

NEUROLOGICAL SYNDROMES WHICH CAN BE MISTAKEN FOR PSYCHIATRIC CONDITIONS

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All illness has both psychological and physical dimensions. This may seem a startling claim, but on reflection it is uncontroversial. Diseases don't come to doctors, patients do—and the processes by which patients detect, describe, and ponder their symptoms are all eminently psychological. This theoretical point has practical implications. If we adopt a “bio-psycho-social” approach to illness generally, one which recognises the biological, psychological, and social aspects of our lives, we become less likely to neglect the treatable psychological origins of many physical complaints (from globus hystericus to full blown conversion disorder) and the treatable psychological consequences (such as depression and anxiety) of much physical disease.

NEUROLOGY, PSYCHOLOGY, AND PSYCHIATRY

Neurology has an especially close relationship with psychology and psychiatry, as all three disciplines focus on the functions and disorders of a single organ, the brain. The main targets of the traditional British “neurological examination” may be elementary motor and sensory processes, but any adequate assessment of “brain function” must take account of cognition and behaviour. The notion many of us bring to neurology—that only a minority of neurological disorders has a significant psychological or psychiatric dimension—is almost certainly wrong. Cognitive and behavioural involvement is the rule, not the exception, among patients with disorders of the central nervous system (CNS). The physical and psychological symptoms of disease can therefore be related in the following ways: (1) physical symptoms come to light by way of complex psychological processes; (2) psychological upset can manifest itself in physical symptoms; (3) physical diseases commonly cause a secondary psychological reaction; (4) one category of physical disease, affecting the brain, can give rise, more or less directly, to psychological manifestations.

The importance of a wide ranging approach to assessment is well illustrated by the example of dementia, a primarily cognitive and behavioural disorder: the clue to diagnosis may come from general medical examination (revealing, for example, the testicular tumour causing limbic encephalitis or the bradycardia of hypothyroidism), from traditional neurological examination (subtle chorea in early Huntington's disease), from cognitive assessment (isolated anterograde memory impairment in early Alzheimer's disease), or from observation of behaviour (the patient with a frontal lobe dementia who leans over your desk and takes apart your pen). Moreover, this type of assessment is essential if one is to do justice to the symptoms of dementia which most bother patients: these are more often “psychiatric” than “neurological”.

In this article we first drive home the general point that CNS disorders tend to give rise to cognitive and behavioural as well as “neurological” manifestations by considering some of the neuropsychiatric associations of the major classes of neurological disease, highlighting some specific examples and case histories as we do so. We then pick out a number of neurological disorders which are particularly liable to give rise to “discipline confusion” by turning up in the psychiatry clinic, grouping these disorders in terms of the neuropsychiatric function which they most conspicuously disturb (for example, memory in the case of transient global amnesia). As you will have gathered, we are not really trying to teach you how to “rescue” neurological patients from the psychiatrists: on the contrary we believe that both psychiatrists and neurologists have much to gain by sharing and exchanging their complementary skills. Judging how far we neurologists can trust our own psychiatric acumen, and when we should ask for help, is necessary but tricky. There is much to be gained from joint work with interested psychiatric colleagues. While the title of this article draws attention to the risk of mistaking “neurological” disorders for psychiatric ones, the opposite mistake is almost certainly more common.

We believe that all neurologists in training would benefit from spending some time with a neuropsychiatrist or with a liaison psychiatrist who is experienced in dealing with “neurological” patients, and should equip themselves to perform at least a basic neuropsychiatric assessment. There are several excellent textbooks which provide a background in the subject.

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We cannot possibly discuss all the neurological disorders which can be mistaken as psychiatric in this short article: we have picked out an illustrative assortment to convey the broad approach we recommend. Throughout the text, you will encounter the words *neurological*, *psychological*, and *psychiatric* enclosed in “scare quotes”. This is to emphasise that, although brain disorders are often carved up into these subcategories for practical or heuristic purposes, these distinctions are often tenuous.

MAJOR CATEGORIES OF NEUROLOGICAL DISORDER AND THEIR PSYCHIATRIC PRESENTATIONS

The cognitive, psychological, and behavioural sequelae of CNS disorders depend, inter alia, on: the tempo of the underlying disorder; the brain regions it affects; the neurotransmitter systems it involves; and various individual characteristics, such as age, sex, and psychosocial background:

- ▶ *Tempo*—Acute pathologies, caused by trauma, metabolic upsets, drugs, and infections, for example, are particularly associated with “delirium” or confusional states, with prominent impairment of attention, while slowly progressive pathologies are more often responsible for “chronic brain syndromes”, such as dementia (table 1).
- ▶ *Site*—Several more or less fine grained anatomico-clinical distinctions can be drawn: in addition to the well established contrast between cortical and subcortical patterns of cognitive impairment (table 2), pathologies in certain brain regions are associated with particular constellations of psychological and behavioural disturbance; right hemisphere stroke, for example, gives rise to mania more often than left, and damage to the orbito-frontal cortex is particularly associated with disinhibited behaviour.
- ▶ *Neurotransmitter system*—The relatively severe depletion of acetylcholine in early Alzheimer’s disease provided the rationale for the development of the current, modestly effective, treatments for the disorder; depression in Parkinson’s disease is associated with involvement of serotonergic and noradrenergic neurotransmission in addition to the classical dopaminergic deficit.
- ▶ *Individual differences*—Factors such as age, sex, educational attainment, and prior psychiatric history can influence the likelihood that brain pathology will give rise to “psychological” symptoms. For example, higher levels of educational attainment offer some protection against Alzheimer’s

disease; a prior history of anxiety disorder may be a risk factor for the occurrence of ictal fear.

A brief survey of the major categories of neurological disorder highlights the importance of neuropsychiatric symptoms across the whole spectrum of CNS disease.

INHERITED DISORDERS

Many of the inherited disorders of the central nervous system have neuropsychiatric as well as traditionally “neurological” manifestations. This is well recognised in some conditions—for example, Huntington’s disease, which is commonly associated with depression, apathy and aggressivity, and sometimes associated with psychosis, obsessive–compulsive disorder and suicide; these features, or the predominantly subcortical dementia of Huntington’s disease, can precede or overshadow the associated chorea. Wilson’s disease presents with primarily neuropsychiatric symptoms including personality change, mood disturbance, psychosis, and cognitive impairment in around one third of cases. Acute intermittent porphyria can give rise to acute psychosis, often in association with abdominal pain. Neuroacanthocytosis is frequently associated with cognitive and behavioural features:

- ▶ *Case history 1*—A 50 year old unemployed man was referred as an emergency to the psychiatric services because of impulsive and disinhibited behaviour—for example, going naked into his back garden and talking loudly to himself in public. He was sleeping poorly. His wife reported that he had been hoarding “junk” in his house for many years. He had been sacked from his work as a chef about 10 years before because of disorganisation. He was an only child and there was no relevant family history. He had been “fidgety” since childhood. Examination revealed lack of insight, an inappropriately jocular manner, chorea, borderline wasting of the lower legs and areflexia. His creatine kinase was elevated at 1350 U/l (normal range 24–161 U/l). Acanthocytes were eventually identified on his blood film. Blood grouping and genotyping confirmed the diagnosis of McLeod syndrome, a subtype of neuroacanthocytosis. His behavioural disturbance progressed, eventually leading to compulsory detention under the Mental Health Act.

Recent research suggests that neuropsychiatric features also occur quite commonly in many inherited disorders regarded as firmly “neurological”—for example, hereditary spastic paraparesis and inherited spinocerebellar ataxia. Both disorders can be associated with “frontal” or dysexecutive features, presumably because prefrontal or cerebellar regions involved in executive functions are implicated. The

Table 1 Delirium versus dementia

Feature	Delirium	Dementia
Onset	Abrupt/sub-acute	Insidious
Course	Fluctuating	Slow progression
Duration	Hours–weeks	Months–years
Alertness	Abnormally high or low	Typically normal
Sleep–wake	Disrupted	Typically normal
Attention	Impaired	Relatively normal
Orientation	Impaired	Intact in early dementia
Working memory	Impaired	Intact in early dementia
Episodic memory	Impaired	Impaired
Thought	Disorganised, delusions	Impoverished
Speech	Slow/rapid, incoherent	Word finding difficulty
Perception	Illusions/hallucinations common	Usually intact in early dementia
Behaviour	Withdrawn/agitated	Varies: often intact early

Table 2 Cortical versus subcortical dementia

Function	Cortical e.g. Alzheimer's disease	Subcortical e.g. Huntington's disease
Alertness	Normal	"Slowed up"
Attention	Normal early	Impaired
Executive function	Normal early	Impaired
Episodic memory	Amnesia	Forgetfulness
Language	Aphasic	Reduced output
Praxis	Apraxia	Relatively normal
Perception ± visual/spacial	Impaired	Impaired
Personality	Preserved (unless frontal type)	Apathetic, inert

cerebellum has been linked specifically with the "cerebellar cognitive-affective syndrome", a putative combination of personality change, dysexecutive syndrome, impairment of visual memory, and subtle language deficits.¹

► *Case history 2*—A 46 year old man was referred with a five year history of personality change, involving labile mood, aggressive outbursts, and inflexibility about routines. He complained of forgetfulness and difficulty in doing more than one thing at a time. His speech had become mildly slurred, his gait slightly unsteady, and his dexterity had declined. Although he scored 30/30 on the mini mental state examination, comprehensive neuropsychological testing on two separate occasions revealed impairment of executive function. His mother proved to have similar cognitive, behavioural, and motor features. Both later tested positive for spinocerebellar ataxia type 8.

