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5 COMPUTERIZED ASSESSMENT OF COGNITIVE FUNCTION IN AGEING AND DEMENTIA

INTRODUCTION

In recent years, computerized testing procedures have become increasingly popular in the assessment of cognitive dysfunction in dementia and related neuropsychiatric disorders. In this chapter the main technological developments in this field will be described and their relevance to both clinical assessment and experimental research discussed.

The advantages of computer systems over more traditional means of assessment will be considered in the context of recent studies that have adopted this technological approach. Specifically, the sensitivity of computerized tests to cognitive changes in dementia and to the effects of pharmacological intervention will be addressed. In addition, comparative studies of human neurosurgical populations and animals with selective neurochemical lesions using analogous computerized tests will be described. The role of such comparisons in defining the specificity of cognitive deficits in dementia and in identifying the underlying neural substrates responsible will be discussed.

Finally, in order to illustrate these points, one particular computerized paradigm, adapted for use with both humans and experimentally lesioned primates, will be described in detail, illustrating how the innovative use of existing computer technology can be used to define the neural and neurochemical basis of specific neuropsychological deficits.

TECHNOLOGICAL CONSIDERATIONS

Hardware

With the widespread availability of computing technology, it is now possible for most research groups to design, implement and standardize computerized psychological testing procedures for routine use in the clinic. The choice of microcomputers is considerable. In recent years the Acorn BBC Master computer has proved to be a popular choice offering high-resolution colour graphics at relatively low cost. However, with the rapid decrease in the cost of computing technology and the development of more powerful and flexible systems, a new

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generation of personal computers (or PCs) have entered the neuropsychological arena. In particular, the IBM PCs (including IBM 'compatibles' or 'clones') are now widely available and have a number of advantages over the more basic Acorn BBC system. As well as increasing overall processing speed, test stimuli can be presented and responses measured with millisecond accuracy. In addition, large amounts of data can be stored on the computer's hard disk and more easily transferred between the neuropsychological test programs and popular statistical and graphics packages.

In relation to dementia, one important attribute of computer technology is the availability of peripheral systems which allow the patient to interact directly with the computer. Many alternative response media are available including single touch key pads, mice, joysticks, tracker balls and light-pens. In recent years, touch sensitive screens have proved to be extremely valuable in assessing patients with neurodegenerative disorders since they enable the subject to respond directly by touching stimuli presented on the monitor (Morris *et al.*, 1988; Sahakian *et al.*, 1988, 1990; Downes *et al.*, 1989). The main advantage of this method is that the stimulus material which guides the decision of the subject is identical to the cues which guide the response. Thus, the patient is not required to divide their attention between the stimulus and the response, an important consideration given that demented patients are known to be impaired on such tasks (Baddley *et al.*, 1986; Morris, 1986). In addition, Carr *et al.* (1986) found that cognitively impaired elderly patients preferred using a touch sensitive screen to a board with illuminated response buttons.

For reaction time studies, single touch key pads may be used in combination with a touch sensitive screen to provide separate and accurate measures of reaction time (i.e. the time to remove the hand from the key pad) and movement time (i.e. the time between moving the hand from the pad and touching the screen) (see Downes *et al.*, 1989; Sahakian *et al.*, 1990).

Software

In principle, it should be possible for most research groups to design and program neuropsychological tests according to their own specific requirements. On the Acorn BBC machine, BBC BASIC is a simple but powerful programming language with a versatile graphics system. For IBM compatible PCs, various packages exist to simplify programming in a number of high level languages including BASIC (e.g. Microsoft QuickBASIC) and C (e.g. Microsoft Quick C).

Alternatively, some existing computerized neuropsychological test packages are commercially available. The main advantage of these systems is that they may already have been extensively used on a number of patient and control populations and relevant data may previously have been published.

For example, the Bexley–Maudsley Automated Psychological Screening Battery (Acker and Acker, 1982) includes tests of visual–spatial memory and spatial orientation, a symbol–digit coding task (similar to the Digit Symbol subtest of the Wechsler Adult Intelligence Scale (WAIS) and a test of concept formation based on the Wisconsin Card Sorting Test, WCST (Grand and Berg, 1948; Milner, 1964). This system was originally programmed for the now largely redundant Commodore PET computer but a version for the Apple II microcomputer has also been produced.

In the evolving world of computing hardware, the most useful neuropsychological tests are likely to be those designed to run on popular 'industry standard' machines such as the IBM PC and compatible systems.

For example, the Cambridge Neuropsychological Test Automated Battery* (CANTAB) is a set of three computerized neuropsychological test batteries designed to test various aspects of visual memory, attention, working memory and planning. In a fourth battery, five parallel versions of many of the tests are supplied which may be useful for longitudinal studies in which subjects are retested on a number of occasions. The tests have been designed and programmed to run on both an Acorn BBC Master microcomputer (using a high-resolution Microvitec Touchtech 501 touch sensitive monitor) and an IBM (or compatible) PC (using a variety of IBM compatible touch sensitive screens). The CANTAB tests were developed by Dr T.W. Robbins and colleagues at the University of Cambridge and at the Institute of Psychiatry, London.

In recent years the CANTAB test batteries have been used extensively to assess cognitive function in a number of clinical groups including patients with dementia of the Alzheimer type (DAT; Sahakian *et al.*, 1988, 1990, 1991; Sahgal *et al.*, 1991, 1992), depression (Abas *et al.*, 1990), Parkinson's disease (Morris *et al.*, 1988; Downes *et al.*, 1989), Korsakoff's syndrome (Joyce and Robbins, 1991), multiple system atrophy (Robbins *et al.*, 1992) and patients with localized excisions of the frontal and temporal lobes (Owen *et al.*, 1990, 1991).

THE ADVANTAGES OF COMPUTERIZED TESTS

Experimentally, computerized testing procedures have many practical and theoretical advantages over more conventional testing methods. For example, response latencies can be measured to millisecond accuracy, which may be important in sophisticated reaction time studies. However, they are also more flexible than traditional neuropsychological techniques with data being recorded, processed and scored automatically during the testing session.

Moreover, computer systems greatly improve the accuracy with which the testing situation can be controlled, isolating the factors of interest and reducing experimental 'noise' which is frequently difficult to achieve in a clinical environment. For example, both stimulus presentation time and intertrial intervals may be held constant for each trial and, more importantly, for each subject. Conversely, they can be precisely and systematically varied to examine the relationship between these factors and performance.

In addition, computers can accurately record and analyse many aspects of performance simultaneously, providing a componential analysis of the behaviour being assessed. In particular, measures of response latency and response accuracy may be combined in order to examine the processes comprising particular cognitive operations in great detail (e.g. response latency for correct responses versus incorrect responses). This is essential, for example, in information processing studies of dementia where it may be necessary to record simultaneous information about the speed and accuracy of the patient.

The detailed analyses produced by computerized systems also increase the accuracy with which 'task difficulty' can be determined and equilibrated across different paradigms. This is particularly important in the assessment of dementia since failure on one task may often reflect a general, nonspecific effect of task difficulty. By comparing performance across a number of tasks of equal complexity, the specificity of observed deficits can be more accurately determined.

Another advantage of computer-controlled tests is that they can be designed

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so that each testing session is administered in a more systematic and objective way than may be possible in a typical clinical setting. For example, the difficulty of a task may be automatically adjusted according to strict and predefined criteria. In this way, tests may be tailored to suit the abilities of each individual, shortening test sessions and minimizing the experience of failure in the severely impaired patient. In a similar way, computer tests can easily be 'fixed' (in terms of the number of successes and failures) such that the subjective experience of being tested is equivalent for each patient.

Finally, using precise computer control, a consistent amount of positive and negative feedback can be given to each subject, increasing inter-rater and test–retest reliability and making computer systems ideal for multicentred trials.

Of course, everything has its price and computerized neuropsychological assessment is no exception. Computer-controlled tests are in general, more expensive and less portable than their more conventional 'paper and pencil' counterparts. Individual items such as touch sensitive monitors are awkward to carry and easily damaged. However, in the near future falling computer prices and the increased availability of truly portable computers or 'laptops' may reduce the importance of these differences.

Computers are also limited in the types of test material to which they are suited. For example, the advantages of a computerized version of a verbally administered test such as the Mini-Mental State Examination (Folstein *et al.*, 1975) are not obvious.

In summary, despite the obvious practical considerations computerized neuropsychological tests have many advantages over more conventional testing methods in terms of improved control over the testing situation and an enormous increase in the depth and breadth of information provided.

THE APPLICATIONS OF COMPUTERIZED TESTS

The relative precision and sensitivity of computerized neuropsychological techniques makes them valuable tools for investigating small, sometimes quite subtle, behavioural alterations which may not be detected using more conventional 'paper and pencil' tests. For example, in a recent longitudinal study of elderly depressed patients, performance on several traditional tests such as the Mini-Mental State Examination (Folstein *et al.*, 1975) and the Kendrick Object Learning Test (Kendrick, 1985) improved significantly on recovery, although residual deficits were detected using computerized tests of memory and learning (Abas *et al.*, 1990). In recent years, computerized neuropsychological testing has become commonplace in a number of research centres and has been successfully applied in many experimental and clinical areas, in particular for:

1. Charting the course of cognitive deficits in dementia and related neurodegenerative disorders
2. Assessing the effects of pharmacological intervention in dementia and other neurodegenerative disorders
3. Distinguishing between different neuropsychiatric disorders
4. Imaging studies
5. Comparative assessment of cognitive dysfunction in experimentally lesioned animals and dementia
6. Comparative assessment of cognitive dysfunction in dementia and patients with localized neurosurgical excisions

Much of this work has been carried out at Cambridge University, the Institute of Psychiatry in London and related research centres using tests from the CANTAB neuropsychological test battery. The results of several of the more important studies will be described below.

Longitudinal and cross-sectional studies of cognitive dysfunction in dementia

Computer-controlled tests are particularly well suited for following the course of many neurological diseases including DAT. Thus, assessments at regular intervals can provide reliable indications of whether the underlying neurological condition is changing, and if so, in what way.

In a recent 5-year study, Sahakian *et al.* (unpublished observations) reassessed 12 patients with mild DAT annually using a number of computer-controlled tests from the CANTAB battery (Morris *et al.*, 1987). Marked differences in visual memory performance were observed between each assessment with the most significant deterioration occurring between the second and third years.

