Multiple roles of neurotrypsin in tissue morphogenesis and nervous system development suggested by the mRNA expression pattern

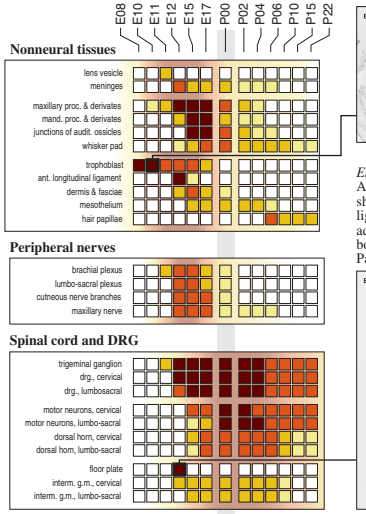
D.P. Wolfer, R.Lang, P.Cinelli, R.Madani, P.Sonderegger
University of Zurich, Institutes of Anatomy and Biochemistry, Zurich, CH-8057

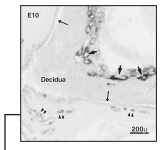
SNF 31-54184.98
Roche Research & Hartmann-Müller Foundations

Summary

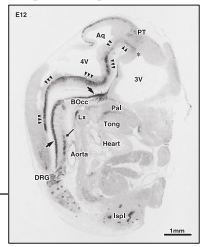
The trypsin-like serine protease neurotrypsin is found in subsets of central and peripheral neurons of the adult mouse. Other serine proteases, such as thrombin, tissue- and urokinase-type plasminogen activator, have been implicated in cell migration, axogenesis, and synapse elimination during development, but also in adult neural plasticity. Because little is known about the developmental role of neurotrypsin, we have used in situ hybridization to map the distribution of its mRNA during pre- and postnatal development of B6D2F1 mice. While the elaborate postnatal expression pattern in the neocortex suggests an involvement of neurotrypsin in synaptogenesis or synapse elimination, its prenatal expression implicates it in target invasion by axons, Schwann cell differentiation and tissue morphogenesis.

1 Strong expression in spinal cord, peripheral NS and nonneural tissue of the embryo



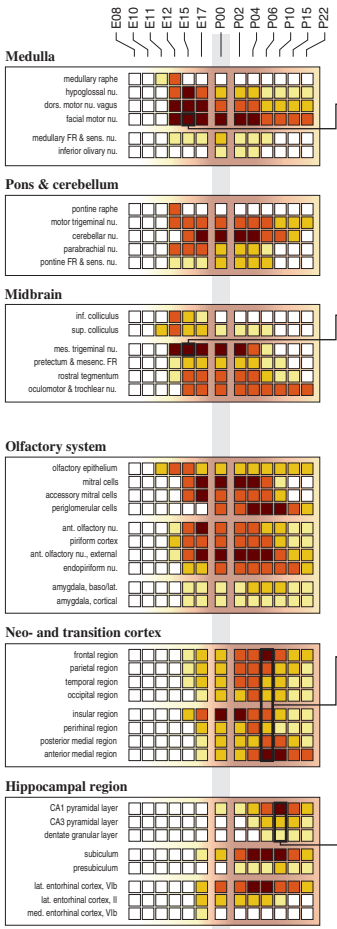


Trophoblast
Arrows: giant cells, long arrows: lumen, arrowheads: uterine epithelium

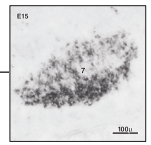


Embryo sagittal
Arrowheads: floor plate/raphe, short/long arrow: post/ant. lon. lig., 3/4V: ventricles, Aq: aqueduct, BOcc: basioccipital bone, lspl: lumbo-sacral plexus, Pal: palate, PT: pretectum.

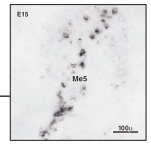
2 Caudo-rostral developmental gradient of neurotrypsin expression in the brain



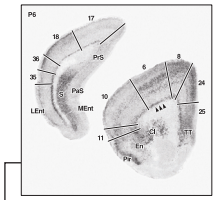
Medulla sagittal
facial motor nu.



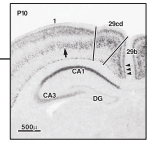
Midbrain sagittal
mesenc. trigeminal nu.



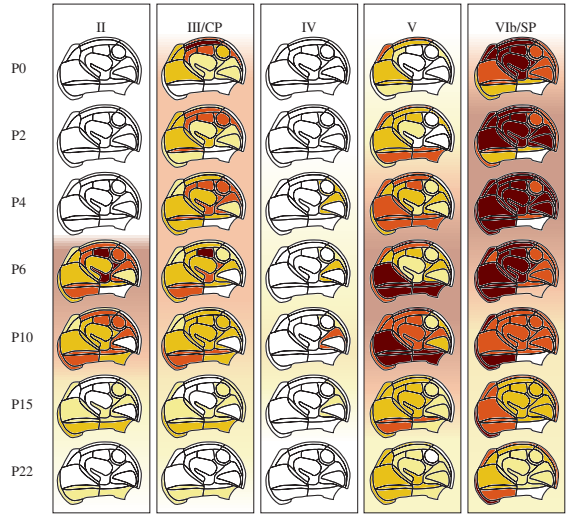
Cerebral cortex coronal
Arrowheads: layer VIb, numbers: cortical fields, Cl: claustrum, En: endopiriform nu., L/MEnt: lat./med. entorhinal area, Pa/PrS: para/presubiculum, Pir: piriform cortex, S: subiculum, TT: tenia tecta.



Hippocampus coronal
Arrow: layer V, arrowheads: layer II/III, numbers: cortical fields, DG: dentate gyrus.

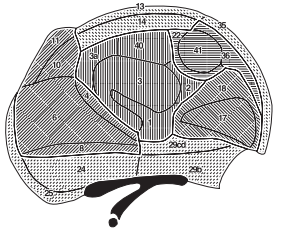


3 Elaborate areal & laminar pattern during postnatal maturation of cerebral cortex



blank, layer not developed weak
moderate strong maximal

Expression projected onto mouse cortical map from Caviness V.S.Jr. JCN 164:247-263, 1975



Neocortex
frontal: 4, 6 (motor), 8, 10, 11
parietal: 1, 2, 3 (barrel field), 3a, 40
temporal: 22, 36, 41 (auditory)
occipital: 17 (visual), 18

Transition zone
lateral:13+14 (insular), 35 (perirhinal)
medial: 24 (cingulate), 25, 29 (retrosplenial)

Methods
Fresh freezing, 20 µm cryostat sections. DIG-labeled anti/sense riboprobes from partial cDNA clone of neurotrypsin in pBluescript using Roche DIG RNA labeling kit. Fragments of 200-300 bp of the cRNA by partial alkaline hydrolysis used at at approx. 300 ng/ml. Visualization with Roche anti-DIG Fab, AP + NBT/BCIP + levamisole.