Introduction

The aim of this book is to review what is known about the neuropsychological or neurocognitive impairments which occur in neurological disorders, and in some general medical conditions which may be seen by neurologists. Such neuropsychological deficits are of course relatively well defined in those disorders which present with, or whose clinical features are largely restricted to, cognitive impairment, specifically the dementia syndromes, of both neurodegenerative and vascular aetiology, and these account for a fair proportion of this book. However, cognitive dysfunction may also occur in other neurological disorders, an observation which may have implications for both clinical diagnosis and case management. Few texts have, to my knowledge, specifically addressed this area (e.g. Grant & Adams, 1996; Green, 2000; Harrison & Owen, 2002), and some only in passing. To be sure, there are a number of excellent texts which tackle the classical neuropsychological syndromes such as amnesia, aphasia, alexia, agraphia, apraxia, agnosia, and executive dysfunction (e.g. Baddeley et al., 1995; Benson & Ardila, 1996; Kirshner, 2002; Heilman & Valenstein, 2003). The case-study approach to the neuropsychological features of neurological disorders (e.g. Kapur, 1996; Ogden, 2005) has even spilled over into populist texts, but though such in-depth case studies are informative, they may not immediately correspond to the case mix seen by clinical neurologists. Textbooks of neurology may mention dementia as a feature of certain neurological diseases, often in a rather diffuse way.

There is a perception in some quarters that neuropsychology is something rather separate from clinical neurology. The case may perhaps be persuasively made for academic cognitive neuropsychology, which aims to infer mental structure from neuropsychological test performance, often in single case studies of highly unusual but instructive patients (Shallice, 1988; Ellis & Young, 1996), and even ‘clinical’ neuropsychology texts (e.g. McCarthy & Warrington, 1990; Groth-Marnat, 2001; Halligan et al., 2003; Devinsky & D’Esposito, 2004) may contain more than a practising clinician would require, or possibly desire. Nonetheless, clinical neurologists neglect cognitive function at their peril. It should not be forgotten that cognitive neuroscience has neurological foundations (D’Esposito 2003; Panegyres, 2004).

It is well recognized that the standard neurological examination is focused predominantly on functions mediated by the parietal and occipital lobes, with frontal and temporal lobe functions being relatively untested. Since, in the context of the clinical history, neurological signs help to focus on the likely locale of pathology (Larner, 2006), it would seem desirable to be able to tap the functions of these areas of the brain as well.

A neuropsychological examination provides the opportunity to do this; such assessment permits a more fine-grained analysis of cognitive function, a refinement which may have localizing and diagnostic value. Just as one would not contemplate omitting the visual field examination or the plantar responses when examining a patient suspected of...
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harbouring neurological disease, so some form of higher cognitive testing should also be undertaken whenever the clinical history suggests possible cognitive impairment. The requirement is for a manual of ‘neuropsychology in clinical practice’. Professor John Hodges’ book on cognitive testing has pointed the way for clinical neurologists to do this without the need for highly specialized equipment or training (Hodges, 1994).

Not only are neuropsychological tests essential in the diagnosis of dementia disorders, but they may also be helpful in differential diagnosis, for example of movement disorders (Pillon et al., 1996). Neuropsychological features may contribute to disease morbidity even where outcome is judged good or excellent on neurological grounds, e.g. in multiple sclerosis (Feinstein, 1999) or subarachnoid haemorrhage (Hüttner, 2000). Neuropsychological parameters may therefore be as appropriate as motor, sensory, or functional scales as outcome measures in the conduct of clinical trials. Early identification and treatment of cognitive impairments would seem the most likely time point at which interventions might show therapeutic efficacy. Part of the desire here, of course, is to identify conditions with neuropsychological deficits that may reverse with appropriate treatment of the underlying condition. Much has been written on the subject of ‘reversible dementias’, no less than 65 such conditions being alluded to in one review (Cummings et al., 1980), although it seems that the overall frequency of such reversible conditions is low, and falling (Barry & Moskovitz, 1988; Waldemar, 2002; Clarfield, 2003).

Part of the problem, of course, is the sophistication of neuropsychological testing, the plethora of possible tests available to bewilder the uninitiated (Lezak et al., 2004; Mitrushina et al., 2005; Strauss et al., 2006), and the lack of time devoted in clinical training to this subject. For this reason, a brief overview of cognitive function and neuropsychological evaluation prefaces the chapters devoted to the neuropsychological profiles of specific disease entities. This modest excursion into applied neuropsychology will in all probability horrify those trained in the art and science of neuropsychology, but the aim has been entirely pragmatic, for the benefit of clinical practitioners. In the chapters which follow, the neuropsychological impairments of neurological and general medical disorders are considered. Detailed discussions of neurological features of the disorders covered are not included, although brief notes are given and, where possible, references to diagnostic criteria are cited. For more information on the clinical features of neurological disease, the reader is referred to other textbooks of neurology (for one of which the current author has a particular, and perhaps forgivable, predilection: Barker et al., 2005). A few comments on the treatment of cognitive impairments are given as a gentle rebuff to those who imagine neuropsychological neurology to be a purely descriptive undertaking.

