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Five-factor model personality traits and inflammatory markers: New data and a meta-analysis

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Abstract The purpose of this research is to examine the association between five major dimensions of personality and systemic inflammation through (a) new data on C-reactive protein (CRP) from three large national samples of adults that together cover most of the adult lifespan and (b) a meta-analysis of published studies on CRP and interleukin-6 (IL-6). New data (total $N = 26,305$) were drawn from the National Longitudinal Study of Adolescent Health, the Midlife in the United States study, and the Health and Retirement Study. PRISMA guidelines were used for the meta-analysis to combine results of up to seven studies on CRP ($N = 34,067$) and six on IL-6 ($N = 7538$). Across the three new samples, higher conscientiousness was associated with lower CRP. The conscientiousness-CRP relation was virtually identical controlling for smoking; controlling for body mass index attenuated this association but did not eliminate it. Compared to participants in the highest quartile of conscientiousness, participants in the lowest quartile had an up to 50% increased risk of CRP levels that exceeded the clinical threshold (≥ 3 mg/l). The

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meta-analysis supported the association between conscientiousness and both CRP and IL-6 and also suggested a negative association between openness and CRP; no associations were found for neuroticism, extraversion and agreeableness. The present work indicates a modest, but consistent, association between conscientiousness and a more favorable inflammatory profile, which may contribute to the role of conscientiousness in better health across the lifespan.

1. Introduction

Inflammatory markers, such as C-reactive protein (CRP) and interleukin-6 (IL-6), are intermediate markers of health that contribute to the development, maintenance, and worsening of disease. Although beneficial in response to an acute injury, low-grade systemic inflammation increases risk for chronic disease, including cardiovascular disease (Kaptoge et al., 2012), type 2 diabetes (Pradhan et al., 2001), and mortality (Harris et al., 1999). As such, there has been considerable interest in identifying factors associated with inflammatory markers, such as CRP and IL-6.

A number of psychosocial factors have been implicated in systemic inflammation (Morozink et al., 2010), including personality traits (Sutin et al., 2010). As operationalized by the five factor model (FFM) of personality (McCrae and John, 1992), an individual's characteristic ways of thinking, feeling, and behaving can be summarized along five broad dimensions: neuroticism, extraversion, openness, agreeableness, and conscientiousness. Of these five traits, conscientiousness and neuroticism are the traits most often associated with morbidity (Sutin et al., 2013) and mortality (Terracciano et al., 2008). These traits may thus also be associated with intermediate markers of health, including inflammation. And, indeed, conscientiousness, the tendency to be organized, disciplined, and self-controlled, has been associated with inflammatory markers: Less conscientious individuals tend to have higher levels of CRP and IL-6 (e.g., Sutin et al., 2010; Turiano et al., 2013; though see Armon et al., 2013; Mõttus et al., 2013). High neuroticism, the tendency to experience negative emotions such as anxiety, anger, and depression, has also been associated with higher levels of inflammatory markers (e.g., Sutin et al., 2010; Armon et al., 2013), but other studies have not replicated this association (e.g., Chapman et al., 2009; Chapman et al., 2011; Mõttus et al., 2013). Fewer studies have addressed the association between the other personality traits and inflammatory markers.

Although the literature on personality and inflammation is growing, there have been relatively few well-powered studies that included all five FFM traits. In addition, previous research on personality and inflammation has been concentrated on middle-aged (Turiano et al., 2013) and older adults (e.g., Mõttus et al., 2013). In fact, the median age of the samples reported in the literature is approximately 52. Thus, it is not yet known whether personality and inflammatory markers share similar associations across younger and older adults.

The present study extends research on personality traits and inflammatory markers in two ways. First, we present new data on the association between personality and CRP from three large national samples of American adults that together cover the adult lifespan: the National Longitudinal Study of Adolescent Health (Add Health; mean age 29), the Midlife in the United States study (MIDUS; mean age 55), and the Health and Retirement Study (HRS; mean age 68). Second, we combine the results from these three new samples with the published literature in a meta-analysis of the association between personality and CRP, and we present a meta-analysis of the published literature on the association between personality and IL-6. Based upon existing research, we expect that conscientiousness will have the most consistent relation with both CRP and IL-6. We also expect neuroticism to be associated with greater inflammation.

2. Methods

2.1. New data

2.1.1. Participants

(1)National Longitudinal Study of Adolescent Health (Add Health): Add Health began as a representative sample of adolescents in grades 7—12 in the United States during the 1994—1995 school year. The sample was followed into young adulthood, with the most recent assessment in 2008—2009, when the sample was aged 24—32. The 2008—2009 assessment was the first to include an FFM measure of personality and inflammatory markers. The current analyses included 13,967 participants (mean age, $M = 29.09$; standard deviation, $SD = 1.75$; age range 25—34; 54.4% female) for whom valid personality and CRP data were available.

(2)Midlife in the United States (MIDUS): MIDUS is a national survey of adults living in the United States, which began in 1995—1996 (MIDUS I). A longitudinal follow-up of the original sample was conducted in 2004—2006 (MIDUS II). This assessment included a measure of personality, and a subset also included biological data, including inflammatory markers. The current analyses included 1040 participants from MIDUS II for whom valid personality and CRP data were available (mean age, $M = 55.25$; standard deviation, $SD = 11.79$; age range 34—84; 54.6% female).

