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Letter to the Editor

Response to Letter to the Editor: "Plasma β-amyloid1–42 reference values"

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1. Response

We thank Dr. Kawada for the interest for our work and the thorough observations [1]. We are pleased to provide further comments to the main conclusions provided by Dr. Kawada that validation study on cutoff value should be conducted by further studies.

In our study, we focused on quantitative measurement of β-Amyloid 1–42 ($A\beta_{1-42}$) in plasma samples of cognitively normal subjects, adopting appropriate procedures according to the guidelines C28A3 of the Clinical and Laboratory Standards Institute (CLSI) [2]. We considered this work as the first step in the process of validation of biomarkers for the diagnosis of Alzheimer's disease (AD) and other forms of dementia. Certainly, we investigated a critical question on the clinical utility of plasma biomarkers of AD.

In our opinion, the levels of $A\beta_{1-42}$ in plasma can be considered a promising blood-based biomarker for dementia with underlying AD pathology. Several studies investigated recently if circulating levels of Aβ could potentially be used as markers of disease risk. Hilal et al. [3] analyzed plasma Aβ levels in 458 individuals from the Rotterdam Study, a prospective population-based study. Their results showed that lower plasma Aβ levels were associated with risk of dementia and incident AD. Moreover, lower plasma Aβ1–42 levels were associated to smaller hippocampal volume, suggesting that plasma $A\beta_{1-42}$, and the novel Aβ peptide 1–38 ($A\beta_{1-38}$) may be useful biomarkers for the identification of individuals at risk of clinical dementia.

In another study, Verberk et al. [4] evaluated the association of plasma Aβ ($A\beta_{1-40}$, $A\beta_{1-42}$) and total tau (tTau) with the presence of Alzheimer's pathological changes in cognitively normal individuals with subjective cognitive decline (SCD). They included 248 subjects with SCD (61 ± 9 yrs., 42%F, 28 ± 2 MMSE) from the SCIENCe project and Amsterdam Dementia Cohort. Plasma $A\beta_{1-42}/A\beta_{1-40}$ ratio has been revealed a potential as useful marker to identify Alzheimer's pathological changes detected with positron emission tomography (PET) in cognitively normal individuals with SCD. For the authors, a blood-marker for Aβ becomes feasible to improve the diagnostic process both in a trial setting where individuals with the earliest AD pathological changes are recruited and also in a clinical primary care setting.

However, we agree with Dr. Kawada about the fact that a validation study on cutoff value should be conducted. The overall data in literature are in some way contradictory and not easily comparable [5]. The existing variability between studies is largely due to the lack of standardization and harmonization of pre-analytic and analytic methods and also to the absence of reference values for appropriate comparison. It would be useful to compare $A\beta_{1-42}$ plasma levels in patients and controls, for a better interpretation of the results and for a better applicability in different clinical settings. Further studies are therefore needed to confirm the real contribution of reference values to the interpretation of laboratory results of $A\beta_{1-42}$ plasma concentrations and to better define their value in medical decision-making with the aim of building biomarker models of AD that combine Aβ status with additional relevant factors and to have an appropriate diagnosis.

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References

[1] C. Zecca, R. Tortelli, F. Panza, et al., Plasma β-amyloid1-42 reference values in cognitively normal subjects, J. Neurol. Sci. 391 (2018) 120–126.
[2] CLSI and IFCC, C28-A3 Document, Defining, Establishing and Verifying Reference Intervals in the Clinical Laboratory: Approved Guideline, 3rd ed., Vol. 28 (2008), pp. 1–76.
[3] S. Hilal, F.J. Wolters, M.M. Verbeek, et al., Plasma amyloid-β levels, cerebral atrophy and risk of dementia: a population-based study, Alzheimers Res. Ther. 10 (1) (2018) 63.
[4] I.M.W. Verberk, R.E. Slot, S.C.J. Verfaillie, et al., Plasma Amyloid as Prescreener for the Earliest Alzheimer Pathological changes, Ann. Neurol. (2018), https://doi.org/10.1002/ana.25334 (Epub ahead of print).
[5] A. Koyama, O.I. Okereke, T. Yang, et al., Plasma Amyloid- β as a predictor of dementia and cognitive decline: a systematic review and meta-analysis, Arch. Neurol. 69 (2012) 824–831.

Abbreviations: Aβ, Amyloid β; AD, Alzheimer's disease; $A\beta_{1-42}$, β-$Amyloid_{1-42}$; Aβ1–40, β-$Amyloid_{1-40}$; Aβ1–38, β-$Amyloid_{1-38}$; PET, Positron Emission Tomography; SCD, Subjective Cognitive Decline

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