CLINICAL SPECIFICATIONS

NEUROFILAMENTS PROTEIN

Function:

Neurofilaments (NTs) are protein polymers. Along with microtubules and microfilaments, NTs form the neuronal cytoskeleton. Their primary function is to provide structural support for axons and to regulate axon diameter, which influences nerve conduction velocity.

Associated With:

Alzheimer's disease[1,2]
Vascular dementia[3]
Creutzfeldt-Jakob disease[4]
Multiple sclerosis[5, reviewed in 6]
Sporadic amyotrophic lateral sclerosis[reviewed in 6]
Optic neuritis [reviewed in 6]
Gullaine-Barré syndrome [reviewed in 6]
Chronic peripheral neuropathy [reviewed in 6]
Neurophychiatric systemic lupus erythematosus [reviewed in 6]

Known Cross-Reactions:
Cytoskeleton from fibroblasts, cytoskeleton from human hepatocellular carcinoma cell lines Hep3B[7]

Clinical Significance:

Neurofilaments provide structural support for the axon and influence nerve conduction velocity. Antibodies against heavy neurofilaments are detected in patients with Alzheimer's disease (AD).[1-3] The presence of Neurofilament (NT) antibodies indicates a disruption in the blood-brain barrier, which puts the brain at greater risk for neurological disorders.[3] NTs may be used to monitor ongoing axonal injury and neurodegeneration.[4] Researchers report varying results on NT antibodies, however, this is due to the different peptides of NTs used in the test. Soussan et al.[8] conducted one such study in healthy subjects, patients with Alzheimer's disease (AD) and patients with multi-infarct dementia. They found higher antibody levels in older (aged 70-79) healthy subjects than younger (aged 40-59) healthy subjects, while NT antibodies were significantly higher in AD than in healthy controls and patients with multi-infarct dementia. A debate also ensues in multiple sclerosis (MS). Some studies conclude that antibodies to NT reflect axonal damage, and are higher in relapsing MS patients compared to MS patients in remission, and might be useful in monitoring the progression of secondary progressive MS.[reviewed in 9] Using anti-$A\beta_{42}$ peptide antibody, Vojdani and Vojdani showed positive reaction between this antibody and neurofilament proteins.[10] Therefore, identifying the triggers that are responsible for the production of these cross-reactive antibodies may be important for the prevention of AD.

References:

1. Chapman et al. Alzheimer's disease antibodies bind specifically to a neurofilament protein in Torpedo cholinergic neurons. J Neurosci, 1989; 9(8):2710-2717.
2. Bartos. Patients with Alzheimer disease have elevated intrathecal synthesis of antibodies against tau protein and heavy neurofilament. J Neuroimmunol, 2012V; 252(1-2):100-105.
3. Mecocci et al. Serum anti-GFAP and anti-S100 autoantibodies in brain aging, Alzheimer's disease and vascular dementia. J Neuroimmunol, 1995; 57(1-2):165-70.
4. Toh et al. The 200- and 150-kDa neurofilament proteins react with IgG autoantibodies from chimpanzees with kuru or Creutzfeldt-Jakob disease: a 62-kDa neurofilament-associated protein reacts with sera from sheet with natural scrapie. Proc Natl Acad Sci USA, 1985; 82:3894-3896.
5. Harris et al. Biomarkers of multiple sclerosis: current findings. Degener Neurol Neuromuscul Dis, 2017; 7:19-29.
6. Rajasalu et al. Demonstration of natural autoantibodies against the neurofilament protein α-internexin in sera of patients with endocrine autoimmunity and healthy individuals. Immunol Lett, 2004; 94:153-160.
7. Gown and Vogel. Monoclonal antibodies to intermediate filament proteins of human cells: unique and cross-reacting antibodies. J Cell Biol, 1982; 95:414-424.
8. Soussan et al. Antibodies to different isoforms of the heavy neurofilament protein (NF-H) in normal aging and Alzheimer's disease. Mol Neurobiol, 1994; 9(1-3):83-91.
9. Teunissen and Khalil. Neurofilaments as biomarkers in multiple sclerosis. Mult Scler, 2012; 18(5):552-556.
10. Vojdani and Vojdani. Immunoreactivity of anti-$A\beta P$-42 specific antibody with toxic chemical food antigens. J Alzheimers Dis Parkinsonism, 2018; 8(3):1-11.