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The association between personality and plasma biomarkers of astrogliosis and neuronal injury

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Abstract

Personality traits have been associated with risk of dementia and Alzheimer's disease neuropathology, including amyloid and tau. This study examines whether personality traits are concurrently related to plasma glial fibrillary acidic protein (GFAP), a marker of astrogliosis, and neurofilament light (NfL), a marker of neuronal injury. Cognitively unimpaired participants from the Baltimore Longitudinal Study on Aging (N=786; age: 22-95) were assayed for plasma GFAP and NfL and completed the Revised NEO Personality Inventory, which measures five domains and 30 facets of personality. Neuroticism (particularly vulnerability to stress, anxiety, and depression) was associated with higher GFAP and NfL. Conscientiousness was associated with lower GFAP. Extraversion (particularly positive emotions, assertiveness, and activity) was related to lower GFAP and NfL. These associations were independent of demographic, behavioral, and health covariates and not moderated by age, sex, or APOE genotype. The personality correlates of astrogliosis and neuronal injury tend to be similar, are found in individuals without cognitive

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impairment, and point to potential neurobiological underpinnings of the association between personality traits and neurodegenerative diseases.

Keywords

Personality; glial fibrillary acidic protein; GFAP; neurofilament light; NfL; plasma biomarkers; astrogliosis; neurodegeneration; Alzheimer's disease

1. Introduction

Personality traits are fundamental measures of individual differences in emotional, cognitive, and behavioral patterns that characterize people over time. Most personality traits can be hierarchically organized under five major traits (neuroticism, extraversion, openness, agreeableness, and conscientiousness), known as the five-factor model or big five (Costa and McCrae, 1992). Individuals who score higher on neuroticism (the tendency to experience more negative emotions, such as sadness and anxiety) tend to have poor cognitive health, whereas individuals who score higher on conscientiousness (a tendency to be organized, reliable, motivated, and disciplined) tend to have better cognitive health. Indeed, higher neuroticism and *lower* conscientiousness are associated with worse performance on standard neuropsychological tests in older adults (Caselli et al., 2016; Luchetti et al., 2021; Sutin et al., 2019a), poor subjective memory (Aschwanden et al., 2020; Smit et al., 2021), and worse informant-rated cognitive functioning in everyday life (Sutin et al., 2019b). Several prospective studies further indicate that personality traits assessed in unimpaired individuals predict the risk of Alzheimer's disease (AD) and related dementias years or decades later; neuroticism and conscientiousness tend to have the most robust and consistent associations with risk of dementia (Aschwanden et al., 2021; Duberstein et al., 2011; Duchek et al., 2020; Johansson et al., 2014; Kaup et al., 2019; Terracciano et al., 2021a; Wilson et al., 2007). At least for neuroticism, comparable associations are found for Alzheimer's Disease (AD) and Vascular dementia, but not frontotemporal dementia (Terracciano et al., 2021a). The associations are also similar for other neurodegenerative conditions, like Parkinson's disease (Terracciano et al., 2021b). In contrast, the associations between the other five-factor model personality traits (extraversion, openness, and agreeableness) and risk of dementia tend to be less consistent across studies (Aschwanden et al., 2021).

There are likely multiple interacting pathways underlying the associations between personality and cognitive health. Since early in life, high neuroticism and low conscientiousness are associated with more emotional distress (Kotov et al., 2010), maladaptive coping skills (Connor-Smith and Flachsbart, 2007), poor job and relationship outcomes (Barrick and Mount, 1991), sleep problems (Sutin et al., 2020), and engagement in health-risk behaviors such as smoking, physical inactivity, and poor dietary habits (Hill and Roberts, 2016; Mõttus et al., 2013). In turn, these stressors can undermine health over time. Indeed, personality traits have been associated with inflammatory and metabolic dysfunction (Luchetti et al., 2014; Tanios et al., 2022; Wagner et al., 2019), even at the level of mitochondrial DNA (Oppong et al., 2022). Individuals who score high on neuroticism and low on conscientiousness are thus more likely to experience emotional and physiological

stressors that expose the brain to repeated micro insults, disrupt homeostasis, and feed vicious cycles that increase the vulnerability of neurons and glial cells to neurodegenerative processes. To support this conceptual model, more research is needed on crucial biological markers that may play a role in the association between personality and dementia. Recent studies have made progress in identifying the neurobiological bases of these associations, including the role of the amyloid (A), tau (T), and neurodegeneration (N) components of the ATN framework (Jack et al., 2016). While there are some inconsistencies across studies and markers of brain health (Baena et al., 2021; Booth et al., 2014; Byun et al., 2020; Yao et al., 2022), a meta-analysis found that neuroticism and conscientiousness were related to amyloid and tau accumulation, the hallmarks of AD neuropathology (Terracciano et al., 2022). The meta-analysis included research based on positron emission tomography (PET), cerebrospinal fluid (CSF), or post-mortem studies (Terracciano et al., 2022). To our knowledge, no study has reported the association between personality and more novel and accessible blood-based biomarkers of neurodegeneration.

