

604-5-430

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FEDERAL PROVINCIAL MENTAL HEALTH GRANT

No. 604-5-430

To Dr. R. A. Cleghorn

Allan Memorial Institute of Psychiatry

McGill University, Montreal, Quebec.

FINAL REPORT

For the period

April 1st, 1961 to March 31st, 1963.

June 20th, 1963.

604-5-430

DRIVE, AFFECT, THOUGHT AND PHYSIOLOGICAL EVENTS

This grant began April 1st, 1961 and terminated March 31st, 1963. It supplied part of the Principal Investigator's salary, his secretary's and 50% of the stipend for a Research Fellow. Several other investigators, supported from other sources, contributed part of their time to the areas under investigation. During the two years' tenure of 604-5-430 the Principal Investigator published seven full papers, eight brief essays, such as book reviews and reports and gave three lectures, so far unpublished, at important medical centres. Some of these publications were already listed in Appendix A of the Final Report made on June 13th, 1962, with respect to the previous grant, No. 604-5-65, entitled Sympatho-adrenal Function in Mental Illness. They are listed again here, as their publication falls within the term of the present grant, though work on many was begun during the tenure of the previous period of support. In the research field, papers represent an arbitrary division in the course of work which is continuous. At this time, the Principal Investigator would like to draw attention to the statement made in the Final Report of grant 604-5-65 regarding the functions of the Director of the unit with widely diversified activities in both basic and applied research areas, such as the one of which he is Director. The activities and responsibilities of the head of such a unit, while furthering research, impinge seriously on his time for personal investigation, so that if he supplies some ideas, leadership, criticism and coordination of endeavour, he has to be content with limited time for his own research efforts. As Chairman of the Programme Committee of the Third World Congress of Psychiatry held in Montreal in June, 1961, and for the publication of the subsequent Proceedings, the Principal Investigator was involved in surveying and adjudicating psychiatric contributions which were world-wide. As a member of a Study Section of N.I.M.H., he enjoyed the privilege of associating with top flight psychiatric investigators and social scientists in reviewing research

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applications from all over the U.S.A. and abroad.

A review of the appended bibliography of the Principal Investigator for the years 1961-62 indicates his concern with various vexed issues, such as psychiatric research and mood disorders, where there is as yet no unanimity as to definition of the most appropriate techniques on the one hand, or of conceptualization on the other. The biological roots of psychiatry were also of particular concern and bid fair to add still more to an understanding of mechanisms and the provision of predictable therapy. At the same time, psychodynamic factors from the individual history of each patient and the contribution to the psycho-social milieu have to be weighed for the manner and extent to which they contribute to the issues at stake.

Studies on pressure changes in the lumen of the gastro-intestinal tract by the open-tip catheter method have been conducted by Dr. Peterfy, who derived \$1800 towards his salary from 604-5-430 annually. In conjunction with Dr. Ivan Beck of the Division of Gastroenterology of the Department of Medicine of the Royal Victoria Hospital, he has made detailed observations which have supplied data of the most basic value for subsequent work using the telemetric capsule. The latter instrument will provide a technique for the non-traumatic study of gastro-intestinal variations in normal individuals and in patients with gastro-intestinal functional disorders. This is an area of considerable importance to the Departments of Medicine, Surgery and Psychiatry. Technical difficulties have prevented further progress with this instrument during the past few months, because it was found that the local radio and T.V. stations on Mount Royal emanate waves which interfere with the recording from this sensitive instrument. Consequently, it has been necessary to employ a thoroughly shielded room. This was found in the Department of Otolaryngology, but is only available in the evenings. In the new research building of the Allan Memorial Institute, which is to open shortly, a suitable shielded room will be available and Dr. Peterfy will be able to conduct his pioneer investigations in a setting

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which should give reliable results. It is anticipated that his observations may make possible the earlier and easier detection of gastro-intestinal disorders which have an emotional basis and therefore warrant better discrimination and more appropriate therapy.

Basal Ganglion Disease.

