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Effect of Acute Exercise on Cerebral Blood Flow in Man.* (32193)

M. RUSSEK† AND J. R. BEATON‡

Department of Physiology, University of Western Ontario, London, Ontario, Canada

Little is known concerning the effects of exercise on cerebral blood flow. This is perhaps due to the difficulties involved in the application of the methods available in the past (inert gas, indicator injection) which require blood samples from the jugular sinus and an artery(1). Only one report could be found in the literature—that of Kleinerman and Sancetta(2) who observed that mild steady-state exercise produced a slight decrease in cerebral blood flow, which they attributed to decreased carbon dioxide in blood(3).

The development of the impedance rheograph offered an opportunity for quantitative but relative measurement with continuous recording of cerebral blood flow before and after a short period of exercise(4-7).

Methods. The experiments were carried out on a group of 11 volunteers (4 males and 7 females). Two of the females were laboratory technicians, the other 9 subjects were fourth year university students enrolled in Physical and Health Education.

Cerebral blood flow was recorded continuously using an E. & M. Impedance Rheograph and scalp plate electrodes 2 cm in diameter, attached to the frontal and parieto-temporal regions. This instrument measures the changes in impedance to an A.C. current of 75 Kc/sec occurring in the tissue between the electrodes, during each systole, these changes being proportional to the instantaneous blood flow(4-7). Thus it provides a flow pulse that reflects any changes in blood flow. To have a better appreciation of the changes in blood flow, the pulses were electronically integrated and the total "pulse area per unit time" was recorded in a second channel of the polygraph (Grass 5A). The electrocardiogram (E.K.G.) in the II standard derivation and the skin temperature between 2 fingers were also recorded simultaneously.

The subjects sat quietly for 5 minutes, during which a basal recording was taken. The E.K.G. in all the standard derivations was also taken in order to obtain information about possible abnormalities that might interfere with the results. All except one of the hearts were electrocardiographically normal and the only abnormality found in one of the females was a right branch block; data on this subject were not included in the general averages.

After basal recordings, the subjects performed a modified Harvard Step-Test (step up and down to a 45 cm block) at a frequency of 20/min for 5 minutes. No recordings could be done during the exercise because of movement artifacts. Immediately after the exercise they sat down again, and recordings were made for at least 10 minutes.

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† Permanent Address: Dept. of Physiology, Escuela Nacional de Ciencias Biologicas, Inst. Politecnico Nacional, Mexico, D. F.

‡ Medical Research Associate of Medical Research Council of Canada.

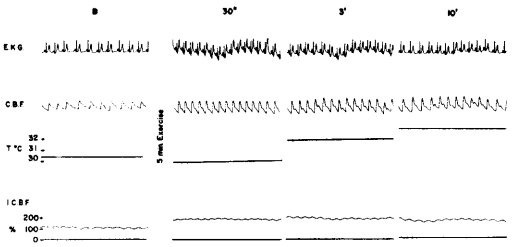

FIG. 1. Recordings of electrocardiogram (EKG), cerebral pulse flow (CPF), skin temperature and integrated CPF in a female subject before (B) and 30 sec, 3 min and 10 min after 5 min of exercise (step test, 20/min).

Results. Cerebral pulse flow was increased by 13 to 50% (average 27.0 ± 8.0) in the males and 22 to 100% (average 49.6 ± 12.9) in females after 5 minutes of exercise. The increase was even greater on the integrated recordings of the cerebral pulse flow, ranging from 40 to 100% (average 68.7 ± 17.3) for males and from 64 to 135% (average 92.0 ± 12.1) for females (Fig. 1 and 2). The average increases in pulse flow and integrated flow were statistically significant when compared to the basal recordings ($p = 0.01$ for the pulse flow and $P < 0.001$ for the integrated flow). The average increases appeared to be larger in the females, but the difference between the two groups was not statistically significant (Fig. 2).