Inherited leucodystrophies can present with neuropsychiatric features. Metachromatic leucodystrophy, for example, caused by a deficiency of the lysosomal enzyme arylsulphatase-A (ASA) leading to demyelination in peripheral and central white matter, has infantile, juvenile, and adult forms. Peripheral nerve involvement and motor dysfunction characterise the initial presentation of the infantile and juvenile forms. In the rarer adult form, cognitive and psychiatric features predominate and patients may present with dementia or psychosis. The latter is particularly associated with onset in adolescence and typically involves auditory hallucinations, complex delusions, inappropriate affect, or bizarre behaviour. A diagnosis of schizophrenia, or occasionally mania, may persist for many years until motor dysfunction, pyramidal or extra-pyramidal, seizures and peripheral nerve involvement become apparent. The psychotic features have been postulated to arise from frontal-subcortical disconnection caused by demyelination. However, age must be an additional determining factor, as a similar pattern of demyelination is seen in all three forms of the disease.

ACQUIRED DISORDERS

Neurodegenerative disorders

CNS degenerative disorders are commonly associated with neuropsychiatric symptoms. In some cases—for example, the frontal variant of frontotemporal dementia (fvFTD)—these symptoms are the most characteristic presentation.

► *Case history 3*—A 63 year old man was referred because of his wife's concerns about a change in his personality. Previously affectionate and meticulous, he had become increasingly detached and self obsessed. On a recent occasion he had walked down the counter of a local café, picking up, sniffing and replacing each cake in turn. His speech was slightly slurred, with mild word finding difficulties. He had bilateral palmo-mental reflexes. He

scored 30/30 on the mini mental state examination but performed poorly on neuropsychological tests of frontal lobe function. A computed tomographic (CT) scan revealed selective frontal lobe atrophy.

Although a rare cause of dementia overall, frontotemporal dementia (FTD) accounts for 10–15% of cases of dementia occurring before the age of 65 years.² Some cases are familial. FvFTD, exemplified here, often presents first to a psychiatrist, typically with a blunting of emotions, apathy, and egocentricity. Some patients become inert and asportaneous, others anxious and restless, leading to a diagnosis of depression or anxiety disorder. Compulsive behaviour and rituals may be prominent: a lack of insight helps to distinguish the condition from obsessive-compulsive disorder. Neglect of personal appearance and hygiene, elevated mood, disinhibition, and poor judgement may cause confusion with personality disorder, alcoholism or hypomania; hallucinations and delusions occur in up to 20% of patients. Examination may reveal utilisation behaviour (an unthinking, apparently automatic, utilisation of objects presented to the patient) and primitive reflexes (pout, palmo-mental, and grasp). The temporal lobe variant of FTD presents most commonly with "semantic dementia", a syndrome of progressive word finding difficulty, loss of language comprehension, depletion of conceptual knowledge (apparent on non-verbal as well as verbal tests), and impairment of object recognition. These features reflect left temporal lobe dysfunction. If the right temporal lobe is more severely affected, prosopagnosia (impaired face recognition) and loss of knowledge about people may be especially prominent. Two other clinical varieties of FTD are recognised: "progressive non-fluent aphasia" occurs in patients with degeneration of peri-Sylvian structures, including the insula, inferior frontal, and superior temporal lobes; "FTD with motor neurone disease" is the combination of frontal variant FTD or progressive aphasia with features of motor neurone disease, usually particularly affecting speech and swallowing ("bulbar" type). Several types of pathology can underlie the features of FTD. The five principle types are: classical Pick's disease pathology, with tau and ubiquitin positive cortical inclusions (Pick bodies) and ballooned neurons; neuronal loss with microvacuolation of outer cortical layers and astrocytosis; tau-positive inclusions in neuronal and glial cells in familial FTD with Parkinsonism, linked to mutations in the tau gene on chromosome 17; motor neuron disease type pathology; and corticobasal degeneration type pathology.

While neuropsychiatric presentation is the rule in fvFTD, it is common in many other neurodegenerative disorders, and neuropsychiatric symptoms are ubiquitous. Examples of

neuropsychiatric presentation include depression or REM (rapid eye movement) sleep behaviour disorder predating the motor onset of Parkinson's disease, sometimes by several years; early hallucinations in diffuse cortical Lewy body disease; delusional jealousy at the onset of progressive supranuclear palsy; or apathy as an early and prominent feature of Alzheimer's disease.

Vascular disorders

Cognitive and behavioural symptoms are a common result of cerebrovascular disease, and are important determinants of long term outcome. Confusional states occur in around one third of patients with acute stroke, and are occasionally its most prominent feature. Focal behavioural disturbance caused by cerebral ischaemia can mimic "functional" disorder.