(3)Health and Retirement Study (HRS): HRS is a nationally-representative longitudinal study of Americans 50 and older, and their spouses regardless of their age. In 2006, half of the participants completed a face-to-face interview that included measurement of inflammatory markers and an FFM measure of personality included in a psychosocial questionnaire; the other half completed the same measures in 2008. The current analyses included 11,298

participants across the combined 2006–2008 interviews for which valid personality and CRP data were available (mean age, $M = 68.06$; standard deviation, $SD = 10.34$; age range 26–100; 60.0% female).

2.1.2. Personality assessment

(1)National Longitudinal Study of Adolescent Health (Add Health): Personality traits were assessed with the Mini-IPIP, a 20-item short form of the International Personality Item Pool (Donnellan et al., 2006). Respondents were asked ''How much do you agree with each statement about you as you generally are now, not as you wish to be in the future?'' The response scale ranged from 1 (*strongly disagree*) to 5 (*strongly agree*). Reliability ranged from .62 (neuroticism) to .71 (extraversion; Baldasaro et al., 2013).

(2) Midlife in the United States (MIDUS) and (3) Health and Retirement Study (HRS): Personality traits were assessed with the Midlife Development Inventory (MIDI) Personality Scales (Lachman and Weaver, 1997; for further information, see Ryff et al., 2012; Smith et al., 2013). Participants were asked how much each of 26 adjectives that assessed neuroticism (''moody''), extraversion (''outgoing''), openness (''creative''), agreeableness (''helpful''), and conscientiousness (''organized'') described themselves on a scale ranging from 1 (*not at all*) to 4 (*a lot*). Reliability ranged from .68 (conscientiousness) to .80 (agreeableness) in MIDUS and from .66 (conscientiousness) to .79 (openness) in HRS.

2.1.3. High sensitivity C-reactive protein

In Add Health and HRS, the participant's finger was cleansed with an alcohol swab, pricked with a sterile lancet, and the blood droplets were placed on specially treated filter paper. CRP was measured using a standard ELISA assay at the University of Washington (Add Health; Whitsel et al., 2012) or at the University of Vermont (HRS; Crimmins et al., 2013). In MIDUS, participants had a fasting blood draw at one of the clinical research centers. CRP was measured using a particle enhanced immunonepholometric assay (BNII nephelometer from Dade Behring Inc., Deerfield, IL) at the University of Vermont (Ryff et al., 2013). CRP measured from blood spots are highly correlated with CRP measured from serum (e.g., Brindle et al., 2010).

2.1.4. Analytic strategy

To normalize the CRP distribution, all values were natural log-transformed. For each of the three samples, we ran a series of linear regressions predicting CRP from each personality trait, controlling for age, age squared, sex, ethnicity, and education. We also performed logistic regressions to test whether personality was associated with risk of CRP above the clinical threshold (i.e. ≥ 3 mg/l).

A series of follow-up analyses were performed to determine the robustness of the findings. First, given that CRP is related to body mass index (BMI) (Visser et al., 1999) and smoking (O'Loughlin et al., 2008), we reran the analyses controlling for participants' BMI and smoking status. Second, to examine whether any of the effects were driven by an acute infection, we reran the analyses excluding participants with CRP values ≥ 10 (i.e., 13% in Add Health, 3% in MIDUS and 9.9% in HRS). Third, we included interactions to test whether the association between personality and CRP varied by age or sex within each of the three samples.

2.2. Meta-analyses

2.2.1. Literature search

The meta-analysis is reported according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses guidelines (PRISMA; Moher et al., 2009). The literature search was carried out using the following datasets: PUBMED, SCOPUS, and WEB of SCIENCE Cited Reference Search. Search terms included: ''five factor model'', ''neuroticism'', ''extraversion'', ''openness to experience'', ''agreeableness'', ''conscientiousness'', and ''inflammatory markers'' or ''inflammation'', ''C-reactive protein'' or ''CRP'', ''interluekin-6'' or ''IL-6''. Search was limited to papers in the English language published up to February 2014. The reference list of each selected study was examined to identify additional relevant work.

2.2.2. Study selection and meta-analytic approach

Two reviewers (JMB and ML) independently selected eligible studies. Disagreement between the two reviewers was settled by discussing it with the third reviewer (ARS). Studies were selected if they met our criteria for study design (correlational design/cross-sectional association), population (adults), and outcomes (one or both inflammatory markers of interest: CRP and/or IL-6). Studies were included only if a Five Factor measure of personality was used (Flow Diagram in Fig. 1).

A total of 236 citations were identified by the initial searches. On the basis of the titles and abstracts, we identified 10 full-text articles. After further evaluation, 2 articles were excluded because of the statistical approach and design used in the studies, and 1 article was excluded because part of the sample was included in a previously published study. No additional studies were identified from reference lists. A total of 7 eligible studies were identified, of which 4 had valid data on CRP and 6 had valid data on IL-6. Of note, given that personality is thought to be relatively stable over time, we included two studies in which IL-6 was assessed a few years after the assessment of personality (i.e., Mõttus et al., 2013; Turiano et al., 2013). To reduce variability across studies, when possible we chose parameters from the main models that adjusted for age, sex, education, and race/ethnicity. We performed random-effect model meta-analyses using the Comprehensive Meta-Analysis software package. We computed the correlation coefficient '*r*' as a measure of effect size calculated from the sample size and *p*-value. Heterogeneity was assessed using the Q statistic, and publication bias was evaluated by both funnel plots and Egger's test. Table 1 illustrates the characteristics of the selected studies for CRP and IL-6, respectively.

