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Personality Predicts Cognitive Function Over Seven Years in Older Persons

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Abstract

Objectives—To determine whether Neuroticism, as well as the less-studied dimensions the Five Factor Model of personality (Extraversion, Openness to Experience, Agreeableness, and Conscientiousness) were associated with 7-year trajectories of cognitive functioning in older persons.

Design—Primary analysis of existing clinical trial data.

Participants—602 persons of average age 79 at baseline.

Measurements—The NEO-Five Factor Inventory of personality, completed at baseline, and the modified Mini Mental Status Exam (3MSE) measured every 6 months for 7 years.

Results—Controlling for demographics, baseline morbidities including depression, health behaviors, Apolipoprotein E4 genotype, and self-rated health, higher Neuroticism was associated with worse average cognitive functioning and a steeper rate of decline over follow-up. Higher Extraversion and lower Openness were both associated with worse average cognitive functioning

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Conflicts of Interest

None of the authors have any financial or personal conflicts of interest to declare.

Author Contributions

Study concept and design – Franks, Chapman, Duberstein, Robbins

Acquisition of subjects and/or data – Robbins

Analysis and interpretation of data – Franks, Chapman, Duberstein, Robbins, Tindle, Sink

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prospectively, while persons higher in Conscientiousness showed a slower rate of cognitive decline.

Conclusions—In addition to Neuroticism, other dispositional tendencies appear prognostically relevant for cognitive functioning in older persons. More work is needed to understand the mechanisms by which traits operate, as well as whether mitigation of certain dispositional tendencies can facilitate a better course of cognitive function.

Keywords

Older persons; primary care patients; cognitive functioning; cognitive decline; personality

Introduction

Cognitive decline in older adults may eventuate in Mild Cognitive Impairment (MCI) and potentially dementia¹, conditions which can involve substantial functional impairment and quality of life decrements. Moreover, rates of MCI and dementia are growing in step with population aging². Treatments are only modestly effective, underscoring the need to examine determinants of the cognitive function that may precede dementia.

The interrelationships between personality and cognitive function have received considerable attention³, because personality tendencies affect sophistication, efficiency, and type of cognitive activity⁴. The model of personality that has proven most fruitful in studying cognition and other aspects of health and aging is the Five Factor Model (FFM) of personality traits. The FFM, empirically derived from over 70 years of research, groups many specific traits along five primary axes of human cognitive, emotional and behavioral variation⁵. These are Neuroticism (tendencies to experience negative emotions), Extraversion (sociability, energy, positive emotions), Openness to Experience (attentiveness to inner experience and sensations, interest in novelty, ideas, values, aesthetics), Agreeableness (altruism, compliance, the pursuit of interpersonal harmony), and Conscientiousness (dependability, orderliness, competence, and goal-orientation). These so called “Big 5”⁵ dimensions peak in stability in mid-life but are not immutable, showing some plasticity even in the latter decades of life⁶. Twin studies suggest that population variance in the Big 5 is roughly 50% genetic, with the remaining coming from non-shared environmental influences⁷.

The Big 5 have been identified as phenotypes at the intersection of the social environment, biology, and health outcomes⁸. As such, research on the Big 5 can identify risk markers, provide important clues about mechanisms driving health outcomes across the lifespan, and suggest populations and avenues for intervention⁸. Personality operates through a wide range of behavioral, social, and biological mechanisms to influence health across the lifespan⁹. Because it is a root etiologic factor for several pathways to more immediate risks, personality’s effects on aggregate health are considerable: meta-analytic evidence places them at a magnitude comparable to SES and IQ¹⁰.

Root causes of complex risk chains are important in the present research context for two reasons. First, one can identify general segments of the population at risk for adverse cognitive outcomes through a variety of channels, rather than focusing on one or a few of more immediate risk factors. Second, addressing the root cause can prevent several paths of a complex risk chain from subsequently unfolding¹¹ and adversely effecting health. This obviates the need for an array of specific interventions each addressing one of several downstream, immediate risks. In the case of personality, interventions at sensitive, early points in the lifespan may be feasible¹². Recent evidence has also shown that the biologic basis of

personality can be leveraged to induce change during adulthood¹³, and that such change can also be induced using an established behavioral intervention¹⁴.

