

Current Understanding of Dysautonomia After Severe Acquired Brain Injury

Dysautonomia is one of a number of names used to describe a clinical syndrome affecting a subgroup of survivors of acquired brain injury (ABI).¹ The syndrome consists of paroxysmal elevations of autonomic nervous system (ANS) parameters, for example, heart rates (HR) up to 190 beats per minute, respiratory rates (RR) of 60 breaths per minute, temperatures to 42°C, arterial blood pressures (BP) of 170/120mmHg and sweating. These signs are accompanied by assorted forms of muscle overactivity such as decerebrate or decorticate posturing, dystonias, rigidity and spasticity.

Traumatic brain injury (TBI) is the most commonly reported causative condition, with an estimated incidence of 8-15% in moderate and severe TBI admitted to an intensive care unit (ICU).² There is no incidence data on other aetiologies, although anecdotally dysautonomia appears to be much rarer. Acute neurological events that have been reported to precipitate dysautonomia include: spontaneous subarachnoid or intracerebral haemorrhages, pressure from tumours, intra-aqueductal abscess, hydrocephalus and cerebral hypoxia in the absence of other trauma.³

In a prospective cohort study,² dysautonomic subjects had a significantly worse outcome, a greater period of hospitalisation and higher estimated costs compared to non-dysautonomic survivors of TBI. However, dysautonomic and non-dysautonomic patients were found to have a comparable degree of improvement with rehabilitation, albeit dysautonomic patients start at a lower point and take longer to improve.¹

There is considerable disparity between the estimated incidence of dysautonomia in prospective research and the quantity of scientific literature. There are a number of plausible explanations for this discrepancy. The most apparent difficulty is the proliferative and synonymous nature of the nomenclature, with at least 10 different names being used for the same condition. These include paroxysmal sympathetic storms, autonomic dysfunction syndrome, acute midbrain syndrome, hypothalamic-midbrain dysregulation syndrome, fever of central origin, hyperpyrexia associated with muscle contraction, dysautonomia, sympathetic or autonomic storming and paroxysmal autonomic instability with dystonia.³

Another explanation for the discrepancy is that dysautonomia is currently a diagnosis of exclusion and relies on a high index of suspicion. Firstly, some degree of autonomic arousal is a common feature during the early post-acute recovery from ABI and there is no clear threshold where this activity should become classified as dysautonomia. Furthermore, dysautonomia shares a high degree of overlap with the presentation of common complications such as opioid withdrawal, epileptic seizures, and sepsis, as well as rarer conditions such as neuroleptic malignant syndrome, malignant hyperthermia and others.³

Natural history / clinical features

Analysis of the hospital course of post TBI dysautonomia suggests that the syndrome follows a common three phase pattern. The first phase runs from admission to ICU to the cessation of paralysis and/or sedation. There is little to differentiate the dysautonomic and non-dysautonomic patients in terms of physiological variables during this stage.¹

The second phase commences with the cessation of regular sedation. The dysautonomic patient will usually have consistently raised HR and temperature, and increasing regional muscle tone. Paroxysms of posturing and ANS

overactivity are superimposed on these elevated baseline levels. In the early parts of this second phase, episodes are frequent, prolonged and intense. Some episodes will be provoked by identifiable stimuli (for example, pain, endotracheal suctioning, passive movements such as turning, bathing and muscle stretching, constipation, a kinked urinary catheter, emotional stimuli, as well as environmental stimuli such as loud noises),³ but others show no overt cause. The pattern of posturing is most often asymmetrical and may not fit into classical decorticate or decerebrate postures.⁴ With increasing time post injury, the paroxysms decrease in duration, frequency and magnitude; resting BP, RR, HR and temperature return to normal. The pattern of posturing may change, revealing an underlying tetraplegia or other focal neurological deficit. Sweating patterns often alter, from whole body to upper trunk, head and neck, before ceasing entirely.⁵ In the majority of patients, background muscle tone increases with variable flexor, extensor or mixed dystonias in the limbs, neck, trunk and facial muscles. The end of phase two is marked by the cessation of regular dysautonomic paroxysms. Extinguishment of episodes usually coincides with improving neurological status, although most are left with some degree of dystonia and spasticity.¹ The high degree of physical disability can prevent voluntary muscle activity, limiting the accuracy of cognitive assessment.

The final phase commences with the termination of regular paroxysms, though by this stage, dysautonomia patients with severe dystonia will have major deformities of joints and markedly reduced range of movement.¹ Although ANS variables are within normal limits, noxious stimuli may still provoke an episode for at least 14 months post injury.⁶ Patients who develop a mechanism for communication often report persistent abnormal painful responses to normally non-noxious stimuli.

Management

Pharmacological management is difficult and there is limited data available to guide decision-making. In the ICU setting, widespread use of paralysis/sedation has been shown to delay the onset of clinical features.¹ Anecdotally, the best available evidence for treatment efficacy includes bromocriptine, gabapentin and intrathecal baclofen (ITB).^{7,8} Intravenous morphine and midazolam are effective but have problematic sedative effects. Drugs with sympathetic activity (particularly clonidine, propranolol and labetalol) are also commonly used; however there are suggestions that these drugs treat the symptoms rather than the underlying disease process. Equally, there is no evidence that anticonvulsants other than gabapentin are effective in this condition. The potential to trigger paroxysms via noxious stimuli has led one author to suggest pre-treatment in this context.⁹

The rehabilitation management of dysautonomia centres on the usual approach of minimising unnecessary disability and complications while maximising the potential for the individual to regain a maximal quality of life. In the rehabilitation setting, this includes adequate fluids, nutrition, and spasticity management including splinting, serial casting and pressure area management. Given the combination of spasticity and nociception, ITB is increasingly being used earlier in the management.

Clinical significance

There are a variety of reasons to believe that dysautonomia warrants active management. A lack of early recognition



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and management contributes to increased morbidity. In particular, core temperatures above 38-39°C produce neuronal death in animal brain injury models.^{10,11} While transient temperatures at these levels occur in 68% of people following severe TBI,¹¹ dysautonomic subjects mean daily maximum temperatures can remain above this level for more than two weeks.¹ The increased metabolic consumption of posturing patients¹² and prolonged irregularities of gastrointestinal tract function¹³ produce a highly catabolic state causing an estimated 25% decrease in body weight.¹ The subsequent malnourishment places the individual at risk of developing critical illness neuropathy. Spastic tetraparesis in patients at rest and dystonic posturing during paroxysms are typical; and combined with weight loss, these lead to increased risk of pain, pressure areas and contractures. Dysautonomic episodes make splinting an extremely difficult prospect, with potential complications such as pressure areas and ruptured tendons. Lack of voluntary movement and the potential for 'locked-in' syndromes to occur¹⁴ can result in under-

managed pain or a misdiagnosis of persistent vegetative state.

Pathophysiology

While the earliest theories proposed an epileptogenic aetiology,¹⁵ multiple attempts to either identify or treat epilepsy in dysautonomic patients have produced negative results.³ There is greater evidence for supporting a disconnection pathogenesis. The limited autopsy and pathophysiological data has recently been reviewed, suggesting that the critical region of interest in dysautonomia is the mesencephalon.³ Conventional disconnection theories suggest that excitatory centre/s located in the upper brainstem and diencephalon drive paroxysms. A more recent disconnection theory, the Excitatory:Inhibitory Ratio (EIR) Model,¹⁶ suggests the causative brainstem/diencephalic centres are inhibitory in nature, with damage releasing excitatory spinal cord processes.

Evidence from literature on dysautonomia and other conditions suggests that disconnection syndromes can result from structural

and/or functional disconnection. Accordingly, functional disconnection may ensue from transient exacerbations of structural change (such as raised ICP) or neurotransmitter abnormalities.

Conclusion

The clinical research clearly shows that dysautonomia places a considerable burden on both patient and health care services and that there is potential for reducing this burden through timely recognition and intervention. However, the field is hampered by under-recognition, misdiagnosis, a poor understanding of pathophysiology and anecdotal management protocols. Recent advances suggest that new physiological investigatory techniques will allow the development of evidence based treatment paradigms for the first time. It is hoped that more effective treatment protocols will, in turn, result in improved outcomes and decreased overall costs. It is recommended that multi-centre research be utilised and targeted towards modifying outcomes for patients with this condition.

References

1. Baguley IJ, et al. *Dysautonomia after traumatic brain injury: a forgotten syndrome?* Journal of Neurology, Neurosurgery & Psychiatry 1999;67(1):39-43.
2. Baguley IJ, et al. *The incidence of dysautonomia and its relationship with autonomic arousal following traumatic brain injury.* Brain Inj 2007;21(11):1175-81.
3. Baguley IJ, et al. *A Critical Review of the Pathophysiology of Dysautonomia Following Traumatic Brain Injury.* Neurocrit Care 2007.
4. Bricolo A, et al. *Decerebrate rigidity in acute head injury.* Journal of Neurosurgery 1977;47:680-98.
5. Bullard DE. *Diencephalic Seizures: Responsiveness to Bromocriptine and Morphine.* Ann.Neurol 1987;21(6):609-11.
6. Baguley IJ, et al. *Dysautonomia and Heart Rate Variability Following Severe Traumatic Brain Injury.* Brain Injury 2006;20(4):437-44.
7. Baguley IJ, et al. *Pharmacological management of Dysautonomia following traumatic brain injury.* Brain Injury 2004;18(5):409-17.
8. Baguley IJ, et al. *Gabapentin in the management of dysautonomia following severe traumatic brain injury: a case series.* Journal of Neurology, Neurosurgery & Psychiatry 2007;78(5):539-41.
9. Lemke DM. *Sympathetic Storming After Severe Traumatic Brain Injury.* Critical Care Nurse 2007;27(1):30.
10. Minamisawa H, Smith ML, Siesjo BK. *The effect of mild hyperthermia and hypothermia on brain damage following 5, 10, and 15 minutes of forebrain ischemia.* Ann Neurol 1990;28(1):26-33.
11. Albrecht RF, Wass CT, Lanier WL. *Occurrence of potentially detrimental temperature alterations in hospitalized patients at risk for brain injury.* Mayo Clinic Proceedings 1998;73(7):629-35.
12. Clifton GL, Robertson CS, Choi SC. *Assessments of nutritional requirements of head-injured patients.* Journal of Neurosurgery 1986;64:895-901.
13. Ott L, et al. *Altered gastric emptying in the head-injured patient: relationship to feeding intolerance.* J Neurosurg 1991;74(5):738-42.
14. Scott JS, et al. *Autonomic dysfunction associated with locked-in syndrome in a child.* American Journal of Physical Medicine & Rehabilitation 1997;76(3):200-3.
15. Penfield W. *Diencephalic autonomic epilepsy.* Arch Neurol Psychiatry 1929;22:358-74.
16. Baguley IJ. *The excitatory:inhibitory ratio model (EIR model): An integrative explanation of acute autonomic overactivity syndromes.* Med Hypotheses 2007.

