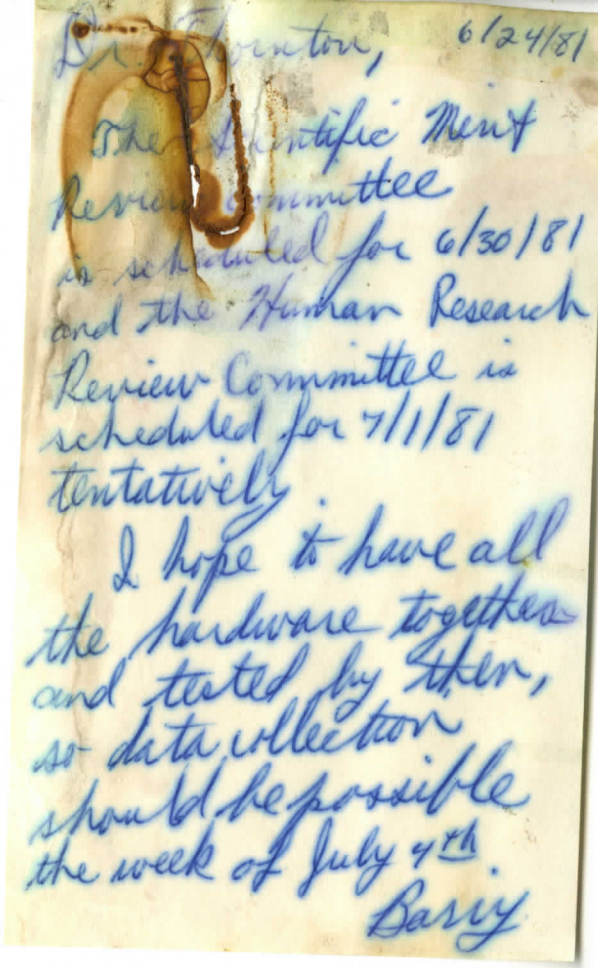

Dr. Thornton, 6/24/81

The Scientific Merit Review Committee is scheduled for 6/30/81 and the Human Research Review Committee is scheduled for 7/1/81 tentatively.

I hope to have all the hardware together and tested by then, so data collection should be possible the week of July 4th.

Barry

NASA LIFE SCIENCES RESEARCH PROPOSAL

1. Title: Pilot Study of Venous Mediated Muscle Pumping Reflex in the Human Lower Limb

2. Sponsor: NASA Johnson Space Center

3. Investigators: B. Linder
W. E. Thornton, M.D.
M. W. Bungo, M.D.

4. Hypothesis:

Distension of the veins in the leg will excite the afferent pathway of the skeletal muscle reflex. The efferent segment of the reflex, after a spinal relay, activates via motor neurons flexor and extensor skeletal musculature of the leg. The effect is an increase in intramuscular pressure and a consequential decrease in venous capacitance of the deep veins in the lower limb.

5. Background:

Astronauts exposed to weightlessness experience a central/cephalad fluid shift which is manifested by loss of intravascular (and probably extravascular) volume from their lower extremities. Skylab data reflect a change in calf compliance in the order of 6 volume percent (1). The result is that when the crewmember is subjected to orthostatic stress, such as lower body negative pressure (LBNP) or the return to gravity, the altered compliance of the venous system and the previous diuresis result in an inappropriate pooling of blood volume in the legs. This may manifest as syncope. The inability of the cardiovascular system to compensate for these changes may be due to a "critical" loss of available volume or a resetting or possibly defective condition in the regulatory mechanisms. The volume contained in the deep venous system of the limb is pumped by surrounding muscles. Thompson, et. al., (2, 3, 4) has reported compelling evidence for a venous afferent mediated skeletal muscle pumping reflex in the cat. He has stimulated femoral venous afferents and recorded a resultant increase in the electromyograph (EMG) in several muscles of the hind limb, including the gastroenemius m. and anterior tibial m. This reflex, however, has not been demonstrated in man.

Furthermore, a modification of A. Guyton's cardiovascular computer simulation model responds poorly to the stress of standing in spite of consideration of volume shifts and neural-humoral reflexes (5). This suggests that some aspect of the physiological system has not been adequately incorporated into the scheme.

6. Rationale:

The healthy human subject does well in response to the stress of standing, at least over the short term. The reflex that Thompson has described changes venous capacitance in a way which is potentially beneficial to the cardiovascular system. The pooling of blood in the limbs due to hydrostatic forces should be limited since there is reflexively a reduction in capacitance of the deep veins which carries the majority of the venous volume in the leg. In our attempt to fully understand the physiology of the human cardiovascular system, it is important to determine whether such a reflex exists in man.

7. Justification:

a. Finding evidence for this reflex in man will aid in the understanding of the response of the cardiovascular system to a variety of stresses.

b. Further understanding of the cardiovascular system in man is important to the understanding of astronaut's responses to varying g-forces and the readaptation which occurs after space flight.

8. Experiment Design:

All of Thompson's work was invasive. This experiment will be noninvasive, but will attempt to duplicate the experimetal conditions of Thompson as completely as possible. Therefore, an occlusive thigh pressure cuff will be used to block venous return and cause distension of the veins of one leg. Changes in calf size will be measured with a Whitney guage. An EMG recording will be made from the gastroenemius muscle as well as the anterior tibial muscle in order to observe the reflex response. The cuff pressure, a trigger, both EMG signals, and calf size will be recorded simultaneously on a Grass polygraph strip chart and FM magnetic tape recorder. If deemed necessary, the EMG from tape can then be rectified and integrated using either Nicolet hardware or using software. We will use four subjects in this pilot study. Each subject will be run through the experimental paradigm three times. A single run will consist of 60 seconds of recording with cuff off, 60 seconds of recording with cuff on at 50 mm Hg, and repeated 4 more times for a total of 5 control-test sets. Calf volume and EMG will be recorded bilaterally although cuff stimulus will only be applied unilaterally.

9. Expected Results:

Based on Thompson's results, a transient increase in EMG activity is expected from the venous distension caused by the pressure stimulus.

10. Management Plan:

The principal Investigator (PI) will be responsible for assembling of hardware/software and collection and analysis of data. The medical monitor will be responsible for the human use aspects of the study. The PI and Co-PI's will share responsibility for the scientific interpretation of the experimental data and for the preparation of written reports detailing the results.

11. Resources Plan:

The facilities of the JSC physiologic performance lab will be utilized for this human research. All equipment is presently on site in Building 37 and will be assembled in the cardiovascular lab to effect the protocol as described above. Computer analysis of the data, likewise, will utilize on-site facilities. A readiness review meeting will proceed actual testing.

Additional Information for the Human Research Review Committee

1. Subjects will be unpaid volunteers from within the NASA JSC community. Each subject will have on file a current Class III NASA physical or pass an equivalent physical exam given by the medical investigator.

2. Four subjects will comprise the first cohort. Additional subjects may be recruited after initial pilot study data analysis.

3. A physician (medical Monitor) will be on call for all aspects of the research which involve human participation as experimental subjects.

4. Written, informed consent will be obtained from each subject on standard NASA consent form.

5. A subject may withdraw from the study at any time he or she so desires.

6. The subject identity will not be released to the general public without his/her consent unless specifically required by law.

7. The research shall be conducted in a manner which will provie coverage for the subjects by the appropriate Federal Employee's Compensation Act or by the Workman's Compensation Act.

8. There are no appreciable hazards associated with the human use of any of the equipment comprising this proposal.

REFERENCES

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2. "Projection of low threshold venous afferent fibers to the spinal cord." Floyd J. Thompson and Charles D. Barnes. Brain Research, 177 (1979) 561-656.

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4. "Properties, projection, and connections of limb venous afferents in the feline central nervous system." Thompson, Barnes, Wald, Lerner, Franzen. 28th International Congress of Physiological Sciences, Budapest 1980.

5. A Systems Approach to Understanding the Challege of Space. Section III, Ron White.