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Plasma amyloid- β is associated with suicidal ideation in older adults: a 15-year follow-up study

INTRODUCTION

Suicide rates in older adults surpass those of other age groups,¹ making suicide a major societal problem in this population. Suicidal ideation (SI) and attempts may be related to increased amyloid burden in non-demented individuals, in addition to psychosocial stress factors. While traditionally associated with Alzheimer's disease, amyloid deposits were recently identified in the frontal and occipital cortex of suicide victims.² They have also been reported to be more frequent in cases of depression,³ although recent contradictory results show reduced A β deposition in depressed older adults compared with cognitively normal non-depressed individuals.⁴ Reflecting the amyloid load in brain, lower A β 42/A β 40 ratio in plasma was associated with depression and with its severity in cognitively normal older adults against healthy controls, after controlling for cognitive performances in a prospective study.⁵ In turn, depressive symptoms may contribute to the emergence of SI and increased suicide risk. A better insight into the role of amyloid-A β peptides on SI may help clinicians to prevent suicidal behaviour. We hypothesise that plasma A β

peptide alterations are associated with the incidence of SI in non-demented older adults.

We used data from the prospective Enquête de Santé Psychologique – Risques, Incidence et Traitement (ESPRIT) cohort to examine the association between plasma A β 42 and A β 40 concentrations, and A β 42/A β 40 ratio, and the incidence of SI over a 15-year follow-up period in older adults. The possible role of late-life depression (LLD) in this association was studied. We also explored the association between plasma A β peptide concentration and the incidence of LLD over time.

METHODS

Data were obtained from the longitudinal ESPRIT study of neuropsychiatric disorders in community-dwelling French older adults aged 65 years and older, part of the 3C multicentre study. Standardised interviews were administered at baseline and at years 2, 4, 8, 10, 12 and 15 of the follow-up. From the 2268 participants recruited, 310 subjects were randomly selected for plasma A β concentration measurement at baseline and were free of dementia. After excluding participants diagnosed with SI at baseline and those without follow-up visits, we analysed the association between plasma A β and the incidence of SI in the 223 remaining

participants. The association between baseline plasma A β and the incidence of LLD was examined in 235 individuals, excluding those with a history of depression and without follow-up visits (online supplemental figure 1). The presence of passive or active SI in the last month was assessed at baseline and at each follow-up visit using the MINI-international Neuropsychiatry Interview (Mini 5.00), based on the Diagnostic and Statistical Manual of Mental Disorders (DSM-4) criteria. LLD was recorded on a positive response to (1) acute major depressive episode (MINI); (2) Centre for Epidemiologic Studies-Depression Scale score ≥ 16 and/or (3) antidepressant intake at each visit. Detailed procedures are provided in online supplemental material.

RESULTS

After a median follow-up of 9.7 years, 42 (18.8%) of the 223 participants reported SI. They showed more frequent LLD and were more frequently treated with selective serotonin reuptake inhibitors (SSRI) than individuals reporting no SI. Other baseline clinical characteristics were not statistically different between groups (online supplemental table 1). The baseline A β 42/A β 40 ratio, categorised into tertiles, was associated with a higher risk of SI, particularly for individuals in the

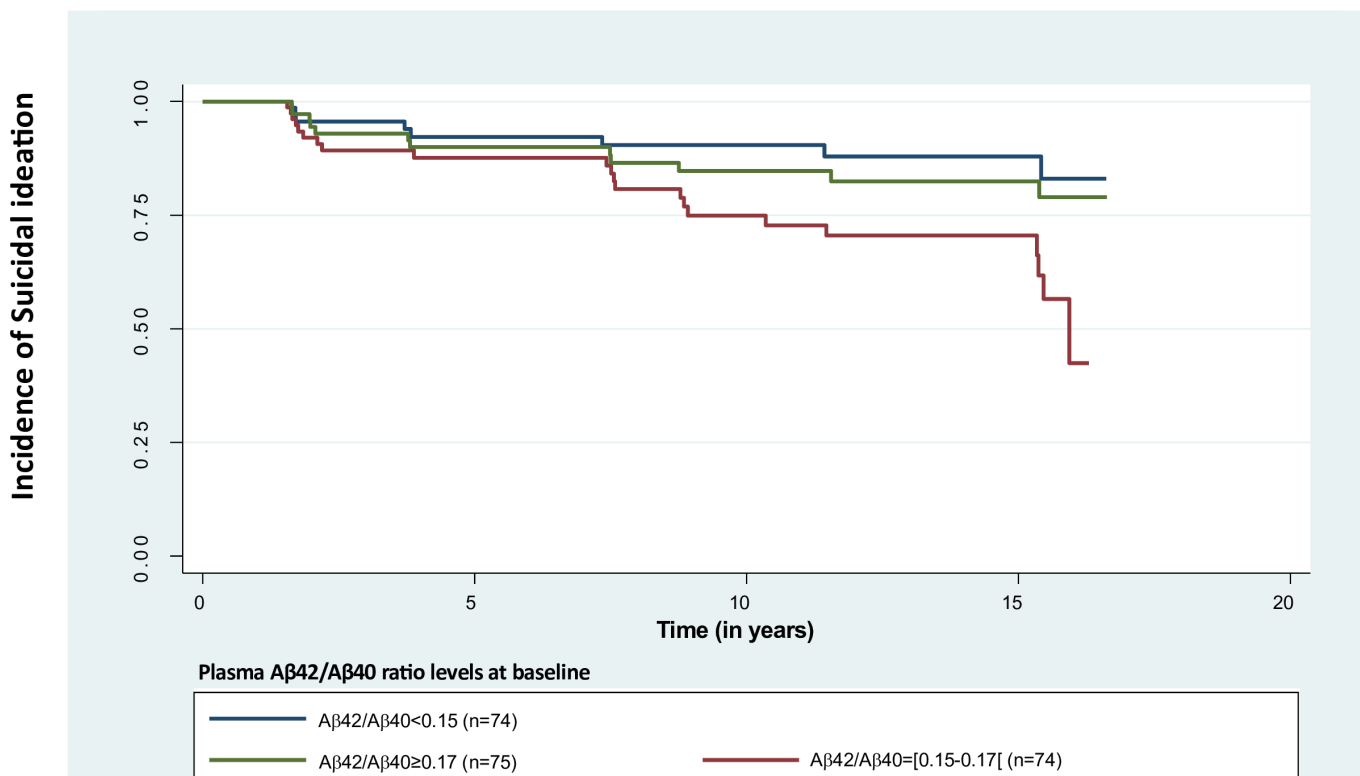


Figure 1 Incidence of suicidal ideation according to plasma A β 42/A β 40 ratio levels at baseline.

middle tertile. This association remained significant even after adjustment for LLD (model 2: HR 2.83 (95% CI 1.24 to 6.45), $p=0.03$), and in sensitivity analyses after excluding individuals taking SSRI or cases of incident dementia (figure 1, online supplemental tables 2–4). The A β 42/A β 40 ratio considered as continuous was not associated with SI incidence. Likewise, no significant associations were found between A β 42 or A β 40 considered separately and the incidence of SI.

Among the 235 non-depressed participants at baseline, 42 (17.9%) reported an LLD over the follow-up period. No association was observed between A β 42, A β 40 or the A β 42/A β 40 ratio at baseline, and the incidence of LLD (online supplemental table 5).

DISCUSSION

In this long-term cohort of older adults, we highlighted an association between plasma A β 42/A β 40 ratio and subsequent SI over a 15-year period, independently of dementia and LLD. This relationship was not linear, as the individuals in the middle tertile were more likely to report SI compared with those in the lower tertile. Our results may have arisen from the selection of cognitively normal participants, less likely to show severe neurodegeneration compared with demented individuals. Non-linear association patterns may account for the absence of relationship between the A β 42/A β 40 ratio when considered as continuous and SI.

We did not find any association between A β 42 and A β 40 considered separately and SI, suggesting that A β 42/A β 40 ratio may be a more sensitive marker of amyloid dynamics in plasma as reported in a prior study.⁵ Furthermore, the absence of relationship between plasma A β concentrations and incident LLD over the 15-year follow-up may potentially result in the restricted sample size as we focused on incident LLD and excluded individuals showing depression with enlarged definition at baseline. The link between depression and A β remains controversial, as decreased brain amyloid deposition, was recently reported in depressed older adults.⁴


A limitation of our study is that we performed a single measurement of A β . However, possible confounding factors were taken into account in the analysis, including SSRI intake, the educational level, living alone or blood creatinine level at baseline. The income level was not included in the model due to its collinearity with the educational level nor the

diagnosis of mild cognitive impairment. Nonetheless, MMSE scores were not associated with SI.

While we showed a strong relationship between amyloid-A β and SI, the association may have been minimised as we excluded institutionalised people at baseline, who are more likely to report incident SI, and suicide deaths following the surge of SI were not recorded. Future studies should confirm the results using more sensitive measures of peripheral A β and also in the CSF.

CONCLUSION

This study highlights an association between A β 42/A β 40 ratio in plasma and the occurrence of SI in late life, independently of depression and dementia. These findings, supporting possible age-related biological pathways underlying suicide, could be of interest for early detection of suicidal risk in older adults as this plasmatic marker is easily accessible.

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