The Authors Reply

We fully agree with Dr. Andreasen and her colleagues that correction for head size and other potentially influential subject characteristics (e.g., age, gender) in measurements of brain structure images is complicated and that "no single approach should be considered appropriate for all analyses."

Whether or not head size or other covariates of brain size should be controlled for depends upon the relevance of this covariation to the research question asked. When the correlation between head size and brain structure size is fundamental to the biological process under investigation, head size correction can potentially deprive the brain data of their essential meaning and may therefore be inappropriate. For example, head-size corrected magnetic resonance imaging (MRI) volumes may obscure the growth patterns of brain tissue types in children whose heads have not yet achieved adult size, whereas uncorrected (raw) MRI volumes preserve the essential maturational processes that drive both brain and head size growth. Raw scores may also provide an appropriate correlate of electrophysiologic measures such as evoked potentials, the amplitude or latency of which may be directly related to the absolute amount of tissue available to drive the response.

When the correlation between head size and brain structure size is irrelevant to the biological process under investigation, head size variation may act as a source of "noise" in the data. Furthermore, head size variation may confound brain structure comparisons across diagnostic groups, since sampling error alone may occasionally produce comparison groups that are nonequivalent with respect to head size. Thus, head size correction may remove irrelevant variance and guard against confounding of brain structure differences with head size differences in group comparisons. For example, adjusting MRI volumes for normal variation in adult head size may facilitate the detection of the effects of normal aging in the adult brain of healthy subjects. Moreover, head size corrected volumes, when further adjusted for the effects of normal aging, may improve the ability to detect brain volume abnormalities that may be present in certain disease states such as schizophrenia.

These presumed beneficial effects of head size correction were corroborated in our recent article (Mathalon et al., 1993). In this study, we replicated the finding reported by Arndt et al. (1991) that head size correction can reduce the reliability of brain imaging measurements by potentially increasing measurement error. However, we extended these findings by showing that head size correction can also reduce reliability by removing *irrelevant* "true score" variance. While increased measurement error would be expected to attenuate criterion validity, we demonstrated that removal of the irrelevant true score variance associated with head size can actually increase the criterion validity of structural brain measures even while lowering their reliability. Based on these results, we cautioned against the use of reliability coefficients to assess the relative merits of raw versus head size corrected measurements, or to choose among various methods of head size correction.

References

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