Less powerful cross-sectional studies have also been successfully used to chart the course of cognitive dysfunction in dementia. For example, Sahgal *et al.* (1991) compared mnemonic and attentional processes in groups of patients with mild or moderate DAT, defined according to their scores on the Mini-Mental State Examination (Folstein *et al.*, 1975). Both groups of DAT patients were significantly impaired on three computerized tests of memory (pattern recognition, delayed matching to sample and paired associative conditional learning) but not on a visual search, matching to sample test of attention. In addition, in the tests of delayed matching to sample and paired associates conditional learning, more severe impairments were observed in those DAT patients who were later in the course of the disease than in those with more mild clinical symptoms.

In a parallel study, visuospatial memory was compared in groups of patients with mild and moderate DAT using computerized tests of spatial recognition, spatial span and spatial working memory (Sahgal *et al.*, 1992). Whilst equivalent deficits were observed in the tests of spatial working memory and spatial recognition only the spatial span task was able to distinguish between the two DAT groups.

The effects of pharmacological intervention

Computerized data are likely to provide the most sensitive indices of the extent to which medication enhances or compromises a patient's mental efficiency. For example, Lange *et al.* (1992) tested a group of patients with idiopathic Parkinson's disease (PD) on a comprehensive battery of automated tests of learning, memory, planning and attention whilst either 'on' or 'off' levodopa medication. Controlled withdrawal of medication interfered with aspects of performance on three tests known to be sensitive to frontal lobe dysfunction (Owen *et al.*, 1990, 1991) but not on tests of visual recognition memory and paired associative conditional learning assumed to depend on more posterior structures.

Despite the previous resistance of cognitive decline in dementia to pharmacological intervention, several recent studies have used computer-controlled tests of cognitive function to examine the effects of experimental drug treatments in patients with DAT. For example, subcutaneously injected nicotine has been shown to produce marked improvements in discriminative sensitivity and reaction times but not short-term memory in both DAT patients with mild

to moderate symptoms and healthy adults using a novel computerized test of attention and information processing (Sahakian *et al.*, 1989).

In a recent double-blind, placebo-controlled crossover trial of patients with DAT treated with the tetrahydroaminoacridine (THA) and lecithin (Eagger *et al.*, 1991a, b) a comprehensive battery of computerized tests was used to assess the effects of the drug as well as more conventional tests of intellectual function. Small but significant improvements were observed on two of the CANTAB computerized tests of attentional ability (Sahakian *et al.*, 1991) although significant improvements were also noted in the Mini-Mental State Examination and the abbreviated mental test score (Hodkinson, 1972).

Comparisons between dementia and other neuropsychiatric conditions

In assessing cognitive dysfunction, the efficacy of a test lies not only in its ability to detect and measure impairments in particular populations of patients but also in its ability to distinguish between those populations. The relative sensitivity and accuracy of computer tests increases the probability that subtle group differences will be reliably detected.

In several recent studies, specific patterns of impairment have been identified in a number of patient groups using a computerized test of simultaneous and delayed matching to sample (Sahakian *et al.*, 1988). Patients are shown a complex abstract pattern in the centre of the computer screen and are then required to match it to one of four choice patterns appearing below the target either simultaneously or after a brief, but variable (0–16 second) delay (Figure 5.1).

Patients with mild DAT exhibited a delay-dependent deficit in choice accuracy but were unimpaired in the simultaneous condition where there is no mnemonic component. In contrast, a group of medicated patients with idiopathic PD showed a delay-*independent* deficit in the delayed matching to sample test and were also significantly impaired in the simultaneous matching condition. On this basis, the cognitive deficits in patients with DAT and PD were differentially described in terms of mnemonic and attentional processes, respectively.

By comparison, the same paradigm has also been used to describe specific patterns of deficit in groups of patients with other neurological and psychiatric disorders. For example, nondemented patients with the progressive neurodegenerative condition multiple system atrophy (MSA), have been shown to be significantly impaired in the simultaneous condition but show normal delayed matching performance (Robbins *et al.*, 1992), the exact opposite of the pattern shown by patients early in the course of DAT. Similarly, using the same task, a unique pattern of prolonged response latencies and errors has been identified in elderly depressed patients, when compared to patients with DAT (Abas *et al.*, 1990).

Imaging studies

Single photon emission tomography (SPET) has recently been used to compare regional cerebral blood flow (rCBF) in relation to cognitive performance in 35 patients with DAT and 35 healthy matched controls. (O'Brien *et al.*, 1992.) In the DAT group, significant correlations were observed between rCBF and many of the neuropsychological measures, assessed using the CAMCOG cognitive subcomponent of the Cambridge Mental Disorders of the Elderly (CAMDEX) schedule (Roth *et al.*, 1986). In particular, memory correlated with left temporal activity whilst praxis, perception object assembly and block design correlated with right parietal activity. A subgroup of 20 DAT patients also received a

