Neuropsychiatry

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Stroke and traumatic brain injury

Neurological symptoms (eg hemiparesis or dysphasia) are the main cause of disability after stroke. Neuropsychiatric complications are likely to make disability worse and possibly increase mortality.

Most traumatic brain injury (TBI) is caused by closed head injury and often complicated by alcohol. The vulnerability to contusions of areas of the brain involved in social behaviour, cognition and regulation of mood (medial orbital frontal and anterior temporal lobes[1]) partly explains why the neuropsychiatric sequelae of TBI usually outstrip the neurological sequelae as predictors of outcome. The best predictor of outcome after TBI is the duration of post-traumatic amnesia (PTA) – the period from injury to the return of continuous day-to-day memory. Those with a PTA duration of longer than one month are unlikely to return to work.

Table 1 illustrates the range of neuropsychiatric sequelae observed after stroke. Similar problems, with similar prevalence rates, are observed after TBI. TBI is associated with higher rates of manic-depressive illness, and may be particularly associated with 'rapid-cycling' manic-depressive illness (ie periodicity of days rather than weeks).

Agitation and aggression, relatively infrequent after stroke, are often seen after TBI and partly reflect the premorbid personality characteristics of those who suffer TBI. Agitation is common in association with the post-traumatic confusional state (see section on delirium). Early agitation predicts long-term aggressive behaviour, which typically is explosive. There is no evidence that aggression differs from agitation in terms of its response to medication[3].

Mood disorders

Mood disorders are common in both stroke and TBI. They are usually like those in the absence of brain injury but there is often more evidence of lability of mood and apathy.

Stroke is a significant risk factor for suicide. After TBI, the standardised mortality rate for suicide is increased threefold so that about 1% will commit suicide over a 15-year follow-up, the risk remaining fairly constant over this period[4].

A recent systematic review suggests that there is no relationship between lesion location and depression after stroke[5]. Significant depressive symptoms should be treated vigorously (Table 2). The fact that they are 'understandable' or consist of symptoms that may be a direct consequence of brain injury (eg apathy) should not prevent a trial of an antidepressant. Several antidepressants have been shown to be effective in post-stroke depression[7]. Selective serotonin reuptake inhibitors (SSRIs), which have fewer side effects, are a reasonable first choice for depression after stroke or TBI (Table 3). If all else fails, ECT is safe for the treatment of depression after both stroke and TBI.

Antidepressants are useful in treating emotionalism (lability of mood, emotional incontinence). Cognitive behaviour therapy may improve adjustment to stroke. Early educational inter-ventions after TBI may prevent later symptoms.

Table 1. Psychiatric syndromes associated with stroke[2].

Syndrome	Prevalence (mean % from prevalence studies)	Clinical features
Depression:		
major	20	Feeling miserable or hopeless, tearfulness, demotivation, decreased appetite, weight loss, reduced interactions
minor/subthreshold	21	
Mania	Rare	Elevated mood, decreased sleep, thought disorder, grandiosity
Bipolar affective disorder	Rare	Alternating symptoms of depression and mania
Anxiety disorder	25	Uncontrollable fear or apprehension, restlessness, somatic anxiety symptoms
Apathy without depression	20	Avolition, anhedonia, demotivation
Psychosis	Rare	Delusions, hallucinations
Emotionalism	20	Impairment in the control of crying and, more rarely, laughing
Catastrophic reaction	20	Bursts of aggressive behaviour, anxiety, crying
Cognitive impairment	25	Visuospatial neglect, apraxia, impaired learning, reduced attention

Other neuropsychiatric sequelae

Psychosis. TBI probably increases two- to threefold the risk of developing a schizophreniform psychosis. Olanzapine or quetiapine are reasonable antipsychotics to use because they have fewer extrapyramidal side effects.

Personality changes. Thoughtlessness, impulsiveness and irritability are particularly troublesome changes in personality after TBI. They are common causes of distress for family and carers, the problems often being compounded by apathy and poor motivation.

