Evaluation of an expert system for dementia diagnostics (EVINCE)

Part II: Factorial analysis showed 5 main factors in the emotional behavior of the patients: Resented irritability, Observed sadness, Observed irritability, Observed blunted affect, Anhedonia. Blunted affect was more pronounced in patients with severe dementia than in patients with mild dementia. There was a dissociation between ressented and observed affects.

It is suggested that dimensions of affect such as irritability, impulsivity on one hand and blunted affect on the other could reflect different biochemical disturbances. Theoretical and practical consequences are underlined.

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DEMENTIA OF FRONTAL LOBE TYPE. *D. Neary, J.S. Snowden, D.M.A. Mann. Department of Neurology, Manchester Royal Infirmary and Department of Pathology, University of Manchester, Manchester M13 9WL, England.

A longitudinal clinico-pathological study of patients with dementia indicates that primary cerebral atrophy leading to dementia represents a heterogeneous group of conditions.

Thirty-eight patients have been studied who presented with striking breakdown in social and personal conduct with ritualistic behaviour and progressive loss of language. They exhibited a frontal lobe syndrome with selective sparing of visuo-spatial function. Neurological signs consisted of primitive reflexes only and the electroencephalogram was normal. Single photon emission tomography revealed selective abnormal uptake in the anterior cerebral hemispheres. A family history of a similar form of dementia was present in 46% of cases.

Pathological analysis at necropsy of the brains of nine cases has revealed fronto-temporal atrophy. The microscopic changes were of large neuronal cell loss, spongiform change and astrocytic gliosis, chiefly affecting layer 3 of the cerebral cortex and especially in the frontal and temporal lobes and the corpus striatum. Neurofibrillary tangles and senile plaques were absent as were Pick cells and Lewy bodies. Neurochemical analysis of cortical tissue revealed normal values for acetylcholine synthesis and choline acetyltransferase activity.

Dementia of frontal-lobe type can be distinguished from Alzheimer's disease neuropsychologically, on brain imaging and pathologically. It appears to be genetically determined, probably by autosomal dominant inheritance and is more common than has previously been supposed.

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LANGUAGE AND MEMORY PROCESSING IN SDAT, DEPRESSIVE PSEUDODEMENTIA, AND MAJOR DEPRESSION/UNIPOLAR. *V.O.B. Emery, R. Arora. Dartmouth Medical School, Hanover, New Hampshire, 03756 USA and Case Western Reserve University School of Medicine, Cleveland, Ohio, 44106 USA.

To contribute to the definition of the structure of cognitive deficits in senile dementia Alzheimer's type (SDAT), language and memory processing were studied in 20 elderly persons with SDAT, 12 elderly with depressive pseudodementia, 20 elderly with major depression/unipolar, and 20 normal elderly. Variables of age, sex, race, education, occupation, native language were controlled. Measures administered included the Western Aphasia Battery, Test for Syntactic Complexity, Chomsky Test of Syntax, Wechsler Memory Scale-Revised, and Katzman Test for Delayed Recall. Significance was determined by ANOVA, followed by Scheffe's test. The Omega Squared statistic was used to determine effect size of tests. Results indicate there are significant differences in patterns of deficits characterizing research groups. Greatest discrimination between SDAT and depressive pseudodementia on measures of memory occurs on Story Recall and Information. Greatest effect size between SDAT and major depression/unipolar occurs with Orientation and Information. Results from the language assessment suggest SDAT is best discriminated from depressive pseudodementia by two simple naming tasks requiring implicit interpretation, i.e., Responsive Speech and Sentence Completion. In contrast, SDAT is best differentiated from major depression/unipolar by the most complex semantic, syntactic, and meta-naming tasks, i.e., Reading Comprehension, Test for Syntactic Complexity, and Word Fluency. Relevance of research results for the differential diagnosis between SDAT and depressive pseudodementia is discussed. The relation between SDAT and pseudodementing illness is analyzed. The issue of nosological validity is addressed.

Preliminary data pertaining to imipramine binding/central serotonergic function in a subset of the study participants are presented. The 'severe' category of SDAT appears to involve significant reductions in platelet 5-HT uptake (V_{max}) (V_{max} = 12 p moles/10^7 platelets/min). Tentative implications of serotonergic function for language and memory processing in research populations are explored.