3. Results

3.1. New data

Table 2 shows the associations between each of the personality traits and CRP in the three datasets; Table S1

Table 1 Characteristics of the studies included in the meta-analyses.

Author (s)	Year	Inflammation markers	*N* sample	Age (mean, *SD*)	Gender (%female)	Personality measures	Association[a]						
							N	E	O	A	C	Design[b]	Controlling for
Chapman et al.	2009	CRP IL-6	103	52.0 (9.0)	76.7	NEO-FFI	n.s.	(−)	NA	NA	NA	CD	Age, sex, race, education
Sutin et al.	2010	CRP	4711	39.3 (14.7)	57.0	NEO-PI-R	(+)	n.s.	n.s.	n.s.	(−)	CD	Age, sex
		IL-6	4923	39.3 (14.7)	57.0	NEO-PI-R	(+)	n.s.	n.s.	n.s.	(−)	CD	Age, sex
Chapman et al.	2011	CRP IL-6	200	72.8 (6.7)	61.7	NEO-FFI	n.s.	n.s.	(−)	n.s.	(−)	CD/PD	Age, sex, education, study variables
Armon et al.	2013	CRP	1709	45.6 (9.6)*	31.0*	Mini-Marker	(+)	(+)	(−)	n.s.	n.s.	CD/PD	Age, sex, education, study variables
		IL-6											
Millar et al.	2013	CRP	324 (MDG)	51.5 (8.5)	51.9	EPQ	n.s.	n.s.	NA	NA	NA	CD	All variables
			342 (LDG)	51.8 (8.0)	50.0	EPQ	(+)	n.s.	NA	NA	NA		
		IL-6	324 (MDG)	51.5 (8.5)	51.9	EPQ	(−)	NA	NA	NA	NA	CD	All variables
			342 (LDG)	51.8 (8.0)	50.0	EPQ	(+)	NA	NA	NA	NA		
Mõttus et al.	2013	CRP	804–806*	69.5 (0.8)	50.2	NEO-FFI*	n.s.	n.s.	(−)	n.s.	n.s.	CD/PD	No variables
		IL-6	592–599*	72.5 (0.7)	49.1	NEO-FFI*	n.s.	NA	n.s.	NA	(−)	PD	Age, sex, social and cognitive background
Turiano et al.	2013	CRP IL-6	1054	54.6 (11.7)	56.0	MIDI	n.s.	n.s.	n.s.	n.s.	(−)	PD	Age, sex, race, education

Note. CRP = C-reactive protein (log transformed); IL-6 = interleukin 6 (log transformed); N = neuroticism; E = extraversion; O = openness; A = agreeableness; C = conscientiousness; (+) = positive association; (−) = negative association; n.s. = non significant; NA = not applicable (not tested or not reported); CD = cross-sectional design; PD = prospective design (personality measured before the inflammatory markers); NEO-FFI = NEO five factor inventory; NEO-PI-R = NEO personality inventory revisited; mini-marker = big five mini-marker scale; EPQ = eysenck personality questionnaire; MIDI = midlife development inventory personality scales; MDG = most deprived group; LDG = least deprived group. In the ''Year'' column it is reported the year of publication.

[a] We reported here the associations of the analytic models selected for the meta-analyses. Most of the studies controlled for demographics (age, sex, race and education).

[b] We selected studies that examined cross-sectional associations or both cross-sectional and prospective associations. Of note, given personality is thought to be stable over time, we also included two studies in which IL-6 was assessed few years after the assessment of personality (i.e., Mõttus et al., 2013; Turiano et al., 2013).

* See original study for further information.