► *Case history 4*—Ten days after undergoing a posterior fossa decompression, an anxious 30 year old man reported that his left limbs felt as if they did not belong to him. He was observed, soon afterwards, to imitate the movements of objects in the room with his normal right arm. When his level of consciousness declined, a brain scan was performed, revealing bilateral ischaemia in the territories of the anterior cerebral arteries, including the anterior cingulate cortices.

Cognitive impairment—caused by widespread subcortical ischaemia, multiple infarcts, or a "strategically placed" single stroke—personality change, affective disorder, and occasionally psychosis, are important neuropsychiatric consequences of stroke. Their cerebrovascular aetiology will usually, though not always, be apparent from the clinical history.

Inflammatory and infective disorders

The majority of CNS inflammatory and infective disorders can present with neuropsychiatric symptoms. For example, multiple sclerosis (MS) occasionally turns out to be the explanation for progressive cognitive impairment in adulthood. MS can also, rarely, present with fatigue, depression, mania or psychosis. The interesting possibility that MS may predispose to "hysterical" presentations, mimicking "functional" neurological disorder, has often been raised but never irrefutably confirmed. Systemic lupus erythematosus (SLE) is particularly associated with a transient encephalopathy—"lupoid psychosis". Worldwide, HIV associated dementia has become a common cause of insidious subcortical dementia: apathy and social withdrawal may be the most prominent features, overshadowing the associated forgetfulness and slowing of cognition. Variant Creutzfeldt-Jakob disease (CJD) provides an especially vivid, recent reminder of the underlying unity of neurology and psychiatry. The initial symptoms of this transmissible spongiform encephalopathy are usually psychiatric, specifically anxiety or depression. These are often sufficiently severe to lead to psychiatric referral. Limb pain or tingling is moderately common early in the course of the illness. After some months cognitive symptoms typically develop, causing difficulty at school or work, together with varied neurological features including pyramidal, extrapyramidal, and cerebellar signs and myoclonus. The disorder evolves more slowly than sporadic CJD, with an average duration to death of 14 months.³

Neoplastic and paraneoplastic

The association between slow growing frontal lobe tumours, anosmia, and personality change is one of the most

celebrated in behavioural neurology. Diffusely infiltrating tumours can also present with behavioural symptoms and are sometimes missed on initial neuroimaging. Paraneoplastic limbic encephalitis, most often associated with small cell lung carcinoma and anti-neuronal antibodies ("anti-hu"), usually causes a profound amnesic syndrome but psychiatric symptoms are sometimes to the fore. Lishman cites the case of a woman of 61 who "developed impairment of memory and difficulty with her secretarial work together with numbness of the limbs. She became depressed, suspicious, confused and severely disorientated". She proved to have a small cell carcinoma of the lung. Recently, a similar syndrome of limbic encephalitis, caused by antibodies to voltage gated potassium channels, has been described in patients without evidence of cancer.⁴

Trauma

Head injury is a common cause of neuropsychiatric symptoms. This will usually be apparent from the history, but occasionally patients with chronic subdural haematomas following minor trauma present with delirium, insidious cognitive decline, or oddities of behaviour.

Metabolic/endocrine

These disorders are not primarily neurological, but may certainly present to both neurologists and psychiatrists. Well known examples include hypothyroidism, associated with lethargy and impaired cognition, sometimes accompanied by hallucinations and delusions, often paranoid; hyperthyroidism, giving rise to anxiety, irritability, delirium, and possibly psychosis; and phaeochromocytoma, which can be associated both with a chronic anxiety state and with paroxysmal fear akin to panic.

Deficiency disorders

The confusional state which accompanies the ataxia and ophthalmoplegia of Wernicke's encephalopathy is a neurological emergency, requiring urgent intravenous thiamine; the cognitive decline and organic psychosis of vitamin B12 deficiency can occur in the absence of anaemia or macrocytosis, requiring B12 assay for diagnosis.

Structural disorders

The ready availability of CT scanning has reduced the risk of missing structural causes for psychiatric presentations. Vigilance is still required.

► *Case history 5*—An elderly woman became progressively withdrawn over the course of several months following minor surgery. Depression was suspected by her general practitioner, and later by a psychiatrist, but she did not respond to antidepressant treatment. Although a CT scan showed somewhat dilated ventricles, the cortical mantle appeared normal and the ventricular dilatation was not considered significant. The patient became stuporose, was admitted under the psychiatry service and treated with electroconvulsive therapy (ECT), with no improvement. Neurological assessment was difficult but revealed hypertonia and possibly extensor plantars. A lumbar puncture showed a cerebrospinal fluid (CSF) protein concentration of 1.8 g/l, and a magnetic resonance imaging (MRI) scan of the brain revealed a meningioma at the foramen magnum. The tumour was thought to be causing hydrocephalus by elevation of CSF protein and interference with CSF reabsorption. The meningioma was

removed and after some months she returned to her normal, independent existence.

