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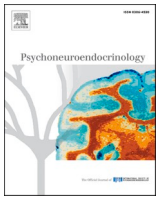

Personality nuances and inflammation: A coordinated analysis of six samples

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ABSTRACT

Five-Factor personality domains are associated with inflammatory markers across adulthood. Personality nuances, the most specific personality characteristics at the bottom of the personality hierarchy that are typically measured by individual questionnaire items, may provide more information on which specific characteristics of traits are related to inflammation. Using six cohort studies (total N > 19,000, age range: 25–104 years) that measured nuances using items from the Midlife Development Inventory (MIDI), this study examined the association between personality nuances and two inflammatory markers: c-reactive protein (CRP) and interleukin-6 (IL-6). Across most samples and a meta-analysis, the extraversion item *lively* and the conscientiousness items *organized* and *hardworking* were related to lower levels of CRP and IL-6. The extraversion item *active* was the strongest item-level correlate of lower CRP in the meta-analysis and across most samples. Domain-level analyses indicated that higher conscientiousness was associated with lower CRP and IL-6, whereas higher extraversion was associated with lower CRP. Neuroticism, openness, and agreeableness domains and items were mostly unrelated to inflammatory markers. The associations between the items *active* and *hardworking* and inflammatory markers persisted in most samples controlling for their respective extraversion and conscientiousness domains. Item-level analyses provide more detailed insights into the specific personality nuances connected to inflammation, showing that the active component of extraversion, rather than components related to sociability, are associated with inflammation.

1. Introduction

Personality traits, relatively enduring patterns of thoughts, feelings, and behaviors (Costa et al., 2019), have a well-established association with health across adulthood (Luo et al., 2023; Wright and Jackson, 2023). Among the traits defined by the Five-Factor Model (FFM, McCrae and John, 1992), higher neuroticism (the tendency to experience negative emotions and vulnerability to stress) and lower conscientiousness (the tendency to be organized and planful) are implicated consistently in a range of health outcomes, including lower functional health (Stephan et al., 2025a), worse cognition (Stanek and Ones, 2023), higher risk of chronic conditions (Weston et al., 2020), higher risk of neurodegenerative diseases such as dementia (Aschwanden et al., 2021), and higher mortality risk (Willroth et al., 2025). To a lesser extent, higher extraversion (the tendency to be sociable and to experience positive emotions), openness (the tendency to be unconventional and curious) and agreeableness (the tendency to be altruistic and cooperative) are associated with some but not with most health-related outcomes (Willroth et al., 2025; Wright and Jackson, 2023).

Personality traits are also associated with physiological markers of health, which may function as early signs of poor health and potentially explanatory pathways between personality and long-term health outcomes (O'súilleabháin et al., 2021; Stephan et al., 2024a; Wright et al., 2022). Among physiological mechanisms, personality traits have been associated with two markers commonly used in clinical care: Interleukin−6 (IL−6), a pro-inflammatory cytokine, and C-reactive protein

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(CRP), a primary marker of systemic inflammation. Elevated values of these two markers predict various adverse health outcomes, including cardiovascular events (Liu et al., 2023) and all-cause mortality (Singh-Manoux et al., 2017). A large literature has already examined the broad FFM personality domains' associations with IL−6 and CRP, with consistent associations found between higher conscientiousness and lower levels of IL−6 and CRP (Allen and Laborde, 2017; Chapman et al., 2011; Graham et al., 2018; Luchetti et al., 2014; Mottus et al., 2013; Stephan et al., 2024a; Turiano et al., 2013; Wright et al., 2022). The evidence is more mixed for the other four traits. Higher neuroticism has been associated with higher levels of IL−6 and CRP in some research (Armon et al., 2013; Graham et al., 2018; Sutin et al., 2010; Wright et al., 2022), whereas no association has been found in other studies (Allen and Laborde, 2017; Chapman et al., 2011; Luchetti et al., 2014; Mitchell et al., 2021; Mõttus et al., 2013; Stephan et al., 2024a; Wagner et al., 2019). Higher extraversion has been related to lower IL−6 and lower CRP in some studies (Allen and Laborde, 2017; Stephan et al., 2024a), higher IL−6 and CRP in some studies (Armon et al., 2013; Wagner et al., 2019), and unrelated with both markers in other studies (Chapman et al., 2011; Luchetti et al., 2014; Mitchell et al., 2021; Mõttus et al., 2013; Sutin et al., 2010; Wright et al., 2022). Some studies found an association between openness and lower IL−6 and CRP (Armon et al., 2013; Chapman et al., 2011; Luchetti et al., 2014; Mõttus et al., 2013), whereas other studies have not (Mitchell et al., 2021; Stephan et al., 2024a; Sutin et al., 2010; Wright et al., 2022). Finally, agreeableness has been associated with higher CRP in some studies (Allen and Laborde, 2017; Armon et al., 2013), whereas no association has been found with either IL−6 or CRP in other studies (Chapman et al., 2011; Luchetti et al., 2014; Mitchell et al., 2021; Mõttus et al., 2013; Stephan et al., 2024a; Sutin et al., 2010; Wagner et al., 2019; Wright et al., 2022).

Existing evidence for the association between personality and inflammation has mostly considered the five broad FFM domains. However, more specificity in the level of analysis can lead to a better understanding of the inconsistent associations between psychological factors and immune processes (Moriarity, Alloy, 2020). Consistent with this approach, the FFM is conceptualized as a hierarchy of traits with increasing specificity, with the five broad domains being decomposed into narrower, lower-order traits such as facets (McCrae, 2015; Mõttus et al., 2017). Some studies have examined the personality facets associated with inflammation. For example, there is an association between the activity facet of extraversion and lower IL−6 (Chapman et al., 2009; Sutin et al., 2010). The order, dutifulness, achievement striving, self-discipline and deliberation facets of conscientiousness have been associated with lower IL−6 and CRP (Sutin et al., 2010, 2018), whereas the angry-hostility, vulnerability, and impulsivity facets of neuroticism have been linked to elevated levels of IL−6 (Sutin et al., 2010).