Studies of basal ganglion disease have continued. So far, the biochemical tests used have indicated that the Huntington's Chorea cases do have changes in amine metabolism, although they are not as clear and stringent as they are in Parkinsonism. Besides that, it has been shown in three cases treated with Alpha-methyl-DOPA, Aldomet, that the drug has a beneficial effect on the main neurological symptoms. The psychiatric syndrome, however, seems to improve only if the deterioration has not reached a very low point. In two of our cases, the psychopathology has shown a very questionable amelioration: the youngest patient, however, has markedly improved. These two findings have justified further search for techniques for studying the biochemical disturbance in these patients, with the aim to make the postulated metabolic "error" more apparent and better defined. A so-called "loading test" was devised. This means that the enzymatic functional circle which is regarded as easily disrupted should be "over-loaded" for a limited time with amines, to test its functional abilities to deal with them. 1-DOPA resp. d-DOPA have been given to the patients and in the consecutive 6 to 8 hours hourly urine collections have been tested with regard to catecholamine excretion. The amino acids were first given by mouth, but, now that we have acquired stable solutions, they are being given intravenously. Control studies on healthy adults have been carried out first, to establish the "normal" curves of excretion and the "normal" quantities of each fraction. So far, we have had only one patient from the Huntington's Chorea family for investigation. It is felt that there are signs suggesting changes in the speed of excretion. We have made arrangements to bring the same, intensely studied patients back to the hospital to

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re-test them as to the long term treatment effects with Aldomet, as well as to make the "loading tests". Only after a number of cases have been examined will we be able to summarize the findings and give them the interpretation which will bring us closer to the enigma of Huntington's Chorea.

A summary of the psychiatric observations is in the course of preparation.

R. A. CLEGHORN

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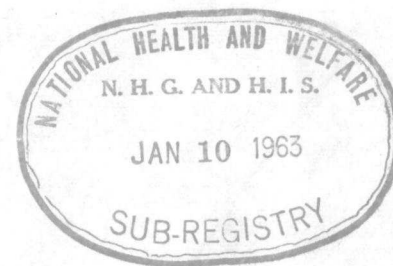
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ANNUAL REPORT

For the period

April 1st, 1961 to March 31st, 1962

September 14th, 1962

DRIVE, AFFECT, THOUGHT AND PHYSIOLOGICAL EVENTS.

The study of psychiatric and biochemical changes in individuals with basal ganglion disease has been extended to cases of Huntington's Chorea. This was done because it became increasingly difficult to get suitable cases of Parkinson's disease for study and in view of the emergence of a rare opportunity to investigate a large number of individuals with Huntington's Chorea from a small community in Quebec. The research thus deviated from the original plan stated in 5(a) and (b) of the original submission, but it is hoped to return later to a more direct attack on the topic envisaged in the title of that project.

So far, biochemical studies of Huntington's Chorea have been carried out on eight persons, with intensive work on three. The aim of the work is two-fold: (1) to determine whether there is a biochemical defect in amine metabolism, as already demonstrated in this laboratory for Parkinsonism; and (2) whether any of the symptoms of the disease can be favourably modified by biochemical means. To achieve the first aim, five different specific amines or products of amines have been measured in a total of 24 urines from patients with Huntington's Chorea. These compounds are dopamine, dihydroxyphenylacetic acid, noradrenaline, adrenaline, and 5-hydroxyindoleacetic acid. A procedure is being worked out now for a sixth compound, homovanillic acid. At the same time, the methods are being applied to urines of normal persons, so that suitable comparisons can be made.

The second aim, the testing of symptom alleviation by a biochemical approach, has been tested on choreic in-patients at the Allan Memorial Institute. Various amino acids were administered by mouth in specific trials. The amino acids being used are dopa and 5-hydroxytryptophan, both precursors of specific amines in the body. Clinical appraisal of the patient following ingestion of the amino acid is made and, independently,

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biochemical analyses. Two points are of interest: (1) Because some of the amino acid gets into the brain, producing its amine there, specific changes in the clinical picture are being watched for, even if fleeting (corresponding to the brief life of the administered material in the body). (2) Again, by comparison of the results of these biochemical tests with those found in normal persons, it may be possible to determine whether the patient with Huntington's Chorea metabolizes the amino acid or its products abnormally. We have already obtained some evidence in this laboratory for a defective conversion of dopa to dopamine in Parkinsonism.

The present results do not permit any generalisation about biochemical factors in Huntington's Chorea, but there are sufficient discrepancies in the analyses from normal to warrant continuing and expanding the pilot endeavour into a more sustained investigation.

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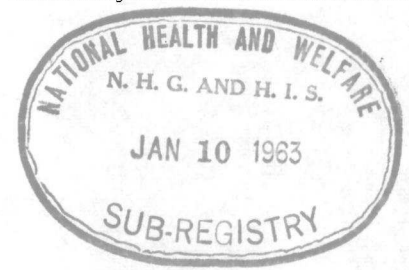
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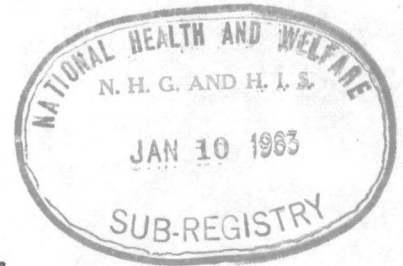
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