PERSPECTIVES

Delayed neural damage induced by lightning and electrical injury: neural death, vascular necrosis and demyelination?

The structural damage to vascular endothelial cell

In a recent article in the journal *Brain Injury*, four potential hypotheses for delayed neurological disorders following lightning and electrical injury were suggested (Reisner, 2013). The phenomenon of delayed neurodegenerative syndromes following lighting and electrical injury has been known since the early 1930s (Critchley, 1934), but to the present day, the mechanisms involved have been poorly understood. An initial and still plausible theory is that the electrical insult causes damage to the vascular structures feeding the spinal cord *via* damage to vascular endothelial cells (Farrell and Starr, 1968). Damage to proteins within these endothelial cells causes this eventual cell death, thus partially explaining eventual starvation of neural tissue in areas of the spinal cord. This theory was added upon (Reisner, 2013) by integrating a recent study which found that lightning and electrical injury can cause an increase in free radicals (Bailey et al., 2003), as well as by citing research suggesting that free radicals caused by glutamatergic overstimulation can damage cerebral vascular endothelial cells (Parfenova et al., 2006). Vascular damage to the spinal cord after lightning injury has been noted post-mortem (Freeman et al., 2004) and there are cases of delayed or progressive spinal damage in cases of electrical and lightning injury (Sirdofsky et al., 1991; Reisner, 2013). The spinal cord is known to contain glutamatergic nerves (Rothstein et al., 1992) and oxidative stress can occur in the spinal cord as well as brain (Juurlink and Paterson, 1998). As capillaries are made up of endothelial cells, it is possible that oxidative stress products from electrically induced glutamatergic overstimulation may eventually cause a breakdown in vascular structures that nourish the spinal cord (Reisner, 2013). Oxidative stress and its resulting free radicals have been previously linked to neurodegenerative diseases (Coyle and Puttfarcken, 1993).

Demyelination following electrical and lightning injury

There is evidence suggesting that glutamatergic overstimulation can bring about damaging free radicals and that some of these free radicals can be derived from lipids (Coyle and Puttfarcken, 1993). Using this evidence, it has been suggested that in cases where delayed demyelinating syndromes occur following electrical and lightning injury, and when vascular damage has not been detected, the electrical overstimulation may create damaging free radicals directly in the lipid-rich myelin cells (Reisner, 2013). Alternately, it has been noted that H_2O_2 (peroxide) can be a product of oxidative stress and can break down to form free radicals (Coyle and Puttfarcken, 1993) and H_2O_2 can lead to "peroxidation of membrane lipids and cell death" (Behl et al., 1997). Oxidative stress-related substances with tendencies to damage lipids in cell membranes (Coyle and Puttfarcken, 1993; Behl et al., 1997) might be particularly destructive to myelin with its high concentration of lipids. Both glutamate receptors and glucocorticoids have been linked to neurodegenerative diseases *via* oxidative stress mechanisms (Coyle and Puttfarcken, 1993; Behl et al., 1997). As previously noted, this type of hypothesis explains demyelination syndromes when no vascular damage around the spinal cord has been found (Reisner, 2013), and such cases (demyelination without vascular damage) have been noted in the literature (Hawkes and Thorpe, 1992).

Reisner (2013) also reviews the already existing electroporation hypothesis, which suggests that electrical over-stimulation causes additional pores to be formed in the cell membranes of neurons. If a moderate amount of electroporation occurs, cell function changes but the cell does not die (Bryan et al., 2009); however, with formation of a critical number of additional pores, the cell membrane ruptures and the cell dies (Freeman et al., 2004). It is unclear, however, whether this cell death would result in delayed versus immediate damage to the brain or spinal cord. Although some of the above hypotheses are speculative, this phenomenon of delayed neurological damage after lightning and electrical injury has been poorly understood since the early 1930s; formation of hypotheses is just one step in the process of achieving an empirically based answer to a decades-old question (Reisner, 2013).