However, the personality trait hierarchy extends even beyond facets into narrower traits called nuances, often indexed by individual questionnaire items (McCrae, 2015; Mõttus et al., 2017). Nuances are the most basic building block of the personality hierarchy and have the hallmark properties of traits, including heritability, cross-rater agreement, and rank-order stability (Mõttus et al., 2017). Theoretically, the examination of items (markers of nuances) offers additional information and a more detailed, granular description of the specific characteristics of traits related to outcomes relative to domain- and facet-level analyses (Mõttus et al., 2017; Seeboth and Mõttus, 2018). Furthermore, personality items have been found to have incremental predictive validity over the five broad domains in some studies (Mõttus et al., 2017; Seeboth and Mõttus, 2018; Stephan et al., 2025d; Stewart et al., 2022), although not in all (Stephan et al., 2024b). A growing body of research suggests that nuances are associated with a range of health outcomes, including psychopathology (Soodla et al., 2025), body mass index (BMI, Arumae et al., 2024), falls (Stephan et al., 2025b), cognitive function (Stephan et al., 2025c), dementia (Stephan et al., 2024b), and even mortality (Stephan et al., 2025d; Deason et al., 2025). Recent studies using the Midlife Development Inventory (MIDI) found replicable patterns of association between personality nuances and health outcomes (Stephan et al., 2024b; Stephan et al., 2025d). Specifically, higher scores on the extraversion items *active* and *lively*, the conscientiousness items *organized*, *hardworking* and *responsible*, the agreeableness item *helpful*, and lower scores on the neuroticism items *moody*, *worrying* and *nervous* were related to lower risk of falls (Stephan et al., 2025b), dementia (Stephan et al., 2024b) and mortality (Stephan et al., 2025d). Despite this accumulating evidence for the association between nuances and health outcomes, to the best of our knowledge, no studies have yet examined the associations between personality nuances and inflammation. The examination of individual nuances could advance existing knowledge by providing a deeper understanding of the specific personality characteristics associated with inflammation. For example, this investigation could help us better understand the mechanisms by which personality becomes linked with physiological processes, and it could help explain inconsistent domain-level findings (studies assess domains through different nuances). A nuance-level approach also has practical implications by allowing for more accurate identification of individuals at risk of inflammation who may be targeted by preventive actions.

Based on a coordinated analysis of six large samples of middle-aged and older adults, the present study examined the association between personality nuances and IL−6 and CRP. In the six samples, personality nuances were operationalized with the items of the MIDI (Zimprich et al., 2012). The coordinated analysis has the advantage of reducing some of the heterogeneity in the results of previous research due to analytic differences across studies. The results from each of the six samples are combined in a random-effect meta-analysis to test whether the association between nuances and inflammatory markers are replicable and generalizable. Hypotheses were derived from the literature on the association between the broad personality domains and inflammation (Luchetti et al., 2014; Wright et al., 2022) and from recent evidence on the association between nuances and health outcomes (Stephan et al., 2024b; 2025d). Based on the literature linking domain-level conscientiousness to both lower IL−6 and CRP (Luchetti et al., 2014; Wright et al., 2022) and the replicable evidence linking conscientiousness items tapping nuances such as being organized, responsible and hardworking to better health outcomes (Stephan et al., 2024b; 2025d), it was hypothesized that these conscientiousness items would be associated with lower levels of both IL−6 and CRP, although the strength could vary. Based on their replicable association with health outcomes, including dementia and mortality (Stephan et al., 2024b; 2025d), it was further expected that higher scores on the extraversion items *active* and *lively* and the agreeableness item *helpful* would be associated with lower levels of IL−6 and CRP, whereas the neuroticism items *moody*, *nervous*, and *worrying* would be related to higher IL−6 and CRP levels. A domain-level analysis of the association between personality and IL−6 and CRP was conducted to complement the item-level analysis.

2. Method

2.1. Participants

Participants were from six samples: The Health and Retirement Study (HRS), the English Longitudinal Study of Ageing (ELSA), the Midlife in the United States Study (MIDUS), the Midlife in Japan Study (MIDJA), the National Social Life, Health, and Aging Project (NSHAP), and the National Health and Aging Trends Study (NHATS). These datasets were selected because they included the MIDI personality questionnaire, an assessment of IL−6 and/or CRP, and were public. CRP was available in all samples; IL−6 was available in HRS, MIDUS, MIDJA, and NHATS. Participants with complete data on personality traits, demographic factors, and at least one inflammatory marker (IL−6 or CRP) were included. Participants provided written informed consent in each study. The present analyses involved publicly available deidentified data and did not require approval from an Institutional Review Board (IRB). Table 1 reports descriptive statistics for the six samples.

Table 1
Descriptive Statistics for the Six Samples.

	HRS		ELSA		MIDUS		MIDJA		NSHAP		NHATS	
Variables	*M/%*	*SD*	*M/%*	*SD*	*M/%*	*SD*	*M/%*	*SD*	*M/%*	*SD*	*M/%*	*SD*
Age (Years)	67.77	10.36	65.74	8.02	52.79	12.63	53.46	13.95	72.41	7.04	77.52	6.55
Sex (% women)	59%	-	55%	-	54%	-	55%	-	53%	-	58%	-
Race (% African American/Black)	15%	-	2%[a]	-	17%	-	-	-	9%	-	10%	-
Ethnicity (% Hispanic)	11%	-	-	-	-	-	-	-	7%	-	7%	-
Education	13.20	2.89	4.31	2.19	7.83	2.50	4.71	2.02	2.77	1.31	5.44	2.28
Neuroticism	1.97	0.61	2.09	0.59	2.06	0.64	2.15	0.58	2.15	0.59	2.17	0.83
Extraversion	3.18	0.58	3.17	0.55	3.12	0.59	2.48	0.66	3.20	0.56	3.21	0.73
Openness	2.95	0.55	2.90	0.53	2.99	0.53	2.23	0.58	2.92	0.65	2.91	0.81
Agreeableness	3.51	0.50	3.51	0.47	3.40	0.52	2.70	0.63	3.47	0.50	3.61	0.50
Conscientiousness	3.37	0.48	3.34	0.48	3.37	0.47	2.66	0.55	3.36	0.54	3.29	0.67
IL−6 (pg/mL)	4.22	10.71	-	-	2.89	2.74	1.63	2.16	-	-	6.90	12.09
CRP (ug/mL)	4.38	6.52	3.52	9.91	2.96	4.79	0.72	2.03	4.29	8.78	2.41	3.16