The average basal heart rate was higher in the females than in the males (68.0 ± 1.3 and 54.0 ± 4.8 b/min, respectively: $P < 0.05$). In both groups the exercise produced a large and significant increase in heart rate. This increase was 20 to 36 b/min (average 32.4 ± 6.4) for the males and 36 to 100 b/min (average 61.6 ± 11.2) for the females (Fig. 2). There was a significant difference between the cardiac response of the two groups ($P < 0.05$); this tachycardia lasted for more than 7 minutes in both males and females. Various degrees of respiratory sinus arrhythmia were observed in both males and females: the ratio between the longer and shorter intervals varied from 1.05 to 1.60 (average 1.29) in the females and 1.25 to 1.50 (average 1.42) in the males. During the tachycardia, the average arrhythmia was reduced to 1.05 in the females and 1.30 in the males.

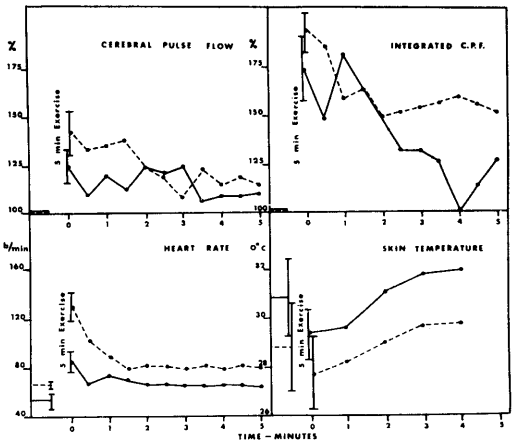

FIG. 2. Cerebral pulse flow (CPF), integrated CPF, heart rate and skin temperature in 6 female (•— — —•) and 4 male (•———•) subjects before and after acute exercise (Harvard step test, 5 minutes).

Skin temperature showed a consistent pattern of change in all subjects: it was decreased immediately after the exercise and then rose to a value higher than basal during the next 3 to 4 minutes (Fig. 2). However, the differences were not statistically significant.

There was no significant correlation between the increase in height of the flow pulse and the increase in cardiac frequency ($r = 0.27$) but there was a significant correlation between the increase in integrated flow and the increase in heart frequency ($r = 0.72$; $P = 0.02$).

Discussion. The observed increase in cerebral blood flow could be interpreted as a combination of a cerebral vasodilation, which causes the increased height of the flow pulse, and an increase in heart rate, which makes the integrated flow increase larger than the increase in flow pulse. It is improbable that the increase in the height of the flow pulse was due to an increased stroke volume since it was as large in the untrained subjects, in which the stroke volume is known to change very little during exercise(8), as in the highly trained ones, in which the stroke volume does increase considerably during exercise. It is also improbable that the increase of the flow pulse was solely due to a passive distention of the cerebral vessels produced by hypertension, since changes in mean pressure from 60 to 150 mm Hg have been shown

to have no effect on cerebral blood flow(9); this includes the range of blood pressures obtained during exercise(8).

The lack of correlation between the increase in height of the flow pulse and the increase in heart frequency suggests that increased stroke volume is not the cause of the increase in flow pulse, because, in the range of heart rates obtained, there is a correlated increase in stroke volume and heart rate(8).

Disagreement between the results obtained in the present communication and those reported by Kleinerman and Sancetta(2) might be due to differences in time of collection of data during the development of exercise and/or in the intensity of the exercise. They reported a rather small decrease in flow (13%) based on the comparison of basal blood samples (nitrous oxide method), with samples taken after 30 minutes of a rather mild exercise (as judged by the increase in heart rate that they report), performed on a bicycle with the subjects lying in a supine position. The data presented here were obtained after 5 minutes of a much stronger exercise (as judged by the tachycardia) performed in a vertical position. It may be that the work performed by the central nervous system, and hence its blood requirements, were very different in the two situations.

An initial decrease in skin temperature, even though not statistically significant, was observed in all subjects, suggesting that the cutaneous blood flow was reduced (or at least not increased) during the maximum increase in cerebral blood flow. Therefore, the participation of the skin in the recorded change in flow was either negligible or opposite in direction.

Respiratory sinus arrhythmia has been shown to be caused by changes in vagal tone synchronous with respiration. Its reduction during the tachycardia elicited by exercise can be used as a relative measure of the vagal inhibition participating in the cardiac response(10).

It has been shown that weak histotoxic hypoxia in the dog elicits tachycardia with reduction or disappearance of the respiratory arrhythmia, increased ventilation which decreases blood CO_2, and a marked increase in cerebral blood flow(10-12). The similarity to the reactions induced by exercise is striking.