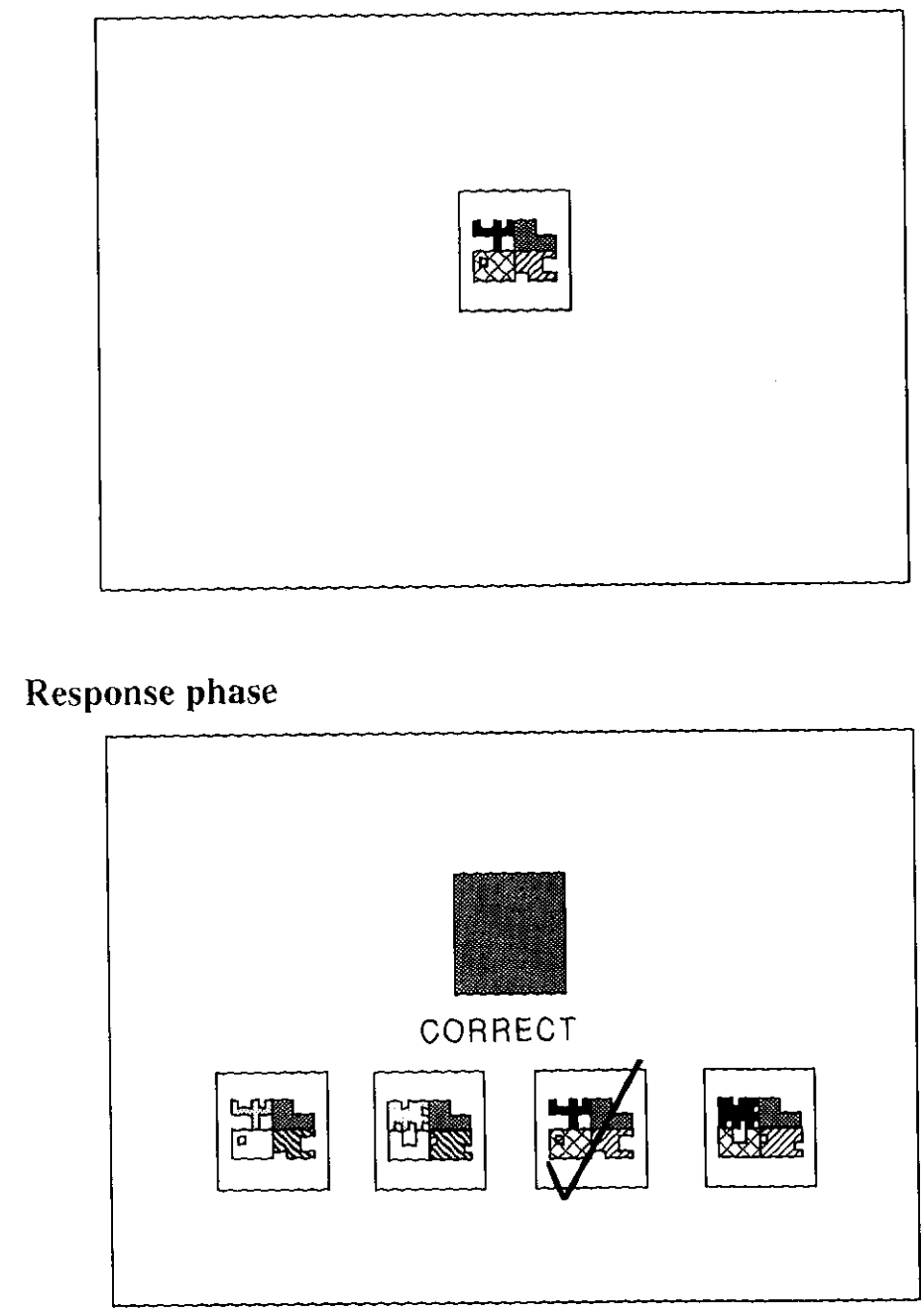


Fig. 5.1 The computerized simultaneous and delayed matching to sample test. In this example, the target stimulus has been correctly identified from among three distractor stimuli after a brief (0–16 second) delay.

number of computerized tests from the CANTAB automated test battery (Morris *et al.* 1987). Performance accuracy on the simultaneous and delayed matching to sample paradigm described above (Sahakian *et al.*, 1988) correlated significantly with posterior temporal and parietal lobe activity, particularly in the right hemisphere (O'Brien *et al.*, personal communication). Thus, it is possible that the severe deficit in visual short-term memory shown by DAT patients performing this test reflects dysfunction of temporal and parietal lobe structures, a possibility consistent with the patterns of neuropathological and neurochemical changes seen in the condition (Tomlinson, 1984).

Additionally, Abas *et al.* (1990) have reported a significant correlation between ventricular–brain ratio (VBR), calculated from mechanical planimetry of CT scans (Jacoby and Levy, 1980) and impaired latency for correct responses on the same computerized delayed matching to sample procedure in a group of elderly depressives.

Comparative assessment of cognitive dysfunction in experimentally lesioned animals and dementia

The specific neural or neurochemical basis of cognitive dysfunction in dementia and related progressive neurodegenerative diseases is particularly difficult to define since extensive primary and secondary pathological changes may preclude such conclusions from being drawn at *post-mortem*. Direct comparison of behavioural or cognitive deficits in patients with dementia and animals with selective neurochemical or neuroanatomical lesions can help to ascertain whether specific neuronal changes are causal to or correlates of impaired cognition.

Unlike human neuropsychology, animal studies have employed computer-controlled testing procedures for many years because of the better control they offer over stimulus presentation, the recording of responses and the programming of feedback contingencies. However, in general, even the relatively complex neuropsychological paradigms designed to assess cognitive dysfunction in nonhuman primates are not sufficiently sensitive for use with human subjects.