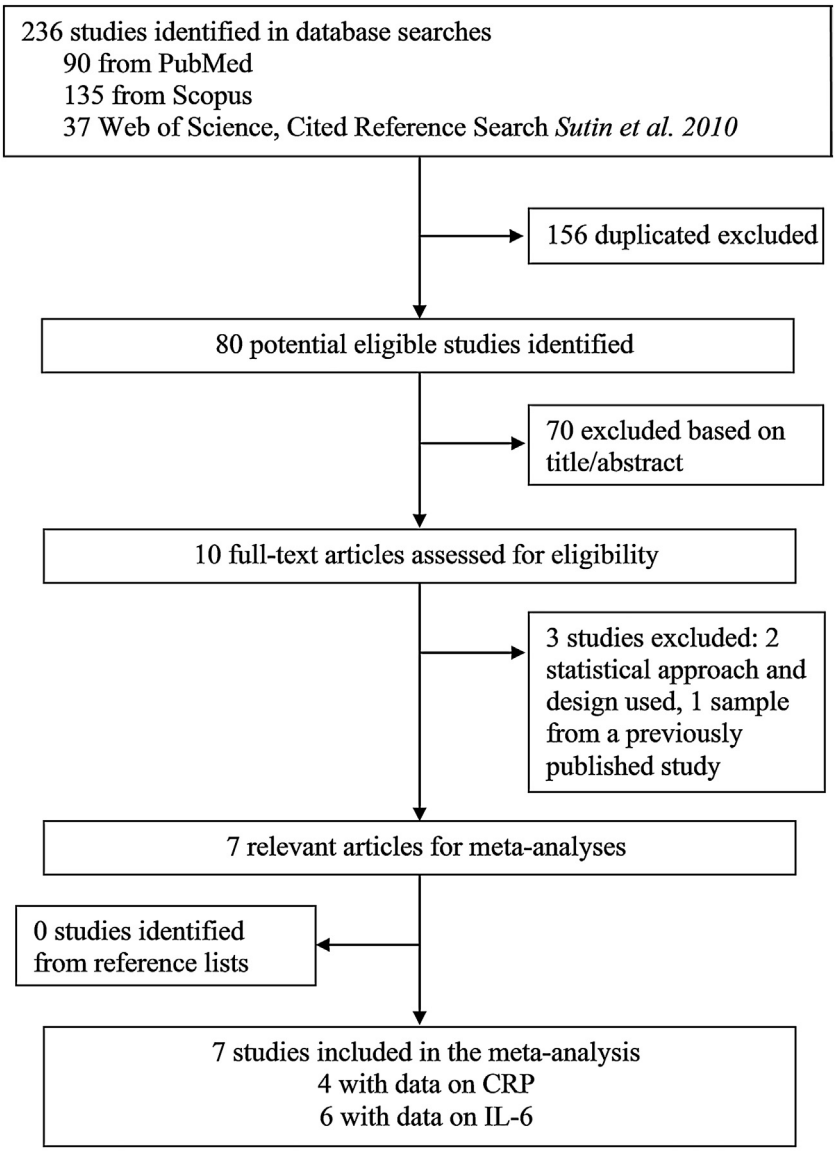

Fig. 1 Flow diagram for studies selection. *Note*. The count for each database includes non-English works.

from Supplementary Material shows the bivariate correlations between the study variables. A significant association between conscientiousness and CRP was found in all three samples: Those who were more organized and disciplined had less systemic inflammation[1]. The results from the logistic regressions paralleled those of the linear regressions (Table 2). For every standard deviation increase in conscientiousness, the risk of exceeding the clinical threshold was reduced by approximately 10—15% across the three samples. In addition, those in the lowest quartile of conscientiousness had an approximately 25—50% increased risk of exceeding this threshold compared to those in the highest quartile (OR = 1.24, 95% CI = 1.11—1.37 in Add Health; OR = 1.54, 95% CI = 1.04—2.28 in MIDUS; OR = 1.30, 95% CI = 1.17—1.45 in HRS). In contrast to conscientiousness, neuroticism was unrelated to CRP in any of the three studies. Mixed results emerged for the other three personality traits across the three samples. Lower openness was associated with higher CRP in Add Health, higher agreeableness was associated with higher CRP in MIDUS, and lower extraversion was associated with higher CRP in HRS. None of these associations replicated in the other two studies. The threshold analyses paralleled the analysis of CRP as a continuous variable.

[1] Given that the HRS sample was composed of spouses, there could be dependency in the data that artificially increased the association between personality and CRP. The intraclass correlations, however, were relatively low for the five traits (neuroticism = .15 [95% CI, lower limit, upper limit = .12, .17], extraversion = .07 [95% CI, lower limit, upper limit = .04, .09], openness = .24 [95% CI, lower limit, upper limit = .21, .27], agreeableness = .06 [95% CI, lower limit, upper limit = .03, .08], and conscientiousness = .14 [95% CI, lower limit, upper limit = .11, .16]), and similar associations were found when we split the sample and ran the analyses separately for each half of the couple. Of note, the association between conscientiousness and CRP was similar across these two subsamples and was of similar magnitude to what has been found in other samples.

Table 2 Associations between personality traits and CRP.

Personality	Bivariate correlations CRP log transformed			Linear regressions CRP log transformed									Logistic regressions (CRP ≥ 3mg/ml)					
	Add Health (rs)	MIDUS (rs)	HRS (rs)	Add Health (N = 13945)			MIDUS (N = 995–999)			HRS (N = 11190–11236)			Add Health			MIDUS		HRS
				B(SE)	β	p-Value	B(SE)	β	p-Value	B(SE)	β	p-Value	OR (95% CI)			OR (95% CI)		OR (95% CI)
Neuroticism	.06**	.01	.03**	.002 (.004)	.005	.556	−.013 (.060)	−.007	.827	.018 (.019)	.009	.341	1.01 (0.97–1.04)			1.01 (0.87–1.17)		1.02 (0.98–1.06)
Extraversion	.00	.04	−.04**	.002 (.004)	.004	.648	.050 (.063)	.025	.434	−.094 (.021)	−.043	<.001	1.00 (0.97–1.04)			1.07 (0.93–1.24)		0.92 (0.88–0.96)**
Openness	−.06**	−.04	−.04**	−.011 (.005)	−.020	.019	−.032 (.071)	−.014	.652	−.030 (.021)	−.014	.156	0.97 (0.94–1.01)			0.91 (0.79–1.06)		0.97 (0.93–1.01)
Agreeableness	.01	.11**	.02*	−.009 (.005)	−.017	.054	.153 (.073)	.068	.037	.020 (.025)	.008	.408	0.97 (0.93–1.00)			1.11 (0.95–1.99)		1.00 (0.96–1.05)
Conscientiousness	−.04**	−.05	−.06**	−.027 (.004)	−.054	<.001	−.154 (.080)	−.060	.056	−.140 (.024)	−.055	<.001	0.91 (0.88–0.95)**			0.85 (0.74–0.99)*		0.90 (0.86–0.93)**

Note. For each sample, regression analyses were controlled for age, age squared, sex, education, and race/ethnicity. r = Pearson correlation; B = non-standardized regression coefficients; SE = standard error of non-standardized coefficients; β = standardized regression coefficients; OR = odds ratio; CI = confidence interval.