UNUSUAL NEUROLOGICAL SYNDROMES THAT MAY PRESENT AS PSYCHIATRIC

In the second part of this article, we highlight a number of neurological syndromes which, because of their predominantly behavioural and sometimes bizarre presentations, are often mistakenly diagnosed as psychiatric. We group these according to the neuropsychiatric function most prominently disturbed.

Consciousness

Consciousness has two key components, arousal (conferring the “capacity” for consciousness) and awareness (conferring the “contents” of consciousness). The modulation of arousal during the sleep–wake cycle is regulated by a network of neurons in the brain stem, diencephalon (thalamus and hypothalamus), and basal forebrain which distribute noradrenaline, acetylcholine, serotonin, dopamine, histamine, and the recently described hypocretins widely throughout the CNS.

Narcolepsy

Narcolepsy is a distinctive disorder of arousal causing excessive daytime sleepiness. This involves both chronic sleepiness and frequent, brief episodes of sleep from which the patient often wakes feeling refreshed.⁵ It is associated with four other characteristic features: cataplexy (70%, an almost pathognomonic partial or generalised loss of muscle tone lasting up to a minute or so, usually in response to emotion, especially amusement), hypnagogic hallucinations (30%), sleep paralysis (25%), and disrupted nocturnal sleep (60–80%). Prevalence is 3–5/10 000, with onset most commonly between 10–30 years of age. The sex ratio is equal; 1–2% of first degree relatives are affected. There is a strong association with the HLA DQB1 0602 allele. Physiological findings characteristically include a reduced mean sleep latency and an early transition to REM sleep (sleep onset REM). Many of the features of narcolepsy can be understood in terms of dysfunctional REM sleep mechanisms (for example, cataplexy and sleep paralysis both reflect inappropriate activation of REM sleep atonia) but the disturbed nocturnal sleep of narcolepsy suggests an underlying instability of conscious states in general. Recent evidence indicates that human narcolepsy is caused by lack of hypocretin, opening up the way to novel therapies.

Late diagnosis and misdiagnosis of narcolepsy are both extremely common. Complaints of tiredness, especially in the context of social or employment difficulties, may lead to diagnoses of chronic fatigue or affective disorder. Vivid hallucinations, sometimes occurring during the day, can be mistaken for a sign of psychosis or sometimes epilepsy, the latter misdiagnosis also being promoted by the twitching which may feature in episodes of cataplexy. Finally, confusion with a psychiatric condition may arise due to the typical precipitation of cataplexy by emotional stimuli.

REM sleep behaviour disorder

Predicted on theoretical grounds before it was described in man, this striking parasomnia is caused by loss of REM sleep atonia; sufferers enact their dreams, which are often aggressive, placing both themselves and their bed partners at considerable risk.⁶ The diagnostic clue is that, once woken, sufferers can generally recall a dream narrative. REM sleep

behaviour disorder is associated with a range of neurodegenerative disorders, particularly Parkinson’s disease and multiple systems atrophy. The disorder may precede the recognisable onset of these conditions by several years. Clonazepam is often an effective treatment.

Attention

Attention is a complex capacity: it can be “selective”, “sustained”, “divided”, or “preparatory”; each of these can be focused on a variety of targets, ranging from spatial events to cognitive tasks. Inability to sustain attention, revealed for example by an inability to recite the months backwards or to perform “serial 7s”, is the neuropsychological hallmark of delirium. The neural systems which direct and maintain our focus of attention are widely distributed in the brain, but the pre-frontal and parietal lobes are crucially involved. Injury to the right parietal cortex, for example, frequently leads to unilateral neglect, a syndrome which may be thought of as an isolated disorder of spatial attention. Biparietal pathology causes a more florid, but less well known, disorder of spatial awareness.

Balint’s syndrome

Balint’s syndrome, originally described in 1909, is usually construed as the inability to see more than one object at the same time (simultanagnosia) and, therefore, as a deficit in visual attention. Balint’s original case report described two additional features: ocular apraxia, an inability to direct voluntary eye movements; and optic ataxia, difficulty reaching for objects under visual guidance. Simultanagnosia most commonly results from biparietal damage, but has also been reported with occipital and thalamic lesions.

► *Case history 6*—An active, 60 year old retired maths teacher was having increasing trouble with her hobbies. She could no longer coordinate moves with her partner in country dancing, was unable to work out where to place the tiles in Scrabble, and kept “missing lines” when reading. She had difficulty placing the cutlery correctly on the table and was unable to locate objects pointed out by her husband, although she felt there was nothing wrong with her eyesight. An MRI scan revealed bilateral, severe atrophy of the parietal and occipital lobes.

Executive function

“Executive functions” include the planning, initiation, and monitoring of movement and behaviour, functions closely linked to social awareness, motivation, and emotion. Executive abilities are particularly associated with the frontal lobes, which subserve them in close collaboration with subcortical structures, the basal ganglia, thalamus, and cerebellum. As discussed in the previous section, disorders of the frontal lobes frequently manifest themselves first and foremost in alterations of behaviour, with the result that psychiatry or psychology services will often be the first port of call.

Memory

Memory complaints are common in clinical practice. The reported problems sometimes reflect lapses of attention: “Where did I put the keys?” This is a common phenomenon in everyday life, but may occasionally be symptomatic of psychiatric or neurological disorder. An insidious, isolated deficit of episodic memory (memory for events) is the most common early cognitive symptom in Alzheimer’s disease,

while semantic memory (factual knowledge about language and the world) is particularly affected by the temporal variant of frontotemporal dementia (see above). Transient disturbances of memory can also cause diagnostic confusion.

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Transient global amnesia

The syndrome of transient global amnesia (TGA) is well defined but poorly understood. The onset of the amnesic attack is abrupt, memory usually returns to normal within a few hours, and recurrence is unusual. During the attack the patient, usually in late middle to old age, is unable to learn new information (anterograde amnesia) and unable to recall events from the more or less recent past (retrograde amnesia). The cause is unknown: a migraine-like depression of temporal lobe function is a favoured possibility. Functional imaging and diffusion weighted MRI scanning have revealed abnormalities predominantly but not exclusively in the medial temporal lobes. Attacks are associated with physical or emotional stress in a significant minority of cases, creating potential for confusion with psychogenic amnesia. Several features should help clinicians to avoid this mistake. Psychogenic amnesia is rare in older patients. It characteristically affects memory for long swathes of the past, sometimes causing a loss of personal identity. Memory difficulties may be restricted to matters of personal concern and there may be inconsistencies in performance or evidence of gain. None of these features are present in patients with TGA, who behave entirely appropriately during their attacks, typically seeking to fill in their memory gap by anxious questioning.

Transient memory disturbances in temporal lobe epilepsy

Transient memory disturbance can be the sole manifestation of temporal lobe seizures.⁷

► *Case history 7*—A 72 year old retired journalist with a history of ischaemic heart disease awoke one morning while on holiday and began to question his wife repetitively “Where am I? What am I doing here?” He appeared unable to remember events of the previous few days. This state persisted while he dressed and had breakfast, but an hour later he had returned to normal. He was partially able to “remember not having been able to remember”. Six similar episodes occurred over the next few months. During one attack, while he was playing bridge, his wife noticed him smacking his lips. An EEG did not reveal any epileptiform abnormalities, but the attacks resolved abruptly upon introduction of carbamazepine. However, the patient began to complain of a patchy but significant loss of memories for events of the past 30 years.

Attacks are typically brief (less than an hour), recurrent, and often occur on waking. They may be associated with other manifestations of temporal lobe epilepsy such as olfactory hallucinations or lip smacking. In addition, interictal memory may be affected: patients sometimes complain of accelerated forgetting and an unusual loss of memories for salient life events in the distant past such as holidays or weddings, autobiographical amnesia. The EEG is often unremarkable, but attacks typically respond well to anti-convulsant treatment. Déjà vu and jamais vu can occur in healthy subjects and in a range of psychiatric disorders but are sometimes symptomatic of temporal lobe epilepsy.

Reduplicative paramnesia

Patients displaying this phenomenon maintain two incompatible attitudes towards their surroundings without seeming to be aware of the inconsistency. They may, for example, assert both that they are in hospital in one town, and that they are at home in another. Such beliefs are maintained side by side in a vacillating manner or may be reconciled by shallow rationalisations such as a recent journey between the two. Reduplicative paramnesia usually occurs in the context of diffuse brain disease.

Perception

Perception is a complex process in which interpretation plays a large role—the consultant neuroradiologist and house officer see an MRI brain scan in very different ways. Complex hallucinations, in which the subject mistakes internally generated imagery for reality, are a fundamental feature of psychotic illness. However, hallucinations and pseudo-hallucinations (where insight is retained) can also occur in a number of “neurological” conditions.

Charles Bonnet syndrome

The Charles Bonnet syndrome is characterised by complex visual hallucinosis occurring in the context of ocular pathology, most commonly macular degeneration in the elderly. The patient typically sees vivid images of scenery, animals or people, often in the evening. Patients usually have full insight and are not generally distressed by the images. Many can stop their hallucinations by simple manoeuvres such as opening or closing the eyes. Functional imaging reveals activation of visual association cortices during these hallucinations.⁸

Peduncular hallucinosis

This phenomenon was first described by Lhermitte in 1922. Pathology in the midbrain and thalamus, often caused by infarction in the rostral basilar territory, may result in vivid, well formed visual hallucinosis sometimes confined to one hemi-field and occurring with or without a visual field defect. The hallucinations characteristically occur in the evening and may be associated with sleep disturbance. They generally begin a few days after the stroke and subside a few weeks later. The mechanism is unclear.