In recent years however, several traditional animal experimental tasks have been adapted using advanced computing technology to enable direct comparisons to be made between human and animal studies. For example, the computerized delayed matching to sample procedure described above (Sahakian *et al.*, 1988; Sahgal *et al.*, 1991) was derived directly from an existing paradigm originally designed to define the neural substrates of visual memory in monkeys (Sahgal and Iverson, 1978; Mishkin, 1982). Recent animal studies have established that performance on this test is critically dependent on cortical structures deep within the temporal lobes rather than on the limbic structures as originally thought (Squire and Zola-Morgan, 1991; Gaffan, 1992).

These findings confirm that the severe deficit in delayed matching to sample performance observed in patients with DAT reflects dysfunction of temporal lobe structures and is again consistent with the neuropathological and neurochemical changes seen in this condition (Tomlinson, 1984).

A computerized test based indirectly on Olton's radial arm maze (Olton, 1982), which has been used extensively in animal neuropsychology, has also been developed to assess spatial working memory performance in human patients (Morris *et al.*, 1988; Owen *et al.*, 1990). In the human version of the task, subjects are required to 'search through' a number of coloured boxes on the screen to find blue 'tokens', whilst avoiding those boxes in which a token has already been found. Importantly, subjects can search through the boxes in

any order they wish although the number of boxes visited before a token is found is determined (unknown to the subject) by the computer. Thus, each subject receives the same degree of feedback prior to making an error.

Significant deficits on this task have been observed in both mildly and moderately demented DAT patients although the two groups were not differentially impaired (Sahgal *et al.*, 1992). Using analogous tasks in animal lesion studies, spatial working memory has been shown to depend crucially on both hippocampal (Olton, 1982) and frontal (Passingham, 1985) structures.

Comparative assessment of cognitive dysfunction in dementia and patients with localized neurosurgical excisions

The neuroanatomical basis of cognitive dysfunction in dementia may also be investigated by comparison with groups of nondemented patients with well-defined, neurosurgical excisions. In this regard, computer-controlled tests are particularly well suited since task difficulty may be systematically varied to allow direct comparisons to be made between high functioning controls, patients with selective impairments of specific abilities and patients with more global deficits in cognition.

For example, the self-ordered searching task described above has previously been used to explore the neuroanatomical substrates of spatial working memory in human neurosurgical patients (Owen *et al.*, 1990). Like patients with DAT, a group of frontal lobe patients was significantly impaired on this test in terms of the number of search errors. However, the frontal lobe patients were shown to be less efficient in the use of a strategy known to improve performance, suggesting that at least some of their impairment in spatial working memory arises secondarily from a more fundamental deficit in the use of organizational strategies. A similar pattern of impairment on this task has recently been reported in a group of patients with alcoholic Korsakoff syndrome (Joyce and Robbins, 1991). In contrast to both groups, patients with DAT are not impaired in terms of their strategy for approaching this task suggesting that their impairment represents a purer memory deficit. This may reflect the involvement of hippocampal (cf. Olton, 1982) rather than frontal lobe (cf. Passingham, 1985) structures.

In a similar way, a modified (but formally similar) version of the computerized delayed matching to sample procedure described above (see Fig. 5.1) has recently been used to compare visual short-term memory performance in patients with localized excisions of the frontal lobes, patients with temporal lobe excisions and patients who had undergone unilateral amygdalo hippocampectomy (Owen *et al.*, unpublished observations). Whilst frontal lobe patients were unimpaired on this task, significant deficits in the delayed but not simultaneous condition were observed in both groups of patients with more posterior lesions, a pattern similar to that previously observed in patients with DAT (Sahakian *et al.*, 1988; Sahgal *et al.*, 1991). This study supports the results of animal lesion studies discussed above (Squire and Zola-Morgan, 1991; Gaffan, 1992) suggesting again that short-term visual memory impairment in patients with DAT reflects dysfunction of temporal lobe structures.

Summary

In recent years, computerized methods of cognitive assessment have been successfully applied in a number of clinical and experimental areas. In dementia, specific patterns of memory impairment have been identified even early in the course of the disease which are clearly distinct from those observed

in related neuropsychiatric populations. Computerized tests have also been employed in both longitudinal and cross-sectional studies of dementia to redefine the characteristic decline in intellectual functioning in terms of the precise cognitive process involved. Recent research has also suggested that in DAT and other neurodegenerative conditions such as PD, the neuropsychological sequelae of pharmacological intervention may be closely monitored using computerized tests of cognitive function. The success of this approach has obvious implications for the assessment of potential treatment strategies in dementia and related disorders.

A number of different approaches have also been used to demonstrate how computerized neuropsychological methods may be important in increasing our understanding of the specific neural and neurochemical basis of cognitive dysfunction in dementia. Comparisons between groups of patients with dementia and related neurodegenerative conditions and nondemented groups of patients with well-defined, neurosurgical excisions have proved to be particularly useful in this regard. Recent imaging studies have also suggested that in future the neural substrates responsible for specific neuropsychological deficits in dementia might be more clearly defined by combining advanced computerized assessment of cognitive function with both dynamic (SPET, PET) and structural (CT, MRI) imaging techniques.

