Reviewer's report

Title: Effects of computerized cognitive training on neuroimaging outcomes in older adults: A systematic review

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Reviewer: Kirsten Hoetting

Reviewer's report:

This review summarized neuroimaging studies examining the effects of computerized cognitive trainings on brain structure and function in older adults. This is a contemporary issue and fits well into the scope of BMC Geriatrics. The literature search and the rating of the included studies are well documented. I agree with the conclusion that the large variability of the studies, with regard to training and assessment parameters, makes it almost impossible to draw any general conclusions. Therefore, more high quality studies are needed in this field. However, I have some concerns that should be addressed by the authors.

Introduction:

The terms "dementia" and "cognitive decline" should be differentiated, as cognitive decline in old age is not necessarily a prodromal phase of dementia. The outcomes of the studies summarized in the review are cognitive scores (not the incidence of dementia) and functional and structural brain changes within the "normal range" (not dementia associated pathologies).

The term "computerized cognitive training" should be defined more precisely. What are characteristics of these trainings? What are distinctions to other kinds of cognitive training? See also my point "selection of studies".

The discussion about transfers to other, non-trained cognitive functions and daily living abilities should be mentioned at least shortly.

Page 6: "To date, it is not well established how CCT impacts regional brain volume, functional activity, and functional or structural connectivity." This might be true for computer-based trainings in older populations (the scope of this review). However, there are studies on the neuronal effects of computerized cognitive trainings in younger age groups and for non-computerized trainings, for example the work of Klingberg and others on working memory training, but also in further cognitive domains (reviewed, for example, in Lövden et al., 2013, Park & Bischof, 2014). These previous studies gave important insights into the neuronal mechanisms of cognitive trainings in general. Therefore, their main results and open questions should be mentioned in the introduction.
Selection of studies:

The paper focuses on computer-based trainings with neuroimaging results in adults aged 55 and older. Given these selection criteria, I am aware of at least two further studies that were not included:

Dahlin et al., Science 2008, computer-based training, single-domain, fMRI, older healthy adults, results were reported separately for younger and older participants, randomized. Although presented in the short format of "Science", all relevant information is available in the supplementary material.

Erickson et al., Neurobiology of Aging, 2006, computer-based training, executive functions, fMRI, older healthy adults, results were reported separately for younger and older participants, randomized.

Moreover, the following studies used computer-based cognitive trainings in older adults and reported neuroimaging results, although the setup was not a typical desktop computer setting:


Mozolic et al., Front Hum Neurosci, 2010.

Quality of studies:

As mentioned on page 19, the quality of the studies varied substantially. The authors systematically assessed and discussed study quality (reported in table 4). I would stress these criteria already when reporting the results and would refrain from interpreting results of studies without random group assignment at all (see also Thomas & Baker, 2012, NeuroImage for a critical discussion of methodological issues in structural MRI studies). I would prefer lowering the inclusion criteria with respect to "computer-based" (see point "selection of studies"), but include randomized studies only.

P10: Subtitle "Volumetric structural imaging": The term "Structural imaging" might be more appropriate, as not only gray matter volume, but also cortical thickness data were reported.

P 10: "However, in the same study they found that cognitive training alone led to atrophy in the posterior cingulated cortex". Suo et al. reported that participants in the CCT training group showed a decrease in cortical thickness in the posterior cingulated cortex compared to a combined physical exercise and cognitive training group. There was no difference between the CCT and a control group. Thus, the results suggest that a combined physical exercise and
cognitive training might delay age-related decline in cortical thickness, but it does not suggest that a CCT induce any atrophy.

Discussion:

Interpretation of differences between studies: the authors claim on page 21 and 22 that differences in functional activation patterns might be explained by multi-domain vs. single domain CCT. Although this is an interesting point, the studies differ with respect to many other variables like training duration, frequency and cognitive domain. Moreover, the conclusion is based on only four studies (2 multi-domain vs. 2 single domain) making it hard to related differences in activation patterns to these characteristics.

Patterns of decreases and increases in functional brain activations and connectivity after trainings are a common finding in neuroimaging studies and possible interpretations have been put forward (e.g. Lustig et al., 2009). Referring to these accounts might help interpreting the diverse findings.

Summarizing more general changes in brain activation patterns and structural connectivity with age and cognitive decline might help the reader to integrate the results (as has been done for functional connectivity on page 24). Moreover, there is literature on neuroimaging effects after cognitive trainings in younger adults. The interpretation of results might benefit from these findings.

Page 26: The term "quasi-experimental design" should be defined more precisely. The lack of blinding and the lack of a control group are not the defining characteristics of a quasi-experiment. Instead, the lack of a proper randomization into a treatment and control group is the main reason for the reduced internal validity of a quasi-experiment compared to a true experiment.

Last paragraph: I agree that there is still a lack of knowledge about the underlying mechanisms of training-induced plasticity in humans and indeed, there is a missing link between histological findings in animals and neuroimaging in humans. However, the present conclusion gives the impression that there is hardly any knowledge about these issues. Animal studies on training-induced plasticity point to the involvement of synaptogenesis, dendritic branching, hippocampal neurogenesis and changes in glia cells and vasculature. Moreover, attempts have been made to link these findings to neuroimaging results in humans (e.g. Zatorre et al., 2012). These findings should be acknowledged (maybe not in the last paragraph but in the discussion of the paper).

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes
Does the work include the necessary controls?
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Unable to assess

Are the conclusions drawn adequately supported by the data shown?
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