Note. [a] Percent of non-white participants

HRS is a nationally representative survey of individuals aged 50 years and older and their spouses in the US. Half the sample had personality, demographic factors, CRP and IL−6 measured in 2014, and the other half had these data measured in 2016. The analyzed sample had 9599 participants aged from 50 to 104 years with complete data on personality and demographic factors and at least one of the two markers (59% women; Mean Age= 67.77; SD= 10.36). HRS data can be downloaded from https://hrs.isr.umich.edu/data-products.

ELSA is a study of a representative cohort of individuals aged over 50 years living in England. Personality and demographic factors were collected at Wave 5 (2010/2011) and CRP was available at Wave 6 (2012/2013). The average time elapsed was 22.94 months (Range: 13.02–33.04 months, SD= 1.60) between personality and CRP assessments. The analyzed sample had 4715 participants aged from 50 to 89 years with complete data on personality, demographic factors, and CRP (55% women; Mean Age= 65.74; SD= 8.02). ELSA data can be accessed at https://www.ukdataservice.ac.uk/.

The MIDUS is a nationally representative study of non-institutionalized adults in the United States. Personality and demographic data were from the MIDUS 2 (2004–2006) and the MIDUS Refresher (2011–2014) samples. IL−6 and CRP were measured in the 2004–2009 and 2012–2016 biomarker projects the MIDUS 2 and the MIDUS refresher samples, respectively. The average time elapsed between assessments was 25.74 months (range: 4.01–62.99 months, SD= 12.63). The two samples were combined for a total sample of 1923 participants with complete data on personality, demographic factors and at least one of the two markers (54% women; age range: 25–84 years; Mean Age= 52.79; SD= 12.63). MIDUS data can be downloaded from https://midus.wisc.edu/index.php.

The MIDJA is a probability sample of Japanese adults from the Tokyo metropolitan area that paralleled the MIDUS survey. Personality and demographic data were collected in 2008, and IL−6 and CRP were collected in 2009–2010. The time elapsed between the waves was 13.91 months (range: 7.04–20.97, SD=4.38). The analyzed sample had 357 participants aged from 30 to 79 years (55% women, mean age=53.46, SD=13.95). MIDJA data can be downloaded from https://midus.wisc.edu/index.php.

The NSHAP is a nationally representative population-based study of older Americans. Personality, demographic factors, and CRP data were collected in Wave 2 (2010–2011). The analyzed sample had 1890 participants (53% women; age range: 62–90; Mean Age=72.41; SD=7.04). NSHAP data can be downloaded from https://www.norc.org/research/projects/national-social-life-health-and-aging-project.html/.

The NHATS is a US nationally representative sample of Medicare beneficiaries aged 65 and older. Personality and demographic data were collected in 2013/2014, and IL−6 and CRP data were collected in 2017. The average time elapsed between personality assessment and inflammatory marker assessments was 40.94 months (range: 29.98–52.04 months, SD= 6.86). The analyzed sample had 1464 participants aged from 67 to 99 years (58% women; Mean Age=77.52; SD=6.55) with complete data on personality, demographic factors and at least one of the two markers. NHATS data can be downloaded from http://www.nhats.org.

2.2. Measures

2.2.1. Personality traits

Personality domains and nuances were assessed with the MIDI (Zimprich et al., 2012) in all samples. Participants rated self-descriptive adjectives that assessed neuroticism, extraversion, openness, agreeableness, and conscientiousness on a scale from 1 (*not at all*) to 4 (*a lot*). A 26-item version was used in the HRS, ELSA, MIDUS, and MIDJA, with 4 items for neuroticism, 5 items for extraversion, 7 items for openness, 5 items for agreeableness, and 5 items for conscientiousness. A 21-item version was used in the NSHAP with 4 items for neuroticism, 5 items for extraversion, 4 items for openness, 4 items for agreeableness and 4 items for conscientiousness. The NHATS used a 10-item version, with two items for each trait. Cronbach alphas ranged from 0.56 to 0.74 for neuroticism, from 0.64 to 0.82 for extraversion, from 0.66 to 0.81 for openness, from 0.55 to 0.88 for agreeableness, and from 0.54 to 0.70 for conscientiousness. The complete list of items and their descriptive statistics is presented in Supplementary Material (Table S1).

2.2.2. Inflammatory markers

Dried blood spots were used to collect blood in the HRS, NHATS, and NSHAP, and whole blood was used in the MIDUS, MIDJA, and ELSA. Fasting blood samples were collected in the MIDUS, MIDJA, and ELSA. In each study, standard CRP and IL−6 assays were performed on the blood samples by certified labs. Plasma-equivalent IL−6 was used in the HRS, the NSHAP, and serum IL−6 was used in the MIDUS and MIDJA. NHANES equivalent CRP was used in the HRS, plasma-equivalent CRP was used in the NSHAP and NHATS, plasma CRP was used in MIDUS and MIDJA, and serum CRP was used in ELSA. Additional information is in Supplementary Material. Normality checks of CRP and Il−6 were conducted using visual inspection of Q-Q plots of residuals, which indicated non-normal values (Supplementary Figures S1 and S2). Furthermore, the distribution of IL−6 and CRP was positively skewed. IL−6 and CRP were thus log-transformed in each study.