Altered perception also occurs in temporal lobe seizures which can cause both distortion of real perceptions, such as macro/micropsia, hyper/hypoacusis and derealisation, and spontaneous hallucinations affecting vision, hearing, taste, or smell.

Misidentification syndromes Capgras delusion

The Capgras delusion (“illusion de sosies”) is the belief that a relative or friend has been replaced by an imposter who resembles the original exactly. The Capgras delusion can occur in paranoid schizophrenia, but is associated with evidence of organic brain disease in 25–40% of cases, including dementia, head injury, epilepsy, and cerebrovascular disease. It has been suggested that the syndrome results from a disconnection of the fusiform face recognition area of the right temporal lobe from the limbic system, impairing the usual emotional response to familiar faces.

Frégoli delusion

This related type of misidentification syndrome is named after the famous Italian actor Leopoldo Frégoli who was a great impersonator. In the condition, a persecutor is believed to have adopted multiple disguises so that, while a number of different people around the patient are recognised as having distinct appearances, they are all thought to represent a single familiar person who is bent on harming the patient. As with the Capgras delusion, there is an association with right hemisphere pathology although Frégoli's delusion has also been reported with bifrontal damage.

Language

Language function is tied to the perisylvian regions of the dominant, usually left, hemisphere, though there is a growing appreciation of the role of the right hemisphere in emotional aspects of language processing. Fluent (Wernicke's) dysphasia sometimes gives rise to exuberant "jargon" aphasia or "word salad" which can be mistaken for the product of psychiatric thought disorder. Occasionally the distinction can be difficult to draw, perhaps because the superior temporal gyrus is involved in both language and thought:

► *Case history 8*—A man in his 50s presented with fluent jargon aphasia. He was initially referred to a psychiatrist who suspected an "organic" cause. It emerged that the patient had a long history of complex partial seizures, with fluent dysphasia occurring post-ictally. Brain imaging revealed an extensive arteriovenous malformation in the left temporal lobe. As his dysphasia resolved, he developed an intermittent formal thought disorder without any other evidence of psychiatric disorder.

Praxis

Praxis is the translation of an idea into action; dyspraxia is usually defined as failure to act effectively despite the will to do so and intact elementary motor capacities. Dyspraxia is sometimes accompanied by performance of relatively complex, apparently *unwilled* actions. These include imitation behaviour (involuntary imitation of an examiner's movements), utilisation behaviour (involuntary utilisation of proffered objects, so that the subject might, for example, don several pairs of glasses simultaneously), and the alien or "anarchic" hand syndrome (see below). The dominant hemisphere is particularly implicated in praxis, especially the parietal lobe and frontal lobes.

Alien hand syndrome

In this syndrome the affected limb performs autonomous complex movements either against the patient's will or at least without his or her bidding. Commonly observed signs include intermanual conflict, in which one hand acts at cross purposes with the other, and impulsive groping towards objects. There are several anatomical bases for alien limb phenomena including pathology in the corpus callosum, disrupting the left hemisphere's normal control of both limbs, and pathology in the medial frontal lobe interfering with the processing of willed movement.

Mood and emotion

Moods and emotions, like anger, sadness, happiness, and fear are complex states with physiological, behavioural, cognitive, and subjective aspects. They are intimately linked to neurological disease through all four mechanisms discussed

in the introduction to this article. Brain lesions affecting the limbic system (including the hypothalamus, amygdala, and cingulate gyrus), or closely associated structures such as the basal ganglia, are particularly likely to be associated with mood disturbance, which can be the first symptom of neurological disease.

► *Case history 9*—A 63 year old retired journalist, with no previous psychiatric history, developed severe, treatment resistant depression, with delusions of persecution and intense feelings of guilt. This spontaneously resolved. Two years later he developed features of idiopathic Parkinson's disease, which initially responded well to levodopa. However, he later became increasingly withdrawn, immobile, and anorectic and suffered from recurrent delusions of guilt. Antidepressants were ineffective, but ECT led to a dramatic improvement in both his mood and mobility.

Depression is common in Parkinson's disease, as was noted in 1817 by Parkinson himself, who referred to patients as "unhappy sufferers" and "melancholy". With an estimated prevalence of 50–60%, it is more common in this group than among age matched controls with a similar degree of handicap from paraplegia, and is occasionally, as in the above case, a presenting symptom before "neurological" signs are evident. The widespread disruption of brain monoamine pathways in Parkinson's disease is likely to underlie the associated mood disturbance.

