EXPLORATORY STUDIES OF PHYSIOLOGICAL COMPONENTS OF MOTION SICKNESS

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Enclosure III:

Project #2: Exploratory Studies of Physiological Components of Motion Sickness

A Pilot Study of Cardiopulmonary Function Differences in High and Low Motion Sickness Susceptibles.

PROGRESS REPORT

Project #2: Exploratory Studies of Physiological Components of Motion Sickness: Cardiopulmonary Differences Between High and Low Susceptibles.

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Funding for this project was delayed, and only arrived in June. We have therefore spent the last four months obtaining equipment and setting up the project. The following is a report on a pilot study conducted in order to evaluate new measures of dynamic cardiopulmonary function and begin to use them to examine possible differences between high and low motion sickness susceptible subjects. In a previous study (1) we demonstrated a strong autonomic nervous system response to motion sickness, with significant changes in heart rate (HR), finger pulse volume (FPV), which is a relative measure of peripheral vascular resistance, respiratory rate (RR) and basal skin resistance (BSR). The heart rate response was the strongest of these, and differences in heart rate response emerged between susceptibility groups even in the first two minutes of the motion sickness test. We therefore designed the present project in order (1)to provide a more comprehensive examination of cardiovascular autonomic response to motion sickness and (2) to determine whether differences in cardiopulmonary function exist in high and low

susceptible groups of subjects. This pilot study was performed in order to develop new measurement techniques, test equipment for its ability to provide accurately new measures of interest and to test the adequacy of these new measures in differentiating between susceptibility groups.

In order to gain a more comprehensive view of dynamic cardiovascular responses during motion sickness we have added the measures of stroke volume, cardiac output, myocardial contractility, pre-systolic and systolic timing intervals (all obtained by impedance cardiography); blood pressure; and total peripheral resistance as calculated from cardiac output and blood pressure measures. In order to assess the interaction of the respiratory and cardiovascular systems we have added the measures of tidal volume, and rib cage and abdominal compartmental volumes. We obtained all measures during resting baseline conditions and during two different types of stressors which are known to affect the cardiovascular system. These were the Valsalva maneuver and mental arithmetic. In order to gain some notion as to whether differences in these measures might be associated with differences in motion sickness susceptibility, we studied subjects who had previously been categorized as either high or low motion sickness susceptible in a standard Coriolis (CSSI) motion sickness test.

METHODS

Subjects were six healthy males 35 to 55 years of age, three of whom were high and three of whom were low motion sickness susceptibles.

The following impedance derived variables were obtained from a Minnesota Impedance Cardiograph with associated microcomputer: stroke volune (SV), cardiac index (CI) which is cardiac output adjusted for body surface

area, cardiac contractility (CC), pre-ejection period (PEP) which is the period of systole before the aortic valve opens, and ventricular ejection time (VET) which is the period of systole during which the left ventricle is actually ejecting blood into the aorta. For these measures, subjects were fitted with four circumferential mylar tape bands, two around the neck and two mid-chest; a microphone for monitoring heart sounds, and a precordial ECG. The microcomputer automatically calculated all five impedance-related variables for heart beats selected by the experimenter, and stored the data on cassette tape. The microprocessor required a minimum of 8 seconds to calculate data from each beat selected; another beat could not be selected until calculations were completed. Blood pressure was recorded twice per minute from an automatic cuff system (Narco Biosystems) worn on the left arm. Systolic and diastolic pressures were derived from Karotkoff sounds picked up by microphone and recorded, along with cuff pressure, on strip chart.

Respiratory tidal volume, and rib cage and abdominal compartmental volumes were recorded using a Respitrace inductance plethysmography system (Ambulatory Monitoring, Inc), calibrated by spirometry prior to each session. A computer program for performing the calibrations, assessing the accuracy of calibration and collecting the data was developed in this laboratory for the project. Heart rate, respiratory rate, finger pulse volume, toe pulse volume and basal skin resistance were also measured as in previous studies in this laboratory in order to compare the new measures with these older ones.

For the resting baseline session subjects sat in a reclining chair for thirty minutes. One-minute means were computed for each variable for the thirty minutes of the session. For the task session, a ten minute resting baseline was recorded, following which subjects performed a Valsalva maneuver.

For this, subjects held their breath in mid-inspiration, contracting abdominal muscles against a closed glottis for 30 sec., then relaxed for a two minute recovery period. A second Valsalva maneuver and recovery were then performed. For the mental arithmetic condition subjects subtracted serial 17's from 500, repeating each answer verbally, for a period of three minutes. Approximately ten to twenty trials were carried out during the three-minute period, depending on the mathmatical prowess of the subject. A mean for each variable was calculated for each minute of the task session.

RESULTS

The impedance cardiography system and the Respitrace inductance plethysmography system were found to be virtually incompatible when used together. The frequency oscillator of the Respitrace system created large artifacts in the impedance cardiography system which often could not be eliminated. We did find that interrupting the mylar tape bands around the chest so that they no longer formed a completely closed loop removed the artifact in some individuals without degrading the impedance signal, but it did not consistently allow us to obtain clean data from both systems. In those instances in which it was impossible to obtain both impedance and respiratory data, we chose to eliminate respiratory measurements. Since our N is small for this pilot study, we did not analyze the respiratory data obtained from those individuals whose data was artifact free. In order to overcome this incompatibility problem we have decided to use the new piezo-electric strain gauge system developed by this laboratory for the SL-3 flight to obtain the pulmonary measures in our formal study. It measures pulmonary volumes using a

different principle which is compatible with the impedance cardiography system. Our software for obtaining respiratory data should require only minor modifications in order to be used with the new transducers.

Our assessment of the impedance cardiography system is that it provides relatively accurate data on a wide range of dynamic cardiovascular variables and appears to be sensitive even to rapid changes in these variables. It is therefore well suited to our purposes in the formal study. The microprocessor designed to work with it we found to be largely unsuited to our purposes. With the microprocessor one can obtain data from one heart beat at a minimun of 8-sec. intervals. Thus much data is lost from the intervening beats, especially when rapid changes in the cardiovascular system are occurring. In the formal study, therefore, we shall tag time periods of interst during experimental runs and obtain impedance data from all beats of interest off-line from tape recorded data using our own software.

In spite of the above equipment limitations, valuable data were gathered. Mean values for all variables across the resting baseline condition for each subject are presented in Table 1. The values for all impedance variables fall within accepted normal values as measured by classical techniques (2).

Correlations were run between ANS variables for both the task and baseline sessions in order to compare old and new measures of autonomic function. Results are presented in Table 2. In general, the higher the correlation between two measures having some relation to each other, the more likely they are measuring identical phenomena. Thus although there is clearly overlap, the relatively moderate correlations between old and new measures indicates that we are measuring new aspects of autonomic function with the

addition of these new variables. We were especially interested in how total peripheral resistance (TPR), which takes into account all vascular beds, compares with finger pulse volume (FPV), a very localized measure of relative vascular resistance. Although relatively highly correlated under resting conditions (r=-Ø.51), there is still a considerable amount of variance in TPR which is not accounted for by FPV, and the correlation is much lower under dynamic conditions (i.e., the presence of stressors). These latter measures are of particular importance because vascular resistance is controlled solely by the sympathetic arm of the ANS and may therefore be a means of dissecting sympathetic and parasympathetic components of motion sickness. Cardiac contractility, which is a measure of how forcefully the heart contracts independently of ventricular filling, is also apparently solely under SNS control. However, it is a cardiac measure, whereas peripheral resistance is a vascular measure; the two may show differential effects depending on the stimulus and the status of the cardiovascular system.

Next, possible differences between susceptibility groups were assessed using analysis of variance. A three-way ANOVA (Epoch X Susceptibility X ANS variable) was performed on the baseline data, where Epoch was each of three consecutive ten-minute periods of the baseline session and Susceptibility was "high" and "low". Results revealed no significant difference between susceptibility groups on any measure, nor was there a significant change in any variable across the session. It appears, therefore, that susceptibility groups cannot be differentiated under resting conditions by any of the physiologic variables we have measured.

A similar ANOVA (task X susceptibility X ANS variable) was performed on data from the task session, where "task" was valsalva maneuver, valsalva

recovery and math. There was a highly significant effect of Task ($p<0.0001$) and of Susceptibility ($p<0.003$). Individual ANOVA's run susequently on each separate variable revealed a significant effect of Task on stroke volume ($p<0.025$), cardiac contractility ($p<0.02$), basal skin resistance ($p<0.006$), and finger pulse volume ($p<0.025$). There was a trend toward a significant effect of Task on pre-ejection period and toe pulse volume ($p<0.10$). These findings verify that the tasks administered did indeed produce changes in dynamic cardiovascular function.

There was a significant effect of Susceptibility on stroke volume ($p<0.005$) and cardiac contractility ($p<0.05$). Additionally, there was a significant Task by Susceptibitlity interaction for stroke volume ($p<0.007$) and BSR ($p<0.01$), and a trend toward significance for total peripheral resistance (TPR) ($p<0.08$). Figures 1-5 present plots of all variables having significant changes related to susceptibility.

As indicated by Figs. 1 and 2, two of the original measures, finger pulse volume and BSR, were significantly different between susceptibility groups. The difference in BSR appears to be attributable to the fact that the low susceptibility group had a much higher resting BSR prior to the tasks than did the high susceptibility group, possibly because they were more relaxed. Paradoxically, heart rate, the measure showing the strongest between group difference in our original motion sickness study, was not different during these non-motion sickness stressors. Three of our new cardiodynamic measures did demonstrate differences, however. Although any conclusions we draw from this small study must be very tentative, our findings may indicate that low motion sickness susceptible subjects have a more flexible autonomic nervous system, able to respond in either direction and return rapidly, whereas high

suscptible subjects may not respond readily to more minor stressors, as the ones in this pilot study certainly were, but respond more extremely to severe stressors such as motion sickness itself. A larger study should help to elucidate these issues. In summary, it appears that motion sickness susceptibility groups can possibly be differentiated using simple, brief stressors and measurments of cardiodynamic function. Further studies are necessary to verify these findings; nevertheless, these results are sufficiently promising to merit a formal study.

PROTOCOL FOR FORMAL STUDY

In the formal study, fifteen subjects previously determined to be high and fifteen determined to be low motion sickness susceptible will participate. They will undergo the following: two days of resting baseline, two sessions with CSSI tests performed in the Rotating Room, and two sessions with psychophysiologic stressors - Valsalva maneuver, cold pressor test, and 30 degree head-up tilt. We have decided to delete the mental arithmetic task because mental arithmetic stress varies considerably across subjects and is subject to movement artifact. Cold pressor has been added in its place. Head-up tilt has been added as an additional pure physiologic stressor.

Measures taken during all sessions will be the old measures of HR, RR, FPV, and BSR, plus the new measures of stroke volume, cardiac output, cardiac contractility, systolic timing intervals, blood pressure, and transcutaneous carbon dioxide tension (Pco2). Total peripheral resistance will be calculated from blood pressure and cardiac output data. Estimates of rib cage and abdominal compartmental volumes and tidal volume will be made from piezo-electric strain gauges calibrated by spirometry. Pco2 will be included

as a further monitor of ventilation, as ventilation and Pco2 are reciprocal as long as metabolic rate is constant (3). Transcutaneous Pco2 has been shown to accurately reflect arterial Pco2 in healthy subjects (4). The transcutaneous electrode heats the skin to 43 degrees C to provide arterialization of capillary blood. The output of the device is electronically adjusted to reflect gas tensions at normal body temperature of 37 degrees C and to compensate for skin metabolism of CO2.

Our first priority will be to develop the software to obtain the impedance cardiography measures and to make any modifications in our respiratory volume software necessary to enable us to obtain volume data with the piezo-electric strain gauge transducers. We will also attempt to modify existing equipment to obtain EEG measures which, along with transcutaneous Pco2, will provide information on Sopite Syndrome, the drowsiness and lethargy often associated with motion sickness.

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Table 1. Mean values for each variable across baseline session.

Subj	CSSI	FPV	TPV	RR (/min)	HR (/min)	BSR (kOhm)	CI (L/min)	CC	PEP (sec)	VET (sec)	SV (ml)	SYS (mmHg)	DIAS (mmHg)	TPR
1	18	54.3	32.6	10.6	66.1	4.7	2.58	9.28	.101	.264	72.6	95	44	23.8
2	630	16.7	26.0	12.0	67.7	97.8	3.98	8.85	.052	.320	82.7	105	76	21.6
3	46	31.4	74.0	18.8	62.2	367	1.65	6.09	.089	.300	56.0	-	-	-
4	180	92.6	38.9	9.0	66.8	181	2.92	14.7	-	.280	79.4	112	72	31.6
5	180	87.3	-	11.8	62.3	186	2.06	8.79	.067	.340	66.9	103	67	38.4
6	18	66.2	14.9	13.6	54.7	47.6	1.97	7.65	.050	.350	69.0	107	77	44.3

"CSSI" = number of rotations tolerated during motion sickness (CSSI) test.

Table 2. Baseline session:Correlations between old and new autonomic measures.

	PEP (sec)	VET (sec)	SV (ml)	CI (L/min)	CC	SYS (mmHg)	DIAS (mmHg)	TPR
FPV	Ø.6Ø*	-Ø.73*	Ø.16	Ø.11	Ø.52*	Ø.Ø1	-Ø.42*	-Ø.51*
TPV	Ø.21	Ø.Ø1	-Ø.26	-Ø.51*	Ø.27	Ø.24	-Ø.Ø3	Ø.51*
HR	Ø.33*	-Ø.66*	Ø.32*	Ø.5Ø*	Ø.37*	Ø.Ø2	-Ø.24	-Ø.72*
BSR	Ø.19	Ø.Ø1	-Ø.44*	-Ø.32*	-Ø.14	Ø.29	Ø.26	Ø.11

*=significant at p<Ø.Ø5

Table 3. Task session: Correlations between old and new autonomic measures.

	PEP (sec)	VET (sec)	SV (ml)	CI (L/min)	CC	SYS (mmHg)	DIAS (mmHg)	TPR
FPV	-Ø.15	Ø.Ø2	Ø.13	Ø.22	Ø.62*	Ø.2Ø	-Ø.18	-Ø.2Ø
TPV	-Ø.11	Ø.23	Ø.Ø5	-Ø.11	Ø.29	Ø.34*	Ø.13	Ø.21
HR	Ø.21	-Ø.37*	Ø.25	Ø.48*	Ø.41*	Ø.38*	-Ø.12	-Ø.38*
BSR	Ø.Ø1	Ø.27	Ø.25	Ø.Ø4	Ø.2Ø	-Ø.15	-Ø.18	-Ø.12

*=significant at p<Ø.Ø5

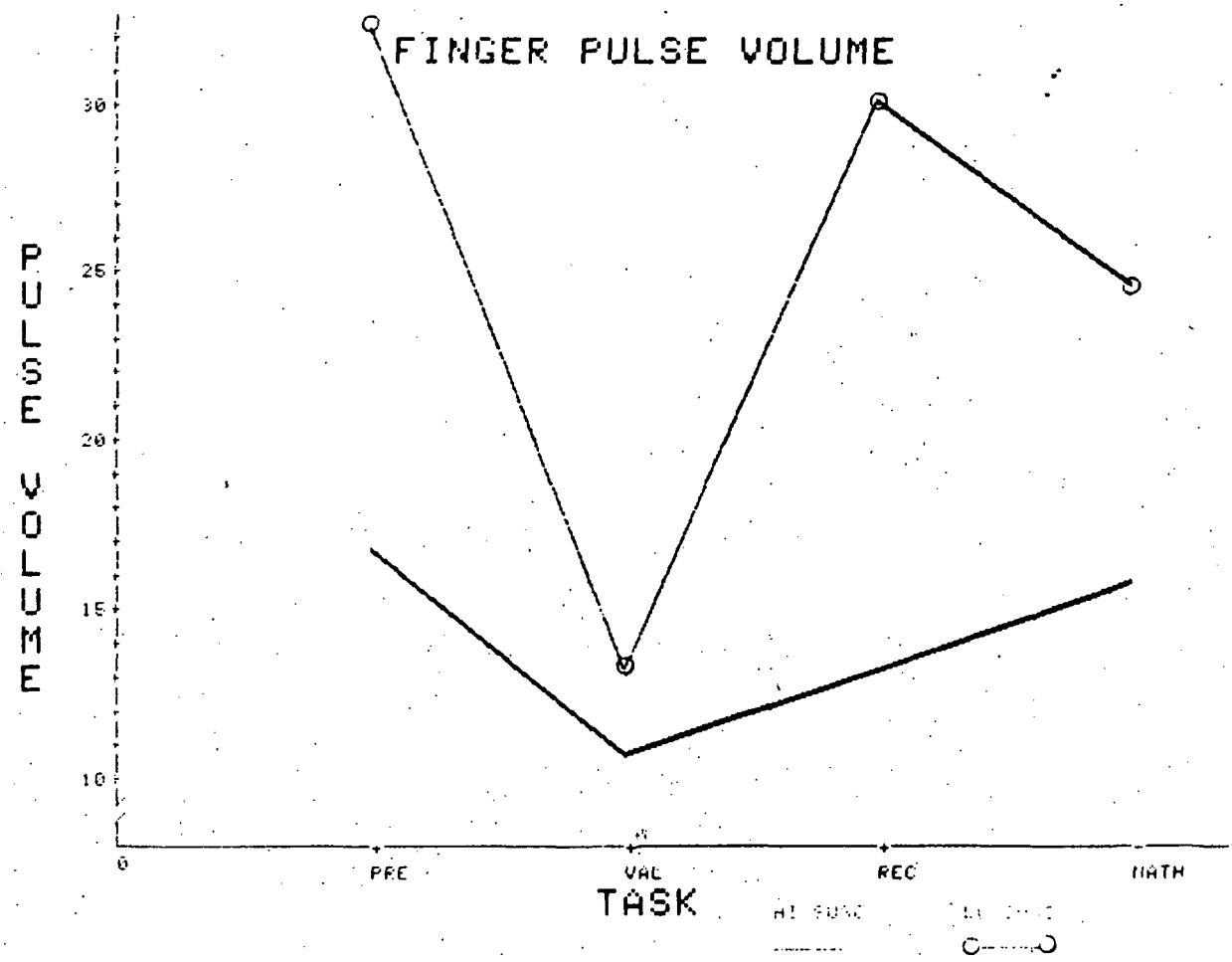
FINGER PULSE VOLUME
PULSE VOLUME
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FIGURE 1.