* p < .05.

** p < .01.

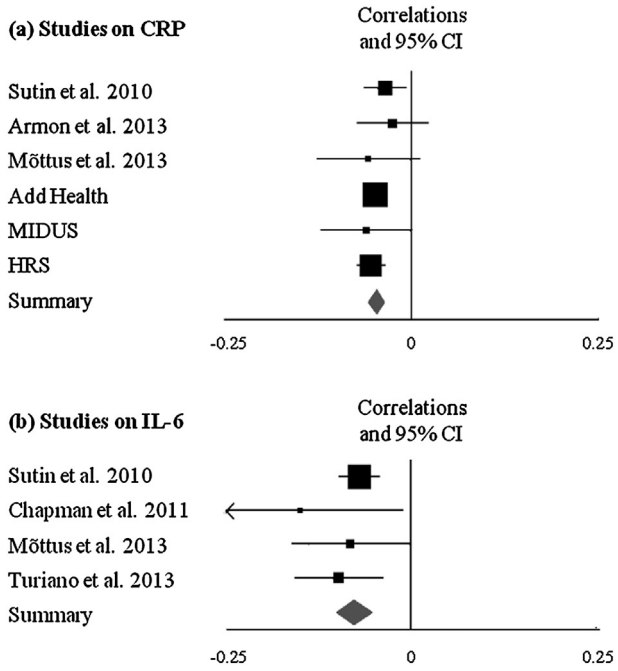

Fig. 2 Results of the meta-analyses for conscientiousness.

When we excluded participants with elevated CRP (i.e. ≥10), the pattern and magnitude of the associations were nearly identical. Moreover, after controlling for BMI, the effect of conscientiousness remained significant in Add Health and HRS, albeit attenuated (both βs ∼ −.02, ps < .05). This attenuation suggested that part of the association between conscientiousness and CRP was due to BMI. Controlling for smoking status did not change the association between conscientiousness and CRP (β = −.05, p < .001 in Add Health; β = −.07, p < .05 in MIDUS; β = −.06, p < .001 in HRS). Finally, in Add Health there were significant interactions with age for neuroticism (β = −.02, p < .05) and openness (β = .02, p < .05), which indicated a slightly stronger positive association between neuroticism and CRP among relatively older participants and a slightly stronger negative association between openness and CRP among the relatively younger participants. In HRS, there was a significant interaction between sex and agreeableness (β = .02, p < .05), with a slightly stronger positive association between agreeableness and CRP among women. None of these interactions replicated in the other two samples.

3.2. Meta-analyses

C-reactive protein: Including the new data from the ADD Health, MIDUS and HRS samples, we identified seven samples with data on neuroticism (total N = 34,026) and extraversion (N = 34,067), and six samples with data on openness (N = 33,369), agreeableness (N = 33,406), and conscientiousness (N = 33,396). Table 3 (see also Fig. S1 from Supplementary material) shows the results of the meta-analysis. By pooling the results across studies, the meta-analysis confirmed a significant association between conscientiousness and CRP (estimate = −0.048; 95% CI = −0.059, −0.037; p < .001) (Fig. 2). In addition, openness was also protective (Estimate = −0.021; 95% CI = −0.033,

Table 3 Correlation coefficients (95% CI) of the five-factor personality traits with CRP and IL-6 for each of the studies included in the meta-analysis.

Studies on CRP	Neuroticism	Extraversion	Openness	Agreeableness	Conscientiousness
Sutin et al. (2010)	0.035 (0.007, 0.064)	0.006 (−0.023, 0.034)	−0.015 (−0.044, 0.013)	−0.021 (−0.049, 0.008)	−0.035 (−0.064, −0.007)
Armon et al. (2013)	0.118 (0.071, 0.164)	0.118 (0.071, 0.164)	−0.061 (−0.108, −0.013)	−0.007 (−0.054, 0.041)	−0.025 (−0.072, 0.022)
Millar et al. (2013) (MDG), (LDG)	−0.052 (−0.160, 0.057), 0.167 (0.062, 0.268)	−0.065 (−0.173, 0.044), 0.092 (−0.014, 0.196)	–	–	–
Mõttus et al. (2013)	−0.037 (−0.106, 0.032)	−0.027 (−0.096, 0.042)	−0.072 (−0.141, −0.003)	−0.041 (−0.109, 0.029)	−0.058 (−0.127, 0.011)
Add Health	0.005 (−0.012, 0.022)	0.004 (−0.013, 0.020)	−0.020 (−0.036, −0.003)	−0.017 (−0.033, 0.000)	−0.054 (−0.065, −0.032)
MIDUS	−0.007 (−0.069, 0.055)	0.025 (−0.037, 0.087)	−0.014 (−0.076, 0.048)	0.068 (0.004, 0.127)	−0.060 (−0.122, −0.032)
HRS	0.009 (−0.010, 0.028)	−0.043 (−0.061, −0.024)	−0.014 (−0.032, 0.005)	0.008 (−0.011, 0.026)	−0.055 (−0.072, 0.036)
Meta−analysis random model (95% CI)	0.027 (−0.003, 0.057)	0.012 (−0.023, 0.047)	−0.021 (−0.033, −0.009)	−0.005 (−0.024, 0.014)	−0.048 (−0.059, −0.037)
Heterogeneity	Q = 34.04	Q = 49.29	Q = 5.69	Q = 10.79	Q = 2.29
Publication bias	($p < .001$)	($p < .001$)	($p = .337$)	($p = .056$)	($p = .807$)
Egger's regression intercept	$t = 0.80$, df = 6, $p = .46$	$t = 0.95$, df = 6, $p = .38$	$t = 1.81$, df = 4, $p = .14$	$t = 0.36$, df = 4, $p = .74$	$t = 0.46$, df = 4, $p = .66$

