Reviewer's report

**Title:** Very long-term effects of cranial irradiation compared with intrathecal chemotherapy in treatment of childhood leukemia: A MEG study of brain oscillatory power differences correlated with cognitive dysfunction

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**Reviewer:** Markus Butz

**Reviewer's report:**

In their work “Very long-term effects of cranial irradiation compared with intrathecal chemotherapy in treatment of childhood leukemia: A MEG study of brain oscillatory power differences and correlated cognitive dysfunction” Daams and colleagues report findings on very long-term changes in oscillatory activity following two different treatments of lymphoblastic leukemia in childhood age. Results show that the two different treatment options result in different oscillatory activity patterns. While the one option leads to severe changes which correlate with substantial deficits in cognitive performance the other is rather close to healthy controls. Results shed further light on the changes in oscillatory activity associated with pathology and limitations of the study are substantially discussed.

In general, I do see the research efforts on this patient population to be both highly relevant and important for the affected patients. Moreover, data from these patient populations offer interesting resources for our understanding of brain oscillations and brain pathology in general.

The question posed by the authors is clear although it might be a bit too enthusiastic. The methods used are appropriate and well describe. They are basic standard procedures used in the field. Data are sound and the manuscript largely adheres to the relevant standards for reporting and data deposition. The language is adequate.

**Major Compulsory Revisions:**

1.) Why did the authors subdivide the alpha band into #1 and #2? The intention of this approach stays vague as they stick to the traditional frequency bands in all other frequency bands. The authors need to substantiate their rationale, especially as main findings are affected by this approach.

2.) In the abstract the authors state that they study the underlying mechanisms of late neurocognitive deficiencies. This statement seems a little bit too ambitious as solely correlations between neurocognitive testing and oscillatory activity are reported which must not necessarily stand for causality. Moreover, correlation might potentially just reflect a side effect or a confound rather than a mechanism.

In addition, I wonder, if it would not be more appropriate to use age as a covariate in the entire analysis rather than only in parts of the analysis?
3.) The authors need to correct for multiple comparisons in the correlation/regression analyses.

4.) The discussion is quite limited. It would significantly profit from a more intensive integration of the present findings in the existing literature of changes of oscillatory activity in pathology. Moreover, the different results for the different frequency bands and the different brain regions need to be discussed. The authors should try to explain why changes appear in only a minority of frequency bands while oscillatory activity in other frequency bands seems to be not affected.

Minor Essential Revisions:

1.) The authors should state how long patients were recorded in the MEG. This information is missing.

2.) The hypothesis of the study at the end of the introduction is not very well integrated in the entire section and can be rephrased more elegantly.

3.) The authors state that they used the two different sample frequencies as covariates. Is this really necessary? Would it not be easier to simply downsample the higher sample frequency data to the lower sample frequency? I cannot think of any effect the sample frequency might have on the reported findings.

4.) On page 7 the authors state that “It seems like the right hemisphere is more affected”. As there is no significant difference between both hemispheres this statement is kind of odd.

Also the statement in the abstract “did not deviate much” is too imprecise.

Discretionary Revisions:

1.) The title is rather long and complicated. The authors might consider to shorten it.

2.) The expression “magnetic induction fields within the brain” sounds a bit odd. The authors might consider to rephrase this chapter.

3.) The description of statistical analyses in the method section might already state that all data was log transformed for the sake of simplicity and clarity.

4.) Fig. 2: Significant differences might be marked by asterisks.

5.) All Figure legends can be more informative.

Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests.