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AGING OF BRAIN AND BEHAVIOUR: BIOMEDICAL, CLINICAL AND BEHAVIORAL RESEARCH IN THE DOMAIN OF AGING AT THE UNIVERSITY OF LIMBURG

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INTRODUCTION

The Aging Programme is one out of the three main research programmes in the faculties of Medicine and Health Sciences in the University of Limburg, Maastricht, The Netherlands. There are two themes namely "Aging of Brain and Behaviour" (leader: Prof. Dr. J. Jolles) and "Social Aspects of Aging" (leader: Dr. A. Ph. Visser). The programme is multi- and interdisciplinary and covers the whole of biomedical sciences, clinical sciences, behavioral sciences and social sciences. The research themes have to do with the process of aging; thus, the research is directed at the period from early adulthood through to the senium and on diseases and health-threatening factors that are thought to influence the aging process. Furthermore, emphasis is given to middle-aged and elderly persons in health and disease. That is, attention is given to people in their second life's half (age above 40 years) and to people in the senium (age above 64 years).

The research theme "Aging of Brain and Behaviour" has started in 1986. Presently, 33 research projects are clustered in this theme according to six research lines (see below). For the present volume of "From gene to man" a selection has been made out of the 33 projects which are presently executed. Thus, 17 papers are presented; a short description of the scope of the research is given in the following paragraphs. The reader is referred to Jolles (1990) for a more elaborate description of all the research projects in the Brain and Behaviour-theme and in the "Social Aspects of Aging"-theme (30 projects; not presented in this volume).

RESEARCH LINE 1. BEHAVIORAL, EMOTIONAL AND COGNITIVE DYSFUNCTIONS.

This cluster of projects is characterized by an angle of incidence from human neuropsychology. This means that analysis from a brain-behaviour perspective takes a central position. It involves persons with (probable) brain

dysfunctions and their expression in terms of disturbed behavioral, emotional and cognitive functions (memory, attention, language, etc.). A strong emphasis is put on the connection between cognition and the compensation for function loss, which occurs on growing older. Related to this is the development of all possibly relevant forms of neuropsychological rehabilitation. Within this cluster, research is carried out:
1. into the development and application of new methods to be used in clinical neuropsychology; 2. into the determination of psychological dysfunctions and their nature; 3. into experimental and psychiatric syndromes; and 4. into experimental forms of neuropsychological intervention with these diseases.

At present, projects are in progress in the following fields:
- early diagnosis and risk factors for Alzheimer dementia;
- differential diagnosis dementia-depression;
- disorders in perception and communication with psychogeriatric patients;
- functional training and function-directed support;
- education about memory disorders and dementia;
- cognitive dysfunctions on growing old.

There is an overlap with projects in research lines 2 and 3.

RESEARCH LINE 2: NEUROPSYCHIATRIC SYNDROMES.

This cluster of projects is characterized by an angle of incidence from neuropsychiatry /biological psychiatry. It involves fundamental and applied research into biological determinants of diseases of Brain and Behaviour. A central position is taken, on the one hand, by the development and evaluation of new procedures for medical diagnosis for neuropsychiatric syndromes, and by their biological treatment, particularly with pharmaca, on the other. An important theme is early detection and intervention of the relevant diseases, while, at the same time, much attention is paid to cognitive deterioration in non-demented persons. Cognitive changes after brain trauma, anaesthesia, alcohol and cerebrovascular disease are the most relevant in this respect. The fundamental and applied research is carried out in particular in the Maastricht Memory Clinic.

At present, projects are in progress in the following fields:
- neuropsychiatric differentiation of demential syndromes;
- evaluation of a memory clinic as provision for the syndromes;
- medical decision-taking and an expert system for dementia diagnostics;
- treatment of cognitive dysfunctions with vasopressin;
- aluminum metabolism in Alzheimer's disease;
- event related potentials in dementia and depression;
- motor reflexes in aging and dementia;

- treatment of Alzheimer dementia with L-acetyl-carnitine and with cholinergic drugs;
- brain imaging techniques Single Photon Emission Computer Tomography, (SPECT), Nuclear Magnetic Resonance (NMR) and Computer Tomography (CT) and dementia.

There is an overlap with projects in all other research lines.

RESEARCH LINE 3: COGNITIVE AGING.

