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Neuroticism, depression, and anxiety traits exacerbate the state of cognitive impairment and hippocampal vulnerability to Alzheimer's disease

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Abstract

Introduction: Certain personality traits are associated with higher risk of Alzheimer's disease, similar to cognitive impairment. The identification of biological markers associated with personality in mild cognitive impairment could advance the early detection of Alzheimer's disease.
Methods: We used hierarchical multivariate linear models to quantify the interaction between personality traits, state of cognitive impairment, and MRI biomarkers (gray matter brain volume, gray matter mean water diffusion) in the medial temporal lobe (MTL).
Results: Over and above a main effect of cognitive state, the multivariate linear model showed significant interaction between cognitive state and personality traits predicting MTL abnormality. The interaction effect was mainly driven by neuroticism and its facets (anxiety, depression, and stress) and was associated with right-left asymmetry and an anterior to posterior gradient in the MTL.
Discussion: Our results support the hypothesis that personality traits can alter the vulnerability and pathoplasticity of disease and therefore modulate related biomarker expression.

Keywords: Alzheimer's disease; Brain; Personality; Neuroimaging; Psychiatry; Prognosis

1. Background

Translational research in Alzheimer's disease (AD) has relied mostly on tests based on the assessment of cognitive state to detect individuals at risk, the individuals with mild cognitive impairment (MCI), and to identify the corresponding disease signatures such as medial temporal lobe (MTL) atrophy [1–3]. Looking beyond the unidimensional concept of MCI, current research aims to identify other important risk factors (genetic, personality traits) that would improve the prognostic accuracy of current tests and explain the high degree of individual variability in MTL atrophy that is not associated with cognitive decline.

In AD, personality changes, like cognitive decline, are also salient features of the disease [2–9]. In previous studies, interest in personality traits, particularly neuroticism (tendency to feel negative emotions such as stress, depression) and conscientiousness (tendency to be self-disciplined), and AD [10–13] was motivated by the fact that personality traits are stable into adulthood [14], have genetic-environmental underpinnings [15], brain anatomy correlates [16], and are also

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predictive of late-life developments such as cognitive dysfunction [7] or psychiatric symptoms [17]. However, the influence of personality traits on disease causation and their biological manifestations still remain unclear [6,8,18].

Our study aims to test whether morbid personality traits relate to individual differences within the MTL independent of cognitive state. To further improve the discrimination between the two groups in term of brain anatomical changes, we aim to identify the personality profile that minimizes the variance within each group (MCI and non-cognitively impaired [NCI]) and maximizes the difference between them. We predict that neuroticism and its underlying facets, anxiety, depression, and stress will have the greatest exacerbating effects on disease stages. We also expect that identified personality profile will correlate with known functional organization within the MTL.

To quantify MTL atrophy, we used structural magnetic resonance imaging and derived measures of gray matter volume (GMV) and gray matter mean diffusivity (GMMD). GMMD is considered a more sensitive marker than GMV to detect MTL abnormalities in MCI [19]. We used a multivariate strategy [20] to provide a comprehensive test of the association between personality traits, cognitive state, and brain anatomy. The method (Fig. 1) is data driven, unbiased, takes into account the multidimensional and hierarchical nature of the five-factor model of personality, and uses anatomical constraints to decompose the different sources of variability.

2. Methods

2.1. Participants

The study included older adults selected from a longitudinal cohort recruited in the psychogeriatric and geriatric memory clinics of the Lausanne University hospital. The local ethics committee gave permission for the research protocol, and all participants gave written informed consent before taking part in the study. All participants completed comprehensive clinical, psychiatric, and cognitive assessments at the time of MRI scanning. Participants with psychiatric or neurological central nervous system disorders (stroke, tumor), dementia, and alcohol or drug abuse were excluded. The 97 participants included in the study were divided into two groups, MCI and NCI, according to the conventional Winblad criteria [2] where MCI is defined as abnormal but does not fulfill the diagnostic criteria for dementia. A total of 29 participants were MCI (8 males, aged 68 ± 8 years, Mini–Mental State Examination [21] [MMSE]: 27.7 ± 1/range [25–29], Clinical Dementia Rating [22] [CDR] = 0.5, with MCI amnestic 23, nonamnestic 6) and 68 were NCI (18 males, aged 66 ± 6 years, MMSE: 29.1 ± 1/range [26–30], CDR = 0).