To identify potential biological underpinnings of the associations between personality and neurodegenerative conditions and further understand the role of psychological traits in the pathophysiology of AD and related dementias (ADRD), this study tests whether personality traits are related to glial fibrillary acidic protein (GFAP) and neurofilament light (NfL) measured from plasma. The markers assessed in plasma have been shown to correlate substantially with the corresponding markers assessed in CSF and with PET measures of β amyloid (Palmqvist et al., 2022; Preische et al., 2019). Astrocytes are glial cells and the most abundant cells in the brain; astrocytes support neurons and are involved in the blood brain barrier and reactive astrogliosis (Escartin et al., 2021). GFAP is the most widely used marker of reactive astrogliosis, that is the morphological and functional changes in astrocytes that occur after brain injuries or during neurodegeneration. While not a specific AD marker, GFAP levels are elevated across the full spectrum of AD (Benedet et al., 2021; Chouliaras et al., 2022; Cicognola et al., 2021), including in the early stage of the disease (Benedet et al., 2021; Chatterjee et al., 2021). GFAP is also related to amyloid pathology (Benedet et al., 2021; Chatterjee et al., 2022) and predicts conversion to AD (Cicognola et al., 2021). NfL is a cytoskeletal protein expressed by neurons. NfL is considered a marker of neuro-axonal damage (Bridel et al., 2019) because it is altered in neurological disorders, including in patients with AD and other dementias (Ashton et al., 2021; Bridel et al., 2019; Chouliaras et al., 2022; Preische et al., 2019). There is some mixed evidence that NfL is related to amyloid pathology in pre-symptomatic stages (Chatterjee et al., 2022; Hu et al., 2019; Verberk et al., 2020). Finding a significant association between personality traits and markers of reactive astrogliosis and neuronal injury in cognitively normal adults would further support the hypothesis that personality and neurodegenerative biology are closely linked, perhaps through stress responses that drive neuroinflammation (Luchetti et al., 2014), even in the absence of clinically meaningful cognitive impairment.

Based on past evidence (Aschwanden et al., 2021; Terracciano et al., 2022), we expected higher neuroticism and lower conscientiousness to be associated with markers of reactive astrogliosis (higher GFAP) and neuronal injury (higher NfL). While meta-analyses suggest that extraversion and openness have a small protective effect against dementia (Aschwanden et al., 2021), the findings tend to be inconsistent, and thus we had no strong hypotheses

for these two traits or for agreeableness, which tends to be unrelated to dementia risk. We further test the facets of each major trait for a more in-depth understanding of which aspects of personality are more strongly related to the different biomarkers. Supplemental analyses tested whether the association between neuroticism and conscientiousness and the biomarkers were moderated by age, sex, or apolipoprotein E (APOE) ε4 carrier status. These moderation analyses explore whether the personality associations are stronger among older, female, and APOE ε4 carrier individuals who are at greater risk for neurodegeneration or ADRD.

2. Methods

2.1 Participants.

The Baltimore Longitudinal Study of Aging (BLSA; ClinicalTrials.gov: NCT00233272) is an ongoing longitudinal study that started in 1958 (Ferrucci, 2008). Participants are community-dwelling adults who are generally healthy at enrollment (e.g., free of severe cardiac or pulmonary disease). Participants receive health and functional screenings during study visits, as described in detail elsewhere (Ferrucci, 2008).

The plasma biomarkers were available for 818 individuals; 20 individuals (about 2%) were not included in the analyses because personality data were missing; an additional 12 individuals (about 1.5%) were excluded because they had dementia or another cognitive impairment at the time of blood collection (cognitive status was determined at a consensus case conference based on neuropsychological battery and clinical examination, including informant- and participant-structured interviews). The remaining sample (n = 786) included in the analyses was 46.1% female and 32.3% non-White (24.5% Black). Table 1 presents descriptive statistics for the included participants.

Local institutional review boards approved the BLSA study protocols. All participants provided written informed consent at each visit. The BLSA complies with the NIH ethical standards and with the Helsinki Declaration of 1975, as revised in 2008. Deidentified BLSA data is available on request (http://blsa.nih.gov).