The results of all of these studies suggest that computerized assessment may have an important role to play in many areas of neuropsychological assessment. In particular, computerized tests appear to be most useful where small changes are espected which may not be detected using more conventional 'paper and pencil' tests. However, it is important to emphasize that few direct comparisons have been made between these novel, computerized techniques and the more traditional methods of assessment. Such comparisons may be essential before the future role of computerized assessment of cognitive function in dementia and ageing can be fully evaluated.

AN ILLUSTRATIVE EXAMPLE: COMPUTERIZED ASSESSMENT OF SET-SHIFTING ABILITY

In the previous sections of this chapter the benefits of computerized neuropsychological tests have been described together with a number of studies that have exploited this advanced technology.

In order to illustrate how these advantages might be applied to a specific neuropsychological question, one particular test designed to assess attentional set-shifting ability will now be described in detail. The task, from the CANTAB attention battery, has recently been used to assess set-shifting impairments in patients with dementia, and to draw comparisons between patients with related neurodegenerative conditions, patients with localized neurosurgical excisions and monkeys with specific neurochemical lesions.

Test rationale and design

Clinically, 'frontal lobe dysfunction' is often assessed using tests assumed to depend on set-shifting ability such as the Wisconsin Card Sorting Test. (WCST; Grant and Berg, 1948; Milner, 1964; Nelson, 1976). Deficits on the this test have also been reported in a number of neurodegenerative diseases including PD (Lees and Smith, 1983), progressive supranuclear palsy (PSP; Pillon *et al.*, 1986) and Huntington's disease (Josiassen *et al.*, 1983). In DAT, significant deficits have not been reported for the WCST (Pillon *et al.*, 1986) although an

impairment has been observed in a related test of tactile reversal learning (Freedman and Oscar-Bermann, 1987).

However, in addition to set shifting, successful performance on the WCST requires a number of other distinct cognitive abilities including matching to sample and the identification of stimulus attributes. These factors may not depend on frontal lobe mechanisms and may independently contribute to some of the deficits described. Thus, across these patient groups, similar impairments may actually reflect deficits in quite different cognitive mechanisms.

Several computerized analogues of the WCST have also been produced (e.g. Acker and Acker, 1982), although in general, these suffer from the same drawbacks as the standard form of the test. Accordingly, a 'purer' computerized test of attentional set shifting has recently been developed that can be related to the WCST but which is derived from the animal learning literature and is based on the concepts of 'intradimensional' and 'extradimensional' shifts. An intradimensional shift (IDS) occurs when a subject is required to cease responding to one member of a particular stimulus dimension (e.g. 'blue' from the dimension 'colour') and begin responding to a new member of that same dimension (e.g. 'red'). An extradimensional shift (EDS) occurs when the subject is required to switch responding to a novel member of a previously irrelevant dimension (e.g. to 'squares' from the dimension 'shape').

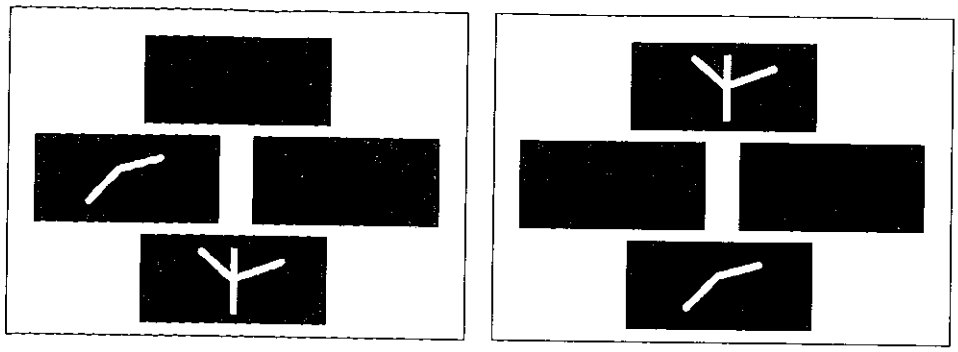
The computerized attentional set-shifting test was specifically designed to improve the comparative assessment of cognition from animals to humans. Therefore, formally identical versions have been developed for use with human subjects and experimentally lesioned monkeys (Roberts *et al.*, 1987). The test was designed and programmed to run on an Acorn BBC Master microcomputer and more recently on an IBM personal computer. In both cases, the programs employ high-resolution colour graphics and responses are made via a touch sensitive screen.