Personality appears to be a potentially salient risk factor for cognitive function in old age. Individuals higher in Neuroticism show greater probability of dementia and lower levels of cognitive function cross-sectionally prospectively, and more rapid declines in cognitive function, largely independent of depressive disorders^{15–18}. This risk does not appear to be mediated by the formation of beta-amyloid plaques and neurofibrillary tangles¹⁷. However, Neuroticism is marked by elevated autonomic reactivity and HPA-axis function^{19,20} and consequent chronic elevations in cortisol are known to produce hippocampal atrophy in animals²¹. Neuroticism may also erode working memory capacity because chronic anxiety involves intrusive and/or ruminative thoughts which compete for limited cognitive resources in the working memory system²². Finally, Neuroticism is a risk factor for depression in old age²³, and depression is a known risk for cognitive dysfunction in the elderly².

Among the other dimensions of the Big 5, Openness may be a predictor of cognitive function in old age. Persons who are more Open engage in greater cognitive activity in everyday life²⁴, a factor contributing to greater cognitive reserve²⁵. Consistent with this evidence, studies showed that persons who went on to develop Alzheimer's disease tended to be rated lower on pre-morbid Openness by proxy respondents^{26, 26, 27}. There has also been some effort to link Openness to dopaminergic systems²⁸, which appear to play some role in cognition²⁹, but this is speculative. Prospective studies also revealed that lower Openness was associated with Alzheimer's Disease (AD; ¹⁶³⁰). One of these studies³⁰ also documented a somewhat more robust protective effect for greater Conscientiousness, suggesting that diligent pursuit of goals and maintenance of everyday life responsibilities may contribute to cognitive reserve. Some weaker evidence from this same study also suggested that lower Extraversion conferred risk for AD as well. Other findings for Extraversion have suggested curvilinear effects or interactions with Neuroticism^{31, 32}, making its role somewhat more difficult to discern. Finally, no evidence or theory suggests a distinctive role for Agreeableness in cognitive dysfunction at this time.

To address these questions, we examined the contribution of all FFM traits to prospective cognitive function in a large cohort of older persons enrolled in a clinical trial. We hypothesized that lower Neuroticism and higher Openness and Conscientiousness would predict better prospective cognitive function. We also explored the effects of Extraversion and Agreeableness. Prior studies have noted an interaction between Extraversion and Neuroticism³², and that risk attributable to each of the Big 5 may be correlated³⁰. Guided by these findings, we examined the effects of all 5 dimensions simultaneously to adjust for any overlap, and also screened all possible 2-way interactions between traits.

Methods

Sample

The sample consisted of older persons enrolled in the Ginkgo Evaluation of Memory (GEM) study. Details of the sample have been published elsewhere^{33,33}. The study was conducted under an investigational new drug application with the Food and Drug Administration under the auspices of the National Center for Complementary and Alternative Medicine (NCCAM) and registered at clinicaltrials.gov. For the larger GEM study, eligible subjects were recruited at 4 sites between 2000 and 2002. This prospective cohort sub-study examining the relationship between personality and cognitive decline includes only subjects enrolled at the University of California, Davis (UCD) site. These UCD subjects were recruited after consenting to the additional data collection.

The GEM study itself built upon the infrastructure of the Cardiovascular Health Study, a longitudinal epidemiological study of normal elderly individuals initiated in 1988. Few subjects of that original study participated in the GEM trial study, and 90% of volunteers were newly recruited through local advertising. Key enrollment criteria included: age over 72 years, availability of a proxy respondent, English as the usual language, and absence of significant morbidity. At the UCD site, 2234 potential subjects participated in an initial screening telephone interview: 551 (24.7%) were ineligible; 761 (34.1%) refused to participate; and 922 (41.3%) attended the baseline study visit. Of these, 916 (99.3%) were randomized. Subjects at the UCD site had characteristics similar to those at the other sites. Because this sub-study was initiated after the start of the main GEM study, only 771 (84.2%) of the 916 enrolled subjects completed the personality inventory and are included in the current analyses. Finally, apolipoprotein E (APOE) genotyping was obtained on 80% of subjects (78.2% of those in Sacramento), and 602 (78.1%) of those completing the personality inventory. Subjects were examined every 6 months until they met the study outcome (diagnosis of dementia, death, or study conclusion, a maximum of 7.3 years (median 6.1 years). Note that the intervention had no effect on outcomes, and did not interact with personality. Nevertheless, we included intervention arm as a covariate in analyses.