2.2 Measures.

Personality traits were assessed with the self-report version of the Revised NEO Personality Inventory (NEO-PI R)(Costa and McCrae, 1992), a reliable measure of personality. The questionnaire included 240 items answered on a 5-point Likert scale, from “strongly disagree” to “strongly agree”. The NEO-PI-R assesses 30 facets, six for each of the five factors. The five-factor scales have high internal consistency (Cronbach alpha ≥ .85) and high test-retest correlations (r_{tt} = 0.78–0.85) over ten years in the BLSA (Terracciano et al., 2006). The NEO-PI-R provides valid assessment across age groups and clinical and non-clinical samples (Bagby et al., 1999; Costa and McCrae, 1992; Islam et al., 2019; Terracciano et al., 2006; Terracciano et al., 2018).

Personality was assessed at the same visit as the biomarker collection for most participants (n=723), or we used the assessment from the previous (n=51; time gap ranged from −19 to

−1 years; M = −4.74, SD = 4.02) or following (n=12; time gap ranged from 1 to 4 years; M = 1.78, SD = 0.88) visit.

2.3 Plasma biomarkers.

Fasting venous blood was collected and processed using standardized methods. Samples were kept at −80°C until the biomarkers were measured in EDTA plasma using the Single Molecule Array (Simoa) Neurology 4-Plex E (N4PE) assay on the Simoa HD-X instrument (Quanterix Corporation). Assays were run in duplicate, and values were averaged. Intra-assay coefficients of variation were 5.0 for GFAP and 5.1 for NfL (Duggan et al., 2022; Peng et al., 2022). To address the right-skewed distributions of the plasma biomarkers, we winsorized (replaced with the closest highest value in the distribution) 3 outliers for GFAP and 5 for NfL (the Winsorized values were identified by visual inspection and were > 3 SD above the mean). The resulting variables had acceptable skewness and kurtosis (< 1.5) and were used in the analyses. Sensitivity analyses that used log-transformation produced similar results (Supplementary Table S1).

2.4 Covariates/Moderators.

Participant-reported age, sex (male/female), race (white/other), education (years), and the time between personality assessment and biomarker assay were included as covariates. CKD-EPI criteria were used for the estimated glomerular filtration rate (eGFR)-creatinine (Levey et al., 2009). APOE ε4 carrier status was coded as 0 for no ε4 allele and 1 for one or two ε4 alleles. Physical activity was assessed with questions on household chores, household updating/maintenance/repair, gardening and yardwork, walking and climbing stairs, exercise, and recreation. Responses were translated into metabolic equivalent of task (MET) minutes per day and coded as 0=Inactive (<50 MET-min/d), 1=Low (50-250 MET-min/d), 2=Moderate (250-500 MET-min/d), and 3=Very active (≥500 MET-min/d). Body mass index (BMI) was calculated from staff assessed weight and height. Smoking was coded as current (vs. other) and former (vs. other) smokers. Disease burden was the sum of the following conditions: depression, hypertension, diabetes, stroke, anemia, cancer, congestive heart failure, ischemic heart disease, and chronic obstructive pulmonary disease.

2.5 Statistical analyses.

We calculated descriptive statistics for study variables as means and standard deviations (SD) or proportions. We computed z-scores for all variables in the regression analyses. The main results are presented as standardized Beta (β) coefficients with 95% confidence intervals (CI) from linear regression analyses with personality traits entered as predictors of the two biomarkers. Model 1 included age and sex as covariates. Model 2 further included the time gap between personality assessment and the blood collection, eGFR, years of education, race, physical activity, BMI, smoking, and disease burden. We ran separate models for each trait to avoid spurious results due to suppression effects. We further tested whether the associations of neuroticism and conscientiousness with the two biomarkers were moderated by age, sex, or APOE ε4 carrier status by testing interaction terms. Because of the a priori hypotheses based on published evidence, and to avoid inflating type I error, we set significance at $p < .05$ for neuroticism and conscientiousness and their facets. For the

other traits, we report the nominal p-value but mainly discuss findings with p < .01. SPSS version 27 was used for the analyses.

3. Results

Accounting for age and sex (Model 1, Table 2), participants who scored higher on neuroticism (β = .08, 95%CI = .02, .14, p = .007) and lower on conscientiousness (β = −.11, 95%CI = −.17, −.05, p < .001) had higher levels of GFAP. Neuroticism was associated with higher levels of NfL (β = .08, 95%CI = .02, .13, p = .009), but not conscientiousness (β = −.05, 95%CI = −.10, .01, p = .119)(Table 3). Higher extraversion was significantly associated with lower GFAP (β = −.10, 95%CI = −.16 −.04, p = .001) and NfL (β = −.10, 95%CI = −.15 −.04, p = .001). Openness and agreeableness were unrelated to the biomarkers. Overall, the pattern of results was similar across GFAP and NfL, with slightly larger effects for GFAP (Figure 1). While the results were similar in model 2, the effect sizes were reduced (particularly for NfL) after accounting for eGFR, years of education, race, physical activity, BMI, smoking, and disease burden. Sensitivity analyses that excluded 63 participants with the personality assessment not at the same visit as the blood collection produced similar results: GFAP was related to higher neuroticism (β = .08, 95%CI = .02, .15, p = .009) and lower conscientiousness (β = −.12, 95%CI = −.17, −.05, p < .001); NfL was related to higher neuroticism (β = .09, 95%CI = .03, .15, p = .004) but not conscientiousness (β = −.05, 95%CI = −.11, .01, p = .088).

