Brain Res. 2009 Mar 3;1258:1-11. Epub 2008 Dec 29.

Differential distribution of neuregulin in human brain and spinal fluid.

Pankonin MS, Sohi J, Kamholz J, Loeb JA.
Center for Molecular Medicine and Genetics, Wayne State University, Detroit, MI 48201 , USA.

Abstract
The neuregulins are a family of polypeptide factors implicated in a wide range of neurological and psychiatric disorders including multiple sclerosis, schizophrenia, and Alzheimer's disease. Many alternatively-spliced forms of the NRG1 gene are released as soluble factors that can diffuse to near and distant sites within the nervous system where they can accumulate through binding to highly specific heparan-sulfate proteoglycans in the extracellular matrix. Here we have determined the sites of synthesis and accumulation of heparin-binding neuregulin forms in human neocortex, white matter, cerebral spinal fluid, and serum by immunostaining and measurement of neuregulin activity. While neuregulin precursors are expressed predominately within cortical neurons, soluble neuregulin accumulates preferentially on the surface of white matter astrocytes. Consistently, neuregulin activity can be released from the extracellular matrix of human brain by protease treatment. Neuregulin activity is also detectable in human cerebral spinal fluid where its expression appears to be altered in neuronal disorders. While cerebral spinal fluid neuregulin levels were unaltered in patients with multiple sclerosis, they were slightly reduced in amyotrophic lateral sclerosis and Parkinson's disease ($p<0.15$), but significantly increased in Alzheimer's disease ($p<0.01$). While not detected in human serum, a novel neuregulin antagonist activity was identified in human serum that could have prevented its detection. These results suggest that human neuregulin is selectively targeted from cortical neurons to white matter extracellular matrix where it exists in steady-state equilibrium with cerebral spinal fluid where it has the potential to serve as a biological marker in human neuronal disorders.

PMID: 19150438 [PubMed - indexed for MEDLINE]