Measures

The *NEO-Five Factor Inventory*³⁴ is a 60-item self-report questionnaire with 12 items measuring each of the five factors that comprise the FFM (Neuroticism; e.g., “I often feel inferior to others;” Extraversion; e.g., “I like to have a lot of people around me;” Openness; e.g., “I have a lot of intellectual curiosity;” Agreeableness; e.g., “I try to be courteous to everyone I meet;” and Conscientiousness; e.g., “I keep my belongings clean and neat.”). Response options comprise a 5-point Likert scale from Strongly Disagree to Strongly Agree. Internal consistency (Cronbach’s coefficient alpha) for the five scales ranged from .75 (Openness) to .82 (Conscientiousness) in the current study. The NEO-FFI’s use in research in gerontology and geriatric psychiatry^{35, 36} attests to its reliability and applicability to older samples.

Subjects also provided other information at baseline, including: age, gender, race/ethnicity, education (years of schooling, coded as <12, 12, 13–15, 16 years), self-rated health (excellent, very good, good, fair, poor), history of five diseases possibly associated with cognitive function (hypertension, diabetes, osteoporosis, cancer, and cardio-vascular disease [any of coronary heart disease, angina, stroke, transient ischemic attack, bypass surgery, or angioplasty]), the CES-Depression score, and smoking status (never, vs. ever). Other measures included body mass index ([BMI] Kg/m², categorized into underweight [<18.5], normal [18.5–< 25], overweight [25–< 30], and obese[>30]) based on measured height and weight at baseline) and APOE genotyping, categorized into e4 allele present or absent. Subjects did not differ statistically by whether or not they completed the personality inventory or by whether or not APOE genotyping was completed.

Outcome Measure

Participants completed an assessment of cognitive function at each 6-month follow-up visit, most consistently the Modified Mini-Mental Status Exam [3MSE]^{37, 37}. Compared with the original Mini-Mental State Exam, the 3MSE incorporates four additional test items, offers more graded scoring (0–100 instead of 0–30, with higher scores indicating better function), and is more sensitive for detecting cognitive disorders.

Analyses

Data were analyzed using Stata (Version 10.1, StataCorp, College Station, Texas). Key analyses were conducted using a series of random effects linear regressions (adjusting for the nesting of repeated measurements on each participant), with the 3MSE score at each visit as the dependent variable. Random effects models provide unbiased estimates even when missing data is tied to observed factors. An unstructured covariance matrix was selected based on likelihood ratio tests of alternative covariance structures. The key independent variables were the scores on the NEO-FFI, standardized to a mean of 0 and a standard deviation of 1 to facilitate interpretation. Analyses adjusted for wave (centered) and wave squared, as well as the covariates noted above. Models included both a random intercept and random slope for wave. To assess whether rate of cognitive decline was affected by personality, an additional analysis included interaction terms between visit number and each personality factor, as well as non-linear effects for each personality factor. Standard errors were obtained via cluster-bootstrap to account for non-normal random effects.³⁸ All reported p-values are from Wald chi-squares with 1 degree of freedom. Main models did not include baseline 3MSE, but secondary analyses included it as either a covariate or outcome.

Secondary analyses examined the following additional covariates: vital status (death any time during follow-up, coded 0 vs. 1), social involvement (questions assessing time spent visiting with others and playing cards) and alcohol use. Additional models excluded subjects with mild cognitive impairment (MCI) status at baseline (defined as a 3MSE score < 88).

