WriteClick® Editor's Choice

Editors' Note: In WriteClick this week, Haliloglu and Topaloglu comment on "Evidence-based guideline summary: Evaluation, diagnosis, and management of congenital muscular dystrophy," and authors Kang et al. answer their points, noting that the guideline generally based its statements on the articles with the best methodology. Dr. Bronstein challenges the conclusion in "Neuropsychological outcome after deep brain stimulation for Parkinson disease" that the subthalamic nucleus is the preferred target in deep brain stimulation over the globus pallidus pars interna. Authors Odekerken et al. summarize their supporting data. It is clear that the matter may not yet be settled.

—Megan Alcauskas, MD, and Robert C. Griggs, MD

EVIDENCE-BASED GUIDELINE SUMMARY: EVALUATION, DIAGNOSIS, AND MANAGEMENT OF CONGENITAL MUSCULAR DYSTROPHY: REPORT OF THE GUIDELINE DEVELOPMENT SUBCOMMITTEE OF THE AMERICAN ACADEMY OF NEUROLOGY AND THE PRACTICE ISSUES REVIEW PANEL OF THE AMERICAN ASSOCIATION OF NEUROMUSCULAR & ELECTRODIAGNOSTIC MEDICINE

Goknur Haliloglu, Haluk Topaloglu, Ankara, Turkey: Kang et al.[1] reviewed congenital muscular dystrophies (CMD), which is a dynamic topic in both pediatric neurology and neuromuscular disease practices.

A distinctive CMD with multisystem involvement and characteristic mitochondrial structural changes due to choline kinase β (*CHKB*) gene defects is commonly referred to as megaconial CMD.[2,3] Core clinical features include intellectual disability (ID), autistic features, ichthyosis-like skin changes, and dilated cardiomyopathy. This form of muscular dystrophy should be considered in children with ID without overt CNS involvement and with increased serum creatine kinase levels and behavioral abnormalities.[4]

In the Turkish population, the A200P haplotype described in *POMT1* is associated almost exclusively with limb-girdle muscular dystrophy (LGMD) and mental retardation phenotype, characterized by abnormal α-dystroglycan expression, and not related to CMDs.[5] In addition, congenital muscular dystrophy type 1C and LGMD2I, which are due to *FKRP* mutations, are both in the α-dystroglycan-related dystrophy group.

The authors noted that evidence is insufficient to determine the capability of muscle biopsies to identify collagenopathies. However, immunohistochemical studies—including collagen VI staining or double labeling with collagen VI and perlecan—are helpful in the diagnosis of Ullrich CMD (UCMD).[6]

Furthermore, *SEPN1* mutations result in both multiminicore disease, which is a congenital structural myopathy, and CMD with rigid spine and early restrictive respiratory insufficiency. Multiminicore disease should not be presented as an unclassified CMD.

For such a heterogeneous condition, it may be inaccurate to cite cognitive involvement as 58%. In collagenopathies, and even in merosin deficiency, intelligence is usually preserved.

Finally, etiologic yield of targeted genetic testing and benefits of genetic diagnoses have been shown. At bedside, this information is also important for genetic counseling and prenatal diagnosis. In merosin-deficient congenital muscular dystrophy type 1A and UCMD, prenatal diagnosis can be made by immunohistochemistry of chorionic villus sample and DNA analysis.[7]

Author Response: Peter B. Kang, Gainesville, FL; Leslie Morrison, Albuquerque; Susan T. Iannaccone, Dallas; Robert J. Graham, Boston; Carsten G. Bönnemann, Bethesda, MD; Anne Rutkowski, Harbor City, CA; Joseph Hornyak, Ann Arbor, MI; Ching H. Wang, Corpus Christi, TX; Kathryn North, Melbourne, Australia: We thank Drs. Haliloglu and Topaloglu for their comments. Evidence-based guidelines, such as ours,[1] are constructed on a specific methodology regarding the literature search and data analysis, and thus differ from consensus statements.[8] Some of our findings highlighted questions that merit further primary research.

The article on megaconial CMD associated with *CHKB* did not meet inclusion criteria. This disease may also be considered as mitochondrial. Mentioning the A200P haplotype was not optimal given the associated phenotype, as the authors indicated. However, the section remains valid, as specific subtypes cluster in various geographic areas and ethnic groups.

The main conclusion of the article regarding immunostaining for collagen VI involved immunostaining

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fibroblasts rather than muscle sections.[6] Collagen VI immunohistochemistry may not always have a high sensitivity, as deficiencies may be subtle.

Multiminicores may coexist with dystrophic pathology.[9] As the distinctions among subtypes of *SEPN1*-related myopathies become blurred,[10] *SEPN1*-related myopathies may represent a single diagnostic entity.

We agree that citing an overall percentage for cognitive involvement in CMD may not reflect the variability among subtypes. The 58% statistic was from a population-based study that was also the most rigorous study (Class II) ascertained for this question.[11]

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NEUROPSYCHOLOGICAL OUTCOME AFTER DEEP BRAIN STIMULATION FOR PARKINSON DISEASE

Jeff M. Bronstein, Los Angeles: Odekerken et al.[1] investigated neuropsychological outcome after deep brain stimulation (DBS) in Parkinson disease (PD). The subthalamic nucleus (STN) is the most common DBS target in PD despite data suggesting that it is not superior to globus pallidus pars interna (GPi).

The aggregate data from the 3 large, head-to-head trials suggested that GPi DBS results in equivalent motor benefits based on their primary endpoints.[2–4] However, Odekerken et al.[1]—and essentially all other studies—have demonstrated fairly consistent neurobehavioral outcomes favoring GPi DBS.[4,5] The significance of these mild to moderate changes in neurobehavior following STN DBS is unclear but the data are clear: STN and GPi DBS result in equivalent motor benefits but STN DBS results in worse neuropsychological outcomes than GPi DBS. This is not surprising given the functional connections of the STN.

Based on these studies, I disagree with the conclusion in the accompanying Commentary that "the data support STN as the preferred target."[6]

Author Response: Vincent J. Odekerken, Judith A. Boel, Ben A. Schmand, Rob M. de Bie, Amsterdam: We thank Dr. Bronstein for his comments. The Netherlands Subthalamic and Pallidal Stimulation (NSTAPS) study showed no difference in the primary outcomes after GPi DBS and STN DBS, but was underpowered on its primary outcome of off/on time-weighted functioning due to incomplete diary data.[3] However, we found a motor improvement in off-drug phase that was twice as large after STN DBS compared to GPi DBS.[3] The other large head-to-head trial, the Veteran Affairs (VA) trial, showed a much lower off-drug motor improvement and less medication reduction after STN DBS.[2] The improvement was not only smaller than in NSTAPS, but also smaller than in other large randomized trials investigating STN DBS.[7]

Regarding cognition, mood, and behavior, we found no clinically significant differences that might justify preference of GPi DBS over STN DBS. Even though some mental speed tests showed larger decline after STN DBS, other tests in the same domain did not. The VA trial results also showed no large between-group differences as far as we can assess.[8]

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Goknur Haliloglu, Peter B. Kang, Haluk Topaloglu, et al.

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