

# Advances in the Neuropsychiatry of Neurorehabilitation

The division of neurology and psychiatry into disciplines seen as dealing with either brain or mind, respectively, is once again being re-evaluated. Increasingly, developments in service provision and core scientific knowledge about mental health mean that the boundary between the subspecialties is being bridged. Neuropsychiatry is best defined as the interest in mental disorder associated with neurological presentations. It is an important discipline, if for no other reason than the significant burden of neuropsychiatric illness on the patient, their carers and society. Furthermore, neuropsychiatric disorders are commonplace in neurology, neurosurgery and neurorehabilitation settings. A study of new neurology referrals revealed that as many as one half of patients met criteria for a neuropsychiatric disorder and up to one third had unexplained symptoms.<sup>1,2</sup>

In this review, the focus is on clinical advances in neuropsychiatric disorders that may be seen on the neurorehabilitation unit. Stroke, traumatic brain injury, multiple sclerosis, delirium and functional neurological presentations, are considered in turn.

## Stroke and Traumatic Brain Injury (TBI)

The prevalence of neuropsychiatric sequelae after stroke and TBI are very similar. In one study, one year after injury around 40% of patients with TBI had three or more neurobehavioural symptoms.<sup>3</sup> Disorders of affect, anxiety and cognitive impairment are most often reported, with a mean prevalence rate of 35% for depression and 25% for anxiety or cognitive disorders. The prevalence of psychosis after injury is rare. In contrast to stroke, TBI is associated with a higher prevalence of bipolar disorder, particularly with a periodicity of affective episodes lasting days, referred to as 'rapid cycling'. These presentations are important not only because they are common, but also as they have a negative impact on rehabilitation outcomes as well as significant effects on quality of life measures.

## Mood Disorders

Mood disorders after brain injury are by and large similar to those in the absence of brain injury, although apathy and emotional lability are more often features. Impairments of communication, emotional and facial expression can make diagnosing depression more difficult. Rating scales such as the Hospital Anxiety and Depression Scale (HADS) or the General Health Questionnaire (GHQ) are useful and well validated screening tools. Stroke and TBI are significant risk factors for suicide.<sup>4</sup> After TBI, the standardised mortality rate from suicide is increased three-fold with 1% completing suicide over a 15-year follow-up period, in one study.<sup>5</sup> Hopelessness and suicidal ideation are the best indicators of suicidal risk in the mental state features identified in brain-injured populations.

## Psychosis

Psychosis can present both early and late in recovery after brain injury. Early on it is most likely a sequelae of delirium. The long held hypothesis that head injury may be a causal factor in schizophrenia has not been supported by a recent comprehensive, critical review.<sup>6</sup>

## Agitation and aggression

Agitation and aggression are more frequently seen after TBI than stroke. The more common premorbid personality characteristics of those at greater risk of TBI are likely to play a role in this. Early agitation, often associated with post-traumatic acute confusional states, predicts long-term explosive aggression.

## Cognitive impairment

Brain injury may also be followed by progressive cognitive decline. Dementia pugilistica may develop years after repeated blows to the head, usually in boxers. Head injuries, particularly in men, may predispose to the devel-



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Indication	Treatments	References
Depression after TBI or post stroke	Tricyclic antidepressants: Likely to be most effective but limited by anticholinergic side effects SSRI's: Such as citalopram have fewer side effects and drug interactions CBT: Inconclusive evidence of benefit for post stroke depression, but most promising psychological treatment. Scarce research of psychological treatment after TBI	Turner-Stokes and Hassan, 2002 <sup>24</sup>  Kneebone & Dunmore, 2000 <sup>25</sup> Lincoln & Flangan, 2003 <sup>26</sup> Khan-Bourne & Brown, 2003 <sup>27</sup>
Treatment refractory or severe depressive episodes with suicidality	Electroconvulsive therapy	Currier et al, 1992 <sup>28</sup>
Prevention of post stroke depression	No evidence of benefit of antidepressants versus placebo May be benefit of treatment in first versus third month on 2 year functional outcomes	Anderson et al 2004 <sup>29</sup> Narushima & Robinson, 2003 <sup>30</sup>
Agitation and aggression after TBI	Beta blockers: Best evidence but limited by large doses required and significant side effects Carbamazepine: Common first line choice but limited evidence Sodium valproate: Alternative choice but limited evidence	Fleminger et al 2003 <sup>31</sup>
Abulia	Bromocriptine: Limited evidence	
Psychosis after TBI or stroke	Quetiapine: Limited evidence but reasonable choice as less associated with extrapyramidal side effects; be aware of possible increased risk of cerebrovascular disease with other atypical neuroleptics	

opment of Alzheimer's disease.<sup>7</sup> This is presumably due to deposition of  $\beta$ -amyloid in the brain at the time of injury, although evidence that it is linked to APOE status is inconsistent.

### **Aetiology**

Fierce debate continues as to whether lesion location and particularly anterior, left hemisphere lesions are associated with post-stroke depression. A recent meta-analysis has suggested that the lesion proximity to the left frontal pole, predicted depressive illness.<sup>8</sup> This has been further supported in another appraisal from Finland.<sup>9</sup> The vulnerability of medial orbital frontal and anterior temporal lobes (being involved in social behaviour, cognition and regulation of mood) to contusions, partly explains why the neuropsychiatric consequences of TBI often supersede neurological sequelae as predictors of outcome.

### **Treatment**

Table 1 briefly outlines treatments for various indications. Depressive symptoms should be identified carefully and treated vigorously. The fact that they are 'understandable' or consist of symptoms that may be a direct consequence of brain injury, e.g. apathy, should not prevent a trial of an antidepressant. If there is a good response, antidepressants should be continued for at least 6 months. Severe, persistent or troublesome tearfulness (emotionalism) should be treated with antidepressants, monitoring the frequency of crying to check effectiveness.