Table 3 (*Continued*)

Studies on CRP	Neuroticism	Extraversion	Openness	Agreeableness	Conscientiousness
Studies on IL-6	Neuroticism	Extraversion	Openness	Agreeableness	Conscientiousness
Chapman et al. (2009)	0.092 (−0.104, 0.280)	−0.197 (−0.376, −0.004)	–	–	–
Sutin et al. (2010)	0.041 (0.013, 0.069)	−0.020 (−0.048, 0.008)	−0.013 (−0.041, 0.015)	−0.025 (−0.053, 0.003)	−0.070 (−0.098, −0.042)
Chapman et al. (2011)	−0.017 (−0.156, 0.122)	0.056 (−0.083, 0.194)	−0.151 (−0.283, −0.012)	−0.054 (−0.191, 0.086)	−0.150 (−0.282, −0.011)
Millar et al. (2013) (MDG), (LDG)	−0.139 (−0.245, −0.031), 0.114 (0.008, 0.217)	–	–	–	–
Mõttus et al. (2013)	0.066 (−0.015, 0.145)	–	−0.012 (−0.093, 0.068)	–	−0.082 (−0.162, −0.001)
Turiano et al. (2013)	−0.035 (−0.095, 0.025)	−0.001 (−0.061, 0.059)	−0.042 (−0.103, 0.018)	0.044 (−0.017, 0.104)	−0.098 (−0.157, −0.038)
Meta-analysis random Model (95% CI)	0.015 (−0.040, 0.069)	−0.016 (−0.061, 0.029)	−0.028 (−0.064, 0.007)	−0.005 (−0.058, 0.049)	−0.078 (−0.101, −0.054)
Heterogeneity	Q = 18.28	Q = 4.71	*Q* = 4.21	Q = 4.44	Q = 1.78
Publication bias Egger's regression intercept	(*p* = .006) *t* = 0.51, df = 5, *p* = .63	(*p* = .194) *t* = 0.25, df = 2, *p* = .82	(*p* = .240) *t* = 1.84, df = 2, *p* = .21	(*p* = .108) *t* = 0.32, df = 1, *p* = .80	(*p* = .619) *t* = 2.94, df = 2, *p* = .10

Note. Add Health = National Longitudinal Study of Adolescent Health; MIDUS = Midlife in the United States; HRS = Health and Retirement Study; CRP = C-reactive protein (log transformed); IL-6 = interleukin 6 (log transformed); MDG = most deprived group; LDG = least deprived group. For the CRP meta-analysis, we included seven samples with data on neuroticism (total *N* = 34,026) and extraversion (*N* = 34,067), and six samples with data on openness (*N* = 33,369), agreeableness (*N* = 33,406), and conscientiousness (*N* = 33,396). For the IL-6 meta-analysis, we identified six samples with data on neuroticism (total *N* = 7538), four samples with data on extraversion (*N* = 6280), openness and conscientiousness (*N* = 6769), and three samples with data on agreeableness (*N* = 6177). All models included in the meta-analysis controlled at least for demographics (age, sex, and/or education), with the exception of CRP data of Mõttus et al. (2013). We used sample size and *p*-values to compute '*r*' parameters of inflammation-personality associations.

−0.009; $p = .001$). There was no evidence of heterogeneity for either conscientiousness or openness (Q $ps > .05$; see Table 3). No significant association was found between CRP and neuroticism, extraversion, or agreeableness, and there was marked heterogeneity across studies for these three traits (Q $ps < .05$; see Table 3). There was no evidence of publication bias as evaluated by the Egger's test (regression intercept, $ps > .10$). See Fig. S2 from Supplementary material for funnel plots. Finally, we performed a meta-regression employing the random-effects model to test whether there was an effect of sample age on the personality-inflammation associations. Sample age was not significantly associated with the relation between personality and CRP, although the small number of samples included in the analysis may limit the power to detect an effect.

