Eric Turkheimer[8] christened this the First Law of Behaviour Genetics over a decade ago. We also know that more accurate measurement produces higher estimates of genetic influence,[9] so I would have been amazed not to see the wide range of estimates this study produced. We know the estimate should not be 0 or 1.00, but what it should be in between is anybody's guess. Based on this study, I would not recommend following Kremen *et al*.'s[6] suggestion that we invest scarce research funding on a genome-wide association study of MCI.

The winter of my discontent with the state of MCI affairs is upon me. What can be done about that? The first step is clearly to come to better agreement on what MCI should represent. Should it be the lower end of the distribution of late-life cognitive function, in general, in any one specific area or in some particular number of specific areas? If either of the latter two, which area(s)? If the latter one, how many? And how far down the distribution? Or should it be a threshold of function level rather than a portion of the distribution? What level? Or should it represent change in function, regardless of level? How can this best be most economically/conveniently tapped, given that prior measures of function are not generally available when a patient presents with a concern about decline in cognitive function? And again, what areas of function and what levels of decline? The Kremen *et al*. study's[6] strongest message, to me at least, is that research surrounding MCI will not make much progress until these questions are addressed.

Conflict of interest: None declared.

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LETTER TO THE EDITOR

Authors' Response to: Commentary by Johnson *et al*.

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We respond here to a commentary by Johnson[1] on our article entitled 'Early identification and heritability of mild cognitive impairment'.[2] We believe that Johnson missed the point of the article. After criticizing much of the article, her own conclusions simply reiterate one of our main points, namely, that considerable study is still needed before we can be confident about a definition of mild cognitive impairment (MCI).

Johnson is experiencing 'discontent' about the state of MCI diagnoses, which she says is 'one messy concept'. She finds our results 'difficult to interpret', and wrote that our reported prevalence rates ranging from 2.57% to 64.74% are 'epidemiologically useless'. She stated that the wide range is due to different thresholds in 'very arbitrary' definitions as well as several generic problems inherent in cognitive assessment, one of which is our use of general cognitive ability to gauge decline, because people differ in their specific cognitive strengths and weaknesses. She was also critical of our reported heritability estimates ranging from 0.0 to 0.56, again suggesting that this reflects the imprecision of measurement of MCI. Finally, she disagrees with our suggestion that MCI is an appropriate phenotype for genome-wide association studies.

We think our approach and results were quite clear. The wide-ranging prevalence rates make one of the key points of our article, namely, that researchers and clinicians do not yet know what are the best cut points or the best set of tests. To model this lack of consensus on what constitutes impairment, our five criteria sets, based on published research,[3] intentionally went from extremely liberal to extremely conservative to reflect the full range of possibilities. Moreover, as we noted, there are similarly wide prevalence ranges across studies of older adults. Given that all current definitions of MCI have high false-positive rates, we also emphasized the point that none of the cross-sectional findings could be sufficient. Rather, we pointed out that determining the optimal criteria set would require longitudinal trajectories, and that it would be valuable to assess people earlier (in midlife) than has been done in almost all previous studies.

Regarding the point about using general cognitive ability to gauge decline, neuropsychologists are, of course, acutely aware of individual differences in cognitive profiles. Yet, routinely, estimates of general premorbid ability are used successfully to gauge whether or not a person's current performance represents a decline. Johnson's critique ignores the reality that this is the standard of care, and is currently the best that can be done in neuropsychiatric diagnosis and assessment. People still must be evaluated and decisions to treat or not still must be made even when we have less than perfect measurement tools and imprecise diagnoses.

Regarding the heritability estimates, Johnson cites Turkheimer's[4] proposition that essentially all human traits measured with some accuracy will be heritable, but as we pointed out, our results challenged previous studies that showed no heritability. Despite the well-known caveats Johnson enumerated about state effects, cognitive tests do consistently have moderate heritability and reasonable test-retest reliability compared with many other phenotypes. Also, the identical set of tests was used in all cases, so measurement precision did not differ across MCI definitions. Rather, as we pointed out, the variability of heritability estimates likely stems from the substantial differences in definitions of impairment. We did not state explicitly that genome-wide association studies should probably wait until there is more of a consensus on optimal MCI definitions, but we do think it was strongly implied by our clear emphasis on the fact that we are some distance from that consensus.

Johnson concludes with some recommendations. First she states that we need 'to come to better agreement on what MCI should represent', raising questions about how many cognitive domains should be included, how far down the distribution of functioning will meet the criteria, should it represent change in function rather than level, etc? The strongest message of our study, she says, is that MCI research will progress little until these questions are answered.We find it rather puzzling that she writes as if we ignored all of these issues in our article, and she questions the usefulness of our findings. We think that any reasonable reading of our article would indicate that we had already made many of the same points enumerated by Johnson in her commentary, and our analysis examining how heritability estimates vary as a function of different definitions of MCI is clearly germane to understanding what MCI represents.

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