ON THE IMPORTANCE OF CONTROL DATA AND BACKGROUND VARIABLES IN THE EVALUATION OF NEUROPSYCHOLOGICAL ASPECTS OF BRAIN FUNCTIONING

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Introduction

Organic solvents have a well-described depressant or narcotic effect on the central nervous system (CNS). Neuropsychological tests have repeatedly been demonstrated to be sensitive measures of this effect both in exposure chamber experiments and field studies (1).

It has been suggested that long-term occupational exposure of organic solvents may also lead to a permanent impairment of CNS functioning. In Denmark this is clinically and legally recognized, and neuropsychological examinations are performed routinely in the evaluation of exposed workers considered for financial compensation for damages.

A number of reports of a high incidence of intellectual impairment as well as other presumed indices of brain damage in referred exposed workers have been published. This may reflect a clinical practice developed from the examination of clear-cut neurological patient categories. A practice, however, which may not be applicable in this context.

In epidemiological studies the influence of confounding variables is sought controlled by careful matching with control groups. In clinical studies, and in individual assessments for diagnostic and legal purposes, age, education, intelligence level and other potential influences on test performance have often been inadequately controlled or even ignored (2, 3, 4).

In Denmark, adequate control data for the neuropsychological interpretation of test data did not exist until recently.

It is the purpose of this progress report to discuss our attempts to redeem this unsatisfactory situation, and to present preliminary results of our current research.

Methods

The basic aim of our efforts is to study different groups of neurological patients (including diagnosed cases of the so-called organic solvent syndrome) either compared with matched normal subjects, or with statistical control of relevant confounding variables, on a battery of neuropsychological tests. In our analyses we seek to extract the information that can be

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applied in the assessment of the individual patient in order to maximize reliability and validity of test results.

Subjects

a) 120 normal subjects recruited among in-patients of our hospital during 1980-83. Only occupationally active persons were included except six age pensioned cases. An uncertain diagnosis, a consumption of more than four beers or equivalent daily, a psychiatric history, regular use of analgetics or psychotropic drugs, or any indication of CNS or systemic disease including hypertension led to exclusion from the study. The sample consists of 70 males and 50 females, with a mean age of 45 years (range 20-73). The distribution over social class is very similar to that of the general population. Education (a combined measure of school and occupational level) was held constant over age groups.

b) 95 patients selected from departments of neurology and industrial medicine on the basis of a clinical neuroradiological diagnosis of cerebral atrophy on the CT (Group A). More than one third of the group had diagnoses of toxic encephalopathy from solvent exposure, the rest comprising many different diagnostic categories.

Test Battery

The subjects were tested with an extensive set of cognitive tasks, of which a variable number have been included in different analyses. The results from 4 verbal subtests of the WAIS have been used as a measure of verbal intelligence. Another set of tests, assumed to be sensitive to brain damage (the Basic Battery (BB)), comprises two abstraction tasks (proverb interpretation and a sorting test), an associate learning and retention test, three measures of memory span (digit repetition and reversal, and sentence repetition), a block design test, a visual gestalt memory test, and three measures of visuo-motor speed (SDMT, Trail Making A and B). Further tests used included recognition memory tests, PASAT delayed repetition and addition, and several perceptual tasks.

The types of data analysis used are described in the result section.

Results

Influence of background variables

The main findings from regression analysis of results from the 120 normal subjects are illustrated in figure 1. Composite scores were first computed in factors determined in factor analysis, with raw scores converted to T-scores with a mean of 50 and a standard deviation of 10. The scores were then

regressed on multiple background variables. The best regression model included age, education, age squared (the influence of age on scores was non-linear), and age x education (the age decrement in some scores was more marked with low education). Inclusion of a measure of verbal intelligence in the regression model greatly increased the amount of explained variance. In the case of mean total BB performance, the amount of explained variance is 56% without the intelligence measure, 80% with intelligence included in the regression. Other variables, including sex, did not improve the model. The influence of age and education, and their interaction, on five factor scores are illustrated in figure 1. Differences between two (arbitrary) educational groups may be seen to increase to about two standard deviations among the older subjects in some measures. It should be noted that these differences may exceed differences between groups of normal subjects and brain damaged patients.

