Dr Peter Shortland: Novel strategies to ameliorate pain associated with avulsion injury

Project report

This one year project has investigated the hypothesis that spinal root avulsion injury produces alterations in blood flow that contribute to avulsion injury induced pain-like behaviour in rodents. Photoplethysmography (PPG) is an established way of assessing blood flow in the CNS (Phillips et al 2009). PPG is the recording of blood volume changes by measurement of changes in light absorption and provides an indication of the availability of blood supply to the tissue. In this study we have combined PPG with Laser Doppler Flowmetry (LDF), the most widely used technique for measuring perfusion, to measure changes in normal and spinal root injured rodents. Initially, we developed a protocol for recording PPG & LDF signals from the surface of the spinal cord (Phillips et al 2013, submitted) and found that signals could be reliably obtained from all subjects; this provided a baseline for comparisons with spinal root injured animals.

Using an established model of spinal root injury (Chew et al 2012) we confirmed that root avulsion produced mechanical hypersensitivity. Then two weeks after injury, the PPG and LDF signals were recorded in animals that had avulsion only or those that had avulsion followed by intraperitoneal injection of erythropoietin (2 injections, spaced 24 hours apart, initially given within 15 minutes of the injury). In animals with spinal root avulsion injury, histological analysis showed loss of motoneurons and significant atrophy of the medial gastrocnemius muscle and soleus muscles. PPG and LDF measurements were assessed on the ipsilateral and contralateral sides of the spinal cord rostral and caudal to the avulsion injury and at the level of the injury. At two weeks post injury, a time when vascular blood vessel endothelial markers are decreased, we did not detect a significant change in the spinal cord blood flow either above, at or below, the site of injury or when comparing the ipsilateral versus contralateral side. When oxygenation levels were assessed, again no significant differences were found between naïve and spinal root injured animals along the rostrocaudal axis (i.e. above, at and below the site of injury or its equivalent on the contralateral side).

Treatment of injured animals with EPO produced no significant effects on motoneuron survival or muscle atrophy or blood flow within the cord. However, it did reverse the mechanical hypersensitivity and increase spinal cord tissue oxygenation in treated animals; these effects were long-lasting considering administration was 2 weeks previously. These results are consistent with the known effects of EPO in healthy individuals and other models of peripheral nerve injury.

From these experiments it is concluded that spinal root avulsion does not significantly alter blood flow or tissue oxygen levels and so ischemia may play a less prominent role in avulsion injury induced pain. Administration of EPO increases tissue oxygen levels without altering flow and this may contribute to amelioration of mechanical hypersensitivity. Future studies will apply this technology to vascular changes associated with spinal cord injuries in rodent (Yip et al 2012).
References

Publications resulting from project