This overview is no small undertaking (I have amongst my papers a draft plan of the book, not too dissimilar from the current contents, dated 27 August 1998), for which reason certain omissions have proved necessary. Perhaps the most important of these is the lack of coverage of neuropsychiatric features of neurological disease (mood disorders, delusions, hallucinations, depression, euphoria, etc.) which often coexist with, and may confound the examination of, neuropsychological deficits. (Pain is also a potential confounder of neuropsychological testing, as in mild traumatic brain injury or headache: Nicholson et al., 2001.) It seems to me that the domain of neuropsychiatry, or behavioural neurology, the overlap between neurological disorders and psychiatric features, has been relatively well addressed, both in general texts (e.g. Lishman, 1987; Trimble, 1996; Moore, 2001; Fincus & Tucker, 2002; Cummings & Mega, 2003; Feinberg & Farah, 2003) and in texts devoted to specific diseases (e.g. stroke: Robinson, 2006; multiple sclerosis: Feinstein, 1999; Parkinson’s disease: Starkstein & Merello, 2002; Alzheimer’s disease: Ballard et al., 2001). As a corollary to this, the grey area of depression-related dementia or depressive pseudodementia (Roose & Devanand, 1999; Kanner, 2005) has been referred to only briefly.

Given my personal clinical training and experience, the perspective is entirely that of adult neurological practice. For childhood disorders
causing cognitive decline, standard texts are available (e.g. Lyon et al., 1996; Brett, 1997; Clarke, 2002; Panteliadis & Korinthenberg, 2005). Learning disability (mental retardation), of which over 2000 different syndromes are described, is entirely eschewed. However, those ‘childhood’ neurodegenerative disorders that may on occasion present as dementia in adults (e.g. Coker, 1991; Doran, 1997; Panegyres, 2001; Sampson et al., 2004) have been included. Some specific topics have not been tackled, again for lack of personal training and experience, most notably head injury and drug-induced cognitive problems (for the latter see Farlow & Hake, 1998; Moore & O’Keefe, 1999), with the exception of antiepileptic drugs, radiotherapy and chemotherapy treatment of brain tumours, and a passing mention of solvent exposure (Berent & Albers, 2005). Neither the management of dementia (e.g. Qizilbash et al., 2002; Baldwin & Murray, 2003; Brown & Hillam, 2004; Curran & Wattis, 2004; Rabins et al., 2006) nor neuropsychological rehabilitation (e.g. Wilson, 1999; Greenwood et al., 2003; Halligan & Wade, 2005; Selzler et al., 2006) is discussed. Since dementia syndromes have been relatively well covered, collectively (e.g. Parks et al., 1993; Hodges, 2001; Mendez & Cummings, 2003; Burns et al., 2005) and individually, the text is slightly weighted towards other neurological disorders. The arrangement of the chapters is somewhat arbitrary, with certain conditions potentially relevant to more than one, but hopefully those scanning rather than reading systematically will find what they are seeking without too much difficulty. Unavoidably, the author’s own interests may appear overemphasized.

This book is envisaged as a reference text relevant to all neurologists, not only those with a declared interest in cognitive disorders; to old age psychiatrists and geriatricians who have to assess patients with cognitive decline; and also as a resource for general physicians and specialists who deal with any endocrine, metabolic, vascular, or infective disorders that may compromise cognitive function. Practitioners of professions allied to medicine which involve contact with cognitively impaired patients (mental health nursing, physiotherapy, occupational therapy, speech and language therapy) may also find material of interest and use.

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Introduction


This chapter seeks to elucidate briefly the various domains of cognitive function, their neuropsychological evaluation, and syndromes of cognitive impairment. It is aimed at the practising neurologist rather than the academic neuropsychologist.

Without necessarily subscribing to an explicitly modular concept of cerebral function, it is nonetheless convenient to think in terms of cognitive domains or functional systems (‘a congeries of mental faculties’) in the brain, specifically attention, memory, language, perception, praxis, and executive function. These subdivisions, all (hopefully) working in concert, not in isolation, to produce in sum what we understand by consciousness, may direct a structured approach to the clinical assessment of cognitive function. Nowadays, a model of distributed neural networks with nodal points more specialized for certain functions has supplanted the idea of particular brain centres (Mesulam, 1990).