Test description

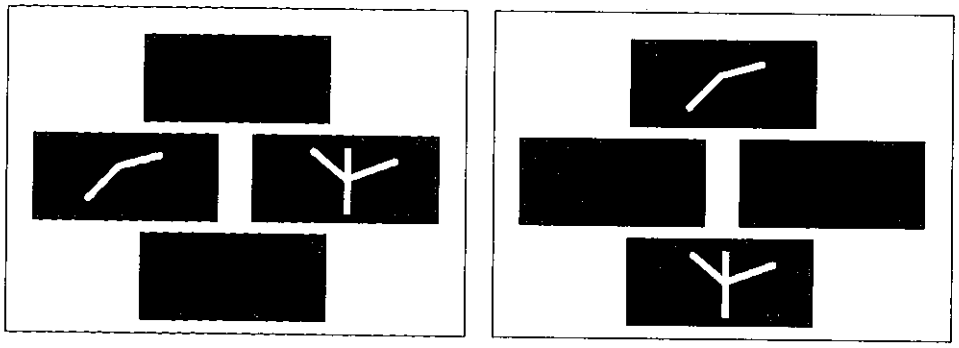
The subject is required to learn a series of discriminations in which one of two stimuli are correct and the other is not, using feedback provided automatically by the computer. The test is composed of nine stages presented in the same fixed order, beginning with a simple discrimination (SD) and reversal (SDR) for stimuli varying in only one dimension (i.e. two white line configurations). In Fig. 5.2, example stimuli from various stages of the test are presented. A second, alternative dimension is then introduced (purple-filled shapes) and compound discrimination (CD) and reversal (CDR) are tested (Fig. 5.2). To succeed, subjects must continue to respond to the previously relevant stimuli (white lines), ignoring the presence of the new, irrelevant dimension (shapes). At the intradimensional shift (IDS) stage new exemplars are introduced from each of the two dimensions (new lines and new shapes) and subjects are required to transfer the previously learnt rule to a novel set of exemplars of the same stimulus dimension. To succeed, they must continue to respond to one of the two exemplars from the relevant dimension (lines). Following another reversal of contigencies (IDR) the extradimensional shift (EDS) and reversal (EDR) occurs and again novel exemplars from each of the two dimensions are introduced. The subject is required to shift 'response set' to the alternative (previously irrelevant) stimulus dimensions (see Fig. 5.2).

At each stage a change in contingencies occurs once the subject has learnt the current rule to a criterion of six consecutive correct responses. Failure to achieve this criterion within 50 trials results in the premature discontinuation of the test.

Simple discrimination and reversal (initial dimension, white lines)



Compound discrimination and reversal (introduce second dimension, filled shapes)



Intra-dimensional or Extra-dimensional shift and reversal (new lines and shapes)

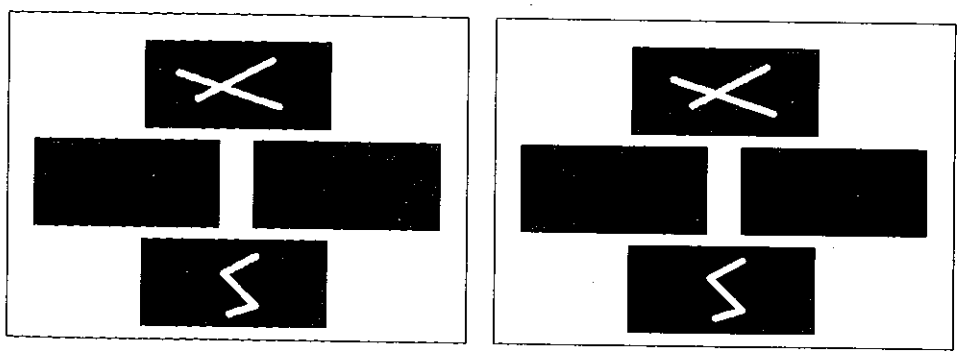


Fig. 5.2 Example stimuli from various stages of the intradimensional and extradimensional set-shifting task. The white line and purple-filled stimuli (shown here in black and white) are presented exactly as they appear on the screen and at each stage, two *typical* trials are given (left box = trial 1, right box = trial 2).

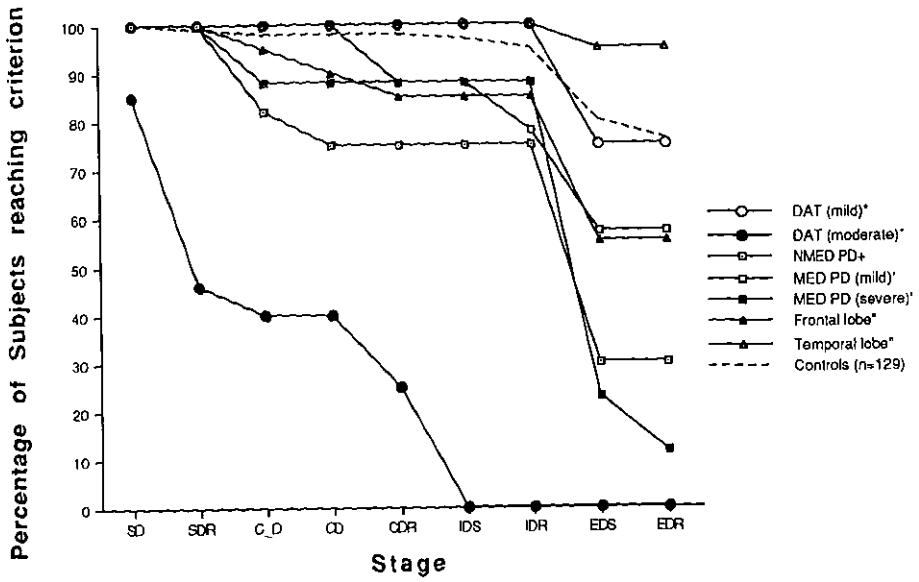


Fig. 5.3 The proportion of subjects reaching criterion at each of the nine stages of the discrimination learning paradigm. *Sahakian *et al.* (1990). +Downes *et al.* (1989). 'Owen *et al.* (1992). "Owen *et al.* (1991). DAT = dementia of Alzheimer type. NMED = non-medicated Parkinson's disease. MEDPD = medicated Parkinson's disease. SD = simple discrimination. SDR = SD reversal. CD = compound discrimination. CDR = CD reversal. IDS = intradimensional shift. IDR = IDS reversal. EDS = extradimensional shift. EDR = EDS reversal.