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ACCELERATED PROGRESSION OF DEMENTIA OF THE ALZHEIMER TYPE BY DEVELOPMENT OF SEIZURES. *L. Volicer, S. Smith. Geriatric Research Education Clinical Center, E.N. Rogers Mem. Veterans Hospital, 200 Springs Road, Bedford, MA, 01730 and Boston Univ. School of Medicine, 80 East Concord Street, Boston, MA, 02118.

The onset of generalized, unprovoked seizures in patients with moderately advanced DAT is well recognized. The consequences of this seizure disorder, however, are unknown. To evaluate the possible sequelae of new-onset seizures, we surveyed 75 patients with clinical diagnosis of probable DAT, hospitalized at the Dementia Study Unit. Seventeen of them (22.7%) exhibited initial seizures after the onset of dementia. Data on the effects of these seizures were collected by means of interview of patients' spouses, chart review and quarterly clinical evaluations. In 7 of the 8 patients (87.5%) who suffered the initial seizure at home, caregivers reported worsening of patient's behavior and increased confusion. In 5 cases (62.5%) the patient developed resistiveness to care, in 4 cases (50%) assaultive behavior and decreased ability to communicate, in 3 cases (37.5%) increased difficulty in walking and in 2 cases (25%) decreased ability to eat after the onset of seizure(s). Four of these patients, who were evaluated before and after the onset of seizures, exhibited significant decreases in their Mini-Mental scores. Seven of the 8 families caring for these patients at home obtained long-term care admission for the patient within 6 months of the seizure onset, with 4 of them being hospitalized within one month. Eight patients developed new onset, generalized seizures after long-term care admission. The impact of seizures on the condition of 6 patients was not possible to assess, because 4 of them developed seizures more than 5 years ago, one had a fluctuating baseline, and one was too advanced to detect any change. In two other patients, who had a moderate degree of dementia before the development of seizures, the language and cooperation with staff worsened while a severity indicator increased after the seizure, although these indices were quite stable for several months before the seizure onset. These results indicate that new-onset seizures result in an acceleration of the progressive course of DAT in most patients and might precipitate a need for institutionalization. Preventive treatment of moderately advanced DAT patients with anticonvulsants should be investigated. (Supported by the Veterans Administration).

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EVALUATION OF AN EXPERT SYSTEM FOR DEMENTIA DIAGNOSTICS (EVINCE): EXPERT SYSTEM PERFORMS BETTER THAN CLINICIANS. *L.A. Plugge, F.R.J. Verhey, J. Jolles. Dept. of Neuropsychology & Psychobiology, University of Limburg, P.O. Box 616, 6200 MD Maastricht, The Netherlands.

The differential diagnosis of Alzheimer's Disease (AD) in the earlier stages is compromized by the fact that the differentiation from normal cognitive aging is not simple. Although the classification was improved by the criteria proposed by DSM-III and the NINCDS-ADRDA Work Group, there is still quite a lack of consensus on the clinical diagnosis and classification of AD. This makes the problem at hand an interesting subject for formalization through the use of an expert system (ES), especially beacuse the results from several examinations of very different natures have to be integrated. The ES EVINCE incorporates internationally accepted standards as described in the DSM-III-R and the report of the NINCDS-ADRDA Work Group. The present paper describes two evaluation studies with the ES EVINCE in diagnosis of dementia. In experiment 1 EVINCE diagnosed 19 patients who were previously diagnosed by a neuropsychiatrist as suffering from some form of dementia and 10 other patients with various disorders without dementia. The main diagnoses present were demential syndrome (DEM), Alzheimer's Dementia (AD), multiple infarct dementia (MID), and depression (DEP). The ES EVINCE and the human expert showed a perfect agreement on the diagnosis DEM, a high level of concordance for the diagnoses AD and MID, and a moderately high assent on the diagnosis DEP. In experiment 2 a comparison was made between EVINCE, 85 clinicians and a multi disciplinary expert committee (EC), in the diagnosis of 10 patients suspected to suffer from dementia. Each patient received a syndromal and an etiological diagnosis. The 85 clinicians (consisting of neurologists, psychiatrists, nursing home physicians, general physicians and psychologists) had an average of 7.6 correct (i.e. in agreement with the EC) syndromal