Summary. Changes in cerebral blood flow (C.B.F.) induced by acute exercise (5 minutes of Harvard Step Test at 20/min) were recorded with the aid of an impedance rheograph in 11 subjects (4 males and 7 females) with various degrees of physical training (2 females completely untrained). Flow pulses and their electronic integration were recorded before and after the period of exercise. A substantial increase in the height of the cerebral flow pulses, (males + 27%; females + 49%) and an even larger increase in the integrated recordings, (males + 68%; females + 92%), were observed in all subjects. The increase in C.B.F. lasted for more than 5 minutes after the end of the exercise. A marked increase in heart rate (+42 b/min for males and +61 b/min for females) and a small initial decrease in skin temperature followed 2 min later by an increase were observed also. Changes in heart rate were highly significant but changes in skin temperature were not. The similarity of these responses to those elicited by hypoxia and the possibility of a participation of the chemoreceptors in the cardiovascular and respiratory reactions observed during exercise were noted.

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A Plaque Neutralization Method for Arboviruses. (32194)

E. EARLEY,* P. H. PERALTA, AND K. M. JOHNSON
Middle America Research Unit, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Balboa Heights, Canal Zone

The plaque technique developed by Dulbecco(1) provides a method for relatively precise infectivity assay of many animal viruses. Although several types of cell cultures have been tried in the past decade (2,3), successful application of this method to the study of arboviruses has been limited to certain members of groups A(4), B(5), and C(6).

Ideal objectives in the case of arboviruses include: discovery of a single cell culture system in which discernible plaques are induced by a wide variety of viruses and the demonstration that cell monolayers of very small size will provide sufficient quantitative accuracy to permit use of the plaque method for routine procedures which require many individual cultures. In the latter regard, encouraging results have been reported by Miura and Scherer(7) and by Rubio-Brito (8), in which individual arboviruses were successfully assayed and specifically neutralized in cell monolayers grown in the wells of leucite trays originally developed for studies on viral hemagglutination.

This communication describes successful production of plaques by many arboviruses from the western hemisphere in a "microsystem" utilizing disposable plastic trays initially used for performing metabolic inhibition tests with polioviruses(9).

Results obtained using this system for measurement of neutralizing antibodies to Venezuelan equine encephalomyelitis (VEE) virus are compared with those obtained in a mouse neutralization test and by hemagglutination inhibition.

Materials and methods. Tissue cultures. Several types of cell cultures were tested in preliminary trials but the MA-111 line of continuous newborn rabbit kidney† was selected because all of the 19 viruses screened produced plaques under agar. Except as specified, all experiments reported were carried out in this cell line. Recent experience suggests that a line of African green monkey (*Cercopithecus aethiops*) kidney cells (VERO) (10) may be superior to the MA-111 cell line. Virus titers were higher in certain instances and plaque resolution was often better. Methods used for preparation of both cell lines were the same.

Monolayer cell cultures grown in 32 oz ungraduated prescription bottles‡ were subcultured twice weekly. The growth medium (GM) consisted of medium 199§ containing 1.25 g of $NaHCO_3$ per liter, supplemented with 5% fetal calf serum, 100 units of penicillin and 100 μg of streptomycin per ml.

Preparation of cell cultures in trays. Cells were grown in two types of plastic trays manufactured by Linbro Chemical Co., New Haven, Conn. Wells in the model 96CV have a slightly concave bottom, provide a cell surface area of about 2.0 cm^2 and have a fluid capacity of 2.2 ml. Those of model 54FB are flat bottomed, with a surface area of 2.2 cm^2 and a capacity of 3.0 ml. Trays were cleaned and sterilized by 5 minutes' immersion in 95% ethanol, followed by exposure to ultraviolet light (GE 30 watt,

* Present address: Dept. of Pathology, School of Med., Tulane Univ., New Orleans, La.

† Microbiological Associates, Inc., Bethesda, Md.
‡ Brockway Glass Co., Brockway Pa.
§ 10 × Concentrate - Microbiological Associates, Inc., Bethesda, Md. Dry concentrate - General Biochemicals Co., Chagrin Falls, Ohio.