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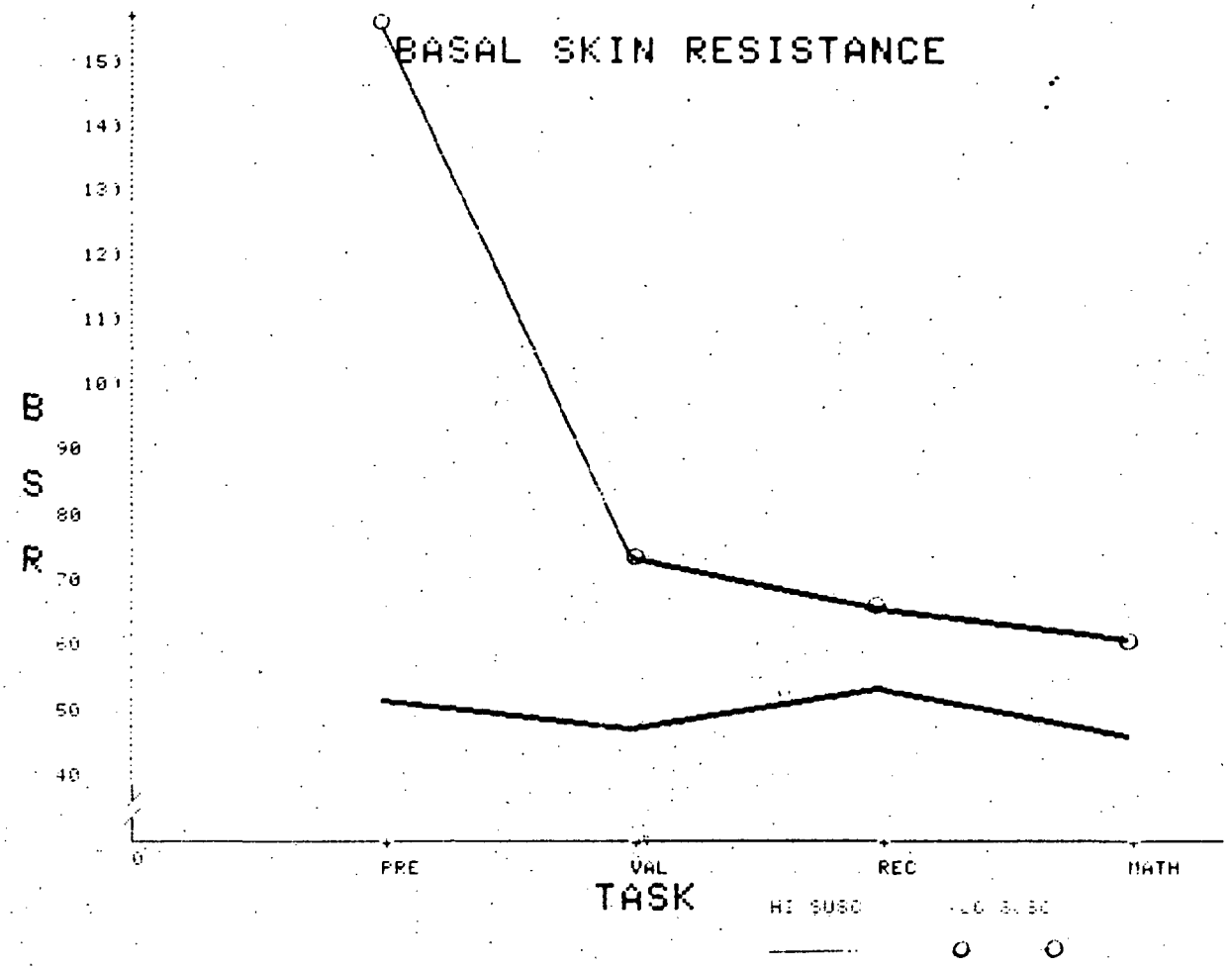
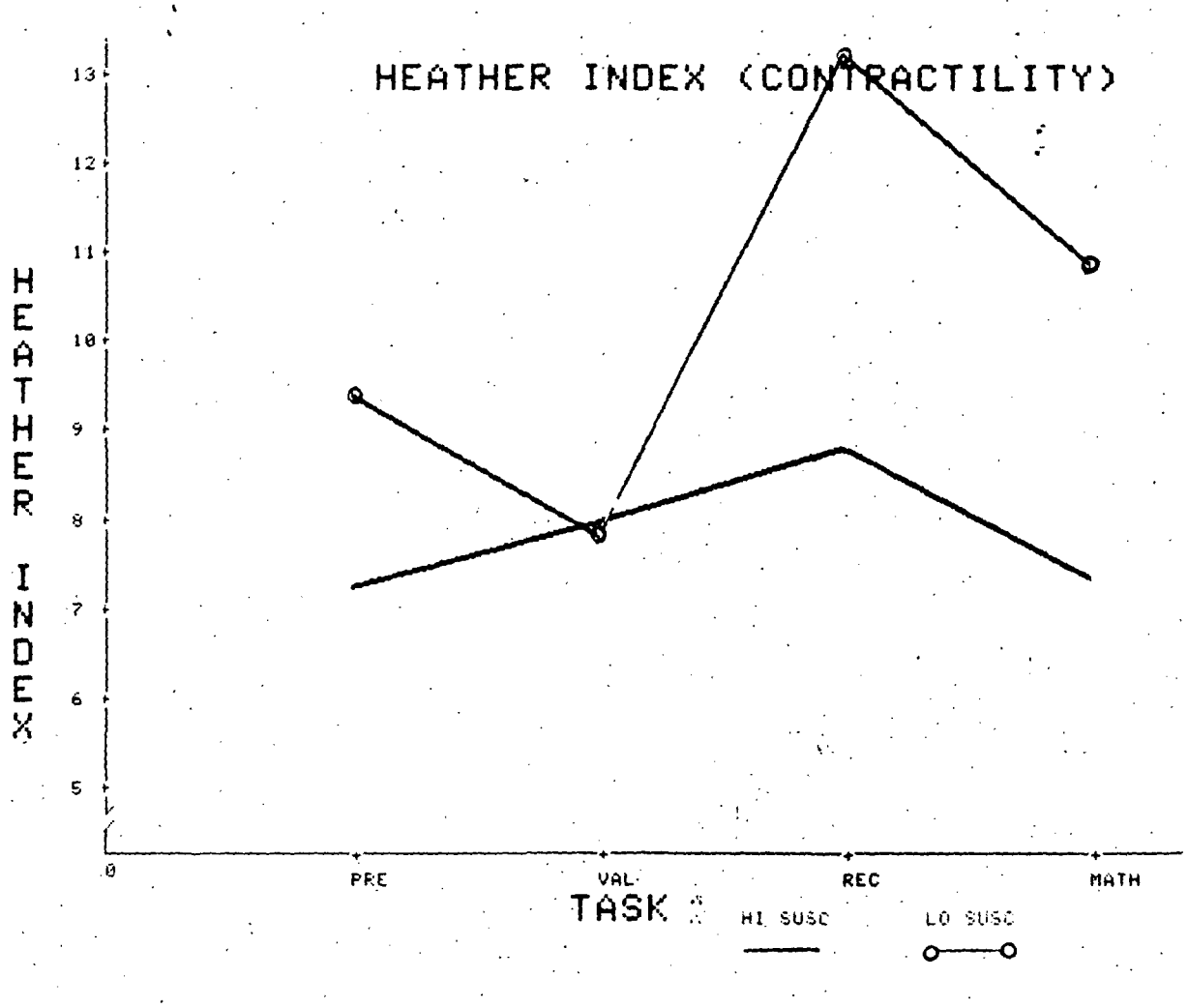