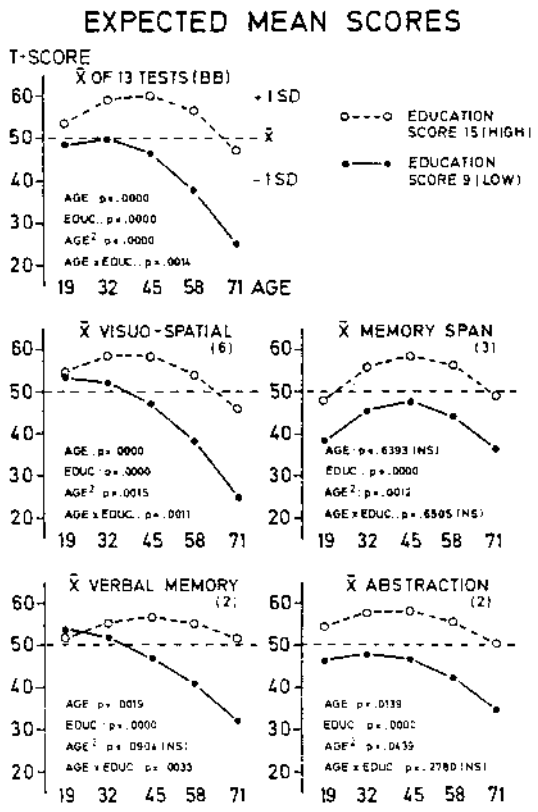

Fig. 1. Expected age curves at two educational levels.

Based on the regression equations we have computed expected scores for each normal subject, and the relationship between these and the observed scores (mean total BB) is shown in figure 2. The observed deviations are symmetrical, and average $\pm$ 3.6 T-score points. 60% of the subjects obtain scores within $\pm$ 3 of the expected values.

Reliability

20 of the normal subjects were retested after an average of about three months. Correlation coefficients between scores from the first and second tests were computed for both single

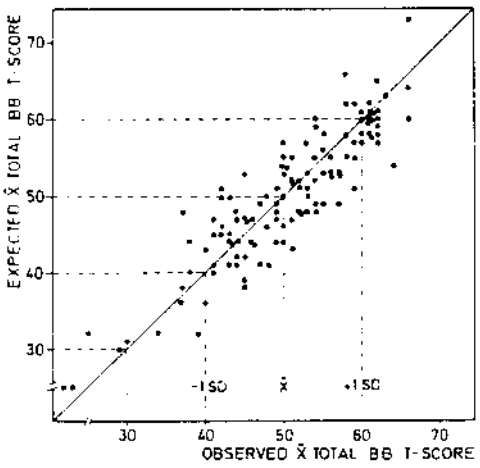

Fig. 2. Expected and observed scores in 120 normal subjects.

measures and factor scores, shown in the table. The reliability of single tests were in some instances unacceptably low, but much higher in factor scores.

Table Test-retest correlations (Pearson r) of factor scores, and mean correlations of component tests

FACTOR	No. of tests	Factor r	Tests $\bar{x}$ r
ABSTRACTION	2	.82	.60
MEMORY SPAN	3	.89	.71
VERBAL LEARNING	3	.56	.47
RECOGNITION MEMORY	5	.87	.68
VISUO-MOTOR SPEED	3	.56	.55
VISUO-SPATIAL	4	.70	.41
PASAT	4	.51	.38
VISUAL S/A	2	.80	.68
VISUAL M/A	2	.74	.63
$\bar{x}$ TOTAL BB	13	.77	.51
$\bar{x}$ TOTAL of 7 factors	24	.90	.54

Discriminations between normal and impaired performance

We hesitate to publish data from our analyses of discrimination rates between normals and atrophic patients before a confirmation from quantitative analyses of CT-scans that our patients in group A indeed suffer from cerebral atrophy.

Preliminary analyses of group A patients with diagnoses other than toxic encephalopathy have indicated acceptable discrimination from carefully matched controls. Group A patients with the diagnosis of toxic encephalopathy were in the majority of cases not significantly different from expected test scores.

We have made no formal reanalysis of previously published groups of patients with diagnosed toxic encephalopathy. It is, however, evident to us that the majority of such patients in neuropsychological tests perform in the normal range as defined by the normal subjects with similar age and education in this study.

Summary and Conclusions

An analysis of the neuropsychological test results in 120 normal subjects has shown that the majority of the variance can be explained by age, education and intelligence. Variability among subjects in raw scores is very great, and without careful matching with controls, or statistical control of the influence of background variables, diagnoses of intellectual impairment in individual referred cases are apt to be misleading. To obtain acceptable reliability it may be necessary to consider test performance in factor or composite scores in addition to single tests.

Our predictive model has been developed in a small country with a rather homogeneous population. It may be expected that a similar model in more heterogeneous cultures must be more complex and include more variables (e.g. sex, ethnic background) and thus also require a larger normal sample as its basis.

Previous studies of solvent exposed workers in our department were uncontrolled. Our experiences during the last few years with both referred cases of suspected toxic encephalopathy and normal subjects have led us to question the conclusions from uncontrolled studies including our own. We believe to have increased the diagnostic validity of our neuropsychological examinations by the knowledge gained on normal test performance, and we now very rarely diagnose intellectual impairment in solvent exposed patients without known or suspected alternative etiologies.

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