

Subject Name: John Hoyte

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Serum Test for Neuronal and Glial Autoantibodies

Report

Sera obtained from John Hoyte and from healthy adults (controls) were assayed for the level of autoantibodies against brain-specific proteins associated with:

1. Neurogenesis, i.e., high molecular weight neurofilament protein (NFP-200, NFH), microtubule associated protein-2 (MAP-2), and Tau proteins;
2. Myelinogenesis, i.e., myelin basic protein (MBP); and
3. Gliogenesis, i.e., glial fibrillary acidic protein (GFAP).
4. Autoantibodies against tubulin, a protein present in all tissues, including the nervous system, have been determined as markers for global tissue damage.
5. Finally, autoantibodies against the glial calcium-binding protein S-100 were determined as markers for acute traumatic brain injury.

These autoantibodies have been used as markers for injury to the central nervous system.

RESULTS

Percentage change of the subjects autoantibodies against neuronal and glial proteins compared to healthy subjects are listed in Table 1. The results that are expressed as percentage (%) of healthy controls represent the mean values of duplicate assays of optical density arbitrary units, following Western Blotting assay of autoantibodies at 1:50 serum dilution.

Serum autoantibodies against neuronal proteins, Tau proteins and MBP exhibited mild and moderate increase, respectively, whereas autoantibodies against MAP-2 proteins were severely higher than that of controls. Autoantibodies against the protein associated with gliogenesis, the glial protein, GFAP were greatly higher than the controls. Autoantibodies against the global protein tubulin were moderately increased than controls.

Autoantibodies against S-100 protein are used as an internal standard to determine the precision of the assay. The results show that the levels of these autoantibodies were low in controls and slightly higher in the subject, indicating high precision of the results. They also suggest the presence of some of acute traumatic or recent brain injury in the subject.

Table 1. Percentage Change in Autoantibodies Compared to Healthy Subjects
 Slight increase (\pm): 100-200; Mild increase (+): 200-400; Moderate increase (++) : 41-600; High increase (+++): 601-800; Severe increase (++++): 800-1,000; Great increase (+++++) >1,000

Brain-Specific Protein	Neurological function	%	Significance	Location of Tissue Injury	Associated Neurological Deficits
Neurofilament protein (NFP-200, NFH)	Neurogenesis	64	\pm	Axonal degeneration	1. Cerebral Cortex Weakness, Deficits in: posture, locomotion and deficits in movements of fingers, speech, and facial expression
TAU Proteins (TAU)	Axonal development and axonal transport	176	\pm		
Tubulin	Axonal Transport Present in other tissues	520	++	Axonal degeneration and damage to other tissues	2. Limbic System Learning, memory deficits
Myelin basic Protein (MBP)	Myelinogenesis Myelin Development	189	\pm	Demyelination	
Microtubule Associated Proteins-2 (MAP-2)	Neurogenesis Dendrite Development Of nerve cell	807	++++	Dendrite Degeneration	Purkinje Cells (Cerebellum): Incoordination, staggering ataxia
Glial Fibrillary Acidic Protein (GFAP)	Gliogenesis Forms scar in injured axons	1,113	+++++	Axonal Injury	Chronic axonal injury
S-100 Protein	From astrocytes in acute injury	193	\pm	Acute, traumatic Brain injury	Acute axonal injury

DISCUSSION

Alterations of the cytoskeletal structure are prominent features in some neurological diseases and chemically induced neurological disorders. Neurofilament and Tau proteins are major constituents of the axon and MAP-2 is mostly present in the dendrites. Increased autoantibodies of these proteins are indicative of axonal degeneration. Also, increased autoantibodies against MBP are consistent with axonal demyelination. Many neurotoxicants, such as organophosphorus insecticides, as well as other insecticides, solvents and heavy metals cause neuronal cell death and axonal degeneration and over-expression of GFAP, with subsequent release of neuronal, myelin, and glial proteins into circulation, followed by the formation of autoantibodies against these proteins.

Increased autoantibodies against axonal proteins are consistent with injury to cerebral cortex resulting to weakness and deficits in posture, locomotion and movements of fingers and facial expression and of limbic system injury leading to cognition, and learning and memory deficits. Increased of autoantibodies against the dendrite protein, MAP-2 resulting from Purkinje cells damage leads to incoordination and staggering ataxia. Increased of autoantibodies against the astrocyte protein, GFAP is consistent with acute axonal injury and behavioral alterations. It is particularly important that the serum of this subject exhibited severe increase in autoantibodies against axonal proteins, MAP-2, and great increase in autoantibodies against the astrocyte protein, GFAP. All other proteins ranged from slight to moderate increase, suggesting neuronal injury.

CONCLUSIONS

While not diagnostic for specific disease, the presence of circulating autoantibodies against neuronal and glial proteins, at higher levels in patients who had been exposed to neurotoxic chemicals and developed neurological deficits, over that of controls, can be used as further confirmation for chemical-induced nervous system injury. The patient's serum profile of autoantibodies against brain-specific proteins shows that the autoantibodies against the axonal proteins, MAP-2 was severely higher than controls, in agreement with the great increase of autoantibodies against GFAP and the slight to moderate of autoantibodies against all other proteins. The moderate increase in the level of autoantibodies of S100 protein in the serum suggests moderate acute traumatic brain injury in the subject. These results are consistent with the presence of severe nervous system injury.

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