FINAL TECHNICAL REPORT
NASA-AMES AGREEMENT NO. NAG 2-427

INSTITUTION: University of Arkansas at Pine Bluff
Pine Bluff, Arkansas 71601

TITLE OF INVESTIGATION: The Neurochemical and Neuropharmacological Basis of Motion Sickness

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PRINCIPAL INVESTIGATOR: Dr. C.A. Walker

The NASA Technical Officer for this grant is Nancy G. Daunton,
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THE NEUROCHEMICAL AND NEUROPHARMACOLOGICAL BASIS OF MOTION SICKNESS

FINAL TECHNICAL REPORT
NASA GRANT #NAG 2-427
PI: Dr. C.A. Walker

A. SCIENTIFIC PRESENTATIONS

The following presentations at scientific meetings have been made on the results obtained from the above named research project funded by NASA:


ABSTRACT

An apparatus suitable for producing motion sickness in laboratory animals and constructed at the university is herein described. The apparatus is a modified version of that previously described by Fox and Daunton (1982).

It consists of a 66-inch steel arm anchored at the center to a wooden platform and attached to a motor that makes the arm move in a see-saw fashion. At each end of the steel arm is mounted an aluminum disc that can be rotated by a motorized device. Detachable cages are mounted on each disc for animal holding. The animal can then be exposed to rotational motion by rotation of the aluminum disc, or to see-saw motion simultaneously (Cross-
The apparatus is presently being used in our laboratory to study the neuropharmacological basis of motion sickness in the rat. The device can be adapted for use with other animal species by modifying the cage mounted on the aluminum discs (supported by NASA grant # NAG 2-427).

ABSTRACT

Travel by land, sea or air sometimes results in motion sickness in man. It is therefore of interest to study brain neurochemical changes that accompany exposure to motion. The purpose of this study was to determine brain dopamine (DA), dopac (DC), 5-hydroxytryptamine (5-HT) and 5-hydroxyindoleacetic acid (5-HIAA) in animals exposed to cross-coupled motion. Adult, male Fisher 344 rats were used in this study. Control and sham animals (n=6) as well as animals (n=6) subjected for 20 minutes during the dark phase of a light-dark cycle to cross-coupled motion were sacrificed by decapitation at 30, 60 and 120 minutes after exposure to motion. The brain was removed and dissected into cortex, medulla and cerebellum for HPLC analysis of biogenic amines and metabolites. Exposure to motion resulted in a significant decrease in the DA level accompanied by an increase in the DC level of the cortex and medulla as well as an increase

in 5-HIAA level in these brain areas. No change in the level of biogenic amines or metabolites was observed for the cerebellum. These findings suggest an involvement of brain biogenic amines in the effect of motion. A similar study is being conducted in animals exposed to motion during the light phase of a light-dark cycle (Supported by NASA grant #NAG 2-427).


ABSTRACT

It is of wide interest to better understand physiologic factors that contribute to motion sickness in man. Therefore, the purpose of this study was to examine brain neurochemical changes that may accompany motion sickness by determining brain dopamine (DA), 3,4-dihydroxyphenylacetic acid (DOPAC), 5-hydroxytryptamine (5-HT) and 5-hydroxyindoleacetic acid (5HIAA) in rats subjected to cross-coupled motion. Adult, male, Fischer 344 rats were used in this study. Control and sham animals, as well as animals (n=6) subjected for 20 minutes to cross-coupled motion were sacrificed at 30, 60 and 120 minutes after exposure to motion. The brain was removed and dissected into cortex, medulla and cerebellum for HPLC analysis of DA, DOPAC, 5-HT and 5-HIAA. Exposure to motion resulted in a significant increase in the DOPAC and 5-HIAA levels as well as an increase in the 5-HT concentration of the cortex and medulla. No change in the levels of biogenic amines or
metabolite was observed in the cerebellum. These findings suggest that biogenic amine levels in the cortex and medulla may be involved in the effect of cross-coupled motion (Performed at NCTR and supported by NASA grant #NAG 2-427).


ABSTRACT

Drugs, x-irradiation, and motion-sickness produce emetic responses and/or taste aversions. Area postrema (AP) lesions attenuate x-irradiation and drug-induced, but enhance motion-sickness-induced taste aversions in rats. To develop other indices of motion-sickness, we measured analgesia (55°C hotplate) before and after 30 minutes of cross-coupled acceleration as well as BE levels. We also evaluated animals with lesions of the AP (and other circumventricular organs, CVOs) produced by neonatal MSG treatment. Motion-sickness produced a brief (< 30 minute) increase in analgesic latency which was greater in MSG-treated than control rats (105% vs 51%, p < 0.01). MSG-treated rats showed the expected decrease in hypothalamic BE (51%, p < 0.01), but in correspondence to the analgesic effects, motion-sickness produced a further and larger relative drop of hypothalamic BE in MSG than control rats (52% vs 16%, p < 0.01). These results identify analgesia as a useful endpoint for motion-sickness,
suggest that BE may mediate certain motion-sickness responses, and confirm that CVO lesions enhance rather than block such responses. Supported by U.S.A. FDA and NASA Grant NAG 2-427.

B. FUTURE PRESENTATIONS

The final aspect of this project which involves determination of brain acetylcholine/choline levels in control rats and in rats subjected to cross-coupled motion during the light and dark phase of a light-dark cycle has been completed. Acetylcholine/choline was assayed simultaneously in brain samples using an HPLC method with electrochemical detection developed by Bioanalytical systems (BAS), West Lafayette, Indiana. The data is presently being analyzed and will be prepared for presentation at the 1991 meetings of the Society for Neuroscience (New Orleans, LA) and Aerospace Medical Association (Cincinnati, Ohio). Copies of the abstracts submitted for the meetings will be sent to NASA-Ames as a supplement to this report.

Attachments

An apparatus suitable for producing motion sickness in laboratory animals and constructed at this university is herein described. The apparatus is a modified version of that previously described by Fox and Daunt (1982).

It consists of a 66-inch steel arm anchored at the center to a wooden platform and attached to a motor that makes the arm move in a see-saw fashion. At each end of the steel arm is mounted an aluminum disc that can be rotated by a motorized device. Detachable cages are mounted on each disc for animal holding. The animal can then be exposed to rotational motion by rotation of the aluminum disc, or to see-saw motion through the up and down motion of the device's steel arm, or to both rotational and see-saw motion simultaneously (Cross-coupled). The apparatus is presently being used in our laboratory to study the neuropharmacologic basis of motion sickness in the rat. The device can be adapted for use with other animal species by modifying the cage mounted on the aluminum discs (supported by NASA grant # NAG 2-427).
BRAIN BIOGENIC AMINES AND METABOLITES IN RATS EXPOSED TO CROSS-COUPL ED MOTION DURING THE DARK PHASE OF A LIGHT-DARK CYCLE.

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Travel by land, sea or air sometimes results in motion sickness in man. It is therefore of interest to study brain neurochemical changes that accompany exposure to motion. The purpose of this study was to determine brain dopamine (DA), dopac (DC), 5-hydroxytryptamine (5-HT) and 5-hydroxyindoleacetic acid (5-HIAA) in animals exposed to cross-coupled motion. Adult, male, Fisher 344 rats were used in this study. Control and sham animals (n=6) as well as animals (n=6) subjected for 20 min. during the dark phase of a light-dark cycle to cross-coupled motion were sacrificed by decapitation at 30, 60 and 120 min. after exposure to motion. The brain was removed and dissected into cortex, medulla and cerebellum for HPLC analysis of biogenic amines and metabolites. Exposure to motion resulted in a significant decrease in the DA level accompanied by an increase in the DC level of the cortex and medulla as well as an increase in 5-HIAA level in these brain areas. No change in the level of biogenic amines or metabolites was observed for the cerebellum.

These findings suggest an involvement of brain biogenic amines in the effect of motion. A similar study is being conducted in animals exposed to motion during the light phase of a light-dark cycle (Supported by NASA grant NAG 2-427).
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BRAIN BIOGENIC AMINES AND METABOLITES IN RATS SUBMITTED TO CROSS-COUPLED MOTION. J.O. Owasoyo, M.M. Akmal and C.A. Walker. UAPB Research Center, University of Arkansas at Pine Bluff, Pine Bluff, AR 71601.

It is of wide interest to better understand physiologic factors that contribute to motion sickness in man. Therefore, the purpose of this study was to examine brain neurochemical changes that may accompany motion sickness by determining brain dopamine (DA), 3,4-dihydroxyphenylacetic acid (DOPAC), 5-hydroxytryptamine (5-HT) and 5-hydroxyindoleacetic acid (5-HIAA) in rats subjected to cross-coupled motion. Adult male, Fischer 344 rats were used in this study. Control and sham animals, as well as animals (n=6) subjected for 20 min to cross-coupled motion were sacrificed at 30, 60 and 120 min after exposure to motion. The brain was removed and dissected into cortex, medulla and cerebellum for HPLC analysis of DA, DOPAC, 5-HT and 5-HIAA. Exposure to motion resulted in a significant increase in the DOPAC and 5-HIAA levels as well as an increase in the 5-HT concentration of the cortex and medulla. No change in the levels of biogenic amines or metabolite was observed in the cerebellum. These findings suggest that biogenic amine levels in the cortex and medulla may be involved in the effect of cross-coupled motion (Performed at NCTR and supported by NASA grant NAG 2-427).