Dysexecutive syndrome. Personality change is often associated with the dysexecutive syndrome in which there is

Table 2. Management of depression: (National Clinical Guidelines for Stroke[6]).

- Provide information, advice and the opportunity to talk about the impact of illness
- Assess psychosocial needs
- Screen for depression and anxiety within the first month of stroke and monitor mood
- Use standardised questionnaires for screening in those who can respond
- Emotionalism after stroke should be confirmed by a few simple questions at interview
- In the presence of one syndrome assess for other mood disorders
- Severe, persistent or troublesome tearfulness (emotionalism) should be treated with antidepressants, monitoring the frequency of crying to check effectiveness
- Consider a trial of antidepressant medication in those with persistently depressed mood of at least one month duration. If there is a good response, antidepressants should be continued for at least six months
- Consider seeking advice from, or co-managing patients with, liaison mental health professionals in cases of persistent distress or worsening disability

Table 3. Factors influencing choice of psychotropic medication.

- Side effects, particularly cognitive due to anticholinergic medication
- Whether the drug is generally sedative, useful in agitation or anxiety, or alerting
- Drug interactions, particularly with anticoagulant, cardiac and antiparkinsonian medications
- Drug efficacy in the population of interest
- Potential for reducing seizure threshold

impaired problem-solving due to difficulties in planning, prioritising and monitoring tasks, and multitasking. Impairments of concentration and memory and psychomotor slowing are also common cognitive symptoms after brain injury. Specialist rehabilitation may be needed.

Post-concussion syndrome. The relative contributions of brain injury and psychological responses may be difficult to disentangle in the post-concussion syndrome. Symptoms include double and blurred vision, noise sensitivity, dizziness, difficulties concentrating, fatigue, head and neck pains. Anxiety and depression tend to occur later after injury. Similar non-specific symptoms are seen in somatisation disorders, including chronic fatigue syndrome. Interventions such as graded exercises and cognitive behaviour therapy are appropriate. As in whiplash, being involved in a compensation claim may increase symptoms, particularly after mild injury.

Cognitive decline. Brain injury may be followed by cognitive decline. *Dementia pugilistica* may develop years after repeated blows to the head, usually in boxers. Severe head injuries, particularly in men, may predispose to the development of Alzheimer's disease, presumably due to deposition of beta-amyloid in the brain at the time of injury. A single stroke may be the precursor of multi-infarct dementia.

Parkinson's disease

Several neural circuits which link frontal cortex, thalamus and basal ganglia are involved in movement, attention, memory and reward processes. This explains why disorders of the basal ganglia, including Parkinson's disease (PD), are characterised by abnormalities of movement, mental state and cognitive function (Fig 1, Table 4)[8].

Depression

Depression is common in PD. It is associated with faster disease progression, more rapid decline in cognitive function and activities of daily living, and is a risk factor for developing dementia. It is probable that both biological and psychological factors explain depression in PD:

- *Biological:* loss of monoaminergic neurones, hypometabolism in caudate, inferior orbitofrontal and medial frontal regions on positron emission tomography.
- *Psychological:* chronic disabling illness, psychosocial stress.

Treatment of depression. Tricyclic antidepressant drugs are effective and may also improve motor symptoms by virtue of

Key Points

Neuropsychiatric sequelae may exacerbate disability, therefore psychosocial problems should be identified early

Always search for physical causes for symptoms, particularly in delirium and agitation, and consider drug effects, both prescribed and abused

Always start drug on low dosage and go slowly when prescribing psychotropics; avoid cocktails

Do not leave depressive symptoms untreated. Selective serotonin reuptake inhibitors are usually a safe first-choice antidepressant

When choosing an antipsychotic for patients after brain injury or with Parkinson's disease, choose one with the least extrapyramidal side effects if possible

When prescribing psychotropics in epilepsy, monitor anticonvulsant levels

KEY WORDS: CPD, delirium, depression, epilepsy, neuropsychiatry, Parkinson's disease, psychopharmacology, psychosis, stroke, traumatic brain injury