Potential mechanisms of glutamatergic overstimulation on the trauma of electrical and lightning injury

Another mystery concerning cognitive functioning decline in electrical and lightning injury is that sometimes the pathway of the electrical current does not directly cross the brain, yet cognitive impairments still occur (Ramati et al., 2009). One study used sophisticated neuropsychological methods, and demonstrated a biological basis for such deficits employing functional magnetic resonance imaging (Ramati et al., 2009). Sometimes lightning injury brings about psychological and cognitive impairments without structural damage to the brain being detected by magnetic resonance imaging (MRI) (Cooper, 2003); but this newer study used functional MRI, and demonstrated differences in brain activity and cognitive functioning between those who have suffered lightning and electrical injury and those who have not (Ramati et al., 2009). It has been suggested that elevations in cortisol, stimulated by the trauma of electrical and lightning injury, may play a key role in subsequent cognitive deficits (Andrews, 2012) and it has long been known that there is a destructive interaction between glucocorticoids and the cytotoxic (Behl et al., 1997) and memory impairing (Chamberlin and Tsai, 1998) effects of glutamatergic receptor hyper-stimulation. In their literature review Chamberlin and Tsai (1998) state: "Some glucocorticoids increase both the frequency of opening and the mean opening time of the NMDA receptor channel." It is thought that glutamatergic hyper-stimulation and cortisol may interfere with memory *via* disruption of long term potentiation in the hippocampus (Chamberlin and Tsai, 1998; Andrews, 2012). It is possible that even if the pathway of electricity does not directly cross the brain, cortisol and the excitatory neurotransmitter glutamate may still be stimulated *via* the physical and psychological trauma and the "excitatory" impact of the electrical insult.

The electroconvulsive therapy (ECT) connection: cortisol, glutamate, and memory

It is noted that Chamberlin and Tsai (1998) are reviewing

literature on a model of ECT and they address hypotheses concerning glutamatergic hyper-stimulation and memory impairment in ECT (a well-known side effect). Some of the physiological mechanisms they review, however, may be relevant to other situations where glutamatergic receptors are over-stimulated, such as with the physical and/or psychological effects of electrical or lightning injury. Andrews' (2013) theory regarding the impact of cortisol on psychiatric and cognitive symptoms derives from the lightning and electrical injury literature; however, it is also found in the ECT literature that high cortisol levels are associated with the highest levels of post-ECT cognitive impairment (Neylan et al., 2001). By comparing certain aspects of ECT, a therapeutic procedure, with the trauma of lightning and electrical injury, the current author does not mean to imply that ECT and lightning/electrical injury are the same thing or are close together with regard to type and intensity of electrical stimulation. Both situations, though, most likely involve stimulation of the excitatory neurotransmitter, glutamate, and cortisol levels are apparently relevant in both situations. A combination of high cortisol levels and glutamatergic over-stimulation may have a negative impact on certain aspects of memory or cognition, and elevations of cortisol and glutamatergic over-stimulation may occur simultaneously in markedly different situations.

Conclusions

The author reviews possible mechanisms by which lightning and electrical injury may cause delayed neural damage as well as ways that cognitive functioning may be impaired by lightning and electrical injury in cases where structural damage is not apparent. The key to structural damage, both vascular and demyelinating, may be an electrically mediated overstimulation of glutamate receptors in a situation where cortisol levels are likely to be high. This may bring about an increase in damaging free radicals. In one case, the free radicals may cause an eventual breakdown of the endothelial cells which make up the capillaries surrounding the spinal cord, and in another case, either free radicals may be formed directly in the lipid-rich myelin, or the free radicals damage the cell membranes of myelin cells. There appear to be at least two different mechanisms for delayed neurological damage following lightning injury. One mechanism involves a vascular breakdown and starvation of parts of the spinal cord. A second mechanism involves a breakdown of myelin without vascular involvement. The literature on the effects of cortisol elevation, glutamatergic over-stimulation, and formation of destructive free radicals was reviewed, and explanations for both forms of delayed neurological damage were offered (Reisner, 2013). With regard to the electroporation hypothesis, it is unclear as to whether electroporation would cause immediate versus delayed neurological damage.

In addition to the above, there are cases where cognitive and psychological disorders become manifest even when the pathway of electrical current apparently does not cross the brain, and when structural damage to the brain is not found (Ramati et al., 2009; Andrews, 2012). Increased cortisol levels in the body brought about by electrical insult and/or extreme psychological and physical stress from electrical trauma may partially account for these cognitive and psychological disorders following lightning and electrical injury. One would expect that excitatory neurotransmitters and receptors, including glutamate and its receptors, would become overstimulated with the physical and emotional trauma of lightning and electrical injury. The synergistic effect between elevated cortisol and excited glutamate receptors may have a damaging effect on memory through disruption in long-term potentiation (Chamberlin and Tsai, 1998). This increases the probability that in these cases, the mechanisms may be physiological as opposed to representing gross structural damage.

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