Biological risk factors for accelerated cognitive aging and dementia

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We investigated survival in 121 consecutive patients affected by clinically diagnosed Alzheimer's Disease (AD), selected among the 146 referred to the seven Neurological Departments involved in the Italian Multicenter Study on Dementia (SMID) project, from April 1982 to December 1983. Clinical diagnosis of AD was made according to rigorous inclusion and exclusion criteria similar to that indicated by the NINCDS in 1984. Included patients were followed for two years at least by every six-month assessments and, then, interviewing the next of kin about patient status, self-care, time and cause of death, whenever direct examination was not possible. Of the 146 mentioned patients, 4 revealed to suffer from other forms of dementia and 21 dropped-out. Their demographic characteristics did not differ from that of the population under study. In this, 43M and 53F (mean age 59.6, SD 6.2) presented presenile AD (onset before than 65 years), while 7M and 18F (mean age 71.3, SD 7.1) presented senile AD. The overall dementia severity at baseline was similar in the two groups. Relative survival curves adjusted by age and sex, as well as curves generated by the Kaplan-Meier procedure using a functional and a cognitive endpoint (score higher than 17 at the Blessed Dementia Scale and score lower than 7 at the Information-Memory-Concentration test) were similar in senile and presenile AD.

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BIOLOGICAL RISK FACTORS FOR ACCELERATED COGNITIVE AGING AND DEMENTIA: FINDINGS FROM A MULTIPLE COHORT STUDY. * J. Jolles, P. Houx, F.W. Vreeling, N. Bohnen, E. Reyersen van Buuren. Dept. Neuropsychology & Psychobiology; Limburg University; Box 616; 6200 MD Maastricht; The Netherlands.

There is a lack of knowledge with respect to the predementing stages of Alzheimer's Disease. Thus it is not clear whether a person who eventually appears to suffer from AD has particular cognitive and/or biological characteristics earlier in his/her life. The present paper defends the notion that minor "Risk Factors for Brain Dysfunction" (RF) are important in this respect, in that they accelerate the normal biological aging process and lead to accelerated cognitive aging. Relevant in this respect are brain trauma, general anesthesia, drinking and toxicological factors. The first line of evidence comes from a controlled clinical experiment in which 15 patients suffering from a possible predementing stage of AD (GDS 3) were compared to carefully matched control subjects. It appeared that the patients were characterised by inferior performance on complex tests of memory; in addition, the prevalence of RF appeared to be significantly increased in the patients. The second line of evidence comes from a multiple cohort study with 250 subjects analysed in 7 cohorts from 20 through 80 years. These subjects were recruited from the normal population and devided into a healthy group and a RF group on the basis of a neurological examination and an extensive clinical interview into the presence of possible RF. It appeared that elderly risc-free individuals (aged 60, 70, 80 years) were hard to find: 2-4 times as many volunteers had to be recruited in order to fill these cells; None of the subjects however suffered from a major neurological disorder. Highly significant findings were done in that the RF group performed significantly inferior to the healthy subjects on all complex and speed-demanding neuropsychological tests. There was an interaction with aging in that the difference between the groups increased with age; quite some individuals aged 70 or 80 in the RF group showed a globally poor performance in all tests, suggesting an incipient dementia. The findings may have serious implications for cognitive aging research in that they attract notice to the importance of risc factors for brain dysfunction. Many of the effects of biological aging reported in the literature, may result from factors other than aging itself. In addition, epidemiological research into predementing stages of AD is directed towards assessing the possible relevance of a cumulation of the relevant risc factors.

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INCIDENCE, PREVALENCE AND RISK FACTOR ANALYSIS OF ALHEIMER'S DISEASE IN ROCHESTER, MINNESOTA: LONG TERM TRENDS OVER TWENTY YEARS. *E. Kokmen, C.M. Beard, R.C. Petersen, D.J. Ballard, L.T. Kurland. Mayo Clinic and Foundation, Rochester, Minnesota 55905.

Rochester, Minnesota is a town of approximately 62,000 population located in southeastern Minnesota. Since the early part of the century, most of the medical services and all specialized medical services have been provided by a large multidisciplinary medical practice, Mayo Clinic, and its affiliated hospitals. A collaborative arrangement with other health care resources in the community including State Hospital, Veterans Hospital, County Hospital, group practices, and nursing homes allow us to review all medical records and all diagnoses that might possibly lead to dementia in a precoded form. Utilizing this resource, incidence rates of dementia of all causes and specifically of Alzheimer's disease were calculated for the period, January 1, 1960 through December 31, 1979. Estimated age- and sex-adjusted incidence rates for Alzheimer's disease for these four quinquennial periods were respectively 54.9, 43.5, 49.9, and 54.7 per 100,000 per year. For dementia of all types, observed ten-year survival from onset was 16%, 17%, 16%, and 18% in these four periods. Prevalence of dementia from Alzheimer's disease on January 1, 1975, and January 1, 1980, was approximately 2.5% of all population over 65 years and older. Risk factor analysis for therapeutic radiation exposure, head trauma, common medical illnesses, surgical interventions, and exposure to general anesthesia was also carried out utilizing matched controls and matched control odds ratios. No risk factors were found to be significant.

When age-specific prevalence rates of January 1, 1975, and January 1, 1980, were compared to each other, the only significant difference was an increase of prevalence of Alzheimer's disease in the population 85 years and older.

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AGING AND RISK FACTORS FOR ALZHEIMER'S DISEASE. *F. Marott Sinex, Boston University School of Medicine Boston, Mass., 02118, USA.

To delay or prevent Alzheimer's disease we must know what factors determine risk. It would be helpful to anticipate the number and type of risk factors for different ages of onset, and the age at which these risk factors have the most effect on the incidence of subsequent disease.

Kannel has discussed the interaction of risk factors and age in cardiovascular disease, where an individual's risk factors may be isolated or found in combination with others. A single risk factor is more readily detected in a younger person where its effect on the relative risk is clear. While a risk factor (for example, hypertension) increases the risk of an older person, the effect is seen against a background of other factors and intrinsic aging. Some of these other factors may be less robust but may have been operating and contributing injury over many years.

There are two major risk factors for Alzheimer's disease, a family history and age. It is tempting to look for factors for aging which also might be present in Alzheimer's disease. Hochschild, Furakawa, and Young and Reichart have shown that it is possible to estimate a biological age with biomarkers, and use this biological age to study the effects of intervention factors. The contribution of these known adult stage intervention factors to the total variability about chronological age is small, equivalent to less than ten percent of the standard deviation of the order or plus or minus 3.5 years.

A number of risk factors for Alzheimer's disease in older subjects remain to be tested. Individual risk factors for the elderly may have small effects on the ascertainable risk, but in the aggregate be significant. There also may be important risk factors which only relate to development, infancy or childhood.

One may speculate that some of these risk factors relate to particular genes, and that the very old express more but less robust genes for the disease than those with earlier onset.

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PREVALENCE OF ALZHEIMER'S DISEASE AND OTHER DEMENTIAS IN ADVANCED AGE.