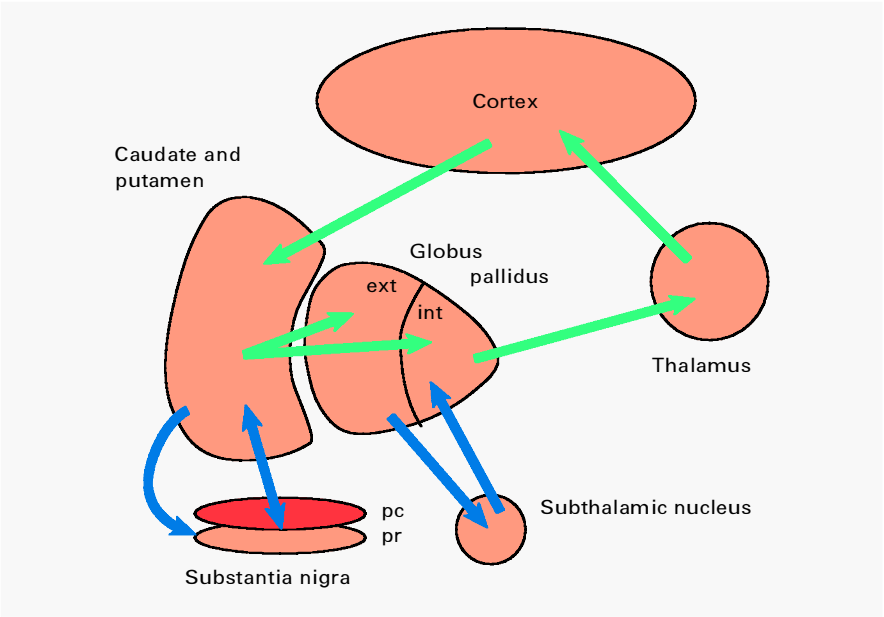

Fig 1. Basal ganglia and their connections (ext = external; int = internal; pc = pars compacta; pr = pars reticulata).

their anticholinergic activity[9], but their side effects, including cognitive impairment, may limit their use. Although SSRIs generally have fewer side effects, the evidence that they work is not as strong, and some have extrapyramidal effects which exacerbate motor symptoms. Psychological treatments for depression in PD have not been fully evaluated.

Hedonistic homeostatic dysregulation

In a condition known as hedonistic homeostatic dysregulation, patients take increasingly more dopamine replacement medication, particularly subcutaneous apomorphine, despite dyskinetic adverse effects. They also show hypersexuality, hypomanic symptoms and pathological gambling.

Psychosis

Psychosis in PD, often with visual hallucinations and persecutory delusions, is associated with cognitive impairment and recent increases in antiparkinsonian medication. Consideration should be given to decreasing or stopping these drugs. Antipsychotic medication should always be used with caution because of the extrapyramidal side effects. There is good evidence that low-dose clozapine can improve psychosis without worsening Parkinsonism[10] but careful monitoring is needed, particularly in the elderly.

Epilepsy and non-epileptic seizures

Depression is the commonest neuropsychiatric disorder associated with epilepsy[11] (Table 5). Post-ictal confusional states can be associated with psychosis and violence. Interictal psychosis resembles schizophrenia. Personality change has been described, but has been poorly validated.

It is important to identify the relationship of the psychiatric disturbance to ictal events, the role of antiepileptic drugs in the aetiology of symptoms, and the importance of psychosocial factors including stigma. For symptoms directly related to the seizure itself, optimisation of seizure control is the treatment of choice.

Psychotropic medication

When considering psychotropic medication for patients with epilepsy there is always the worry that it will decrease seizure threshold. However, a recent retrospective study suggests that psychotropic medication does not increase mean seizure frequency[12]. It is important to start psychotropic medications at low dose and increase slowly. It has been suggested that SSRIs are less likely to reduce seizure threshold than tricyclic anti-

Table 4. Neuropsychiatric complications of Parkinson's disease (PD).