In agitation and aggression after head injury response to medication is usually seen early, within the first six weeks, and it is suggested that this is an adequate treatment period during which clinical benefit should be expected before switching to an alternative treatment. There is no evidence that aggression is different from agitation in terms of its response to medication.<sup>10</sup>

### **Multiple Sclerosis**

Neuropsychiatric presentations include mood, anxiety, cognitive and psychotic disorders. The prevalence of depression in multiple sclerosis (MS) has been suggested to be higher than that seen in control groups with different neurological illnesses. However, methodological problems with regard to clinician blinding and diagnostic criteria are likely to be confounding this. A recent evaluation suggests that the lifetime prevalence rate for depressive symptoms is 40-50%.<sup>11</sup> Psychotic illness in MS is most commonly seen in the context of treatment with steroids, where it is often an affective psychosis, although schizophreniform psychoses are also seen. Cognitive impairment in MS has been estimated to have a prevalence of up to 50% in community samples.

### **Mood Disorders**

Fatigue and cognitive impairment are probably more common in depressive episodes in MS and have received the most attention. The most recent studies have supported positive correlations particularly suggesting that mental fatigue<sup>12</sup> and impaired effortful information processing<sup>12</sup> are features of depression in MS. Suicide rates in patients with MS have been shown to be twice the mean rate seen in the adjusted population<sup>14</sup> and are most frequently correlated with living alone, alcohol misuse and depressive disorder.

### **Cognitive Impairment**

Cognitive deficits arise early in the course of MS and often before the diagnosis has been made. The course of cognitive decline would appear to be slow in the majority of

cases and risks factors for a more rapid decline include disease progression, age and worsening of physical disability. Particular impairment is seen in verbal fluency, comprehension, naming and executive dysfunction as well as memory.

### **Aetiology**

$\beta$ -interferon has been implicated in causing depression, although the evidence for this is contentious. Studies of lesion location utilising neuroimaging have been conducted in patients with MS and depression as well as psychosis. The most robustly reported findings in depression implicate more hyperintense lesions in left inferior medial frontal and greater atrophy of left anterior temporal regions.<sup>15</sup> It has been suggested that temporal lobe lesion location may correlate to psychotic illness.<sup>16</sup>

### **Treatments**

Desipramine has been shown to be more effective than placebo in depression in MS, although anticholinergic side effects may preclude its use. SSRI's are a good first line option but the risk of causing sexual dysfunction should be monitored.

Limited evidence exists regarding the best choice of antipsychotic for treatment of psychoses in MS, although an atypical antipsychotic is a sensible choice. Cognitive impairment showed improvement in an open trial of donepezil in patients with MS.<sup>17</sup>

Fatigue may benefit from approaches utilised in chronic fatigue syndrome. Cognitive Behavioural Therapy for depression in MS is likely to be useful and had similar outcomes to treatment with an SSRI.<sup>18</sup>

### **Delirium**

Delirium, classified as acute confusional state in the International Classification of Diseases (ICD-10), is characterised by a disturbance of conscious level. The patient is obtunded, or drowsy, or highly distractible. Attention and concentration are impaired, e.g. as demonstrated by poor performance on a digit span. They are neither alert nor orientated and the mental state may fluctuate. The patient is 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.

### **Aetiology**

Numerous physical problems, including drugs and drug withdrawal, may be aetiological factors. 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 playing a part.

### **Treatment**

Management consists of making the patient safe and then finding the cause. Nursing should be in a side room with consistent staff and plenty of light. It should be a calm environment with opportunities for undisturbed sleep.<sup>19</sup>

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 observations, monitoring respirations and neurological state. If sedation is required for more than one or two days, use atypical antipsychotic medications, e.g. olanzapine or quetiapine, which have less chance of producing extrapyramidal side effects. Valproate, carbamazepine and beta-

blockers may also be helpful in the management of agitation and aggression as alternatives to antipsychotics where these are not tolerated or cause intolerable side effects. Avoid drug combinations that may increase agitation and aggression by increasing confusion.

## Functional neurological presentations

The many different names that have been given to functional neurological symptoms including hysterical, psychogenic, somatoform, dissociative and conversion disorders is representative of the complexity of these presentations and the difficulty that doctors often have in explaining them to their patients. Nonetheless, functional symptoms are common in neurological settings with estimates of their prevalence in 10-30% of outpatients. They are associated with significant burden, particularly in terms of health economy and are enduring in around 50% of patients.

There is a wide range of possible presentations and functional symptoms can mimic most neurological disorders. The most commonly reported in one sample included pain, anaesthesia, paresis and headache.<sup>19</sup> Non-epileptic seizures have been estimated to be seen

in 9-50% of patients in a specialist centre and can co-exist with epilepsy.

## Aetiology

Despite attempts to investigate the neurobiological correlates of functional symptoms, the existing studies are small and difficult to generalise. The most popular aetiological model formulates presentations from a bio-psycho-social perspective taking into account the impact of life events (such as sexual abuse), coping style and comorbid illness. A past psychiatric history may be an important risk factor.

## Treatment

The importance of communicating the diagnosis to the patient in such a way that they are not offended and engage in your management plan, is paramount.<sup>21</sup> Multidisciplinary rehabilitation, utilising the skills of physiotherapists, occupational therapists and cognitive therapists has been shown to be effective, although the studies that have considered this have not been randomised. A systematic review has shown that cognitive therapy is beneficial.<sup>22</sup> Antidepressants have been shown to be effective for both those with comorbid depression and for functional symptoms alone.<sup>23</sup>

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