Interleukin-6: We identified six samples with valid data on neuroticism (total $N = 7538$), four samples with data on extraversion ($N = 6280$), openness and conscientiousness ($N = 6769$), and three samples with data on agreeableness ($N = 6177$). The meta-analysis confirmed a significant effect for conscientiousness (see Fig. 2; estimate = −0.078; 95% CI = −0.101, −0.054; $p < .001$): higher scores on conscientiousness were associated with lower IL-6. Neither neuroticism nor any of the other three traits were associated with IL-6. Similar to CRP, there was no evidence of heterogeneity for conscientiousness (Q $p > .05$; see Table 3); the negative direction of this association was consistent across studies. There was no evidence of publication bias (i.e., Egger's regression intercept, $ps > .10$). Finally, sample age did not moderate the association between personality and IL-6, although the small number of samples included in the analysis may limit the power to detect an effect.

4. Discussion

The present research took a comprehensive approach to the association between personality traits and inflammation by (a) using new data from three large national samples and (b) performing a meta-analysis of published studies on two different inflammatory markers, CRP and IL-6. Consistent with previous research (e.g., Sutin et al., 2010; Chapman et al., 2011), across both inflammatory markers, conscientiousness was the most consistent personality correlate of systemic inflammation. The meta-analysis also revealed a significant association between CRP and openness, but not for IL-6. Neuroticism, extraversion, and agreeableness were unrelated to inflammation in the meta-analysis of CRP and IL-6. In addition, the average age of the sample had no systematic effect on the association between the inflammatory markers and personality traits, indicating this association is consistent across adulthood.

Higher conscientiousness was associated with lower CRP with remarkably similar effects across the three new samples and the meta-analysis. For every standard deviation increase in conscientiousness, the risk of exceeding the clinical threshold (i.e. ≥3 mg/l) was reduced by approximately 10—15%. Moreover, those in the highest quartile (vs. the lowest quartile) of conscientiousness had an up to 50% reduced risk of exceeding this clinical threshold. Of note, the new data indicated a similar association between conscientiousness and inflammation in younger as well as older adults: The protective effect of conscientiousness starts early in adulthood and extends into later life. One short-term longitudinal study found that conscientiousness was associated with maintaining a stable level of low inflammation over time (Chapman et al., 2011). Although the current cross-sectional data cannot address stability (or change) over time, the similar associations between conscientiousness and CRP found in younger, middle, and older adulthood suggest that conscientious individuals may maintain their healthier inflammatory profiles as they age. In contrast, individuals who are less organized, disciplined, and self-controlled (lower conscientiousness) may have fewer adaptive resources to effectively respond to repeated exposure to stress, which may contribute to elevated inflammatory markers.

There are at least two non-mutually exclusive pathways through which conscientiousness may be associated with inflammation. Preliminary evidence has linked higher conscientiousness to lower stress-related activation of hypothalamic-pituitary-adrenal (HPA) axis (Zobel et al., 2004). Conscientious individuals also tend to maintain a healthier weight across adulthood (Sutin et al., 2011), which is associated with a healthier inflammatory profile. Furthermore, individuals higher in conscientiousness also tend to engage in fewer health-risk behaviors, such as physical inactivity, unhealthy dietary patterns, and smoking (Terracciano and Costa, 2004; Roberts et al., 2005), which may contribute to chronic inflammation (e.g., Fröhlich et al., 2003; Fischer et al., 2007). As such, conscientiousness may be directly associated with inflammation through physiological mechanisms and indirectly associated with it through health-related behaviors. Future research could consider the possible effects of these behavioral and lifestyle factors, which were not accounted for in the present study; such factors may mediate the association between conscientiousness and systemic inflammation.

More broadly, the consistent association between conscientiousness and the inflammatory markers suggests that higher inflammation could be a potential mediator of the link between low conscientiousness and worse health outcomes across the lifespan (Friedman et al., 1995; Kern and Friedman, 2008; Friedman and Kern, 2014). For example, elevated CRP has been implicated in cardiovascular disease (Kaptoge et al., 2012), and lower conscientiousness is also a risk factor for cardiovascular mortality (Terracciano et al., 2008; Jokela et al., 2014). The systemic inflammation of individuals low in conscientiousness may thus partly contribute to their increased risk of cardiovascular mortality. A similar process may contribute to the association between low conscientiousness and risk for morbidity.

In the present research, our correlational data could not address the direction of the association between conscientiousness and the inflammatory markers. That is, individuals who are less organized and disciplined may have higher levels of inflammation in part because of their tendency to engage in unhealthy behaviors. At the same time, however, systematic inflammation may have an effect on personality by depleting the physical, emotional, and cognitive resources necessary to engage in adaptive behaviors. Over time, higher inflammation may reduce the energy and ability to foster and sustain the pattern of

industriousness, self-discipline, organization, and diligence that define conscientiousness. We could not tease apart these two possibilities with the current data.

The meta-analysis also revealed an inverse association between openness and CRP. Although statistically significant in only three out of the six samples, the direction of the association was consistent across studies. Individuals higher in openness tend to engage in a wide range of physically and cognitively stimulating activities (Stephan et al., 2013) that may help reduce systemic inflammation (e.g., Hamer et al., 2012). Moreover, lower openness is associated with worse cognitive function in old age (Sharp et al., 2010; Williams et al., 2013), and increased risk of incident dementia (Terracciano et al., 2014), and higher systemic inflammation is commonly associated with cognitive decline (e.g., Schram et al., 2007). Thus, openness may be protective of cognitive functioning in part through its association with lower inflammation across the lifespan.

