In the current report Tohda and collaborators, indicate that two water extracts of *Eleutherococcus senticosus* leaf and rhizome of *Drynaria fortunei* enhance cognitive function according to the results from a placebo-controlled, randomized, double-blind study in healthy adults. The design of the current study is correct and results are interesting and similar to another recent study performed from the same authors regarding the enhancement of cognitive function in healthy adults following treatment with Diosgenin-Rich extracts. However, some parts of the manuscript need to be addressed.

**Introduction**

Introduction is generally well written although is relatively short; however, a small paragraph should be devoted to the description of molecular mechanisms of both water extracts activity, that have been used against some pathological conditions, as indicated by the authors. Moreover, authors could indicate some other examples of natural derived compounds with similar abilities in terms of cognitive improvement in healthy adults.

In addition, authors indicate that according to a recent patent (#JP6165380) simultaneous treatment of ES and DR extracts synergistically improved memory dysfunction in 5XFAD mice. However a reference is missing and should be added.

**Materials and Methods**

2.2 Participants

Line 88: …being inappropriate by other reasons: Which ones? Please state them

2.3 Intervention

Lines 101-102: Was the intake dose determined in both cases by animal studies, or that was only the case for DR extracts? Please provide more detailed informations

2.4/2.5/2.6

In all three sections, text is quite similar with the respective sections of a recent publication from the same group "Diosgenin-Rich Yam Extract Enhances Cognitive Function: A Placebo-
Controlled, Randomized, Double-Blind, Crossover Study of Healthy Adults.” I recommend that authors should re-phrase the respective sections.

2.7. Randomization

Line 128: …by a third party: Which one? Please state

3. Results

Lines 136-138 should be removed

3.1 Baseline characteristics of the study design

Although it is indicated that sociodemographic and baseline characteristics included IQ values in the Materials and Methods section, they are missing in Table 1 and should be added.

3.2 Neurophysiological functioning

Authors should indicate at least in the first appearance in the manuscript the meaning of the “95% CI” value present in different tables as well as the difference between comparison of pre and post treatments and that of intragroup comparison, in order to be more comprehensive to the readers.

Moreover in Table 2, according to the respective values ”language” was increased significantly but an asterisk is missing in the “Intragroup comparison” and should be added

In addition in Lines 162-163, it is indicated that intergroup comparison showed no significant changes in all items, but in Table 4 there is an asterisk with value of 0.022. Was that a mistake?

3.3 Safety measures

Line 177: According to the respective values, HDL-cholesterol was also significantly reduced and should be added.
To Referee 3

1) About active compounds acting in the brain and their molecular mechanisms are already written in Introduction and Discussion (lines 549 – 56, 62 – 67, 246 – 257). In addition, other similar our study has been mentioned (lines 2630 – 262) and cited as reference #16.

2) Thank you for very important comments. We already cited the patent information in lines 275 - 276, because it’s not like a paper, but searchable in a patent platform by the registry number.

3) In 2.2 Participants, “(d) subjects judged being inappropriate by other reasons” has been deleted, because no subject was judged as like this.

4) Effective minimum doses and best combination of doses had been determined by our animal studies. This has been added in lines 115 – 116.

5) We have tried to re-phrase sections 2.4/2.5/2.6. However, those parts are just definitions and simple explanations of used tests. Therefore, it is difficult to re-word. Since we used identical tests previous we used, so similar explanations are not avoided.

6) Thank you for very important comments. Randomization procedure has been added in lines 146 – 147.

7) Previous unnecessary sentences line 136 – 138 has been removed.

8) IQs have been added in Table 1. Assumed IQs were not also significantly different between groups. Since averaged IQ in Japanese is around 100, subjects in this study have normal level of intelligence. This mention was added in lines 164 – 166.

9) 95% CI has been explained in line 150 – 152.

10) We confirmed asterisks in Table 4.

11) Thank you for your correct comment. We added a description of HDL-cholesterol in line 216.