

P003 Identification of Glycine Receptor Associated Gephyrin Splice Variants

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Gephyrin is a protein involved in synaptic anchoring of glycine receptors (GlyRs). The binding of gephyrin to the GlyR depends on an amphipathic motif within the large intracellular loop of the GlyR β subunit. The mouse gephyrin gene consists of 30 exons. Ten of these exons, called cassettes, are subject to alternative splicing (C1 to C7, C4' to C6'). Since one of the cassettes, C5', has recently been reported to exclude GlyRs from inhibitory synapses, we investigated the gephyrin splice variants associated with the GlyR in rat tissue. Gephyrin variants were purified from spinal cord, brain and liver by binding to the GST-tagged GlyR β loop or copurified with native GlyR from spinal cord by affinity chromatography, and analyzed by mass spectrometry. In addition to C2 and C6', already known to be prominent, C4 was found to be abundant in all tissues examined. C5 was detected in brain and spinal cord, while C5' was found mainly in liver. Binding of C5'-containing gephyrin to the GST-tagged GlyR β -loop was confirmed by using recombinant C5'-gephyrin. Therefore, C5' does not interfere directly with GlyR β binding. The functions of C4 and C5, shown here the first time to be present in GlyR associated gephyrin, remain to be investigated.