FIGURE 2.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HEATHER INDEX
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FIGURE 3.

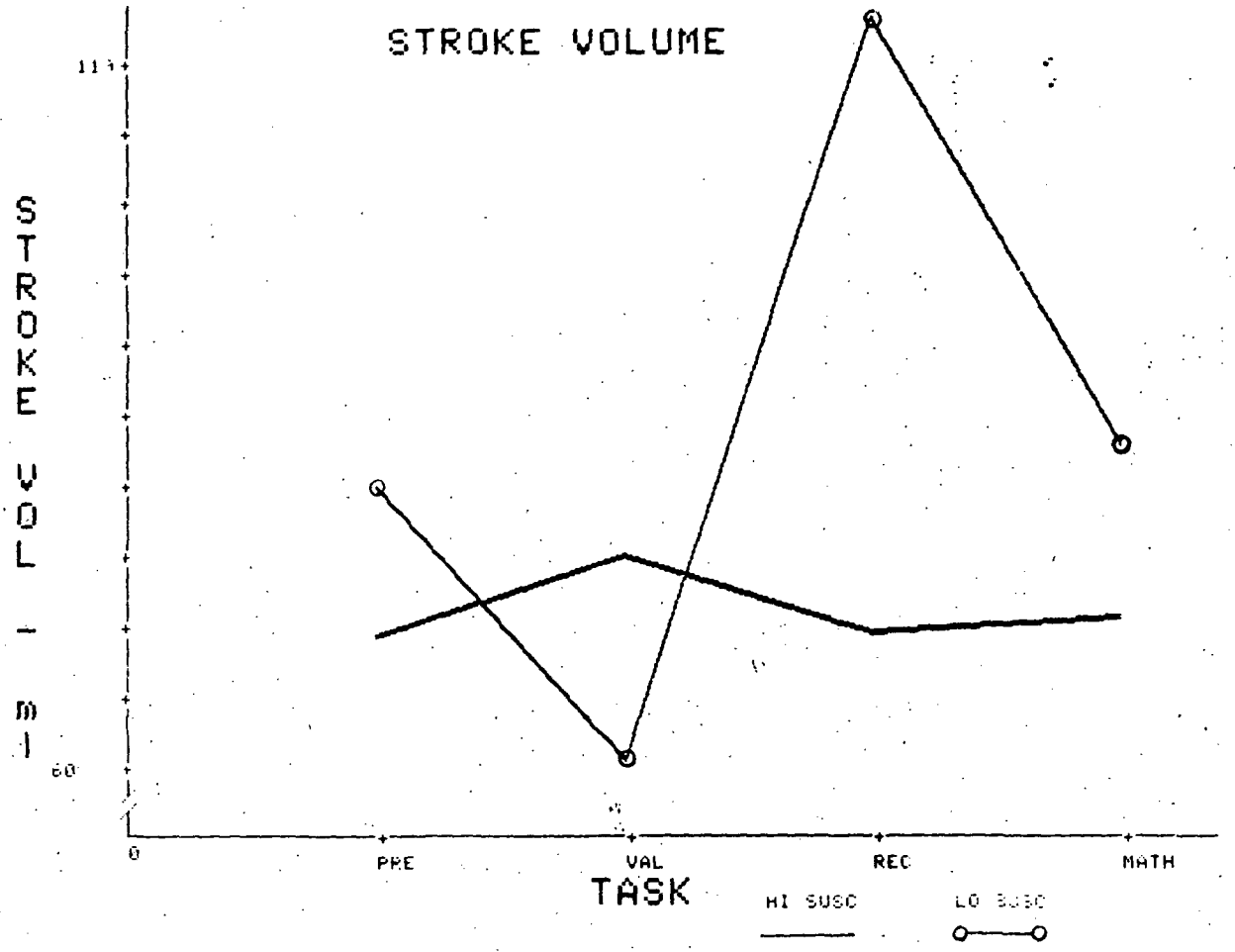
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FIGURE 4.

