WEIGHT LOSS IN HUNTINGTON DISEASE INCREASES WITH HIGHER CAG REPEAT NUMBER

To the Editor: I read the article by Aziz et al.1 with interest. The authors present a strong case for a hypermetabolic link between expanding CAG repeat number and the characteristic weight loss in Huntington disease (HD). It is notable that such recognized hypermetabolic disorders as thyrotoxicosis may also cause chorea. Perhaps therapeutic efforts to lower the metabolic rate by suppressing thyroid function should be investigated in patients with HD.

Gordon J. Gilbert, St. Petersburg, FL
Disclosure: The author reports no disclosures.

Reply from the Authors: We appreciate Dr. Gilbert’s interest in our findings.1 The concept of suppressing thyroid function in HD in order to counteract weight loss is intriguing. In addition, as Dr. Gilbert also points out, thyroid hormone excess has been associated with chorea, so altering thyroid function might also influence the choreatic movements in HD.2 However, a number of caveats should be considered.

First, although we found an increased rate of weight loss in patients with HD with higher CAG repeat number, the precise mechanisms underlying this association are unclear.1 A higher metabolic rate due to mitochondrial dysfunction may be involved, but whether mitochondrial dysfunction in HD would respond to changes in thyroid hormone levels has yet to be investigated.3

Second, the hypothalamic-pituitary-thyroid axis function has rarely been studied in patients with HD.3 Although normal basal levels of thyroxine, triiodothyronine, and thyroid-stimulating hormone (TSH) have been reported in patients with HD, others have found an impaired TSH response to thyrotropin-releasing hormone stimulation.3 Therefore, more detailed studies of thyroid function in HD are needed.

Third, besides regulating the body’s metabolic rate, thyroid hormones also have a myriad of other effects, including the regulation of normal brain function, heart rate and myocardial contractility, gastrointestinal motility, and renal water clearance. Moreover, as thyroid hormones affect protein synthesis and degradation, they can also alter the production, responsiveness, and metabolic clearance of other hormones. Therefore, iatrogenically induced changes in thyroid function are likely to entail complex alterations in systemic physiology.

However, the concept of direct modulation of the metabolic rate in HD remains intriguing and should be tested in the transgenic disease models now available. It is interesting that caloric restriction, which is known to lower basal metabolic rate, has been shown to slow disease progression, ameliorate weight loss, and increase survival in an HD transgenic mouse model.4

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4. Duan W, Guo Z, Jiang H, Ware M, Li XJ, Mattson MP. Dietary restriction normalizes glucose metabolism and BDNF levels, slows disease progression, and increases survival in huntingtin mutant mice. Proc Natl Acad Sci USA 2003;100:2911–2916.

PRESTROKE PHYSICAL ACTIVITY IS ASSOCIATED WITH SEVERITY AND LONG-TERM OUTCOME FROM FIRST-EVER STROKE

To the Editor: I read the article by Krarup et al.1 with interest. The definition of long-term outcome was only outlined in the abstract. The previous study by Krarup et al.2—the ExStroke Pilot Trial—provided information in the Methods on when the PASE questionnaire was obtained (within 90 days, median 10 days).

The authors appeared to have followed the subjects at earlier time intervals, yet it would have been interesting to note when physical activity influenced the odds ratio (OR) of an increasing modified Rankin scale score (mRS) after stroke. Table 2 and figure 2 do not indicate how the variable mRS was treated, presumably as a binary categorical variable given the use of an OR. If so, it would have been helpful to see what the mRS cutoff points were to derive a higher level, and the rationale for that cutoff point.

Another helpful analysis could have used the change in mRS from the time immediately after stroke and 2 years. In light of other reports indicating exercise training may also improve recovery after stroke, analyzing the pattern of physical activity after enrollment could be an interesting corollary to this study.3

Krarup et al. have made an important contribution to the literature regarding prestroke level of functioning and stroke recovery. They have also confirmed the importance of physical activity not just in
stroke onset prevention but in prevention of a more severe stroke and stroke recovery.

Joshua Z. Willey, New York, NY

Disclosure: The author reports no disclosures.

Reply from the Authors: We thank Dr. Willey for his interest in our article. In the ExStroke pilot Trial, we included stroke patients within 90 days of stroke and followed them for 2 years. The median time from stroke onset to inclusion was 10 days and the information was provided in table 1.

In the current article, we wanted to examine the association between prestroke physical activity and stroke severity and between prestroke physical activity and long-term outcome. Therefore, we chose to include only the Rankin scores from the end of trial visit to best answer our scientific question. We have data on Rankin scores from other time points and plan to publish these data in the future.

The mRS is an ordinal scale. For the main analyses, we used ordinal logistic regression, the so-called shift analysis, which, contrary to binary logistic regression, uses all possible cutoff points and gives one cumulative OR as a result. This method omits the need for dichotomization and the problems that arise when ordinal scales are reduced to binary scales. Physical training may be a way to improve recovery after stroke although further studies are needed.

In a paper currently under review, we address the effect of repeated encouragement to be physically active as a way to generally increase physical activity. Our goal is that this will then affect stroke recovery and risk of recurrent stroke.

Lars-Henrik Krarup, Thomas Truelsen, Gudrun Boysen, Copenhagen, Denmark

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CORRECTION

Reduced circulating angiogenic cells in Alzheimer disease

In the article “Reduced circulating angiogenic cells in Alzheimer disease” by S.-T. Lee et al. (Neurology® 2009;72:1858–1863), there is an error in the funding information. It should read as follows: “Supported by a grant (SC4120) from the Stem Cell Research Center of the 21st Century Frontier Research Program funded by the Ministry of Science and Technology, South Korea.” The authors regret the error.

CORRECTION

Correspondence regarding “Assessment: Botulinum Neurotoxin in the Treatment of Autonomic Disorders and Pain (An Evidence-Based Review): Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology”

In the Correspondence regarding the article “Assessment: Botulinum Neurotoxin in the Treatment of Autonomic Disorders and Pain (An Evidence-Based Review): Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology” (Neurology® 2009;72:1367–1368) by Alexander Mauskop and Ninan Mathew, the disclosures listed for the authors were incomplete. Dr. Mauskop has participated in clinical trials sponsored by Allergan, Inc., maker of Botox, and has been paid for lectures on this topic. Dr. Mathew has received grants for clinical trials from Allergan, Inc., maker of Botox. He has also served on the advisory board for Botox in Migraine.