The angle of incidence in this cluster of projects is cognitive-psychological, which means that man is considered to be an adaptive information-processing system. The point-of-view of cognitive psychology is that it is possible to obtain knowledge of separate aspects of the cognitive (c.q. brain-)functioning of man by an accurate selection and application of tasks developed for that purpose. In this way, insight can be gained into the specific disturbed stages of information processing, while laws which lie at the root of it can be described. Within this line of research a strong emphasis is laid on biological and psychosocial risk factors for cognitive aging; coupled to this is large-scale population c.q. epidemiological research as well as longitudinal investigations with persons who are at risk for accelerated cognitive aging and dementia. The projects in this line of research have an overlap with those of research lines 1 and 2. At this moment, investigations are in progress in the following fields:

- information processing in depression;
- risk factors in age-associated cognitive deterioration;
- automatic and controlled information processing in Alzheimer;
- solvents and other risk factors for neurasthenic symptoms in aging;
- memory training;
- episodic memory in middle-aged and elderly subjects.

A project in the field of artificial intelligence c.q. our expert system for dementia diagnostic are in progress, in connection to cluster 2.

RESEARCH LINE 4: ANIMAL MODELS FOR DISEASES OF BRAIN AND BEHAVIOUR.

The projects in this cluster are concerned with experimental behaviour research on laboratory animals. Specifically, new methods are being developed and applied for sensitive and specific measurement of aspects of memory. Another purpose of this cluster of projects is to gain more insight into the cerebral processes underlying memory disturbances on aging. Specifically, investigations are carried out about cholinergic and peptidergic systems in the

brain and about pharmaca, while also risk factors such as alcohol and anaesthesia, as well as dietary factors and cerebrovascular parameters are studied in this connection. Rats of various ages and history record (e.g. inbred strains, chronically enriched environment, etc.) are studied. Current projects are:
- cholinergic neurotransmission and an animal model for memory disturbances;
- effects of cortical cholinergic denervation on memory processes;
- lecithin-enriched food, memory and hippocampal morphometry;
- aging and the effect of chronic alcohol consumption on memory;
- nootropics, particularly acetyl-carnitine and memory of the old rat.

There is an overlap with projects in research lines 1-3 and 5.

RESEARCH LINE 5: NEUROCHEMICAL ASPECTS OF DEVELOPMENT AND AGING.

This cluster of projects is characterized by an approach from experimental and clinical neurochemistry. The central themes are neurochemical changes in components of brain cell membranes; brain hormones and neurotransmitters in relation to neurological and neuropsychiatric syndromes. Thus, an emphasis is on functional relationships between neuro(bio)chemical processes on the one hand, and clinical/behavioral studied diseases on the other. Current projects are specifically concerned with problems that are also studied in other research lines from a different angle of incidence. The neurochemical investigations are carried out on human brain material (in particular Alzheimer dementia and controls) and on brain tissue from rats of various ages. Current projects are:
- metal ions as risk factors for brain aging;
- inositol lipid metabolism on aging and in Alzheimer disease;
- vasopressin in the brains on aging;
- effects of the immuneresponse on brain function.

In 1989, several new studies were started, namely into neurochemical changes in multiple sclerosis and into aluminum and polyphosphoinositides in brain change. There is an overlap with projects in the 2nd, 4th and 6th research line.

RESEARCH LINE 6: THE ELDERLY PATIENT.

In this cluster, projects are combined in which, from a clinical-medical angle of incidence, older patients are studied with whom - in some way or other - the central or peripheral nervous system is at stake; primarily neuropsychiatric projects, such as those related to dementia, are placed in research line 2. Currently, investigations are carried out concerning:

- cerebral haemorrhage;
- lacunary infarcts;
- prophylactic X-ray treatment in order to prevent brain metastases;
- brain imaging techniques (CT-scan, NMR, SPECT) and neurological diseases on aging;
- sleep disturbances in war victims;
- geriatrics as a health care provision for patients with multiple diseases. In 1989, new projects were started in the fields of epilepsy, in particular post-cerebrovascular accident (CVA) epilepsy; and miction disorders and incontinence in older people.

There is an overlap, particularly with research line 3.

REFERENCES

Jolles J., The research programme on AGING at the University of Limburg, 1990, Report 9001.