Results for the facets were generally consistent with the factors, with some notable differences. Among the facets of neuroticism, vulnerability was the facet with the strongest association with both GFAP (β = .12, 95%CI = .06, .18, p < .001) and NfL (β = .10, 95%CI = .04, .16, p = .001)(Table 2 and 3, Model 1). The neuroticism facets of anxiety and depression were also related to higher GFAP (anxiety: β = .10, 95%CI = .04, .16, p = .001; depression: (β = .08, 95%CI = .02, .14, p = .01) and NfL (anxiety: β = .07, 95%CI = .01, .13, p = .02; depression: (β = .08, 95%CI = .03, .14, p = .009). The extraversion associations with lower GFAP and NfL were driven by the facets of positive emotions (GFAP: β = −.12, 95%CI = −.18 −.06, p < .001; NfL: β = −.12, 95%CI = −.18 −.07, p < .001), assertiveness (GFAP: β = −.11, 95%CI = −.17 −.05, p < .001; NfL: β = −.09, 95%CI = −.15 −.03, p = .002), and activity (GFAP: β = −.11, 95%CI = −.17 −.05, p < .001; NfL: β = −.07, 95%CI = −.12 −.01, p = .025). The extraversion facets that tap sociability were unrelated to either marker. The facet openness to feelings was related to both low GFAP and NfL. The facets of agreeableness were largely unrelated to both markers. Most facets of conscientiousness were related to GFAP, whereas only competence (β = −.09, 95%CI = −.15 −.03, p = .002) was related to NfL.

Age, sex, and APOE ε4 risk variant did not moderate the associations between neuroticism and conscientiousness and either biomarker (all p > .05).

4. Discussion

This study provides novel evidence for the personality correlates of astrogliosis (GFAP) and neuronal injury (NfL) markers assessed in plasma in a cognitively unimpaired sample.

Consistent with the broader literature on personality and dementia (Aschwanden et al., 2021), individuals who scored higher on neuroticism and lower on conscientiousness had elevated levels of GFAP. For NfL, the expected association was found for neuroticism, but it did not reach statistical significance for conscientiousness. Thus, neuroticism was similarly related to astrogliosis and neuronal injury markers, while conscientiousness may be more relevant to reactive astrocytes and astrocyte-mediated neuroinflammation. The results were robust when accounting for demographic, behavioral, and health covariates and were not moderated by age, sex, and the APOE variant. These findings complement previous work on amyloid and tau (Terracciano et al., 2022), which found higher neuroticism and lower conscientiousness to be associated with more brain amyloid and tau deposition. In addition, individuals who scored higher on extraversion also had lower levels of GFAP and NfL, while no associations were found for openness and agreeableness. This work expands knowledge on plausible neuropathological processes that underlie the association between personality and risk of dementia (Aschwanden et al., 2021).

One major contribution of this study was the in-depth assessment of personality. The assessments of facets provide an opportunity to get a more granular understanding of which aspects of the five broader factors are driving the associations. For neuroticism, the largest effects were found for the facet labeled “vulnerability”, which assesses the ability to cope with stress and remain calm in difficult or threatening situations. The people who reported the most emotional vulnerability (e.g., those who may panic or feel helpless when facing emergencies, problems, or stressful conditions) had the highest levels of GFAP and NfL. Similar effects were also found for anxiety and depression, two facets of personality that overlap with common neuropsychiatric symptoms, as well as anxiety and depressive disorders. This finding is consistent with clinical evidence that elevated GFAP and NfL are associated with anxiety and depressive symptomatology (Lange et al., 2022; Steinacker et al., 2021). The association between extraversion and the biomarkers was not due to the sociability component of extraversion. Instead, it was the cheerful (positive emotions), forceful (assertiveness), and energetic (activity) dispositions of those high on extraversion that seemed to be protective against neurodegeneration. This finding seems consistent with evidence that individuals who report greater well-being, such as more happiness or purpose in life, tend to have better cognitive health and lower risk of dementia (Sutin et al., 2021; Zhu et al., 2023). People who score higher on the personality facet of activity tend to have more energy, vigorous movement, and a faster tempo compared to individuals who score lower on this facet; the finding that the personality facet activity is related to lower levels of GFAP and NfL, especially in older adults, is consistent with the evidence on the neuroprotective effects of physical activity (Maugeri et al., 2021; Raffin et al., 2021). Openness to feelings (high scorers have more differentiated and deeper emotional states and feelings, while low scorers are characterized by alexithymia) was the facet of openness with the strongest inverse association to GFAP and NfL. Facets of agreeableness were unrelated to the biomarkers. There was little differentiation among the facets of conscientiousness in its association with GFAP. However, only competence (a sense that one is efficient and capable) was related to NfL.

The current study design cannot determine causality. The observed associations could be due to multiple and non-mutually exclusive interpretations, including (a) neurodegeneration

could cause change in personality, (b) personality could modulate risk of neurodegeneration, (c) bidirectional or reciprocal influences between personality and neurodegeneration, (d) other variables (e.g., genes, trauma) influence both personality and neurodegeneration, and (e) confounding factors leading to spurious associations. Next, we discuss the evidence related to the first two interpretations. The neurodegenerative processes leading to higher GFAP and NfL may impact personality, especially after the onset of cognitive impairment. Indeed, about a dozen studies of knowledgeable informants have reported large changes in personality among people with dementia (Islam et al., 2019; Siegler et al., 1991). Astrogliosis and neuronal injury may also interact with personality to manifest in neuropsychiatric symptoms. However, the current study was based on healthy individuals and excluded cognitively impaired participants. Thus, to explain the current findings, neurodegeneration would need to cause change in personality before causing cognitive impairment. But, substantial changes in personality are generally not apparent before the onset of MCI or dementia: A long-term longitudinal study found no evidence of personality change in the preclinical phase for people who developed AD (Terracciano et al., 2017). An alternative interpretation of the observed association is that personality traits modulate the trajectory of brain health over the lifespan by, for example, supporting brain maintenance (Nyberg et al., 2012) and resistance (Arenaza-Urquijo and Vemuri, 2018) against the risk of astrogliosis and neuronal injury. Early in life, these traits are related to educational achievement, and higher education can protect health and cognitive function in later life (Crimmins et al., 2018; Dumfart and Neubauer, 2016; Seblova et al., 2021). Personality traits also shape behaviors and lifestyles, including health risk behaviors that may influence brain health, such as physical activity and cigarette smoking (Hampson et al., 2006; Kekäläinen et al., 2022). However, in this study, the observed associations were mostly independent of the effect of the educational, behavioral, and health covariates, especially for GFAP (Model 2). Personality traits are related to other constructs that may contribute to brain health, including stress reactivity, coping skills, social connection (e.g., loneliness)(Buecker et al., 2020), and well-being (e.g., purpose in life)(Sutin et al., 2021; Zhu et al., 2023), as well as key biological pathways such as inflammation and neurotrophic factors (Hill and Roberts, 2016; Luchetti et al., 2014; Terracciano et al., 2011). High neuroticism and low conscientiousness are also major risk factors for mental health conditions (Bucher et al., 2019; Kotov et al., 2010), which can have a detrimental impact on neurodegenerative processes. Thus, these enduring personality dispositions that emerge early in life are likely to engage multiple psychosocial and neurobiological mechanisms that may regulate neurodegenerative processes; the reverse (i.e., neuropathology inducing changes in personality) may occur later, along with the onset of clinical impairment.

4.1. Strengths and limitations

The current study had several strengths, including the relatively novel assessment of GFAP and NfL in plasma, the detailed assessment of all five major personality traits and 30 facets, and the well-characterized sample of participants who underwent rigorous testing, including clinical diagnoses of MCI and dementia. There are also limitations that should be considered. We tested several traits and facets in this study and some results could be due to chance. For example, the association of Extraversion with GFAP and NfL found in this study was surprising given the inconsistent associations between extraversion and

health (Hill and Roberts, 2016), and particularly with markers of brain health (Terracciano et al., 2022), cognitve function (Caselli et al., 2016; Sutin et al., 2019a), and risk of dementia (Aschwanden et al., 2021). The sample included a substantial portion of African Americans, but the BLSA participants tend to have a high level of education, which may limit the generalizability of the findings. More research is clearly needed to test whether these associations are replicable, especially in samples with a broader range of education and economic status, from the US and other countries. While we discuss the findings in the context of neurodegenerative diseases like AD, both GFAP and NfL are not specific markers of AD. Another limitation was that covariates like physical activity were assessed with few items. While we found that age, sex, and APOE did not moderate the reported associations, future studies should test other potential moderators, including whether the associations change with the transition from amyloid negative to positive, or with the onset of cognitive impairment.