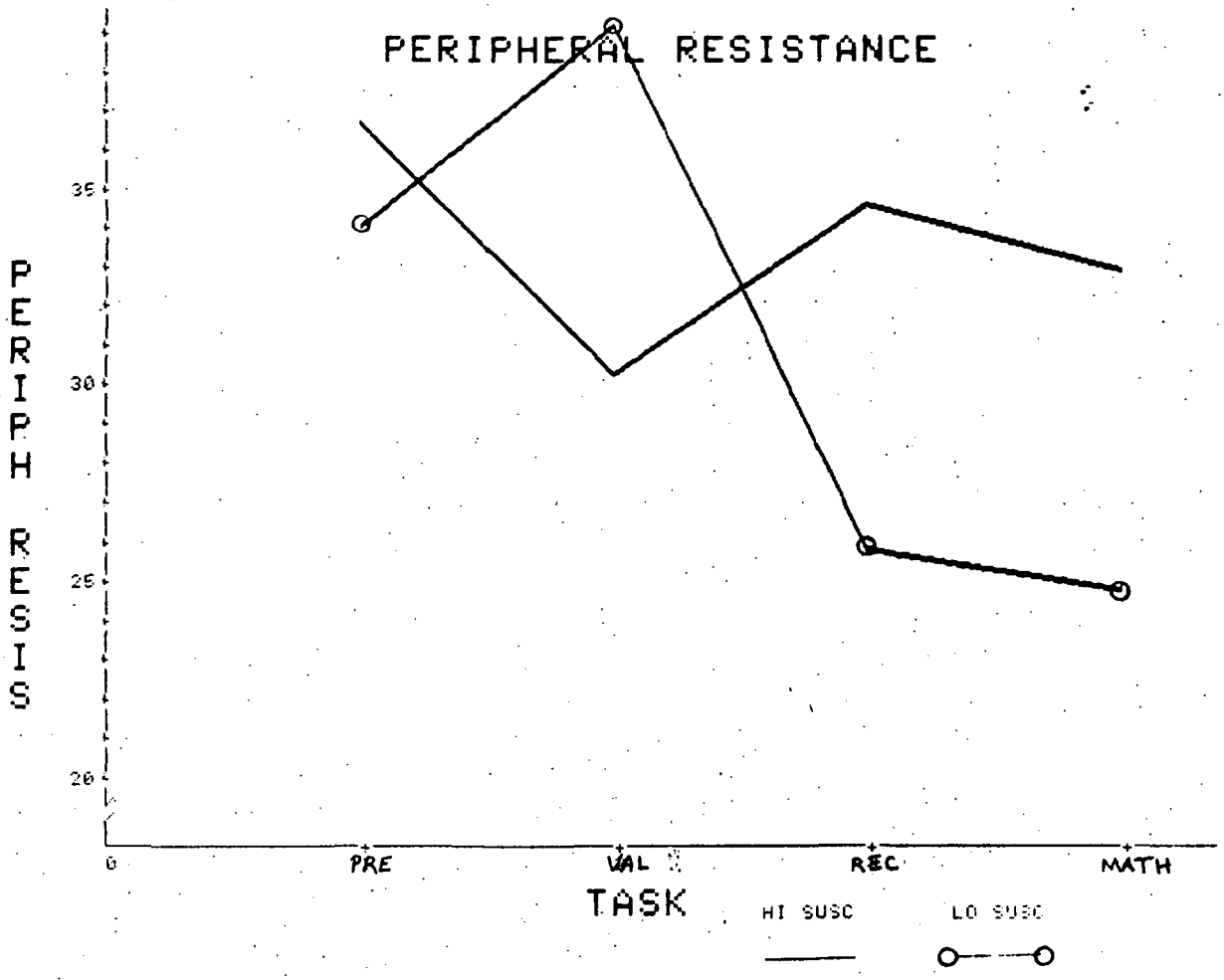
PERIPHERAL RESISTANCE
PERIPH RESIS
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FIGURE 5.