2.2. Personality and neuropsychological/psychiatric assessments

To obtain reliable measures of current personality profiles, we asked relatives of participants to complete the

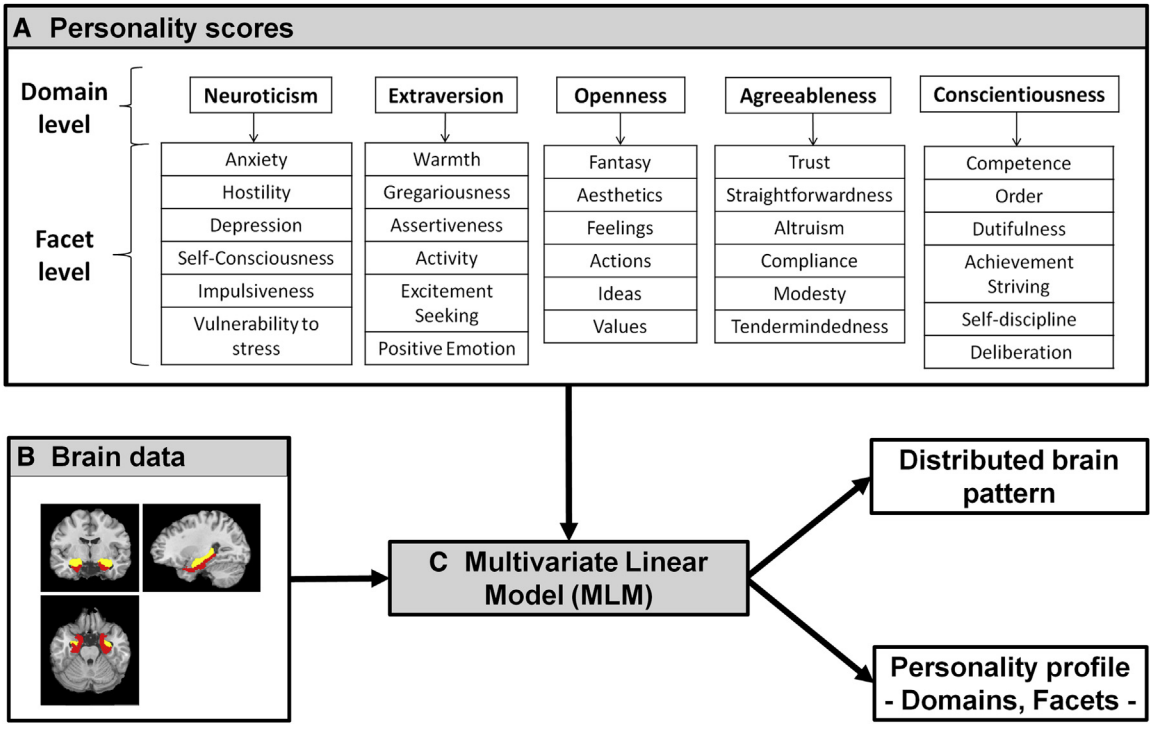

Fig. 1. (A) NEO Personality inventory (NEO-Pi-R) is hierarchical construct composed of 5 domains and 6 facets for each domain. (B) Search volume of interest with the hippocampus in yellow and parahippocampal cortex in red. (C) Multivariate Linear Model (MLM) identified the personality profile and the brain distributed pattern that best explain the covariance between personality scores and anatomical measures.