From Gene to Man - Gerontological Research in The Netherlands
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AGING AND DEMENTIA RESEARCH IN THE NETHERLANDS INSTITUTE FOR BRAIN RESEARCH (NIBR)

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In the Netherlands Institute for Brain Research (NIBR) a number of projects deals with (1) the infrastructure necessary for aging and dementia research, (2) the diagnosis of Alzheimer's disease symptoms (see Ravid and Swaab) and treatment of symptoms of Alzheimer's disease (see Witting et al.), and (3) research on the basis of neuronal changes in aging and Alzheimer's disease and ways to influence these processes (see Van Zwieten et al. and Goudsmit et al.).

Infrastructural provisions are the bank for old animals of NWO and the Netherlands Brain Bank. Aged animals have to be bred years before experiments are carried out; they need much space and care and, therefore, are extremely expensive. Experimental work on aged animals is possible in the NIBR only because NWO and EURAGE are subsidizing the costs of such facilities in the Institute for Experimental Gerontology (IVEG), Rijswijk. The Netherlands Brain Bank was organized in order to provide research teams with clinically and neuropathologically well characterized human brain material of rapid autopsies. Permission for autopsies is obtained in advance. A 24-hours on-call system and the collaboration of neuropathologists from the Free University and the Academic Medical Center (AMC) made it possible to provide in 4 years time 60 research groups with material from 183 Alzheimer's disease patients and 136 controls (Ravid and Beek, 1989). In the framework of EURAGE, European contacts on tissue banking are developing (Swaab et al., 1989).

EURAGE contacts also form the basis for studies on the international standardization of the neuropathological diagnosis of Alzheimer's disease. New developments concerning the diagnosis of Alzheimer's disease include the biochemical determination of Alzheimer's disease associated protein (ADAP) in cortex and of ubiquitine in cerebrospinal fluid of Alzheimer's disease patients. The former is a quantitative assay, easy to perform and might, therefore, be of help in estimating the gravity of the Alzheimer changes. The latter, the ubiquitine assay, is a first step towards an in vivo diagnosis of Alzheimer's disease.

One of the characteristic symptoms of Alzheimer's disease is a disturbed day/night rhythm. Earlier we found that the cell number of the suprachiasmatic nucleus (SCN) decreased strongly in Alzheimer's disease (Swaab et al., 1985). This might be the anatomical basis for the loss of circadian rhythmicity in Alzheimer's disease leading to the sleep disturbances that often necessitate admission of Alzheimer patients to homes. Current research is directed towards the question how normal day/night rhythms can be restored in Alzheimer patients. This line of

research includes both experiments with aged animals and observations in Alzheimer patients.

The search for neuronal changes in aging and Alzheimer's disease includes the hypothesis of enhanced DNA damage in this condition (in collaboration with E. Mullaart and J. Vijg, IVEG) and the alterations in peptidergic and other systems in the human hypothalamus. This latter line of research is partly carried out in cooperation with the University of Leiden (see H.P.H. Kremer elsewhere in this volume). A leading idea in this line of research is our hypothesis that during aging and Alzheimer's disease neurons might survive better by activation. This hypothesis is paraphrased as "use it or lose it" (Swaab, in press). An illustration of this principle is the loss of vasopressin innervation in various areas of the aged rat brain that appeared to be associated with decreased testosterone levels. Testosterone treatment of aged rats was found to restore the vasopressin innervation in the rat brain (Goudsmit et al., 1988).

REFERENCES

Goudsmit E., E. Fliers and D.F. Swaab, Testosterone supplementation restores vasopressin innervation in the senescent rat brain, Brain Res. 473 (1988) 306-313.

Ravid R. and G.J. Beek, The Netherlands Brain Bank, Progress Report 1989.

Swaab D.F., Brain aging and Alzheimer's disease: "wear and tear" versus "use it or lose it", Neurobiol. Aging (1990) in press.

Swaab D.F., E. Fliers and T. Partiman, The suprachiasmatic nucleus of the human brain in relation to sex, age and dementia, Brain Res. 342 (1985) 37-44.

Swaab D.F., J.-J. Hauw, G.P. Reynolds and S. Sorbi, Tissue banking and EURAGE, J. Neurol. Sci. 93 (1989) 341-343.