Distribution of the multidomain serine protease neurotrypsin in the mouse suggests multiple roles in pre- and postnatal development

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The mosaic protein neurotrypsin, whose mRNA is found in distinct subsets of central and peripheral neurons of the adult mouse, contains a trypsin-like serine protease domain. Other serine proteases such as thrombin, tissue- and urokinase-type plasminogen activator, have been implicated in cell migration, axogenesis, and synapse elimination during development, but also in neural plasticity of the adult. As a first step toward understanding the developmental role of neurotrypsin, we have used in situ hybridization to map the distribution of its mRNA during pre- and postnatal development. B6D2F1 mice were analyzed at developmental stages E8, E10, E11, E12, E15, E17, P0, P2, P6, P10, P15, and P22.

On E8, expression was seen in the chorion. On E10, it appeared in the maxillary process. Mesenchymal expression expanded rapidly, concentrating at boundaries to epidermis, mucosal epithelia and cartilage. Expression in the peripheral nervous system began at E11 in sensory ganglia, olfactory epithelium, and Schwann cells. Central neuronal expression started on E11 in the midbrain, spreading to various cell groups in the spinal cord, brainstem and olfactory system. On E15, signal appeared in the cortical subplate of the insular region. During the first postnatal days, expression expanded over the whole cortical mantle including the hippocampal formation and reached its overall maximum at the end of the first postnatal week with a complex and time dependent laminar and areal distribution. During the second postnatal week, when subcortical expression and expression outside the CNS had largely reached the adult pattern, cortical signal remained high and reached the adult pattern only by the end of the third week.

While the elaborate expression pattern in the developing neocortex is highly suggestive of an involvement of neurotrypsin in synaptogenesis or synapse elimination, its widespread expression during prenatal development suggests additional roles in developmental processes such as cell migration and axogenesis.