Author's response to reviews

Title:A systematic review of the evidence that brain structure is related to muscle structure and their relationship to brain and muscle function in humans over the lifecourse

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Author's response to reviews: see over
Dear Editor of BMC Geriatrics,

We are pleased to submit a revised version of our article entitled, “A systematic review of the evidence that brain structure is related to muscle structure and their relationship to brain and muscle function in humans over the lifecourse”.

We thank the Reviewers for their useful comments, which we have addressed below. The most considerable addition to the review was updating the search. This was performed on 6th March 2014, which added a further 4167 articles to be screened, with 29 articles added to the review itself.

We hope you feel these changes make a much improved article and look forward to hearing from you in due course.

Thank you for your ongoing input.

Yours faithfully,

Dr Alixe HM Kilgour

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Reviewer 1's report

Title:

A systematic review of the evidence that brain structure is related to muscle structure or function or that brain function is related to muscle structure in humans.

Version: 1
Date: 13 December 2013
Reviewer: Xiaowei Song
Reviewer's report:

The objective of this article is to review evidence on brain-muscle relations in humans with healthy ageing. The authors conducted a literature searched using several major databases including the Medline on November 30th 2011, supplemented by citation searches. The review is made based on a final set of 55 original research records published between 1994 and 2011.

Overall, it can potentially be an interesting paper that provides novel information to better understanding possible associative and/or predictive relationships between brain structure (e.g., total volume, white matter hyperintensity, frontal gray matter volume) and muscular structure and function (e.g., lean mass, gait speed, grip strength). The work can potentially contribute to the body of the literature on ageing and would be of some interests of the BMC readers.

However, the current version of the manuscript needs much work. My concerns are listed below.

Major

1. If the paper is to review evidence on brain-muscle relations in ageing, it needs to be focused more on searching for relevant evidence, instead of proving proof of specific hypotheses as stated in the paper. There exist different theories and hypotheses on how we age and why people vary in the process of ageing. The proposed hypothesis may serve as one explanation to interpret the research findings. Alternatively, other hypotheses may also be applicable (e.g., refer a most recent paper by Mitnitski et al Biogerontology 2013 Dec;14(6):709-17: Biological ageing at the system level can be expressed by deficit accumulation in multiple organ systems, reflecting the reduction in the pace of the recovery).

We thank the reviewer for this useful comment. We now include several potential hypotheses as to why brain and muscle may change in tandem over the lifespan in our introduction. We hope this has added to our introduction section to provide a carefully reasoned argument for the review. Naturally, the purpose of performing a systematic review, and including all evidence found by our extensive search, is to ensure that results are not selected eclectically to support any particular theory.

2. If the paper is to review evidence on brain-muscle relations, then the results should be presented around this. This is not the case in the manuscript, For example, the contents in the first two paragraphs of the Results section did not report any results.
Thank you for this useful comment. We have now removed the section on contacting the authors from here and put it in the methods section. This has left a small paragraph detailing the main outcome of the literature search in terms of numbers of studies identified. We feel this is necessary here. The following three large subsections go on to detail the evidence we found.

3. In fact, portions of the data reported here were produced by the authors of the present article, through analyzing data of the original studies under this review. In this regard, it is difficult to tell whether the current manuscript is more like a secondary analysis study or a systematic literature review as it is claimed to be.

We thank you for this useful comment. The topic of this paper has not been subject to systematic review previously and as such we were unsure at the start of the review how much literature we would find. We therefore decided to include studies which contained the data we were looking for without the associations to ensure we had a yield of papers we could examine. We feel this was the correct thing to do, as for example, in the section examining studies which included a measure of brain function and muscle structure, we could only have included 2 studies if we had relied on studies including the associations we were looking for [1, 2] and we were able to increase this to 14 studies. We have clearly detailed in our results section and in the tables whether the associations were: a) included in the original study; b) given to us by the authors on request; or c) calculated by us using raw data supplied by the authors. The studies we included which did not contain the associations in their original paper, were found using the same systematic literature search and underwent the same inclusion and exclusion criteria and review of methodology. Also, the majority of the papers included in the review had relevant associations included in the original paper: 38 out of 53 papers (72%).

Minor

1. The title of this article is too long and difficult to follow. It also did not directly address the key points of the article, e.g., “with ageing”, “for changes”, and “limited evidence”.

