PSYCHOPHYSIOLOGIC IMPAIRMENTS IN PATIENTS EXPOSED TO NEUROTOXINS. NEUROPSYCHOLOGICAL ASSESSMENT IN DIFFERENTIAL DIAGNOSIS

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Neurobehavioral methods should discriminate not only between normal and abnormal functioning, but also between abnormalities of different origin. In behavioral toxicology, it is essential that disturbances due to toxic effects be differentiated from those caused by emotional and motivational factors such as fear of poisoning or of brain damage, suggestibility, and attempts (conscious or unconscious) to imitate brain dysfunction. Emotional and motivational states are notoriously difficult to assess in an objective and quantitative way, and they do not readily lend themselves to experimental manipulation. Little is known about their effects on neurobehavioral measures.

In a retrospective study, we have analyzed the neuro- psychological test performance of patients whose symptoms — at first suggestive of toxic encephalopathy — were found to be psychogenic. The results of this analysis may serve to illustrate the potentials and limitations of some current neuropsychological methods in differential diagnosis.

A short introduction to the "Zeitgeist" in Denmark may be essential for apprehension of the findings to be reported. In this country, it has been widely accepted that organic solvents (other than alcohol) pose serious hazards to health. Particularly in the last few years, the news media have taken great interest in the so-called "painters' syndrome", which is depicted (often in a dramatic fashion) as a chronic disease characterized by brain shrinkage, tiredness, impaired concentration, forgetfulness, emotional lability, sexual dysfunction and other psychological and physiological impairments. This syndrome was legally recognized in 1976 and it has since reached almost epidemic proportions, as reflected by central statistics of compensation claims. Thus, the Industrial Injuries Security Office ("Sikringstyrelsen") has reported a rise in de jure re-

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cognized cases of occupational disease due to solvents from 15 in 1976/1977 to 593 in 1982/1983. The majority of these cases obtained a diagnosis of chronic brain damage. There have been several instances of local epidemics in factories with minimal air concentration of neurotoxins.

Since traditional neurological or other medical examinations are generally negative, neuropsychological assessment is often decisive for a diagnosis of solvent-induced encephalopathy. According to Danish practice, even a remote suspicion of intellectual impairment frequently occasions examination by a neuropsychologist.

**Subjects and Methods**

Patients referred to the authors with the tentative diagnosis of toxic encephalopathy due to occupational exposure (in most cases involving organic solvents) are extensively examined through interviews and formal testing of cognitive functions. The tests have been standardized at Rigshospitalet in Copenhagen; the battery has been shown to contain tests with widely different degrees of sensitivity to atrophic brain disease (A. Gade et al., the current proceedings and in preparation).

In the focus of our present interest is a group of patients, tested during the last three years on the suspicion of toxic encephalopathy, who obtained a severely depressed overall score on the test battery, but who showed curious within-test variability and other behavioral inconsistencies incompatible with a genuine "organic" dementia. Hence, they received a diagnosis of pseudodementia (Ref. 1). Fourteen of these patients fulfilled the following criteria for inclusion in the study group: a) Subjective complaints of serious cognitive impairment. b) Significantly depressed overall level of test performance, as evaluated on the basis of at least 10 completed tests (irrespective of pattern of test results. c) A clear discrepancy between the present, poor test results and proficient functioning in other respects, e.g. as revealed in history and/or general conduct in the hospital. (One exception). d) A normal neurological examination (except for "functional" signs, which were

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1 Alotted space does not allow a listing of such inconsistencies. Examples include one patient who failed in simple tests of calculation and showed extreme amnesic difficulties in formal testing, but was able to give a detailed account of the complicated family economy, past and present. Another patient, diagnosed as demented, successfully took up studying.
often present. e) A normal CT-scan. f) A history not suggestive of subnormal intelligence, alcohol abuse, neurological or major psychiatric disease or family disposition for presenile dementia. There were 11 men and 3 women; the age range was 23-60 years (mean 42.6). Half of the patients had previously been diagnosed as demented.

The test results of the pseudodemented patients (group PD) were compared to those of two groups of neurological patients with a clinical neuroradiological diagnosis of cerebral atrophy on the CT-scan. The groups were etiologically heterogeneous. They did not include patients suspected of solvent-induced encephalopathy. In neuropsychological examination, 14 of these patients showed signs of minimal or mild intellectual impairment (group AM: mean age 41.9, range 18-68). Another 14 patients had moderate to severe impairment (group AS: mean age 45.2, range 20-62). The three groups were matched for educational level.

In addition, the pseudodemented subjects were compared with: a) 14 patients with more severe psychopathology (manifest or suspected incipient schizophrenia, delusional hypochondriasis, borderline states). Most of these patients already had a psychiatric diagnosis, but none of them was currently hospitalized. All were referred on a suspicion of organic solvent-induced encephalopathy (age 19-57, mean 40.5). These patients will be referred to as psychotic/borderline states (PBS); b) 11 patients suffering from normal pressure hydrocephalus (NPH), tested before shunting (age 22-62, mean 49.1).

Further information about the patient groups is available upon request.

All test scores were converted to T-scores (mean 50; standard deviation 10), based on the distribution in the normal standardization sample. Hence, all behavioral measures can be represented in comparable "profiles". For brevity and increased reliability most measures are expressed in composite scores based on factor analysis. Differences between groups have been tested by analysis of variance and comparisons by T-tests.

Results and Discussion

Pseudodementia vs. atrophic encephalopathy. On an overall measure of test performance (mean score of the "Basic Battery", A. Gade et al., the current proceedings), the PD patients did not differ from the AS group (X: 19.5 and 22.1 respectively), while both of these groups attained a level significantly lower than the AM subjects (X: 40.6). However, an analysis of test-profiles revealed striking differences also between the pseudodemented and the AS patients, as illustrated in the figure.

Group PD performed better in block designs (p < .05), but considerably worse in measures: Verbal IQ (WAIS-R vocabulary, p < .01), memory sentence repetition; p c of choice, words and faces, (STRE II) fragmented pictures, lapping objects in a photo. All designs and visuo-spatial span are relatively intact here in near identical scores. Similarly, the visual tests for reading test failed to discriminate with brain atrophy. In the test performed at chance level (acquisition of paired associates; (Trail Making A and B) and the PD subjects did not
Group PD performed significantly better than the AS group in block design (p < .01) and in visuo-spatial learning (Ref. 2; p < .05), but considerably worse than the AS patients in four measures: Verbal IQ (WAIS Information, Similarities and Vocabulary, p < .01), memory span (digit repetition and reversal and sentence repetition; p < .0001), recognition memory (forced choice, words and faces, Ref. 3; p < .0001) and visual tests (STREETF fragmented pictures and a test of perception of overlapping objects in a photograph, p < .05). In contrast to block designs and visuo-spatial learning, both verbal IQ and memory span are relatively insensitive to brain damage, as reflected here in near identical scores in the AM and AS groups. Similarly, the visual tests did not discriminate between the groups with brain atrophy. In the recognition tests, our PD patients performed at chance levels as a group (mean 26.6 correct in 50 words and 27.7 in 50 faces), with a few subjects obtaining scores significantly below chance level (lowest score to date at 24% correct). In some tests, i.e. measures of verbal learning (acquisition of paired associates) and of visuo-motor speed (Trail Making A and B and the Symbol Digit Modalities Test), the PD subjects did not differ from group AS. Also the DART reading test failed to differentiate between the groups.
Pseudodementia vs. normal pressure hydrocephalus. The NPH patients were only tested with the Basic Battery. Their overall performance was subnormal (X 32.8), but significantly superior to that of the pseudodemented. Profile analysis revealed different patterns of impairment, with the NPH-subjects performing significantly better in memory span (p < .01), and the PD patients performing significantly better in block designs (p < .05). The same double dissociation was reported above in comparison between groups PD and AS.

Pseudodementia vs. psychotic/borderline states (PBS). Our patients with psychiatric disease performed significantly better than the pseudodemented patients in every test except block designs. In fact, the PBS patients as a group did not differ significantly from the mildly impaired, atrophic patients on any measure. Thus, rather severe psychopathology does not necessarily cause more than slight difficulties on our test battery.

The cognitive profile found in group PD is distinct and, to our experience, practically unique to pseudodementia. Twelve of the 14 patients of the present PD series showed this pattern to a more or less pronounced degree. We have tested several hundreds of solvent-exposed subjects, including the present PBS group, who did not present a similar pattern of deficits. On the other hand, we have seen this profile in a number of non-exposed patients (e.g., a few patients with mild head trauma), who were also diagnosed as pseudodemented. Hence, there is no reason to believe that the profile of group PD represents an impairment characteristic of solvent-induced encephalopathy.

Level of intelligence. In subscales of the WAIS, the PD patients attained remarkably poor scores, with an average level corresponding to mild mental retardation. However, it is our conviction that this measure does not reflect a genuine intellectual deficiency. No patients with a history suggestive of low premorbid intelligence was included in the group. The PD patients did not differ from the other groups in the DART reading test, which is claimed to give a good estimate of premorbid intelligence. Several patients have shown remarkable fluctuations in repeated assessments of intelligence, occasionally demonstrating normal abilities. In no case did the clinical impression suggest mental retardation. It should also be noted that the cognitive profile seen in group PD cannot be attributed to low intelligence. The recognition memory tests have a modest correlation with intelligence. One group of patients with parathyroid disease and low intelligence have demonstrated normal recognition memory (R.G.T. Oberg et al., in preparation).

Incidence of pseudodementia factors, including "Self-control," unemployment rate, and diagnostic practice. Our patients referred to us for pseudodementia presented a prevalence of possible mild incapacity.

The personality characteristics were varied. Neuroticism was not a feature, and most of the presently referred pseudodemented patients were not depressed pseudodemented patients.

Psychogenic impairments were not diagnosed in any of the patients, as overall scores in neuropsychological tests were not suggestive of the syndrome of dementia. However, the patients tend to perform exceedingly well on tasks (notably memory span and tests of recognition) that do not appear to be particularly well correlated with pseudodementia. In most cases, the patients were able to perform well on memory tasks, even when the clinical impression suggested more severe impairments.


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Incidence of pseudodementia is presumably dependent on numerous factors, including "Zeitgeist" as depicted above, working conditions, unemployment rate, possibility to attain compensation and diagnostic practice. During the last 2 years, at least 10% of the patients referred to us on the suspicion of toxic encephalopathy presented a pronounced psychogenic "dementia". The incidence of possible milder forms cannot be estimated at present.

The personality characteristics of the pseudodemented patients were varied. Neurotic or hysterical traits were noted in most of the presently reported patients. There was no case of depressive pseudodementia. Malingering was strongly suspected in a few cases. Further discussion of underlying psychopathology will be presented elsewhere.

Conclusion

Psychogenic impairments may lead to a severe reduction of overall scores in neuropsychological tests and to a false diagnosis of dementia. However, analysis of test profiles may be a powerful tool in differential diagnosis. Pseudodemented patients tend to perform exceedingly poorly on some dementia-resistant tasks (notably memory span and verbal subtests of the WAIS) and on tests of recognition memory; the same patients show disproportionate sparing of function in block designs and visuo-spatial learning. In our experience similar profiles are rarely - if ever - seen in impairment due to brain disease.

References


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