



Information for ME/CFS Physicians

Autonomic Function in CFS

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The autonomic nervous system affects virtually every aspect of body functioning. It regulates most involuntary functions such as heart rate (HR), blood pressure (BP) and gut and bladder function. Autonomic symptoms are not included in the diagnostic criteria of CFS. Never the less many CFS patients have clinical symptoms which suggest autonomic dysfunction. These include: increases heart rate, dizziness, fainting, delayed gastric emptying, urinary frequency and orthostatic intolerance.

Orthostatic intolerance refers to symptoms caused or worsened by standing. There are two types of OI. Neurally Mediated Hypotension (NMH) is a neurally mediated sudden drop in BP which causes fainting upon standing. Postural Orthostatic Tachycardia Syndrome (POTS) is an increase in HR of over 30 bpm from sitting to standing without loss of consciousness. The gold standard of diagnosis for OI is the onset of dizziness or fainting during tilt table testing.

Bou-Holaigah et al from Johns Hopkins in 1995 were the first to note the connection between CFS and OI. They found that 22/23 CFS patients had abnormal responses on tilt table testing (Bou-Holaigah et al, 1995). Since then the finding of autonomic dysfunction has been validated as occurring in a subset of CFS patients.

Research findings include:

- increased incidence of abnormal tilt table response in CFS (30 - 95%) (Bou-Holaigah et al, 1995;Freeman & Komaroff, 1997;Gibson et al, 1993;Stewart et al, 1999;De Lorenzo et al, 1997) Not all agree (Duprez et al, 1998)
- increased resting heart rate (Duprez et al, 1998;LaManca et al, 1999)
- decreased vagal power (parasympathetic activity) (Freeman & Komaroff, 1997)
- decreased sympathetic activity response to physical stress (Stewart et al, 1999;Freeman & Komaroff, 1997;Duprez et al, 1998) and mental stress (Soetekouw et al, 1999)
- decreased night-time systolic BP (van deLuit et al, 1998)

- increased postural drop in BP (Soetekouw et al, 1999)
- increased HR and sympathetic activity after tilt table testing (De Becker et al, 1998)
- improvement of CFS symptoms by treating the autonomic dysfunction (Bou-Holaigah et al, 1995;De Lorenzo et al, 1997)
- some studies show no abnormalities (Yataco et al, 1997)

Possible mechanisms of orthostatic intolerance: The most likely mechanism for OI is decreased vascular tone in the periphery. Rowe has reported several cases of CFS in persons with Erlans Danlos syndrome a disorder of connective tissue elasticity associated with neurally mediated hypotension (NMH) as measured by tilt table testing (Rowe et al, 1999). Poor elasticity causes blood pooling in the peripheries and orthostatic intolerance.

The autonomic parasympathetic nervous system decreases vascular tone by through a cascade of events. The vagal signals activate muscarinic acetylcholine receptors on the endothelial cell surface. This activates G proteins, promoting the conversion of L-arginine to nitric oxide, which diffuses into the smooth muscle cells and stimulates guanylate cyclase to produce cyclic GMP, thereby causing relaxation. In the presence of excess NO vascular tone will be decreased and OI (either NMH or POTS) may result. Therefore the abnormality could occur at any point on this cascade.

Most researchers are currently hypothesizing the problem lies with the cholinergic system. A recent report shows cholinergic supersensitivity in CFS (Spence et al, 2000). Work from the University of Newcastle (Australia) shows increases in serum concentrations of the amino acid ornithine in the serum of CFS patients. Ornithine varies with NO production (Dunstan et al, 2000). Therefore, increased ornithine correlates with increased NO activity. A recent report from the Mayo Clinic shows that some people with OI have antibodies which block the function of the ganglionic cholinergic receptors (Vernino et al, 2000).

Treatment: The treatment of choice for CFS patients with orthostatic intolerance is added salt

and water. The amount of salt and water taken daily should be titrated to best health and blood pressure must be monitored during this treatment. The second line treatments for OI are florinef a salt saving hormone and midodrine a peripheral alpha (sympathetic) agonist. In some cases beta blockers or calcium channel blockers are helpful. Unfortunately all of the drug treatments for OI have side effects which can limit their use in CFS patients.

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