diagnoses, and 5.3 correct etiological diagnoses. In contrast, all syndromal and etiological diagnoses made by EVINCE were correct. Moreover, the disciplines displayed significant preferences for certain diagnoses. For example, neurologists used the diagnosis AD more often than clinicians from other disciplines. The experiments show that EVINCE can be considered a good replica of medical expertise on the subject matter. Because standardized diagnostic procedures are essential for research into etiology, pathogenesis and experimental interventions in dementia patients, especially in Alzheimer's Disease, the ES EVINCE could be an important tool.

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NEUROPSYCHOLOGICAL EVALUATION OF PATIENTS SUSPECTED OF EARLY ALZHEIMER'S DISEASE: EXPERIMENTAL STUDIES WITH AGE ASSOCIATED MEMORY IMPAIRMENT AND DYSTHYMIA. * E. Reyersen van Buuren, J. Jolles and P.J. Houx. Dept. Neuropsychology & Psychobiologie; Limburg University; Box 616; 6200 MD Maastricht; The Netherlands.

It appears to be very difficult -if at all possible- to detect Alzheimer's desease in stages in which no dementia is present. In the earlier stages (2 and 3 on the Global Derioration Scale-Reisberg) cognitive dysfunctions can be assessed but it is not clear whether these subjects may develop AD later in life. Longitudinal research is necessary to evaluate such a hypothesis. As a first step in a large longitudinal followup study in the Alzheimer research center in Maastricht, The Netherlands, we evaluated the nature of the cognitive dysfunctions in patients who are suspected to be in an early stage of primary degenerative dementia or to be at risc to be afflicted by such a condition. In a first experiment, 15 subjects aged 41 through 60 who were diagnosed as suffering from dysthymic disorder were compared to 15 healthy age matched controls. It appeared that there were deficits in secondary memory like aquisition and active retrieval from memory; in addition, memory consolidation and general speed of information processing were inferior in the patients. There were no deficits in primary memory such as in digit span and in block span. Identical findings were done in the second experiment in which 20 patients suffering from Age Associated Memory Impairment (AAMI, age 40-70 years) were compared to matched controls. A two years follow up of subjects from the 2 studies has been done. At the follow up assessment it appeared that the performance of patients without depression was inferior to that of patients with depression. The results of these studies are indicative of the relevance of neuropsychological contributions to early diagnosis of degenerative brain disease, especially AD. The sensitivity of cognitive neuropsychological methods enables an objective establishment of minor cognitive dysfunctions which are not evident with gross, psychometric tests and observation scales. The use of these measures for longitudinal research on early phases of Alzheimer's disease is recommended.

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CLINICAL MARKERS OF EARLY ALZHEIMERS DISEASE. *S.H. Ferris, C. Flicker, B. Reisberg, M.J. de Leon. Aging and Dementia Research Center, NYU Medical Center, New York, 10016 USA.

We will review recent research seeking to identify or develop an early clinical marker for Alzheimers disease (AD), i.e., a reliable and valid measure that can be detected before the onset of cognitive symptoms or before these symptoms are severe enough to warrant a clinical diagnosis of AD. Such an early marker would be extremely useful for studying the early course and pathophysiology of AD, since the marker would enable reseachers to select "enriched" study samples containing subjects at high risk for developing AD clinically over the subsequent several years. Promising research directions in the search for early predictors of AD include study of specific patterns of mild cognitive deficit, use of in vivo brain imaging techniques to detect signs of early atrophic change, sensory system deficits and patterns of electrophysiological abnormality. The status of these and other current approaches will be discussed.

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PSYCHOPATHOLOGY AND FRONTAL LOBE INVOLVEMENT IN PRIMARY DEGENERATIVE AND VASCULAR DEMENTIA. 1. CLINICAL ASPECTS. Lars Gustafson*, Department of Psychogeriatrics, Arne Brun Department of Pathology, University of Lund, Lund, Sweden

The aim of the study was to analyse the diagnostic significance of frontal lobe symptoms in dementia. These symptoms are most frequent in Pick's disease and frontal lobe dementia of non-Alzheimer type. Their presence in other dementias may complicate the diagnostic decision.

These clinical questions have been analysed in a longitudinal dementia study. The patients went trough a neuropsychiatric investigation including EEG, regional cerebral blood flow (rCBF) measurement (133 Xe inhalation technique) and in most cases CT. 28 patients with progressive dementia and marked personality changes and other indications of frontal lobe dysfunction were selected for the study.

Results from five patient groups based on the neuropathological findings are presented. Group 1) Dementia of Alzheimer type (DAT) with frontal predominance. This group contained four cases with a mean age at death of 78 ± 7,6 years. They showed a typical Alzheimer type dementia with dysmnesia, dysphasia, dyspraxia and spatial disorientation. In addition to this however they showed aggressiveness, inadequate laughing, vocally disruptive behaviour and other frontal lobe symptoms already at an early stage of the disease. Group 2) Three cases with mainly fronto bilateral selective incomplete white matter infarction (SIWI). The mean age at death was 72 ± 13 years. The patients showed progressive personality changes with an irritability and unrestrained behaviour in combination with memory failure and gait disturbances. Psychotic reactions with visual hallucinosis were found in two cases and the differential diagnosis against nonorganic mental diseases was difficult. Blood pressure was generally low in this group (mean blood preasure 96 ± 12 mm Hg). Group 3) Binswanger's disease. Three cases with a mean age at death of 74 ± 7 years. The dementia was progressive with episodic deterioration and epileptic phenomena. The frontal lobe involvment was mainly indicated by emotional symptoms such as euforia and apathy. Vascular dementia was indicated by the clinical features but differential diagnosis against DAT was difficult. Group 4) contained two unique cases with frontal vascular lesions. Group 5) contained sixteen cases of degenerative frontal lobe dementia of non-Alzheimer type (FLD).
In conclusion. Symptoms indicating frontal lobe damage are common in both vascular and primary degenerative dementias. Differential diagnosis of dementia has to consider the type and severety of the frontal lobe symptoms, the time of debut, and the combination with other psychiatric and neurological symptoms. Differential diagnosis against nonorganic mental diseases may be difficult especially in dementia with duration over 15-20 years, as was the case in several of our patients.

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A BRIEF ASSESSMENT BATTERY FOR THE DIAGNOSIS OF PROBABLE ALZHEIMER'S DISEASE. * M.C.Tierney, G. Snow, A. Nores, M.L. Zorzitto, R. Fisher, D. Reid. Sunnybrook Health Science Centre, University of Toronto, Toronto, Canada, M4N3M5.

The NINCDS-ADRDA diagnostic criteria for Alzheimer's Disease have received wide acceptance in research protocols. Studies examining their validity have been promising. Use of these criteria, however, necessitates lengthy and costly assessment of patients. The purpose of this study was to determine whether a reduction in the number of assessments could produce as accurate a discrimination as the full battery. Our sample consisted of 197 participants each of whom had individual medical, neuro-psychological and behavioural assessments based on the NINCDS-ADRDA criteria. Participants were then classified as neurologically normal (N=96), Probable Alzheimer's (N=56) or 'Other Dementias' (N=45). More than 50 clinical measures were administered to our participants as part of the diagnostic work-up. Discriminant function analyses indicated that a small battery of neuropsychological and neurological measures differentiated among the three groups with 100% accuracy. This battery requires no more than thirty minutes to administer. While this level of accuracy has been reported in some studies which differentiated normals from dementing individuals, no previous study to date has ever reported such high accuracy rates in the distinction among the dementias.

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INCREASED SERUM INSULIN-LIKE GROWTH FACTOR-I CONCENTRATIONS IN INSTITUTIONALIZED WOMEN WITH ALZHEIMER'S DISEASE. LR Donahue, *CJ Rosen, AA Spindler, JF Nichols, JW Ramsdell, and MJ Renvall. Dept. of Internal Medicine, University of California San Diego, and the Dept.of Nutrition, University of Maine, Orono Maine 04473, USA.

Variable changes in growth hormone (GH) concentration have been reported in Alzheimer's patients (ALZ). Insulin-like growth factor-I