Psychiatric manifestation	Frequency (%)	Associations
All psychiatric symptoms	70	
Depression	50	Female; younger onset; bradykinesia and gait disturbance. ?Correlated with disease progression. cognitive status and ADL
Hypomania/euphoria	2/10	Levodopa and DA agonist treatment especially in pre-existing BPAD
Anxiety	40	Depression; younger patients
Apathy	common	Executive impairment
Psychosis	40 (drug related)	Dopaminergic/anticholinergic medications; hallucinations 20% (esp. visual); delusions 3–30%
Cognitive impairment	19 with no dementia 15–40 with dementia	Older patients, late onset PD; low SES and education; severe EPS

ADL = activities of daily living; DA = dopamine; BPAD = bipolar affective disorder; EPS = extrapyramidal signs; SES = socio-economic status.

depressants. Anticonvulsant drug levels should be closely monitored because there may be an interaction between psychotropics and anticonvulsant drug levels, for example fluoxetine may increase blood levels of carbamazepine. Haloperidol and sulpiride may be less epileptogenic than other antipsychotics, and are therefore the treatment of choice for epileptic psychoses.

Non-epileptic seizures

An important differential diagnosis of epilepsy is non-epileptic seizures. These come under the rubric of conversion disorders or dissociative states; they can co-exist with epilepsy and are associated with sexual abuse and female sex. Recent unpublished work suggests that cognitive behaviour therapy may be effective.

Delirium

Delirium, often called an acute confusional state, is characterised by a disturbance of the level of consciousness. The patient is obtunded, drowsy or highly distractable. Attention and concentration are impaired (eg as demonstrated by poor performance on a digit span). They are neither alert nor oriented and likely to be agitated and frightened. Psychotic symptoms with hallucinations, often visual, and fleeting delusions may be elicited. Delirium may also present as a hypoactive withdrawn state akin to stupor.

Management of delirium

After making the patient safe, an attempt should be made to find the cause. Numerous physical problems, including drugs and drug withdrawal, may be responsible. Nursing should be in a calm environment in a side room with opportunities for undisturbed sleep, consistent staff and plenty of light and things to occupy the patient[13].

Agitation

Agitation is often present in delirium. If the patient has been treated with antipsychotics, an important differential diagnosis of the agitation is akathisia. Poor sleep, pain, constipation and systemic illness may be contributory factors.

Management of agitation. Some patients will settle with reassurance and explanation. Relatives may be able to help. Haloperidol and lorazepam may be used to produce rapid sedation. The patient should be placed on regular nursing observation, monitoring respiration and neurological state. If sedation is required for more than one or two days, atypical antipsychotic medication should be used (eg olanzapine or quetiapine) with which there is less chance of producing extrapyramidal side effects. Valproate, carbamazepine and beta-blockers may be helpful[3]. Drug combinations should be avoided as these may increase agitation and aggression by increasing confusion.

Table 5. Neuropsychiatric associations with epilepsy.

Symptoms/syndromes	Frequency and associations
Depression	30–50% Possible relationship with lesion location (eg TLE) Demoralisation and stigma Increased mortality secondary to suicide
Panic disorder	Lifetime prevalence 21% Can be interictal and peri-ictal Need for differentiation of panic from seizure activity
Psychosis	Prevalence 3–7% but failed to use operationalised criteria for SCZ or differentiating SLPE/episodic psychosis More common in partial epilepsies Possible role of mesial temporal and extratemporal damage as risk factor
Episodic	Most commonly post-ictal or drug-induced Affective, psychotic and confusional phenomena lasting up to a week
Chronic interictal/(SLPE)	Debate as to whether chance association or separate disorder Inconclusive evidence of increased risk of psychosis in TLE or with left-sided focus
Non-epileptic seizures	Abnormal illness behaviour Generally lack features of epileptic seizures but can be difficult to differentiate Can co-exist with epilepsy Possible physical and sexual abuse in childhood

SCZ = schizophrenia; SLPE = schizophrenia-like psychoses of epilepsy; TLE = temporal lobe epilepsy.

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