26468 - NOVEL EXTRASYNAPTIC GABAA RECEPTOR POPULATIONS IN MURINE SPINAL CORD

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INTRODUCTION: Certain components of the anesthetic state including immobility and analgesia are mediated by actions on the spinal cord; however the underlying receptors have not been identified. In the brain, GABA(A) receptors (GABA(A)Rs) generate two distinct conductances including fast synaptic and tonic extrasynaptic inhibition. In the brain, the tonic conductance is highly sensitive to anesthetics and is generated by GABA(A)Rs containing either $\alpha 2$ or $\alpha 5$ subunits. Little is known concerning extrasynaptic GABA(A)Rs and tonic inhibition in spinal neurons. The aim of this study was to identify the subunit composition and sub-cellular location of GABA(A)Rs in spinal neurons.

METHODS: All experimental protocols used in this study were approved by the local animal care committee. Standard western blot analysis was used to confirm expression of subunits, at the protein level, from the brains and spinal cords isolated from Swiss White mice. In addition, immunofluorescence labeling of the spinal cord, brain sections and primary cultured murine neurons was used to visualize the expression and location of various GABA(A)R subunits.

RESULTS: Western Blot analysis showed that both brain and spinal neurons expressed $\alpha 5$ and $\alpha 2$ GABA(A)R subunits. Immunofluorescent staining revealed a distinct pattern of distribution of $\alpha 2$ and $\alpha 5$ subunits within the spinal cord. High levels of the $\alpha 2$ subunit were expressed throughout the spinal cord whereas the $\alpha 5$ subunit staining was more localized with staining also present in the dorsal root ganglia. Both $\alpha 5$ and $\alpha 2$ subunits displayed a punctate pattern, possibly indicating receptor clustering within the spinal cord.

DISCUSSION: To the best of our knowledge, these results provide the first evidence for extrasynaptic GABA(A)Rs in spinal neurons as both $\alpha 5$ and $\alpha 2$ subunits were expressed. These results raise the possibility that modulation of $\alpha 5$ or $\alpha 2$ subunit-containing GABA(A)Rs may be efficacious in analgesia and/or anesthesia.