4.2. Conclusions

This study found that neuroticism and conscientiousness are related to markers of reactive astrogliosis and neuronal injury. The associations were similar across markers, but conscientiousness may be more relevant to reactive astrocytes and astrocyte-mediated neuroinflammation, whereas neuroticism was similarly related to astrocytes and neuronal injury. The associations were evident in a sample of cognitively healthy adults, some of whom are in the preclinical stages of AD and related neurodegenerative conditions. The findings complement other research on amyloid and tau (Terracciano et al., 2022) and point to potential neurobiological underpinnings to the broader epidemiological and clinical evidence linking personality traits to neurodegenerative diseases (Aschwanden et al., 2021).

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- Personality traits are related to measures of astrogliosis and neuronal damage.
- High neuroticism and low extraversion are associated with higher GFAP and NfL.
- High conscientiousness is associated with lower GFAP.
- The associations are independent of other risk factors for neurodegeneration.
- The associations are evident in the absence of cognitive impairment.

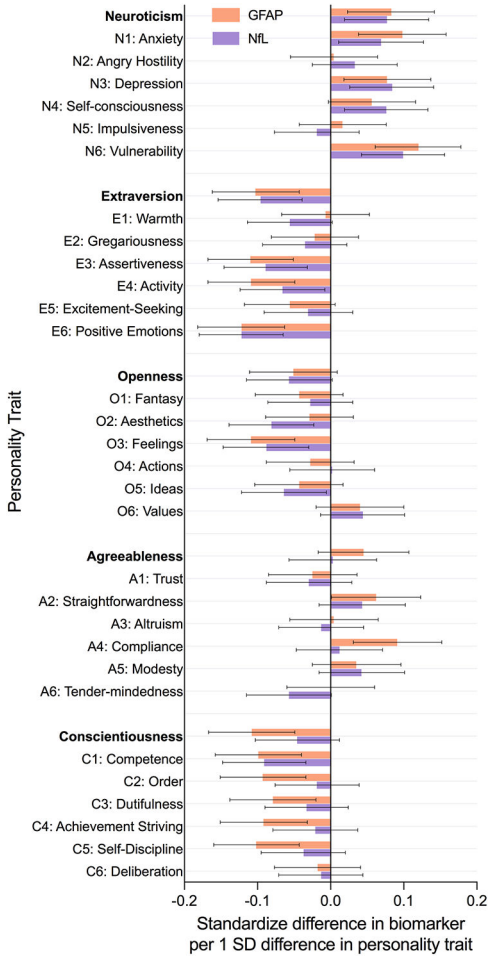

Figure 1.

Clustered bar chart of the sex and age-adjusted associations between personality traits and measures of neurodegeneration.

Table 1.

Descriptive statistics

Variable	Mean [or N (%)]	SD	Minimum	Maximum
Age, yr.	66.53	14.89	22.4	94.7
Education, yr.	17.07	2.37	8	21
Sex (Women)	362 (46.1%)	-	0	1
Black	193 (24.5%)	-	0	1
White	532 (67.7%)	-	0	1
Other race	61 (7.8%)	-	0	1
GFAP	165.39	101.57	31.59	1621.35
GFAP-Winsorized	163.69	86.67	31.59	521.89
NfL	21.26	12.25	2.98	112.43
NfL-Winsorized	21.11	11.57	2.98	59.76
Neuroticism	45.13	9.19	17	78
Extraversion	51.34	10.04	19	82
Openness	53.55	10.59	20	85
Agreeableness	52.57	9.89	9	79
Conscientiousness	52.99	10.00	11	81

N = 786. Age and education are in years. Personality traits are in T-scores, which are simple linear transformation based on combined gender norms that have a mean of 50 and SD of 10, see NEO-PI-R manual (Costa and McCrae, 1992).

Table 2.

Standardized beta regression coefficients from regression models with personality traits predicting glial fibrillary acidic protein (GFAP).