Comparative studies of dementia of the Alzheimer type, Parkinson's disease and normal ageing

This paradigm has now been used to compare shifting ability directly in patients suffering from neurodegenerative disorders including DAT, PD, PSP and MSA as well as neurosurgical patients with localized excisions of the frontal and temporal lobes.

The combined results of these investigations have shown that impairments on this computerized set-shifting task are both psychologically and pathologically specific (see Fig. 5.3). For example, both medicated and particularly nonmedicated patients with PD are selectively impaired in their ability to perform an extradimensional shift but not an intradimensional shift (Downes *et al.*, 1989). In addition, whilst medicated patients with PD are specifically impaired at the EDS stage of the test, compared to age-matched controls, this deficit is somewhat worse in patients with very severe clinical symptons (Owen *et al.*, 1992).

In contrast, a subgroup of elderly patients in the mild stages of DAT are not impaired on this test of visual discrimination learning despite having significant deficits in short-term visual recognition memory (Sahakian *et al.*, 1990). However, compared to age-matched controls, patients with more severe DAT (unlike severe PD patients) are impaired *throughout* the test, even at the simplest reversal stage. This may reflect a more global deterioration of cognition in this group.

Thus the psychological specificity of the set-shifting deficit is shown by the patients with PD who are selectively impaired on the EDS but not the IDS stage of the test. The neural specificity is shown by the fact that mild DAT patients

are far better than even the nonmedicated PD patients with mild clinical symptoms.

The EDS stage of this test is also sensitive to the effects of normal ageing. In a recent study, a group of healthy control subjects of 70+ years with no known neurological condition were significantly impaired at the EDS stage of the test when compared to younger, IQ-matched controls (Owen *et al.*, 1991).

Clearly, in assessing set-shifting ability, this computerized paradigm can distinguish between the patterns of impairment observed in specific neurological populations as well as reliably differentiate between groups of patients at different stages of the disease process.

Comparisons with neurosurgical populations

Comparative studies of neurosurgical patients with localized neurosurgical excisions suggests that impairments at the EDS stage of this test may be related to a disruption of frontal lobe function. Whilst patients who have undergone unilateral temporal lobe resection or unilateral amygdalo hippocampectomy reach criterion at every stage of the test, patients with excisions restricted to the frontal lobes are specifically impaired at the EDS (Owen *et al.*, 1991). This suggests that whilst the severe deficits exhibited by patients late in the course of DAT may reflect a global deterioration of cognition, the specific EDS impairment observed in patients with medicated and nonmedicated PD may follow disruption of frontal or frontostriatal mechanisms.

Lesion studies with nonhuman primates

In order to investigate the neuropathological substrates of the set-shifting impairments described above, comparative studies are also being conducted in nonhuman primates, with selective lesions of defined neurochemical systems. Since this computerized test of set-shifting ability employs nonverbal stimuli and requires nonverbal responses, only slight modifications to the basic design were necessary to make the test suitable for primate studies.

Experimental marmosets with damage to the cholinergic projection to frontal cortex, similar in extent to that seen in PD, are unimpaired on this task (Roberts *et al.*, 1992). In contrast, attentional set-shifting ability is altered following damage to the dopaminergic projection to the frontal cortex (Roberts *et al.*, 1991). This suggests that in PD at least, the deficits in set-shifting ability seen early in the course of the disease may reflect disruption of dopaminergic rather than cholinergic neurotransmitter systems.

The studies described above illustrate how carefully designed computerized tests can be used to establish the neural and neurochemical causes of specific neuropsychological impairments in human patient populations. In this case, a test of attentional set-shifting ability has been used to distinguish groups of patients with different, though related, neurodegenerative conditions and to differentiate between patients at different stages of the disease process. In addition, comparative studies with human neurosurgical patients and primates with selective neurochemical lesions can help to address the question of whether specific neuronal changes are causal to or correlates of these cognitive deficits.

CONCLUSIONS

This chapter has described how recent developments in computing technology can be exploited for the neuropsychological assessment of cognitive function in ageing and dementia. The advantages of computer-based systems over more

traditional methods of neuropsychological assessment have been described in the context of several recent studies that have adopted this technology. The sensitivity of computerized tests to cognitive changes during the course of dementia and other neurodegenerative disease and to the effects of pharmacological intervention has been discussed. In addition, a role for computerized neuropsychological testing in other rapidly advancing fields of technology such as neuroimaging has been suggested. A number of comparative human and animal studies which have used analogous computerized tests have also been described. Such comparisons are helping to define the specificity of cognitive impairments in dementia and other neuropsychiatric conditions and the underlying neural substrates responsible.

In future, parallel computerized tests in comparative neuropsychology may guide the direction of research into appropriate treatments for the alleviation of various neurological conditions including dementia and, in addition, may have some diagnostic value. For example, they may provide a means of assessing the probable loci of neuropathology in the early stages of a neurodegenerative disease when other methods are unavailable or insufficiently sensitive to do so.

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