Reviewer's report

Title: The impact of early life factors on cognitive function in old age. The Hordaland Health Study (HUSK).

Version: 1 Date: 17 May 2013

Reviewer: Jaana Halonen

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Manuscript Title: The impact of early life factors on cognitive function in old age. The Hordaland Health Study (HUSK)

This is an interesting study on the impact of early life circumstances on late life cognitive function. The Introduction is fluent and the study question is clearly defined and justified.

Major Compulsory Revisions

1. The methods are well described and appropriate; however, my concern is that the results are presented for unadjusted models, and that age and sex adjusted results are only briefly mentioned in the text. As the authors have stated in the Introduction, adjustments may well have effect on the findings (ref 23), thus, I would prefer seeing age and sex adjusted effect estimates in the tables. Other ways it should be well justified why crude models were used (or show results for both analyses).

2. Also, individuals’ own SES (e.g. measured by education) was not considered in the analyses although it seemed that it was requested from the HUSK participants at some point (under “Additional information – follow-up from HUSK at age 72-74”). Could the authors run sensitivity analyses adjusting for education and self-rated health?

3. Please provide more information about the statistical analyses performed, e.g. did the authors use logistic regression or what? In the "statistical analyses" paragraph it is only stated that: "Bivariate and age- and gender-adjusted associations were then investigated". (and non-adjusted results were reported in the tables)

Minor Essential Revisions

1. Has the z-scored composite cognitive scale (described just before “Context for the birth cohort”) been used elsewhere? If so, please provide a reference. If not, please explain why this would be a good outcome measure.

2. Table 2: in the top row authors could join “Mean” and “Standard deviation” as “Mean (SD)” and give explanation for SD in the footnote.
3. Also in Table 2, the familial characteristics could be presented in the same direction as in the results in Table 4, i.e.: Mother’s condition after birth (% good), Tuberculosis in family (% no), etc.

4. In Table 3 the title could state: “individual risk factors at birth” and in Table 4: “familial risk factors at birth”, or such, to make the difference between the exposures.

5. If presenting age and sex adjusted results in the tables, please indicate model adjustments in the footnotes.

6. In the second paragraph of the Results, please discuss the results of Table 3 before the results of Table 4.

7. In paragraph “Additional information – follow-up from HUSK at age 72-74” it was not clear to me where the data for APOE genotype was from. From HUSK records? When was the genotyping done?

8. The authors mention in the paragraph “Context for the birth cohort” that “three social classes began to dominate in Bergen during the same period”, but in the analyses only two social classes were used (lower/higher). So what is the meaning of this information of the context? Why was not three social classes used in these analyses?

9. In paragraph “Additional information – follow-up from HUSK at age 72-74”, the first sentence is a bit vague, perhaps reword it as: “As a crude assessment of potential demographic differences between the participants of this study and the rest of the HUSK participants, we were able to trace gender, self-reported level of educational attainment and general health from the HUSK records.”

(Were the data from records? When were these data collected?)

10. The Discussion part is also well written and relies on the presented results although in some places the statements are rather strong in regard of the consistency of the results.

For example, the last sentence of the first paragraph of Discussion could be modified as: “This highlights the importance of parental SES in relation to SOME specific domains of cognitive functioning in old age (20, 23), perhaps relatively independent of birth size (23), a notion which was confirmed ALSO in our study SAMPLE.”

In the last paragraph of Discussion the link between these sentences is vague: “…it is generally accepted that childhood SES is an important predictor for later cognitive function (10, 42), and cognitive reserve (40). Thus, it is possible that, even though anthropometric measures obtained at birth might predict cognitive function later in life…”

The first sentence tells about childhood SES and the second about anthropometric measures. Perhaps delete word “Thus”, or re-word the latter sentence with something like: “Even though anthropometric measures obtained
at birth did not predict cognitive function later in life in this study, it is possible that
other unmeasured factors mitigated these initial differences, and reduced or
eliminated their influence in later adult life."

11. In all places, please indicate to which direction the association is in
statements like:
Abstract “head circumference at birth predicted cognitive function”
page 14 “between higher parental SES (as measured by father’s occupation) and
global cognitive function in old age”
page 16 “Both of them seemed to predict cognitive function…”
–better or worse cognitive function?

Discretionary Revisions
1. The reference list seems good, but perhaps some other work not sited here
could also be checked:
Childhood living conditions, socioeconomic position in adulthood, and cognition
in later life: exploring the associations.
aging. (and references within)
2. In the Methods section of the abstract I was missing the definitions of the
exposures that are now presented in the Background section. Perhaps move the
sentence “we investigated the prospective associationS…” to be the second
sentence of the next paragraph.
3. Abstract: Authors could also mention that the outcomes were individually
analyzed, as results by individual scores are given.

Minor issues not for publication
1. Abstract: The first time “head circumference” is mentioned in the Results, it is
not clear that it refers to head circumference at birth.
2. In the paragraph “Modified version of the Digit Symbol Test (Digit Symbol)”: the
Digit Symbol Test measures perceptual and psychomotor speed, focused ON
attention
3. In the first paragraph of “Statistical analyses” the first sentence is lacking
definition “remainder” of what?
4. In the second paragraph of “Statistical analyses”: “Post-hoc analyses were
also performed to investigate WHETHER the effect of SES on cognitive function
WAS independent of anthropometric measures, as well as WHETHER the effect
of head circumference on cognitive function WAS independent of SES.”
5. In the second paragraph of the Results, please write open what is “SD” (in: by 0.25 SD)

6. The last paragraph of the Discussion: Other studies have ALSO found that social disadvantage and early life stressors are related to cognitive function in later life (10, 41).

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests.