Associations between behavioral factors and Alzheimer’s pathology: Findings from cognitively normal older adults at risk of AD and presymptomatic ADAD mutation carriers

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BACKGROUND AND OBJECTIVES
Cognitive lifestyle factors (e.g., education, cognitive activity) and neuropsychiatric factors (NPF) (e.g., anxiety, depression) are associated with an increased risk of sporadic Alzheimer’s disease (AD) (Lingvist et al., 2017). Recent evidence also linked personality traits with progression to dementia (Terracciano et al., 2017). The relationships between those factors and AD pathology still remain to be understood better, both in the preclinical phases of sporadic AD and of autosomal dominant AD (ADAD). We investigated whether combinations of cognitive lifestyle, NPF & personality traits are related to AD pathology (amyloid [Aβ] and tau deposition) in cognitively normal older adults at risk of sporadic AD, and to Aβ deposition in presymptomatic ADAD mutation carriers.

METHODS - PARIAL LEAST SQUARES ANALYSIS

PARTICIPANTS

SUVR, sporadic AD, and to Aβ deposition in presymptomatic ADAD mutation carriers. The relationships between those factors and AD pathology still remain to be understood better, both in the preclinical phases of sporadic AD and of autosomal dominant AD (ADAD). We investigated whether combinations of cognitive lifestyle, NPF & personality traits are related to AD pathology (amyloid [Aβ] and tau deposition) in cognitively normal older adults at risk of sporadic AD, and to Aβ deposition in presymptomatic ADAD mutation carriers.

Participants
- 111 asymptomatic older adults with a family history of AD
- 117 presymptomatic ADAD mutation carriers

Behavioral factors
- Big5 Inventory (John et al., 1991)
  - Neuroticism
  - Extraversion
  - Agreeableness
  - Conscientiousness
  - Openness

Neuropsychiatric factors
- Geriatric depression scale (Yesavage et al., 1983)
- Geriatric anxiety inventory (Folstein et al., 1981)
- Neuroticism

Cognitive lifestyle
- Years of education
- Lifetime Cognitive activity (Wilson et al., 2002)
- Social isolation (Donald & Ware, 1984)

PET imaging
- Aβ ([18F]NAV4694
  (ref. region: cerebellum GM)
  ([18F]AV1451
  (ref. region: whole cerebellum)

 tau
- florbetapir - [18F]AV1451
  (ref. region: interior cerebellum GM)

Standardized uptake value ratio (SUVR) were extracted in regions from the FreeSurfer Desikan atlas

ANALYTICAL METHODS

A multivariate approach, Partial Least Squares (PLS) analyses was used to evaluate the relationship between personality traits, NPF and cognitive lifestyle (behavioral factors) with AD pathology (Aβ and tau in PREVENT-AD; Aβ in DIAN).

Permutation tests were used to assess the significance of the latent variables derived from the PLS. For each behavioral factor, confidence intervals were derived from bootstrapping. For AD pathology, the top 10 regions contributing to the relationship are displayed.

Exploratory analyses were also run in DIAN taking advantage of the more fine-grained personality assessment, the NEO-IPPI having 30 subscores of personality facets. For comparison purposes, a PLS was also performed on 127 DIAN mutation non-carriers.

CONCLUSIONS

Our multivariate approach revealed that both in individuals at risk of sporadic AD and in the presymptomatic phase of ADAD, combinations of different behavioral factors are associated with AD pathology.

Personality traits and NPF seem to be more related to Aβ, while personality traits and cognitive lifestyle are more related to tau in preclinical sporadic AD.

In the preclinical phase of ADAD, mostly cognitive reserve-related factors (education and intellect facet of personality) and NPF seem to influence Aβ.

Longitudinal evaluations will clarify whether such factors are drivers, consequences of accumulating AD pathology, or both.