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The neurocognitive domains may be described as either localized, implying lateralization to one hemisphere of part thereof, focal damage to which may impair that specific function; or distributed, implying a non-localized function often involving both hemispheres and/or subhemispheric structures (basal ganglia, brainstem), widespread damage being required to impair these functions (Hodges, 1994). Moreover, particular domains may be subdivided, or fractionated, into subsystems or specific functions which may be selectively impaired, suggesting the existence of functionally distinct neuropsychological substrates.

There are many tests available to the neuropsychologist for the evaluation of cognitive function, either global function or individual domains (Lezak et al., 2004; Mitrushina et al., 2005, Strauss et al., 2006). The variety of tests available may bewilder the non-specialist. Moreover, the choice of different test instruments in different studies may make direct comparisons difficult. Of course, it must be remembered that any neuropsychological test may have multiple sensory, motor, perceptual, and cognitive demands, and hence ‘pure’ tests of any single cognitive domain are the exception, rather than the rule.

Neuropsychologists insist, rightly, that special training is required in the administration and interpretation of neuropsychological tests. Clinical neurologists will therefore rely on their neuropsychologist colleagues for the performance and interpretation of these ‘formal’ tests, is the exception, rather than the rule.

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1.1 Attention

It is perhaps redundant to point out that before any meaningful assessment of ‘higher cognitive function’ can be made, it should be ascertained that ‘lower cognitive function’ is intact, assuming that the workings of the nervous system are hierarchical in their operation. To indulge in *reductio ad absurdum*, it would not be reasonable to expect a comatose patient, or a sleeping subject, to perform well on tests of memory, although that memory function may be intact or impaired on recovery from coma or awakening from sleep. The nature of consciousness is an area of great interest to both neuroscientists and philosophers (e.g. Dennett, 1993; Penrose, 1995; Zeman, 2001, 2002; Libet, 2004), but other than to assume that it is an emergent property of brain function, nothing further about its possible neuroanatomical and neurophysiological basis will be considered here. Dissociation between apparent preservation of consciousness and absence of cognitive function may occur, for example in vegetative states (Jennett, 2002).

Disturbance of consciousness may encompass both a quantitative and a qualitative dimension. Hence one may speak of a ‘level’ of consciousness, perhaps in terms of arousal, alertness, or vigilance, forming a continuum from coma to the awake state; and an ‘intensity’ or quality of consciousness, in terms of clarity of awareness of the environment, and ability to focus, sustain, or shift attention. Coma obviously implies a state of unresponsiveness from which a patient cannot be roused by verbal or mechanical stimuli. Lesser degrees of impaired consciousness, sometimes labelled clinically as stupor, torpor, or obtundation (although these terms lack precision, their meaning often varying between different observers) may also interfere with cognitive assessment. There are many causes of coma (Plum & Posner, 1980; Young et al., 1998). These states may be obvious clinically, such as drowsiness, or difficulty rousing the patient, but may also be occult, perhaps manifesting as increased distractibility. Impairments in level of consciousness are a *sine qua non* for the diagnosis of delirium (see Section 1.10), as enshrined in the diagnostic criteria of DSM-IV and ICD10, although these deficits may be subtle and not immediately obvious at the bedside though yet sufficient to impair attentional mechanisms. These attentional deficits may be responsible for the impaired cognitive function that is also a diagnostic feature of delirium (Burns et al., 2004; Larner 2004; Inouye, 2006).

Attention, or concentration, is a non-uniform, distributed cognitive function. It may be defined as that component of consciousness which distributes awareness to particular sensory stimuli. Bombarded as the nervous system is with stimuli in multiple sensory domains, only some reach awareness or salience, whilst many percepts are not consciously taken notice of. Attentional resources, which are finite, are devoted to some channels but not others. Attention is thus effortful, selective, and closely linked to intention. Distinction may be made between different types of attentional mechanism: sustained attention implies devotion of most attentional resources to one particular stimulus;
selective attention is the directing of attentional resources to one stimulus amongst many (‘cocktail party phenomenon’); divided attention implies a division of attentional resources between competing stimuli. Neuroanatomical structures thought to be important in mediating attention include the reticular activating system in the brainstem, the thalamus, and prefrontal cerebral cortex of multimodal association type, particularly in the right hemisphere, since damage to any of these areas may result in impairments of attention. Dopaminergic and cholinergic pathways are thought to be the important neurotransmitters mediating attention (Perry et al., 2002).

The term ‘working memory’ is used by neuropsychologists to describe a limited-capacity store for retaining information over a short term, 1–2 minutes, and for ‘online’ manipulation of that information. This system has a limited capacity wherein information rapidly degrades unless continuously rehearsed (hence ‘unstable’, compared to longer-term memory). Working memory may be fractionated into verbal (phonological or articulatory loop) and visual (visuospatial sketch pad) components, governed by a supervisory central executive (Baddeley, 1986). Working memory function is dissociable from ‘long-term memory’ function (see Section 1.3); for example, in patients with amnesia as a consequence of Wernicke–Korsakoff syndrome working memory is preserved (Section 8.3.1). Working memory is perhaps better envisaged as a component of the selective attention system (the ‘specious present’ of William James), and is certainly not congruent with the term ‘short-term memory’ often used by patients, which refers to recent long-term memory. Grammatical complexity, for example in sentence construction, is associated with working memory capacity, which mediates the need to keep many elements in play and not lose the train of thought before completing the sentence.

Neglect, sometimes known as inattention, is a failure to orient to, respond to, or report novel or meaningful stimuli in the absence of sensory or motor deficits such as hemiparesis or hemianopia that could explain such behaviour. Extinction, the failure to respond to a novel or meaningful sensory stimulus on one side when a homologous stimulus is given simultaneously to the contralateral side (i.e. double simultaneous stimulation), sometimes called ‘suppression’, may be a lesser degree of neglect. In the visual domain, neglect may be categorized as a disorder of spatial attention, which is more common after right rather than left brain damage, usually of vascular origin, an observation accounted for by the ability of the right hemisphere to attend to both sides of space whereas the left hemisphere attends to the right side of space only (i.e. there is some lateralization of function). The angular gyrus and parahippocampal gyrus may be the critical neuroanatomical substrates underpinning the development of visual neglect (Husain, 2002; Chatterjee, 2003; Heilman et al., 2003).

The Glasgow Coma Scale (GCS) is the instrument most commonly used for monitoring level of consciousness (Teasdale & Jennett, 1974). Introduced to assess the severity of traumatic head injuries, it has subsequently been applied in other clinical situations (e.g. delirium, stroke) although its validity in some of these circumstances remains to be confirmed. In the individual patient, use of the individual components of the GCS (eye, verbal, motor response = EVM) is more useful than the summed score (out of 15), although for demographic research use of the summed score is preferable. A GCS score of 15/15 does not guarantee intact attention, since deficits may be subtle, and it may therefore be necessary to undertake tests of attentional function before any other neuropsychological instruments are administered.

Many tests of attention are available (Strauss et al., 2006), such as the Trail Making Test, the Continuous Performance Test, the Paced Auditory Serial Addition Test (PASAT: Gronwall, 1977), and the Symbol Digit Modalities Test. Simple bedside tests which tap attentional mechanisms include orientation in time and place, digit span forwards and/or backwards (also WAIS-R Digit Span subtest), reciting the months of the year or the days of the week backwards, or counting back from 30 down to
1. Distractibility may be evident if the patient loses his or her way, or starts the more automatic forward recital. In the Mini-Mental State Examination (see Section 1.8), performing serial sevens (subtracting 7 from 100 repeatedly 93, 86, 79, 72, 65, etc.) or spelling the word WORLD backwards are labelled as tests of attention or concentration, but it should be realized that failure in these tests may be for reasons other than impaired attention (e.g. poor mental arithmetic abilities in serial sevens).

Neglect may be clinically obvious, for example if a patient fails to dress one side of the body, but is sometimes more subtle, in which case its presence may be sought using cancellation tests (e.g. stars in an unstructured array, or letters in a structured array), figure copying (e.g. the Rey–Osterreith figure), line bisection tasks, numbering a clock face, or drawing from memory.

REFERENCES


1.2 General intelligence, IQ

Formal neuropsychological assessment often involves testing of general intelligence, before any specific assessment of the individual domains of cognitive function. This is legitimate since a general intelligence factor, g, seems to account for a significant proportion of the individual differences among test scores for groups of people (Deary, 2001). General intellectual function is most often measured by administration of one of the Wechsler Intelligence Scales, most often the Wechsler Adult Intelligence Scale–Revised (WAIS-R: Wechsler, 1981) or the Wechsler Adult Intelligence Scale–III (WAIS-III: Wechsler, 1997). (There is a separate scale for children, the Wechsler Intelligence Scale for Children, WISC.) Updating of these tests is required periodically because of changes in the abilities of the normative group from which standardized scores are derived (Deary, 2001).

Administration of these tests may take anything up to 2 hours or more, sometimes necessitating more than one testing session to avoid patient fatigue. Subtests in these batteries fall into two categories, verbal and performance, the former