BHBI-Funded Research*

Abstract 5

Identification and Characterization of Autonomic Dysfunction in Migraineurs With and Without Auras: Phase I

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Objectives: To identify and characterize the presence, if any, of autonomic dysfunction among migraineurs suffering from orthostatic intolerance (postural dizziness, presyncope, and syncope) and to simultaneously compare neurocardiac physiological parameters with morphometrics of sudomotor innervation on skin biopsy.

Methods: In this phase of the study, 30 male and female adults (ages 18–75) who suffered from migraines without and with auras, as defined by the International Headache Society, and who complained of orthostatic intolerance, underwent the following studies: passive upright tilt table testing, clinical autonomic reflex testing, quantitative sudomotor axon reflex testing (QSART), and punch biopsy for evaluation of sudomotor nerve fiber density. The results of clinical autonomic testing were then compared with the morphometric findings supporting small fiber neuropathy involving sweat gland innervation on skin biopsy.

In phase II, the same studies will be performed on age-matched patients suffering from migraines without and with auras but who do not complain of postural instability or intolerance, including presyncope and syncope. The two populations will then be compared.

Results: Among 30 consecutive migraine patients seen in an active neurology practice between January 2008 and June 2009, there were 27 females and 3 males with a median age of 33 (range 18–71). Fifty-seven percent (17 patients) had migraines with and without auras, 33% (10 patients) had basilar-type migraines, 7% (2 patients) had migraines with auras only, and 3% (1 patient) had migraine without aura.

Seventeen of 30 skin biopsies (57%) exhibited small fiber sensory neuropathies (SFSN) by accepted morphometric standards, and 8 of these (47%) demonstrated reduced sweat gland (sudomotor) innervation in addition to reduced innervation to somatic structures. Eleven of 17 biopsies (65%) qualifying as SFSN were classified as length dependent and 6 (35%) as non-length dependent. Among the SFSN group, 5 (29%) exhibited normal QSART results and 12 (71%) had abnormal QSART results. Of the remaining 13 normal skin biopsies, which demonstrated normal nerve fiber densities to both somatic or sudomotor dermal structures, 10 were from patients who had accompanying QSART studies available for comparison; 3 of these (30%) were abnormal while 7 (70%) were normal.

Of 26 available QSART studies, twelve (46%) were normal and 14 (54%) were abnormal (reduced). Three of 12 normal QSARTs (25%) showed sudomotor involvement on skin biopsy while 9 (75%) had no such morphometric abnormality. Among the 14 patients with abnormal QSARTs, only 5 (36%) had biopsy evidence of sudomotor nerve involvement while the remaining 9 (64%) had normal biopsies.

There was a strong association between an abnormal tilt table response in patients with biopsy-proven SFSN; 17/17 (100%) had either orthostatic hypotension with or without a vasovagal syncopal response, postural tachycardia with or without a vasovagal syncopal response, or both. Among the 13 SFSN-negative patients with migraines and orthostatic intolerance, 12 (92%) had abnormal passive head upright tilt table responses.

Among the entire population, one-third had had either head trauma or a craniotomy within 6 months of the onset of symptoms.

Conclusions: In this, the first phase of our study of autonomic dysfunction in migraine sufferers complaining of orthostatic intolerance, we measured clinical neurocardiac parameters of autonomic function—the response to passive head upright tilt table testing, standard autonomic reflex testing, and QSART—and compared the results with morphometric analysis of small fibers, including sudomotor fibers, on skin biopsy. Skin biopsy nerve fiber analysis is presently considered to be the gold standard for diagnosis of SFSN.

In this predominantly female population, all but one patient had migraines with auras and one-third met criteria for basilar-type migraines. While a normal QSART result was able to predict normal sudomotor innervation on biopsy, an abnormal QSART result failed to predict a deficiency of sudomotor fiber innervation of sweat glands. In this symptomatic population, tilt table testing was abnormal and revealed either postural tachycardia or orthostatic hypotension in 29 of 30 patients regardless of biopsy results, suggesting that neurocardiac abnormalities may result not only from peripheral neuropathic autonomic defects but also from central autonomic mechanisms. This may be related to either the migrainous diathesis or another unexplained condition, such as head trauma or surgery.

* BHBI = Bakken Heart-Brain Institute