2.2.3. Covariates

CRP and IL−6 have been found to vary according to demographic factors (Lam et al., 2021). For example, older age, Black race, low socioeconomic status and being female have been associated with higher CRP and IL−6 (Lam et al., 2021). Therefore, age (in years), sex (1 =female, 0 =male), and education were included as demographic covariates in the analyses. Years of formal education were used in the

HRS, whereas education was reported on a scale from 1 (no qualification) to 7 (NVQ4/NVQ5/Degree or equivalent) in ELSA, from 1 (no grade school) to 12 (doctoral level degree) in MIDUS, from 1 (8th grade high school) to 8 (graduate school) in the MIDJA, from 1 (less than high school) to 4 (bachelors or more) in the NSHAP, and from 1 (no schooling completed) to 9 (Master's, professional or doctoral degree) in NHATS. Race was included in all samples except the MIDJA and was coded as 1 (African American/Black) and 0 (not African American/Black) in the HRS, MIDUS, NSHAP, and NHATS, and as 1 (not white) and 0 (white) in ELSA. Ethnicity (1 =Hispanic or Latinx, 0 =non-Hispanic/Latinx) was included as an additional covariate in HRS, the NSHAP, and the NHATS. Wave of personality assessment was controlled for in the NHATS (1 =2013, 0 =2014).

2.3. Data analysis

In each sample, linear regression analyses were conducted to test the association between personality and inflammatory markers. Inflammatory markers were the dependent variables. Log-transformed IL−6 was predicted from personality items in the HRS, the MIDUS, the MIDJA and the NHATS, and log-transformed CRP was predicted from personality items all six samples. All covariates were controlled for in these analyses. Time elapsed between personality and inflammatory marker assessments was controlled for in ELSA, MIDUS, MIDJA and NHATS. All continuous variables, including personality traits, were standardized to z-scores. Each item (z-scored) was tested in separate analyses. The standardized regression coefficients from each sample were pooled in a random effects meta-analysis using the JAMOVI 2.6.13 software. Standardized betas were the common metric across the samples, and arise from the same regression models across the samples. The meta-analysis of standardized regression coefficients provides an accurate estimate of association between a predictor and an outcome after controlling for covariates that are also related to the outcome variable. Coefficients were estimated using restricted maximum likelihood. Heterogeneity was assessed using I^2. Consistent with existing criteria (Higgins et al., 2003), no, low, moderate, and high heterogeneity were indicated by I^2 estimates around 0%, 25%, 50%, or 75%, respectively. Separate meta-analyses were conducted for CRP and Il−6. The association between personality domains and inflammatory markers was examined in additional regression analyses. Across the analyses and samples, the significance was set at p less than.01 (.05 / 5 traits =.01).

Sensitivity analyses examined the association between personality items and inflammatory markers, controlling for their corresponding personality domain. These analyses aimed to test whether the items have incremental predictive validity beyond the effect of their personality domain. In these analyses, the domain scores were calculated without the individual item examined.

3. Results

The results of the meta-analysis and individual studies for CRP and IL−6 are in Table 2 and Table 3, respectively. The conscientiousness items *organized* (CRP: β= −.05, 95%CI: −0.062; −0.034; Il−6: β= −.04, 95%CI: −0.060; −0.022) and *hardworking* (CRP: β= −.08, 95%CI: −0.102; −0.050; Il−6: β= −.06, 95%CI: −0.083; −0.043) were associated with lower CRP and IL−6. The *hardworking* item was the strongest conscientiousness item associated with the two markers. The extraversion item *lively* (CRP: β= −.04, 95%CI: −0.072; −0.014; Il−6: β= −.04, 95%CI: −0.059; −0.020) was associated with lower levels of both CRP and IL−6 levels. The forest plots for the *lively*, *hardworking* and *organized* items for CRP and IL−6 are in Fig. 1 and Fig. 2, respectively.

There were also some marker-specific associations. The extraversion

Table 2
Summary of regression analysis predicting crp from personality domains and items.

	HRS[a]	ELSA[b]	MIDUS[b]	MIDJA[c]	NSHAP[a]	NHATS[d]	Random Effect	Heterogeneity I^2
Personality domain								
Neuroticism	-.005	-.009	-.002	-.014	.028	-.009	-.003 (-.017;0.011)	0
Extraversion	**-.054**	-.03	-.020	.042	**-.070**	.011	**-.03(-.057;-.009)**	53.12
Openness	-.012	.008	.018	.031	-.035	-.012	-.006(-.020;.008)	0
Agreeableness	-.0098	.024	.044	.033	-.022	.021	.01(-.012;.032)	45.34
Conscientiousness	**-.065**	**-.061**	-.044	.045	**-.098**	-.066	**-.06(-.077;-.049)**	0.01
Personality items								
Moody	.020	.027	.018	-.049	.059	-	**.02(.010;.039)**	1.48
Worrying	-.025	-.020	-.017	-.004	-.0001	.009	-.02(-.034;-.005)	0
Nervous	-.009	-.013	.007	.006	.004	-.027	-.008(-.022;.006)	0
Calm	-.002	.017	.013	-.011	-.022	-	.002(-.012;.017)	0
Outgoing	-.002	.026	.026	.006	-.003	.006	.009(-.007;.024)	8.77
Friendly	.007	.021	.025	.042	-.041	-	.008(-.012;.027)	31.83
Lively	**-.069**	**-.044**	.002	.020	**-.068**	-	**-.04(-.072;-.014)**	65.89
Active	**-.140**	**-.152**	**-.165**	.040	**-.144**	-	**-.14(-.158;-.129)**	0
Talkative	.016	**.050**	.035	.056	.002	.014	**.03(.008;.044)**	24.37
Creative	-.006	.003	-.004	.005	-.031	.001	-.005(-.019;.009)	0
Imaginative	.003	.012	.023	.058	-.028	-.022	.003(-.011;.017)	0.11
Intelligent	.005	.031	**.075**	.063	-	-	.04(.001;.069)	70.09
Curious	.001	-.005	.023	-.027	.004	-	.001(-.013;.016)	0
Broad-minded	-.005	.032	.005	.038	-	-	.01(-.013;.035)	42.43
Sophisticated	-.021	.004	-.016	.007	-	-	-.01(-.029;.005)	11.36
Adventurous	**-.028**	-.031	-.007	.014	-.046	-	**-.03(-.042;-.013)**	0
Helpful	**-.035**	-.002	.034	.0004	-	-	-.005(-.039;.028)	68.66
Warm	.012	.025	.029	.005	-.006	.011	.01(.001;.029)	0
Caring	.002	.006	.010	.061	-.005	.026	.006(-.008;.020)	0
Softhearted	.0001	**.041**	**.066**	.012	.004	-	.02(-.003;.052)	61.2
Sympathetic	-.015	.011	.013	.052	-.058	-	-.007(-.034;.019)	58.68
Organized	**-.047**	**-.053**	-.050	.068	-.047	-.062	**-.05(-.062;-.034)**	1.29
Responsible	**-.049**	-.013	**-.080**	.061	**-.079**	-	-.04(-.077;-.010)	74.19
Hardworking	**-.086**	**-.074**	-.043	.014	**-.12**	-	**-.08(-.102;-.050)**	58.04
Careless	.008	.017	-.019	.006	-	-	.007(-.008;.023)	0
Thorough	-.018	-.037	-.005	.013	-.042	-.045	**-.02(-.039;-.011)**	0