Surprisingly, there was no association between neuroticism and inflammation in any of the three new samples or in either meta-analysis. There was, however, evidence for heterogeneity across the studies. While some work has found a positive relation between neuroticism and inflammation (Sutin et al., 2010; Armon et al., 2013), others reported no association (Mõttus et al., 2013; Turiano et al., 2013). The differences across studies might be due to several factors, including sample size and the personality questionnaire used. Studies with smaller samples tend to report larger effects, which may overestimate the overall meta-analytic effect size. A second possibility is that differences in the quality and content of the personality questionnaires across studies contributed to the heterogeneity. For example, using the NEO-PI-R, Sutin et al. (2010) found that the inflammatory markers were most associated with facets of neuroticism related to angry hostility, impulsivity, and vulnerability but not with facets related to anxiety and depression. In contrast, The NEO-FFI, a shortened version of the NEO-PI-R, the Mini-IPIP and the MIDI Personality Scales have items that tap primarily into anxiety and depression and not the hostility, impulsivity, and vulnerability facets of neuroticism. As such, scales that have items that reflect the anxiety and depression aspects of neuroticism, but not the hostile, impulsive, and vulnerable aspects of neuroticism, may not be associated with inflammation. This hypothesis is supported by other research that has found links between inflammatory processes and an aggressive disposition (e.g., Coccaro et al., 2014) and the tendency to give into cravings and urges (Sutin et al., 2012). Although depressive symptoms are both concurrently and longitudinally associated with inflammation (Howren et al., 2009; Valkanova et al., 2013), the somatic aspects of depression (which are not captured on personality inventories) tend to be more strongly related to inflammation than aspects related to negative affect (Deverts et al., 2010), and it may be that more severe forms of depression are associated with inflammation (Wium-Andersen et al., 2013), rather than the general emotional instability that is captured by neuroticism.

Finally, no significant association was found for extraversion or agreeableness in either meta-analysis. Similar to neuroticism, the findings for extraversion have been mixed, which may be due in part to differences across scales. For example, both Chapman et al. (2009) and Sutin et al. (2010) found an association between the Activity component of extraversion and inflammatory markers, but only marginal or non-significant associations for the broad extraversion dimension. Thus, differences across studies might depend on how much the scale captures extraversion's activity component versus its sociability component. Though commonly associated with health-conditions such as cardiovascular disease (Costa et al., 1989) that are characterized by chronic inflammation, no significant association was found for agreeableness.

Among the strengths of the current study were the use of three large national samples (total $N = 26{,}305$) that together covered most of the adult lifespan, including a large sample of young adults, and a meta-analysis of two different inflammatory markers. The present study also had several limitations. First, we only focused on the broad dimensions of personality, whereas detailed measures of the facets would be more informative. Although our findings replicated and extended previous research, future research should move from factor-level to facet-level analysis. There are also other important traits, not considered here, that fall between Five Factor Model traits (e.g., hostility; Smith and Williams, 1992) that have been associated with inflammation (e.g., Suarez et al., 2004). Second, there was evidence of heterogeneity for three of the traits (neuroticism, extraversion, and agreeableness) among the studies included in the meta-analyses. As noted above, in the case of neuroticism, inconsistent results across studies were likely due to differences in the scales used to assess this trait—i.e., which component of neuroticism were captured. Third, from our findings, we cannot speak to the direction of causality. The way that people think, feel and behave shapes the circumstances that lead to greater inflammation, but at the same time, systemic inflammation may have an effect on personality development across adulthood. Further studies are needed to test this potential reciprocal relation.

Lastly, inflammation is complex, and a variety of factors modulate it (e.g., exercise, diet, etc.). As such, psychosocial factors, such as personality traits, are likely to have only a modest effect. Despite the modest effect, the strength of the present research is that it identified a psychological factor — conscientiousness — that is associated reliably with inflammatory markers. That is, meaningful individual differences in the tendency to be organized and disciplined are associated with a more beneficial inflammatory profile, a pattern that replicated across samples. And, even modest effects can be important for predicting health outcomes (Roberts et al., 2007). The association between personality and CRP may also have theoretical and practical implications by outlining possible pathways of vulnerability or resilience to stress and disease. For example, systemic inflammation may be one intermediate marker of health that contributes to the association between conscientiousness and risk of morbidity and mortality.

In sum, the present research identified conscientiousness as the personality trait with the most consistent association with inflammation. Identifying personality traits and specific facets associated with inflammation may help health professionals target populations that are at higher risk of morbidity and mortality to prevent disease and promote healthy aging.

Contributors

A.R. Sutin and A. Terracciano designed the research. M. Luchetti, J.M. Barkley, and A.R. Sutin managed the literature searches and studies selection for the meta-analysis. M. Luchetti, Y. Stephan, and A.R. Sutin performed the statistical analyses. All authors contributed to and have approved the final manuscript.

Role of the funding source

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Conflict of interest statement

All authors confirm that there are no known conflicts of interest associated with this publication and there has been no financial support for this work that could have influenced its outcome.

The manuscript has been read and approved by all named authors and there are no other persons who satisfied the criteria for authorship but are not listed. The order of listed authors has been approved by all of them.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at http://dx.doi.org/10.1016/j.psyneuen.2014.08.014.

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