KEY WORDS: Biogenic Amines, Brain, Motion, Rats.

In an effort to characterize vestibular pathways in the gerbil, immunocytochemistry was combined with retrograde identification of neurons. Small injections of 20% horseradish peroxidase (HRP) were made into the C5-C6 cord of anesthetized gerbils. Sections were reacted with nickel acerate-diaminobenzadine, giving a black reaction product. Sections were incubated in polyclonal antisera to HRP (Dako) for 12 h. The sections were then back incubated in biotinylated-anti-rabbit, followed by avidin-biotin-peroxidase complex, and finally reacted with diaminobenzadine to give a brown reaction product. Brown cells, stained with peroxidase-like immunoreactivity (ASP-lir), were located in all four major vestibular nuclei. These included small and medium and cells in the medial (MVN) and descending (DVN) vestibular nuclei and medium and large ASP-lir cells in the lateral (LVMN) and ventromedial (VMVN) nuclei. In MVN, more cells were stained for ASP-lir caudally than rostrally. After the small injections of HRP into the cervical cord most cells were labeled in the caudal two-thirds of MVN and the adjacent DVN. Double-labeled cells (containing both the black and large ASP-lir) were also present. Some of these cells resembled those of vestibulocollic reflex were exhibiting spatio-temporal convergence which had different response properties (Baker et al., 1982). We examined the response properties of neurons in the lateral, medial, and descending vestibular nuclei of gerbils. Desynchronization of the responses could be antidromically activated from mid-C1, but not from C5. The tilt direction evoking neuronal modulation, and the response dynamics of these neurons, were examined using planar and rotating (wobble) sinusoidal tilts (0.02 to 2 Hz). The response properties of this neck population resemble those of vestibular neurons in an earlier study whose projection was not identified (Kasper et al., 1988). A larger fraction of the neck sub-population has advanced phase (> 90° at 1 Hz), suggesting a contribution from irregular afferents. Most neurons projecting to the neck exhibited the same temporal response to varying spatial stimuli. Some neurons exhibiting spatio-temporal convergence (Baker et al., 1984) were observed, but apparently too few to account for vestibulocollic reflex behavior; this behavior may be due to convergence of inputs from different spatial and temporal properties at other levels of the reflex pathway. (Supported by NIH grants NS02619, NS24930, NS08560).

CONTRIBUTION OF MEDIAL VESTIBULOSPINAL NEURONS (VSNs) TO SPATIAL TRANSFORMATION IN THE VESTIBULOCOLIC REFLEX (VCR). S.J. Perlmutter, J.W. Krampe, J.E. Bahn, B.W. Wintor*, Northwestern Univ., Chicago, IL 60611.

We are investigating the neural substrates of spatial motor patterns of the VCR by recording VSN and neck muscle EMG activity. In 2 alert and 11 decerebrate cats (naloxone, 200 mg/kg/h, i.v.), VSNs were identified by their responses to electrical stimulation of the labyrinthine and descending MLF. The direction of rotation producing maximal activation (MAAD) was determined via micron-traction. Connections of VSNs to neck motoneurones were being studied with spike-triggered averaging and cross-correlations.

Motion sickness and motor strategy.


Different spatial tilts (e.g. roll ± pitch) evoked peak responses in vestibulocollic reflex which have different temporal properties (Baker et al., 1985). Furthermore, the dynamics of the reflex suggest that input from different vestibular afferents differ (Bilotta et al., 1982). We examined the response properties of neurons in the lateral, medial, and descending vestibular nuclei of alert cats, tonic vestibular neurones were antidromically activated from mid-C1, but not from C5. The tilt direction evoking neuronal modulation, and the response dynamics of these neurons, were examined using planar and rotating (wobble) sinusoidal tilts (0.02 to 2 Hz). The response properties of this neck population resemble those of vestibular neurons in an earlier study whose projection was not identified (Kasper et al., 1988). A larger fraction of the neck sub-population has advanced phase (> 90° at 1 Hz), suggesting a contribution from irregular afferents. Most neurons projecting to the neck exhibited the same temporal response to varying spatial stimuli. Some neurons exhibiting spatio-temporal convergence (Baker et al., 1984) were observed, but apparently too few to account for vestibulocollic reflex behavior; this behavior may be due to convergence of inputs from different spatial and temporal properties at other levels of the reflex pathway. (Supported by NIH grants NS02619, NS24930, NS08560).

MOTION SICKNESS AND MOTOR STRATEGY.