Paroxysmal attacks of intense fear associated with a range of somatic symptoms, such as palpitations, sweating, dyspnoea, and hyperventilation, are characteristic of panic disorder, a psychiatric diagnosis classified by DSM-IV as an anxiety disorder. An identical clinical picture may be seen in some patients with temporal lobe epilepsy, whose attacks are similarly spontaneous, unexpected, stereotyped, and self limiting over a few minutes. Discriminating between an epileptic or psychological origin can be extremely difficult: panic disorder can occur in the absence of other psychopathology; seizure activity arising deep in the temporal lobes can be undetectable on a surface EEG.

Thought

Disturbance of the content, as opposed to the form, of thought is a fundamental feature of delusional disorders. Delusions may occur in a number of the "global" neurological conditions already discussed such as MS, Alzheimer's disease, and SLE. Focal lesions can also lead to abnormalities of thought content, as in anosognosia following a right parietal lobe stroke, when the patient denies weakness, disability, or even ownership of the affected limb, or in Anton's syndrome where the patient with cortical blindness may deny any visual disturbance despite all evidence to the contrary.

Epilepsy can be responsible for a transient disturbance of thought content as in per-ictal, post-ictal, and inter-ictal psychosis. Post-ictal psychosis is the most commonly encountered—it may follow a generalised or focal seizure and, particularly if the preceding convulsion has gone unrecognised, can result in presentation to psychiatric services. There is frequently a lucid interval after the seizure before the onset of psychosis. The ensuing mood changes, delusions, and hallucinations may last for days or even weeks. Serious behavioural disturbance, physical aggression, and suicide attempts have all been well documented. The prevalence of schizophrenia-like psychosis ("inter-ictal psychosis") is probably increased in patients with temporal lobe

epilepsy. "Alternating psychosis" refers to psychosis occurring at times when the seizure frequency falls; "forced normalisation" refers to the related phenomenon of psychiatric disturbance occurring when EEG manifestations of epilepsy are abolished by drug treatment.

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Behaviour and personality

Behaviour and personality sit at the top of the tree in the classification of neuropsychiatric functions. They are at least in part an expression of the other functions we have listed. They are often singled out by informants as the main areas of change in patients with neuropsychiatric disorders. A gradual change in personality and behaviour is, for example, a cardinal sign of frontal lobe disease, but can also occur with damage to other areas of the brain, such as the basal ganglia, and even in systemic illness such as hyperthyroidism.

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REFERENCES

- 1 Schmahmann JD, Sherman JC. The cerebellar cognitive affective syndrome. *Brain* 1998;**121**:561–79.
- 2 Hodges JR, ed. *Early-onset dementia*. Oxford: Oxford University Press, 2001.
- 3 Spencer MD, Knight RSG, Will RG. First hundred cases of variant Creutzfeldt-Jakob disease: retrospective case note review of early psychiatric and neurological features. *BMJ* 2002;**324**:1479–82.
- 4 Vincent A, Buckley C, Schott JM, et al. Potassium channel antibody-associated encephalopathy: a potentially immunotherapy-responsive form of limbic encephalitis. *Brain* 2004;**127**:701–12.
- 5 Zeman A, Douglas N, Aylward R. Lesson of the week: narcolepsy mistaken for epilepsy. *BMJ* 2001;**322**:216–18.
- 6 Schenck CH, Mahowald MW. REM sleep behavior disorder: clinical, developmental, and neuroscience perspectives 16 years after its formal identification in SLEEP. *Sleep* 2002;**25**:120–38.
- 7 Zeman AZJ, Boniface SJ, Hodges JR. Transient epileptic amnesia: a description of the clinical and neuropsychological features in 10 cases and a review of the literature. *J Neurol Neurosurg Psychiatry* 1998;**64**:435–43.
- 8 Fytche DH, Howard RJ, Brammer A, et al. The anatomy of conscious vision: an fMRI study of visual hallucinations. *Nat Neurosci* 1998;**1**:738–42.
- 9 Cummings JL, Mega MS. *Neuropsychiatry and behavioural neuroscience*. Oxford: Oxford University Press, 2003.
- ▶ A wide ranging North American introduction to the diagnosis and management of neuropsychiatric disorders.
- 10 Gazzaniga MS, Ivry RB, Mangun GR, et al. *Cognitive neuroscience: the biology of the mind*. New York: WW Norton & Company Ltd, 2002.
- ▶ An excellent, well illustrated introductory text discussing the clinical and experimental basis for contemporary neuroscientific theories of cognition.
- 11 Hodges JR. *Cognitive assessment for clinicians*. Oxford: Oxford University Press, 1994.
- ▶ A valuable practical guide for clinicians through the sometimes baffling world of neuropsychological testing.
- 12 Lishman WA. *Organic psychiatry: the psychological consequences of cerebral disorder*. Oxford: Blackwell Science, 1997.
- ▶ A comprehensive, popular but somewhat dated reference tome that emphasises the cognitive and behavioural features of the principal neurological conditions.