	Model 1				Model 2			
Trait	**β**	**L95%CI**	**U95%CI**	**p**	**β**	**L95%CI**	**U95%CI**	**p**
Neuroticism	**0.083**	**0.023**	**0.142**	**0.007**	**0.079**	**0.018**	**0.140**	**0.012**
Extraversion	**−0.103**	**−0.162**	**−0.043**	**0.001**	**−0.085**	**−0.147**	**−0.024**	**0.007**
Openness	−0.051	−0.111	0.009	0.097	−0.047	−0.111	0.016	0.146
Agreeableness	0.045	−0.017	0.107	0.151	0.041	−0.022	0.106	0.199
Conscientiousness	**−0.108**	**−0.167**	**−0.049**	**<0.001**	**−0.098**	**−0.160**	**−0.038**	**0.002**
N1: Anxiety	**0.098**	**0.038**	**0.158**	**0.001**	**0.093**	**0.031**	**0.154**	**0.003**
N2: Angry Hostility	0.004	−0.055	0.064	0.883	0.007	−0.054	0.069	0.811
N3: Depression	**0.077**	**0.018**	**0.137**	**0.010**	**0.075**	**0.014**	**0.137**	**0.016**
N4: Self-consciousness	0.056	−0.003	0.116	0.063	0.039	−0.022	0.100	0.208
N5: Impulsiveness	0.016	−0.043	0.076	0.590	0.039	−0.023	0.101	0.222
N6: Vulnerability	**0.120**	**0.061**	**0.178**	**<0.001**	**0.103**	**0.042**	**0.164**	**0.001**
E1: Warmth	−0.007	−0.067	0.053	0.825	0.012	−0.049	0.074	0.693
E2: Gregariousness	−0.022	−0.081	0.038	0.475	−0.012	−0.072	0.048	0.692
E3: Assertiveness	**−0.110**	**−0.168**	**−0.051**	**<0.001**	**−0.088**	**−0.149**	**−0.026**	**0.005**
E4: Activity	**−0.109**	**−0.168**	**−0.049**	**<0.001**	**−0.118**	**−0.183**	**−0.057**	**<0.001**
E5: Excitement-Seeking	−0.056	−0.118	0.006	0.079	−0.043	−0.108	0.021	0.183
E6: Positive Emotions	**−0.122**	**−0.182**	**−0.063**	**<0.001**	**−0.110**	**−0.172**	**−0.048**	**0.001**
O1: Fantasy	−0.043	−0.103	0.017	0.163	−0.039	−0.102	0.024	0.221
O2: Aesthetics	−0.029	−0.089	0.031	0.349	−0.025	−0.087	0.037	0.427
O3: Feelings	**−0.109**	**−0.169**	**−0.049**	**<0.001**	**−0.102**	**−0.164**	**−0.040**	**0.001**
O4: Actions	−0.028	−0.088	0.032	0.363	−0.028	−0.090	0.033	0.364
O5: Ideas	−0.043	−0.104	0.017	0.160	−0.040	−0.104	0.023	0.212
O6: Values	0.040	−0.020	0.100	0.188	0.047	−0.016	0.111	0.141
A1: Trust	−0.025	−0.085	0.036	0.418	−0.022	−0.085	0.040	0.481
A2: Straightforwardness	**0.062**	**0.001**	**0.123**	**0.048**	0.048	−0.014	0.111	0.129
A3: Altruism	0.004	−0.056	0.065	0.887	0.015	−0.047	0.077	0.632
A4: Compliance	**0.091**	**0.031**	**0.152**	**0.003**	**0.082**	**0.020**	**0.146**	**0.010**
A5: Modesty	0.035	−0.025	0.096	0.252	0.024	−0.039	0.088	0.446
A6: Tender-mindedness	0.000	−0.060	0.060	0.990	0.009	−0.053	0.072	0.767
C1: Competence	**−0.099**	**−0.158**	**−0.040**	**0.001**	**−0.076**	**−0.137**	**−0.015**	**0.014**
C2: Order	**−0.093**	**−0.151**	**−0.034**	**0.002**	**−0.091**	**−0.150**	**−0.031**	**0.003**
C3: Dutifulness	**−0.079**	**−0.138**	**−0.020**	**0.008**	**−0.078**	**−0.139**	**−0.017**	**0.012**
C4: Achievement Striving	**−0.092**	**−0.151**	**−0.032**	**0.003**	**−0.086**	**−0.149**	**−0.025**	**0.006**
C5: Self-Discipline	**−0.102**	**−0.160**	**−0.043**	**0.001**	**−0.097**	**−0.159**	**−0.037**	**0.002**

	Model 1				**Model 2**			
Trait	**β**	**L95%CI**	**U95%CI**	**p**	**β**	**L95%CI**	**U95%CI**	**p**
C6: Deliberation	−0.018	−0.077	0.041	0.556	−0.008	−0.069	0.053	0.795

Notes: Model 1 N = 786; Model 2 N = 761. Model 1 include age and sex as covariates. Model 2 further include the time gap between personality assessment and the blood collection, eGFR, years of education, race (other vs. white), smoking, physical activity, body mass index, and disease burden. L95%CI and U95%CI are the lower and upper bound of the 95% Confidence interval. $p < .05$ and related β are bolded.

Table 3.

Standardized beta regression coefficients from regression models with personality traits predicting neurofilament light (NfL).