Thank you for this comment. We have now changed the title to, “A systematic review of the evidence that brain structure is related to muscle structure and their relationship to brain and muscle function in humans over the lifecourse”. Most of the data in the review is cross-sectional and the subjects now cover a wide age range, albeit mainly in the older spectrum (please see point 4 on the next page), and we feel the new title accurately reflects the content of the review.

2. The literature under review is not up to date (i.e., by 2011). An update for including publications during the past couple of years from 2011 to 2013 is required.

Many thanks for this input. We have now updated the search (on 6th March 2014) which retrieved a further 4167 articles which were longlisted and then shortlisted. This led to a further 29 articles being included in the review which is now up to date. The paper thus provides a comprehensive systematic review which is up-to-date and will be, we think, exceedingly helpful to researchers in the field.

3. Tables 2-4 need to have more sensible titles (e.g., “sent” does not make sense).
We have changed the titles in the tables so that they are clearer and have added a legend under the table.

4. It was stated in the article, “This systematic review identified studies ... in healthy children and adults”, but the article is basically on ageing and most of the research articles under this review involved older adults, i.e., with a mean age of ~70 years.

Many thanks for this useful comment. In our systematic review protocol we included children and young people and it was our intention to include all articles we found using our search protocol whatever the age of the subjects. Whilst indeed most of the articles identified include older subjects there are studies looking at children and young people (ie under 50y) also (eg Bove et al mean age 31.6y [12]; Chowdhury mean age 35y [9]; FITKids mean age 8.8y [7, 8]; Hardan et al mean age 18.6y [5]; Heymsfield et al mean age male 45.1y, female 38.6y [3]; Magri et al mean age 33.3y [6]; Masley et al mean age 43.5y [13]); Schwartz et al mean age male 14.9y, female 15.1y [11]; Sullivan et al mean age 45.2y [10]; and Weise et al mean age 32.1y [4]).

5. Result presentation needs to be better structured, emphasizing key findings and also balancing weights for various sections. Summarized the main findings using figure/tables may also help.

Thank you for this comment. We have now added four tables to help summarise the main findings and show the size of the studies involved. We think this has improved the interpretability of the results section. Please see table 6, 7, 8 and 9. In addition we have largely rewritten our results section.

6. Conclusions drawn in the paper did not seem to have properly wrapped up the review. Conclusions and the major findings sometimes contradicted each other.

For example, “There exists only limited evidence about the relationship between brain structure and muscle structure” versus “Relationships between brain structure and physical function are well documented.”

Thank you for this comment. We have now completely rewritten our conclusion to make it an accurate reflection of the results of the review. We hope you find it much improved.
Reviewer 2's report

Title:

A systematic review of the evidence that brain structure is related to muscle structure or function or that brain function is related to muscle structure in humans.

Version: 1
Date: 24 January 2014
Reviewer: Laura E Middleton
Reviewer's report:

You undertake a broad review of muscle function/structure and brain function/structure. While the topics are each individually interesting, together the result is a bit unwieldy and projects as a list of studies rather than a cohesive review. The topics may be better served in 2-3 papers rather than amassed into one.

We thank the reviewer for this comment. We agree that the review is large, however we feel it is important that the topics are reviewed as one, to enable the reader to see the differences and parallels in the associations between structure and function. One of the major advantages of submitting it to BMC Geriatrics is that the electronic format facilitates the handling of such comprehensive reviews allowing readers to open separate windows for Tables etc.

Major Compulsory Revisions:

1. The results, discussion, and conclusion are largely repetitive with increasing levels of summary. Discussion could include the proposed mechanisms or explanations (e.g. common cause hypothesis as introduced earlier) among other points. This may also increase the interest in this paper dramatically.

Thank you for this comment. We have now extensively reviewed our results and discussion sections and have included further details on possible underlying mechanisms and possible explanatory theories for associations that were found to be significant and some for those that were not also.

Discretionary Revisions

2. The introduction seems relatively unrelated to the rest of the content of the paper. I suggest either altering the introduction so that others reasons to be interested in the brain/muscle relationship are mentioned OR at least touching back on the topic of the introduction later in the paper.

Thank you for this comment. We have now adapted out introduction to include several theories on the possible mechanisms underlying the relationship between brain and muscle. We hope you feel this has improved this section.


