Carrageenan evoked P-Akt in deep dorsal horn neurons is prevented by loss of neurokinin1 positive neurons in superficial dorsal horn

(continued from page 1) targeted Saporin or [Sar⁹Met(O₂)¹¹] substance P coupled to saporin (SSP-SAP, Cat. #IT-11). Injection was at the level of the thoraco-lumbar junction. It has been reported that this treatment results in loss of neurons with NK1 receptors (substance P receptors) in the superficial, but not the deep dorsal horn (Wiley et al., 2007). Two weeks post-injection, rats were tested for locomotor ability using a rotorod or for carrageenan-induced cutaneous sensitization to mechanical stimuli. Some animals with paw carrageenan were perfused at 45 min or 2 hrs post injection and their lumbar spinal cords processed and reacted for NK1 receptor, P-Akt and a variety of cell markers.

Immunohistological staining demonstrated that NK1 receptor was gone from lamina I-III (p≤ 0.01) of the dorsal horn with no loss in lamina V compared to SAP-pretreated animals. SSP-SAP animals had no carrageenan-associated induction of P-Akt in any spinal lamina at any time point. Behavioral testing indicated a significant loss in mechanical sensitization compared to the SAP animals (p≤ 0.001), with no loss of motor ability. Despite this, SSP-SAP animals still had substantial mechanical sensitization (p≤ 0.001), which peaked 2 hrs after paw injection. We interpret these data as meaning that loss of NK1 receptor bearing neurons in the superficial dorsal horn blocks a large component of spinal sensitization. It is likely that paw carrageenan-induced expression of P-Akt in motor neurons requires an excitatory interneuronal link, which is not required for normal locomotor activity. Inflammation-induced activation of P-Akt in lamina V also requires a superficial dorsal horn linkage (either via excitatory interneurons or the lamina I projection neurons). Allodynia seen in the SSP-SAP animals is probably due to peripheral sensitization of primary afferent fibers and a resultant heightened afferent drive, rather than to a significant spinal sensitization component.

References

Note: Dr. Sorkin is a runner-up for the 2010 SfN Poster of the Year Award. We are delighted she was able to provide this cover article.