	Model 1				Model 2			
Trait	**β**	**L95%CI**	**U95%CI**	**p**	**β**	**L95%CI**	**U95%CI**	**p**
Neuroticism	**0.077**	**0.019**	**0.134**	**0.009**	**0.060**	**0.003**	**0.117**	**0.040**
Extraversion	**−0.096**	**−0.154**	**−0.039**	**0.001**	**−0.059**	**−0.117**	**−0.002**	**0.042**
Openness	−0.057	−0.115	0.002	0.056	−0.040	−0.100	0.019	0.178
Agreeableness	0.003	−0.057	0.063	0.922	−0.013	−0.073	0.046	0.658
Conscientiousness	−0.046	−0.103	0.012	0.119	−0.026	−0.084	0.031	0.362
N1: Anxiety	**0.069**	**0.011**	**0.127**	**0.020**	0.052	−0.006	0.109	0.078
N2: Angry Hostility	0.033	−0.025	0.091	0.260	0.031	−0.026	0.088	0.285
N3: Depression	**0.084**	**0.026**	**0.141**	**0.004**	**0.077**	**0.021**	**0.134**	**0.008**
N4: Self-consciousness	**0.076**	**0.019**	**0.133**	**0.009**	0.047	−0.010	0.104	0.103
N5: Impulsiveness	−0.019	−0.077	0.039	0.516	−0.002	−0.060	0.056	0.941
N6: Vulnerability	**0.099**	**0.042**	**0.156**	**0.001**	**0.060**	**0.003**	**0.117**	**0.039**
E1: Warmth	−0.056	−0.114	0.002	0.056	−0.036	−0.094	0.021	0.210
E2: Gregariousness	−0.035	−0.093	0.022	0.227	−0.028	−0.084	0.028	0.328
E3: Assertiveness	**−0.089**	**−0.146**	**−0.032**	**0.002**	−0.037	−0.095	0.020	0.203
E4: Activity	**−0.066**	**−0.124**	**−0.008**	**0.025**	−0.056	−0.115	0.003	0.061
E5: Excitement-Seeking	−0.031	−0.091	0.030	0.322	−0.005	−0.065	0.055	0.874
E6: Positive Emotions	**−0.122**	**−0.180**	**−0.065**	**<0.001**	**−0.087**	**−0.144**	**−0.029**	**0.003**
O1: Fantasy	−0.028	−0.086	0.030	0.345	−0.015	−0.073	0.043	0.616
O2: Aesthetics	**−0.081**	**−0.139**	**−0.023**	**0.006**	−0.057	−0.114	0.000	0.050
O3: Feelings	**−0.088**	**−0.147**	**−0.030**	**0.003**	**−0.078**	**−0.136**	**−0.020**	**0.009**
O4: Actions	0.002	−0.056	0.060	0.953	0.020	−0.037	0.078	0.490
O5: Ideas	**−0.064**	**−0.122**	**−0.006**	**0.032**	−0.052	−0.111	0.007	0.086
O6: Values	0.044	−0.014	0.101	0.140	0.034	−0.025	0.093	0.259
A1: Trust	−0.030	−0.088	0.029	0.320	−0.042	−0.101	0.015	0.148
A2: Straightforwardness	0.043	−0.016	0.102	0.152	0.021	−0.038	0.080	0.481
A3: Altruism	−0.013	−0.071	0.045	0.662	−0.007	−0.065	0.050	0.797
A4: Compliance	0.012	−0.047	0.071	0.699	−0.017	−0.076	0.041	0.557
A5: Modesty	0.042	−0.016	0.101	0.153	0.026	−0.032	0.086	0.374
A6: Tender-mindedness	−0.057	−0.115	0.001	0.056	−0.038	−0.097	0.020	0.193
C1: Competence	**−0.091**	**−0.148**	**−0.034**	**0.002**	**−0.061**	**−0.118**	**−0.005**	**0.034**
C2: Order	−0.019	−0.076	0.039	0.526	−0.008	−0.065	0.048	0.768
C3: Dutifulness	−0.033	−0.090	0.024	0.254	−0.044	−0.101	0.013	0.127
C4: Achievement Striving	−0.021	−0.079	0.037	0.482	0.009	−0.049	0.067	0.760
C5: Self-Discipline	−0.037	−0.095	0.020	0.199	−0.020	−0.077	0.037	0.485

	Model 1				**Model 2**			
Trait	**β**	**L95%CI**	**U95%CI**	**p**	**β**	**L95%CI**	**U95%CI**	**p**
C6: Deliberation	−0.013	−0.071	0.044	0.645	−0.003	−0.060	0.053	0.910

Notes: Model 1 N = 786; Model 2 N = 761. Model 1 include age and sex. Model 2 further include the time gap between personality assessment and the blood collection, eGFR, years of education, race (other vs. white), smoking, physical activity, body mass index, and disease burden. L95%CI and U95%CI are the lower and upper bound of the 95% Confidence interval. $p < .05$ and related β are bolded.