Note. HRS: N = 9534, ELSA: N = 4715, MIDUS: N = 1912, MIDJA: N = 357, NSHAP: N = 1890, NHATS: N = 1398; [a]Adjusted for age, sex, education, race, and ethnicity; [b] Adjusted for age, sex, education, race, and time elapsed between assessments [c]Adjusted for age, sex, education, and time elapsed between assessments, [d] Adjusted for age, sex, education, race, ethnicity, wave of personality assessment, and time elapsed between assessments. Bold p < .01

Table 3
Summary of regression analysis predicting IL−6 from personality domains and items.

	HRS[a]	MIDUS[b]	MIDJA[c]	NHATS[d]	Random Effect	Heterogeneity I^2
Personality domain						
Neuroticism	-.012	.035	-.032	-.008	-.001(-.027;.025)	28.18
Extraversion	**-.035**	**-.061**	-.027	.039	-.02(-.067;.021)	69.92
Openness	-.012	-.028	-.015	.008	-.01(-.031;.006)	0
Agreeableness	-.016	.007	-.007	.044	.003(-.027;.032)	37.9
Conscientiousness	**-.057**	**-.074**	.019	-.015	**-.05(-.074;-.026)**	20.45
Personality items						
Moody	.011	.044	-.014	-	.02(-.006;.042)	14.1
Worrying	-.018	.002	-.024	-.0004	-.01(-.031;.006)	0
Nervous	-.014	.045	-.035	-.014	-.0002(-.033;.034)	50.57
Calm	.015	-.018	.007	-	.006(-.020;.031)	17.08
Outgoing	-.015	-.005	-.039	.028	-.009(-.028;.010)	0
Friendly	.006	-.017	.009	-	.002(-.018;.021)	0
Lively	**-.040**	-.039	-.032	-	**-.04(-.059;-.020)**	0
Active	**-.088**	**-.198**	-.043	-	-.12(-.207;-.027)	90.65
Talkative	.015	.025	.001	.038	.02(.000;.038)	0
Creative	-.007	-.007	.004	.021	-.003(-.022;.015)	0
Imaginative	-.007	-.010	-.014	-.009	-.008(-.027;.011)	0
Intelligent	.008	.026	.004	-	.01(-.008;.031)	0
Curious	-.013	-.008	-.10	-	-.02(-.035;.005)	0.19
Broad-minded	-.011	-.019	-.006	-	-.01(-.032;.007)	0
Sophisticated	-.006	-.043	.010	-	-.02(-.044;.013)	26.34
Adventurous	-.018	-.051	.041	-	-.02(-.050;.003)	19.44
Helpful	-.029	-.010	-.038	-	-.03(-.045;-.006)	0
Warm	-.006	-.007	.001	.032	-.001(-.020;.017)	0
Caring	.003	.015	-.017	.042	.009(-.010;.028)	0
Softhearted	.003	.010	.022	-	.005(-.015;.025)	0
Sympathetic	-.027	.015	.003	-	-.010(-.044;.023)	40.89
Organized	**-.039**	**-.074**	.034	-.023	**-.04(-.060;-.022)**	0
Responsible	**-.032**	**-.091**	-.002	-	-.05(-.097;-.002)	66.11
Hardworking	**-.067**	-.052	-.041	-	**-.06(-.083;-.043)**	0
Careless	.016	.005	-.071	-	.01(-.010;.031)	1.23
Thorough	-.027	-.032	.003	-.002	-.02(-.043;-.005)	0

Note. HRS: N = 7472, MIDUS: N = 1922, MIDJA: N = 357, NHATS: N = 1299; [a]Adjusted for age, sex, education, race, and ethnicity; [b] Adjusted for age, sex, education, race, and time elapsed between assessments, [c]Adjusted for age, sex, education, and time elapsed between assessments, [d]Adjusted for age, sex, education, race, ethnicity, wave of personality assessment, and time elapsed between assessments. Bold $p < .01$

item *active* (β= −.14, 95%CI: −.158; −.129) was associated with lower CRP. Notably, across all domains, *active* was the strongest item-level correlate of CRP in the meta-analysis and across all samples, except MIDJA (see Fig. 1). The conscientiousness item *thorough* was associated with lower CRP (β= −.02, 95%CI: −0.039; −0.011) and the extraversion item *talkative* was associated with higher CRP (β=.03, 95%CI: 0.008; 0.044) (Table 2). The neuroticism items were mostly unrelated to the two inflammatory markers, exception for the item *moody* and higher CRP (Table 2). Unexpectedly, the openness item *adventurous* was related to lower levels of CRP (β= −.03, 95%CI: −0.042; −0.013) (Table 2). Agreeableness items were unrelated to CRP and IL−6 (Table 2 and Table 3).

Domain-level conscientiousness was associated with lower levels of both CRP (β= −.06, 95%CI: −0.077; −0.049) (Table 2, Fig. 1) and IL−6 (β= −.05, 95%CI: −0.074; −0.026) (Table 3, Fig. 2). The size of these associations was lower than for the item *hardworking*, but stronger than the other items. Domain-level extraversion was related to lower CRP (β= −.03, 95%CI: −0.057; −0.009) (Table 2, Fig. 1). This association was weaker than the association between the extraversion items *lively* and *active* and CRP. Domain-level neuroticism, openness and agreeableness were unrelated to either CRP or IL−6 (Table 2 and Table 3).

Many of the associations persisted in sensitivity analyses controlling for the respective personality domain. Controlling for the conscientiousness domain, the item *hardworking* remained significantly associated with lower CRP in HRS (β= −.08, $p < .001$), ELSA (β= −.07, $p < .001$), and NSHAP (β= −.11, $p < .001$). Controlling for the extraversion domain, the item *active* remained significantly associated with lower CRP in the HRS (β= −.17, $p < .001$), ELSA (β= −.23, $p < .001$), the MIDUS (β= −.22, $p < .001$), and the NSHAP (β= −.16, $p < .001$), the item *lively* remained significantly associated with CRP in the HRS (β= −.07 $p < .001$), the item *talkative* remained significantly associated with higher CRP in ELSA (β=.11, $p < .001$). For IL−6, the item *hardworking* (β= −.06, $p < .001$) remained significantly associated with lower IL−6 in the HRS adjusting for the conscientiousness domain. The items *hardworking*, *active*, and *lively* thus have incremental predictive validity accounting for their corresponding personality domain.

4. Discussion

Based on six samples with more than 19,000 middle aged and older adults, the present study examined the association between personality nuances, operationalized by individual questionnaire items, and inflammation. Meta-analytic results indicated that the conscientiousness items *organized* and *hardworking* and the extraversion item *lively* were associated with lower CRP and IL−6. These associations were largely replicable across different inflammatory markers and samples with different demographic characteristics and from different countries. The extraversion item *active* was the strongest item-level correlate of lower CRP in the meta-analysis and across most samples. There was less consistent evidence for a relationship with neuroticism and openness items, and agreeableness items were unrelated to both markers. Consistent with existing literature (Luchetti et al., 2014; Stephan et al., 2024a; Wright et al., 2022), domain-level conscientiousness was associated with lower CRP and IL−6. Surprisingly, higher extraversion was linked to lower CRP – an association driven mainly by the item *active*. The nuance-level analysis advances these domain-level findings and existing knowledge on the personality-inflammation link (Luchetti et al., 2014; Wright et al., 2022) by providing a more granular, detailed understanding of the specific personality characteristics associated with inflammatory markers.

The overall pattern of association between nuances and inflammation is broadly consistent with the growing literature that links

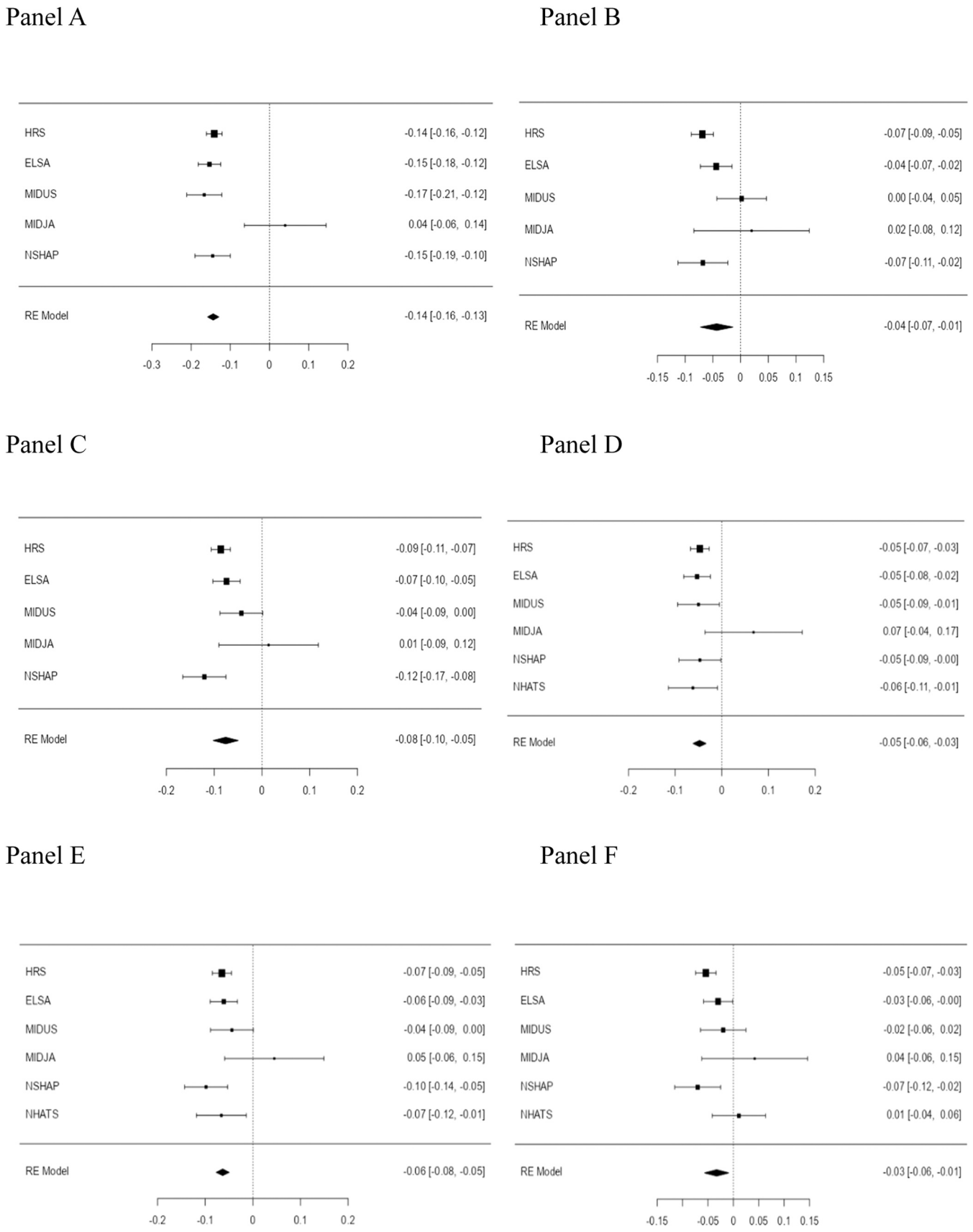

Fig. 1. Forest plots of the association between the items active (Panel A), lively (Panel B), hardworking (Panel C), organized (Panel D), conscientiousness (Panel E) and extraversion (Panel F) and CRP in each sample and the meta-analysis.

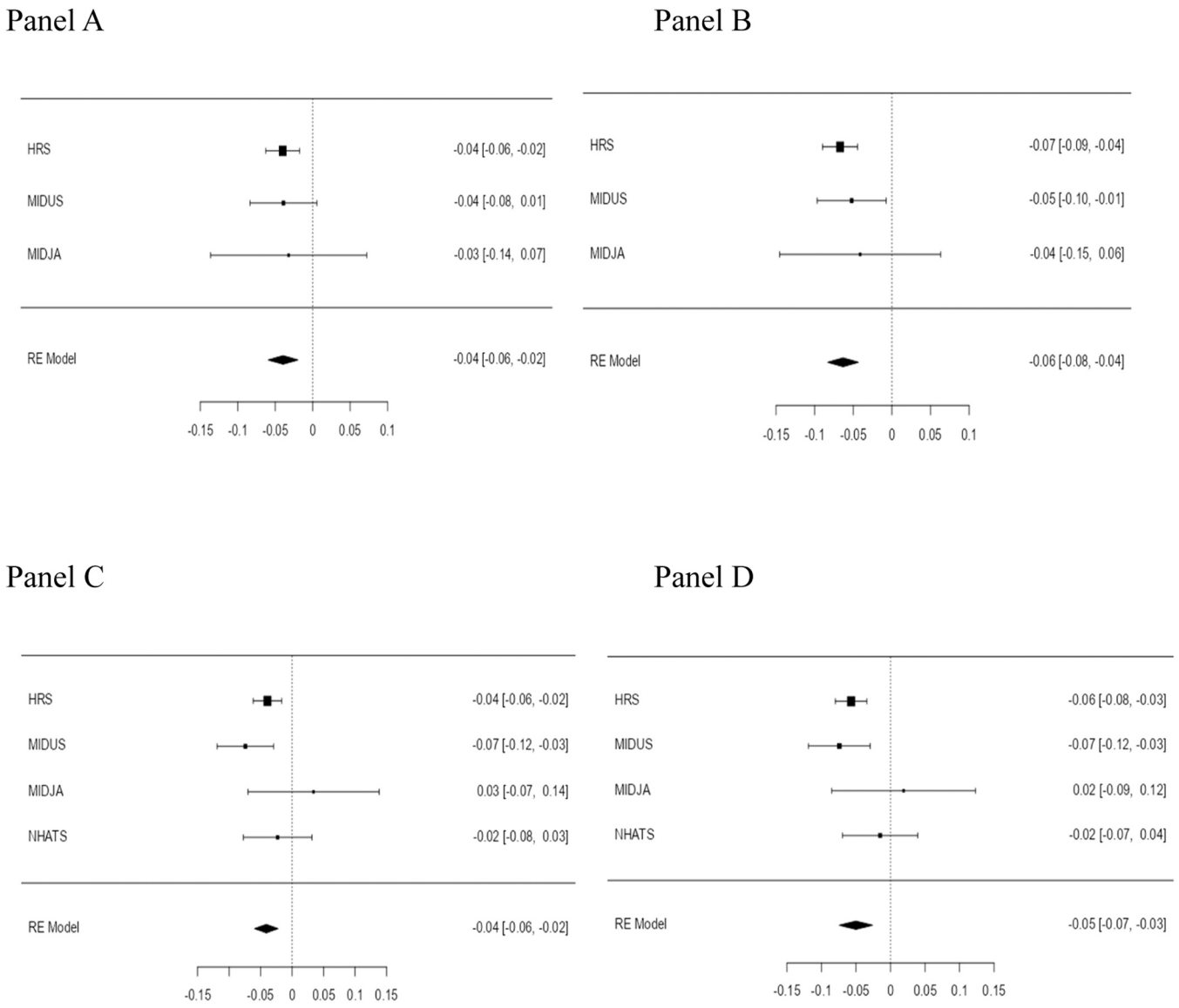

Fig. 2. Forest plots of the association between the items lively (Panel A), hardworking (Panel B), organized (Panel C), and conscientiousness (Panel D) and IL−6 in each sample and the meta-analysis.

personality nuances to health (Arumäe et al., 2024; Stephan et al., 2024b; Stephan et al., 2025d). For example, higher scores on the MIDI items *organized*, *hardworking*, *active*, and *lively* have generally been related to better health across a range of health outcomes, including lower risk of falls (Stephan et al., 2025b), dementia (Stephan et al., 2024b), and mortality (Stephan et al., 2025d). The present study extends this literature by providing evidence of an association between these nuances and measures of physiological health, indexed by CRP and IL−6. This study further supports the argument that health-related outcomes, ranging from physiological function to mortality, are predicted by a relatively similar set of personality nuances. The overall pattern of association observed between nuances and inflammatory markers could also be interpreted with regard to existing literature on personality facets and inflammation. For example, the association between the extraversion nuances *active* and *lively* and lower inflammation are consistent with evidence for the extraversion facet of activity (Chapman et al., 2009; Sutin et al., 2010). In addition, *hardworking* is a nuance of the industriousness/achievement striving facet (Costa, McCrae, 1992; Roberts et al., 2005) and being organized is a nuance of the order facet (Costa, McCrae, 1992), which have been associated with lower CRP and IL−6 (Sutin et al., 2010, 2018).

