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**Differences between cortical and spinal cord astrocytes in the induction of reactive gliosis**

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**Introduction:** Astrocytes are thought to play an important role in the development of chronic pain, but the basis of astrocyte involvement is not well understood. It is apparent that astrocytes become reactive during the onset of pain to form of reactive gliosis in the spinal dorsal horn[1]. The factors which lead to activation the astrocytes in the spinal cord are poorly characterized.

**Method:** To investigate the mechanisms of gliosis, the responses to a range of different stimulants known to induce gliosis (forskolin, lipopolysaccharides and tumor necrosis factor alpha) were compared in primary cultures of spinal cord and cortical astrocytes. The reactive astrogliosis was quantified by calculating the percentage of stellate GFAP-expressing cells, measuring the intensity of phosphorylated-Stat3 in nucleus[1], and testing the sensitivity of cells to the $P2Y_{14}$ receptor agonist UDP-glucose by measuring the $Ca^{2+}$ release, as this receptor is upregulated in reactive astrocytes[2].

**Results:** Cortical astrocytes demonstrated time-dependent gliosis in response to forskolin and LPS with a significant increase in percentage of stellate cells compared to control, but TNFα was not effective. An increase in percentage of stellate cells in spinal cord astrocytes was also observed for forskolin and LPS, but this was significantly less than for cortical cells (30% in spinal versus 70% in cortical). The intensity of p-Stat3 in the nucleus in the case of cortical astrocytes was higher than control after 3h of forskolin treatment, and then decreased over 24h. For spinal cord astrocytes there was no significant difference in nuclear p-Stat3 staining between control and treated cells. Forskolin also increased the percentage of cortical cells responding to UDP-glucose (from 18% to 37%), but no increase was observed for LPS and TNFα. In contrast, for spinal cord astrocytes, 26% of the untreated astrocytes respond to UDP-glucose while just 13%, 18% and 8% of the astrocytes were responsive after forskolin, LPS and TNFα treatment, respectively.

**Conclusion:** Spinal cord astrocytes exhibited a less reliable and less pronounced response than cortical astrocytes to stimuli known to induce reactive gliosis. These differences illustrate the heterogeneity of astrocyte responses in different parts of the CNS and that the role of reactive gliosis in spinal cord astrocytes in the development of pain and spinal nociceptive signalling may be more complex than originally thought.

**References:**

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3. Hamby, M.,et al (2012). *Journal of Neuroscience* **32(42):**14489-14510.