## Hypomyelination Versus Delayed Myelination

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We read the article of Vaurs-Barrière et al,[1] reporting on a Pelizaeus-Merzbacher-like phenotype in male *MCT8* mutated patients, with interest. We share the experience that in infancy, magnetic resonance imaging (MRI) shows a severe lack of myelin in these patients and that the MRI improves over time. This has also been confirmed by other groups.[2] We would, however, like to object to the word "hypomyelination" in this context, because it causes confusion.

MRI is an excellent tool to document myelination of the brain at a certain moment and to follow its progress over time in infants and children. If MRI shows less myelin than normal, the first question should always be whether myelination is delayed or whether the deficit is permanent. Hypomyelination and delayed myelination have a similar appearance on a single MRI, especially if done at an early age, but sequential studies can distinguish between them, showing increasing myelin content in delayed myelination, but an unchanged lack of myelin in hypomyelination. Normal myelination occurs mainly in the first 2 years of life. Within the first year of life, there is so little myelin in normal infants that it is not possible to diagnose permanent hypomyelination. The MRI definition for permanent hypomyelination is an unchanged pattern of deficient myelination on 2 MRIs at least 6 months apart in a child older than 1 year.[3]

The differentiation between delayed myelination and permanent hypomyelination is important. Delayed myelination is a rather nonspecific feature observed in most children with a delayed development of any cause.[4,5] Permanent hypomyelination comes with a specific differential diagnosis.[3] *MCT8* mutations are not on the list. A correct MRI diagnosis prevents the confusion.

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## Potential Conflicts of Interest

Nothing to report.

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## Does Body Mass Index Increase Risk of Hemorrhagic Stroke?

Ivy Shiue, MSc

In the article entitled "Body Mass Index and Risk of Stroke among Chinese Men and Women" by Lydia A. Bazzano and her colleagues,[1] it is very interesting firstly to disclose the association of body mass index (BMI) with risk of stroke by its subtypes among Chinese populations, suggesting a somewhat different profile compared to Western populations. Although the predictive values of lean BMI and risk of subarachnoid hemorrhage (SAH) were found to be statistically nonsignificant and discordant between case-control and longitudinal studies previously,[2] no significant association for SAH and BMI was revealed in the Asia-Pacific region either, and these did not differ much between Asian and Australasian regions.[3] It is known that SAH has a different etiology from other subtypes of stroke including intracerebral hemorrhage (ICH). Therefore, putting SAH and ICH together may confound the association with BMI. Among Koreans and Japanese, an increase in the risk of ICH was observed, but not among patients with SAH.[4,5] Lastly, the cutoff point for BMI use should also be clearly addressed, because the Chinese population tends to be slimmer and the threshold for overweight and/or obesity measurement could be different.[6] It is recommended that the effect of BMI on risk of SAH and ICH should be examined separately.

## Potential Conflicts of Interest

Nothing to report.

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## Reply

Lydia A. Bazzano, MD, PhD

We would like to thank Dr Shuie for these comments. In our study of 169,871 Chinese men and women aged 40 years or older, we identified a linear association between increasing body mass index (BMI) and incidence of hemorrhagic stroke, which included both subarachnoid hemorrhage and intracerebral hemorrhage. Unfortunately, our data do not allow a separate analysis of the association between BMI and subarachnoid hemorrhage, and thus we cannot contribute to the knowledge base on this specific point. However, in regard to the categorization of BMI among Asians, we have published our results from the same cohort examining the relationship between BMI and mortality.[1] Our study included information from more than twice the number of individuals included in a previous examination of this issue,[2] and findings from our study support the use of a single common recommendation for defining overweight and obesity. Furthermore, we conducted analyses of the relationship between BMI and stroke incidence and mortality using quintiles of BMI for Chinese men and women (which closely parallel the suggested cutoffs for Asian populations) and identified the same linearly increasing relationship between BMI and stroke incidence and mortality.

## Potential Conflicts of Interest

Nothing to report.

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## Reply

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The March 2010 issue of this journal contained 2 letters commenting on our recent review of the neurobiology underlying complex regional pain syndrome (CRPS).[1]

We appreciate the plaudits of Moseley et al[2] and their agreement with our central tenet that dysfunction of small-diameter axons in peripheral nerve is critical for persistent CRPS, uniting CRPS-I with CRPS-II. Although our review focused on symptom mechanisms rather than therapies, we recognize the potential value of cognitive behavioral and rehabilitation methods for treating chronic pain. However, like most neurologists, we have no experience with these methods and so could not discuss nor recommend them authoritatively. We hope that better understanding of CRPS biology will improve diagnostic criteria and enable the high-quality clinical trials required to strengthen and broaden treatment recommendations.

The letter by Lang and Chen[3] largely concerns a secondary CRPS feature—distal tonic dystonia,[4] which we had suggested is unlikely to be caused by pure small-fiber axonopathy. Their letter promotes the idea of psychogenic causality in many CRPS patients, particularly in the small subgroup with dystonia. We know that others in the neurological community agree with Lang and Chen, but we take strong issue with the position that because some CRPS symptoms remain poorly understood, their cause is likely psychogenic. Nor does the fact that CRPS/dystonia is unlike other movement disorders support the conclusion that it or concomitant tremors are psychogenic.[5] We would also like to clarify Lang and Chen's mention of debating a CRPS/dystonia patient whose case one of us (A.L.O.) published.[5] We were not invited to the meeting at which Lang and Chen report using our patient's video to demonstrate psychogenic movement disorder. The "regular debate at international meetings" has not included us. Of note, nearly 10 years of medical records on this patient show no somatization or psychiatric difficulties. Her medical complaints remain limited to her persistent stable CRPS/dystonia, unresponsive to multiple treatments. Independent psychological evaluations identified no psychopathology.

Lang and Chen take issue with the alternative hypothesis that we raised—that developing dystonia in CRPS may require concomitant involvement of large-diameter motor axons. This was clearly framed as a hypothesis rather than a conclusion. We mentioned this particular hypothesis because it is the only one for which there is at least some experimental support. In contrast, the theory of psychogenic causality is based mostly on circular reasoning and pattern recognition by movement disorder specialists. It also seems improbable to us that an unrelated stereotypic movement disorder of psychogenic origin should so frequently coexist with a highly characteristic post-traumatic pain syndrome diagnosable by multiple objective findings, as outlined in our review. In support of our conclusion, epidemiological studies of CRPS consistently find no association between CRPS and psychological factors.[6]

Lang and Chen's suggestion that to invoke motor ax-