occurred half an hour after glucose nadir), supporting Taylor and Rachman's first hypothesis. Their second hypothesis garnered less support, and authors advise that defining low blood glucose on basis of nadir is not advisable because it's possible that all participants experience symptoms below a certain level of blood sugar. Another point they bring up is that of the rate of the fall in blood sugar – that, some support was shown for increased symptoms with more rapid decreases in blood sugar. The strongest support was demonstrated for the hypothesis that symptoms are greater with higher hypoglycemic (index) scores. The hypoglycemic index takes into account several factors such as; the level of nadir, the speed of the drop in blood glucose, and the amount of decrease in blood glucose. Authors discuss the over-prevalence of claims of hypoglycemia and psychological changes/problems and address the importance of randomized double-blind experiments with glucose and placebo tests (test-retest evaluation), as well as within subject designs. An interesting caveat in their study was that they let participants go for short strolls between testing periods.

Van Cauter, E., Polonsky, K., & Scheen, A. J. (1997). Roles of circadian rhythmicity and sleep in human glucose regulation. *Endocrine Reviews, 18*(5), 716–738.
Researchers from the University of Chicago, IL and University of Liège, Belgium, provide a thorough review of the relationship between circadian rhythms and blood glucose regulation. The review covers several interesting issues such as glucose regulation in normal young participants, 24–hour variations in glucose regulation, the "dawn phenomenon," time of day effects, glucose regulation and aging, hormone secretion, obesity, and quality of sleep on glucose regulation. One key point is the difference in how blood glucose is maintained during the night (remaining relatively stable) while during the day, glucose levels fall on average 9–18 mg/dl over a 12-hour period, without physical activity.

Wenk, G. L. (1989). An hypothesis on the role of glucose in the mechanism of action of cognitive enhancers. *Psychopharmacology, 99,* 431–438.
A review by Wenk, from the Neuromnemonics Laboratory at John Hopkins University, MD, describes the hypotheses proposed about the effect of glucose uptake and utilization on learning and memory and other substances that may also create an effect on performance. The current thought is that cognitive enhancing drugs create their effect by increasing glucose uptake and utilization in the brain. The article provides a discussion on nootropic (psychoactive compounds) and other drugs (amphetamine, etc.) as well diagrams the hypothesis of the model of such effects. Glucose crosses the blood-brain barrier while other drugs do not yet, these drugs can affect learning and memory by affecting glucose levels through the adrenal glands. To illustrate, a painful/stressful situation stimulates the adrenal glands, which release epinephrine, which then induces the liver to secrete glucose into the blood. However, some substances that do not affect the adrenal glands, do affect performance – that is, the adrenal glands are not critical for learning and memory under normal conditions. Interestingly, some cognitive enhancing substances are only effective when injected peripherally but not directly. He describes how glucose easily passes the blood-brain barrier, unlike epinephrine, and is also effective in enhancing memory (e.g., retention in adult/aged rats and mice) when injected peripherally. The author describes the effect of various substances on performance in humans and

rats (e.g., epinephrine, norepinephrine, vasopressin, naloxone, ACTH, amphetamine). One main point focuses on the importance of glucose regulation and utilization, and how it may be a sensitive and accurate indicator of underlying memory and learning function.

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14. ABSTRACT

The purpose of this review paper is to discuss the research literature on the effects of blood glucose levels on executive and non-executive functions in humans. The review begins with a brief description of blood glucose, how it has been studied, previous syntheses of prior studies, and basic results regarding the role of blood glucose on cognitive functioning. The following sections describe work that investigated the effect of blood glucose on both non-executive and executive functions (e.g., sensory processing, psychomotor functioning, attention, vigilance, memory, language and communication, judgement and decision-making, and complex task performance). Within each section, summaries of the findings and challenges to the literature are included. Measurement conversions of blood glucose levels, blood glucose values, and associated symptoms are depicted. References to the types of tests used to investigate blood glucose and cognitive performance are provided. For more detailed descriptions of references within (and in addition to) this paper, an annotated bibliography is also provided. Several moderator variables including individual differences and contextual variables related to the effects of blood glucose levels on performance (e.g., age, gender, time of day, familiarity with the task and symptom awareness, expectancy effects, dose dependent effects, time dependent effects, task specific effects, rising and falling blood glucose levels, and speed and/or accuracy trade-offs) are addressed later in the paper. Some suggestions for future experimental methodologies are also made.

15. SUBJECT TERMS
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