The *active* and *hardworking* nuances were the strongest and most consistent nuance-level correlates of inflammation across the different samples. In addition, these nuances were driving the association between their respective personality domains and inflammation. Indeed, the effect size of the association between *active* and CRP and between *hardworking* and both CRP and IL−6 were stronger than the size of the association between their respective domains and the inflammatory markers. Building upon past research (Arumäe et al., 2024; Seeboth and Mõttus, 2018; Stewart et al., 2022; but see Stephan et al., 2024b), these findings suggest that the association between these personality domains and inflammation is mostly driven by narrower nuances. Furthermore, these items were associated with the inflammatory markers independent of their respective domains in most samples, which suggests that these nuances contain unique information relevant for inflammation. In particular, being active and hardworking may reflect a higher energy level and better overall health that may manifest in lower inflammation. This hypothesis is supported by existing evidence for an association between the activity and industriousness/achievement striving facets and better cardiorespiratory fitness (Terracciano et al., 2013).

The present study found that the neuroticism, openness and agreeableness domains were unrelated to inflammatory markers. These null

associations have been reported in past research (Luchetti et al., 2014; Wright et al., 2022). There were also weak and mostly unreplicated associations with the items of these domains, as indicated by a small association between the neuroticism item *moody* and higher CRP and between the openness item *adventurous* and lower CRP. The mostly null findings for the neuroticism domain and items are surprising given that neuroticism is associated with poor mental and physical health (Wright and Jackson, 2023).

Several pathways may explain the association between personality and inflammation. Indeed, personality is related to a range of behavioral, psychological and clinical factors that have implications for inflammatory markers. For example, recent research found that higher conscientiousness and extraversion are associated with lower immunoscenescence through their association with higher physical activity, lower disease burden and lower BMI (Stephan et al., 2023). These factors are also likely to explain part of the association between the conscientiousness and extraversion domains and nuances and inflammation. Furthermore, higher conscientiousness and extraversion are characterized by lower stress reactivity (Chopik et al., 2025) and lower risk of depressive symptoms (Hakulinen et al., 2015) which may lead to lower inflammation.

The present study extends models of personality and health (Chapman et al., 2014; Friedman and Kern, 2014). Indeed, these models are mostly focused on the contribution of personality domains more than lower order traits. This study indicates that the nuance-level approach provides a more detailed picture of this association by highlighting the specific personality characteristics associated with physiological marker of health. Furthermore, the identification of an association between nuances and inflammatory markers may inform the potential mechanisms that explain their link with critical outcomes such as dementia and mortality. For example, lower CRP and IL−6 may explain part of the association between being active, lively, hardworking and organized and lower risk of dementia and mortality (Stephan et al., 2024b; Stephan et al., 2025d).

The present study has several strengths, such as the six samples of middle-aged and older adults from different cultures, the use of the MIDI across samples, the inclusion of both IL−6 and CRP, the coordinated analysis that used the same statistical approach across samples, and the meta-analytic synthesis of the findings. There are also several limitations. The observational design of the present study precludes causal interpretation. Although personality nuances may be predictors of inflammatory markers, it is also possible that higher inflammation may result into being less active, lively, hardworking, and organized – or that all these variables share causes. Furthermore, the present study focused on two common inflammatory markers, and more research is needed to test whether the pattern of association with nuances replicates using other inflammation measures. In addition, the set of items examined was relatively limited – in fact, the items were selected to measure nothing but the domains in the first place. As a result, the contribution of personality nuances of inflammation is very likely underestimated. Future research could use longer inventories such as the 240-item NEO- PIR (Costa, McCrae, 1992) or item pools specifically designed to assess a broad range of personality nuances (Condon et al., 2020). Although this study was conducted across several samples from different countries, additional research is needed to test for generalizability in low and middle-income countries.

To conclude, the present study found new evidence for an association between personality nuances and inflammation among middle-aged and older adults. Being active, lively, hardworking and organized are related to lower inflammation, indexed by CRP and/or IL−6.

Ethical approval

The HRS was approved by the University of Michigan Institutional Review Board (IRB). ELSA was approved by the National Research Ethics Service. The MIDUS and MIDJA studies were approved by the Education and Social/Behavioral Sciences and the Health Sciences IRB at the University of Wisconsin-Madison. The NSHAP was approved by the Social and Behavioral Sciences IRB at the University of Chicago and the NORC IRB. The NHATS was approved by the Johns Hopkins Bloomberg School of Public Health IRB. This study was based on publicly available de-identified datasets and therefore was exempt from Institutional Review Board review.

CRediT authorship contribution statement

stephan yannick: Writing – review & editing, Writing – original draft, Visualization, Supervision, Project administration, Methodology, Formal analysis, Conceptualization. **Martina Luchetti:** Writing – review & editing, Visualization, Methodology. **Antonio Terracciano:** Writing – review & editing, Writing – original draft, Visualization, Supervision, Methodology, Formal analysis, Conceptualization. **Angelina R. Sutin:** Writing – review & editing, Visualization, Methodology, Conceptualization. **René Mõttus:** Writing – review & editing, Methodology, Conceptualization.

Declaration of Competing Interest

None

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.psyneuen.2026.107916.

Data Availability

HRS data are publicly available at http://hrsonline.isr.umich.edu/. ELSA data are publicly available from the UK Data Service (UKDS, https://www.ukdataservice.ac.uk/). MIDUS and MIDJA data can be accessed at http://midus.wisc.edu/index.php. Information on how to access the NSHAP data can be found at: http://www.norc.org/Research/Projects/Pages/national-social-life-health-and-aging-project.aspx. NHATS data are available for public download at: http://www.nhats.org.

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