Results

Complete baseline data were available on 602 participants (Table 1). The sample ranged in age from 72–91 years, and was predominantly non-Hispanic White and well-educated. Personality scores suggested levels of Neuroticism about .5 standard deviations (SD) below and Conscientiousness roughly .4 SD below those of the NEO standardization sample³⁴. Overall, baseline 3MSE scores tended to be near the upper end of the scale, i.e. 93–94 out of 100 possible points. **Mean (SD) scores on the 3MSE by assessment point were 1: 94.1 (4.4); 2: 94.2 (4.3); 3: 94.2 (4.3); 4: 94.3 (4.3); 5: 94.4 (4.2); 6: 94.4 (4.3); 7: 94.5 (4.2); 8: 94.6 (4.1); 9: 94.5 (4.1); 10: 94.7 (4.0); 11: 94.6 (4.0); 12: 94.9 (3.9); 13: 94.6 (4.2); 14: 95 (3.7).** Table 2 shows the results of the random effects regression of 3MSE on participant characteristics. Worse adjusted average cognitive function over the follow-up was associated with lower Openness and higher Extraversion and Neuroticism. Higher Neuroticism was also associated with a steeper rate of cognitive decline. Higher Conscientiousness was associated with a more gradual rate of decline (i.e., the trajectories were such that while persons in higher Conscientiousness started with non-significantly worse 3MSE scores, they were surpassed in rate of deterioration by persons low in Conscientiousness at year 5).

Controlling for death during the follow-up period, social involvement, baseline 3MSE, and alcohol consumption and restricting the analysis to those without initial MCI produced very similar findings.

Discussion

We observed that persons higher in Extraversion and Neuroticism and lower in Openness showed worse average cognitive function over 7 years, independent of several potential confounders. Notably, a two standard deviation change in the level of both Neuroticism and Openness was associated with differences in cognitive function larger than that associated with the APOE genotype. As in prior work, higher Neuroticism was also associated with a steeper rate of decline in cognitive function. The trajectory for persons higher in Conscientiousness was more complex, however: although such persons appeared to begin

the study with slightly worse cognitive function, the difference was not significant. Instead, persons higher in Conscientiousness showed *slower* rates of decline than those who were less Conscientious. The differences in rates of decline indicated that by year 5, persons higher in Conscientiousness began to show better cognitive function than those low in this trait.

The steeper rate of cognitive decline marked by high levels of Neuroticism is consistent with prior reports reflecting actual^{15, 17, 18} as well as subjective³⁹ cognitive performance. A possible pathophysiologic mechanism may involve hippocampal atrophy due to chronic elevations of cortisol resulting from overactivity of the HPA Axis⁴⁰. Such a mechanism might account for the link between chronic depression and memory problems, and Neuroticism is a widely known risk-factor for depression in older adults.²³ Of note, however, the relationship between Neuroticism and cognitive function was independent of baseline depression symptoms and the APOE genotype, suggesting independent effects of chronic distress, current depressive symptoms, and a well-known genetic risk marker. Taken together, these findings also support processing efficiency theory, which suggests that ruminative and anxious tendencies squander precious working memory resources, leading to worse cognitive performance²².

Our results demonstrate a new finding concerning the role of Openness and cognitive performance. The intellectual activity and engagement in cognitive processing signified by Openness^{41, 42} appears to prognosticate slightly better average cognitive function over time, even when the effects of education are controlled. The tendency of more Open persons to pursue and encounter novel situations, people, and activities likely facilitates processing of new information⁴. Such active cognitive engagement may help maintain cognitive function²⁴.

Prior findings have suggested both that higher Extraversion conveys greater risk for cognitive impairment³¹, as well as lower risk for Alzheimers when Neuroticism is low³². In this study, we observed no interaction between Extraversion and Neuroticism. Instead, Extraversion was associated with worse average cognitive function over the follow-up period. One possible reason is that the external stimulation sought by persons higher in Extraversion in order to maintain optimal levels of physiological arousal²⁰ actually impedes processing on cognitive tasks. Future work is needed to further explore the association of Extraversion with cognitive function in old age.

In this cohort, higher levels of Conscientiousness mitigated the rate of cognitive decline. The lower rate of cognitive decline is consistent with reports of reduced risk for AD and MCI in conscientious clergy³⁰, if one considers MCI and AD as progressively lower thresholds on the 3MSE that will be more rapidly approached by persons of lower Conscientiousness. Persons who are more Conscientious are organized and deliberative³⁴, which may help preserve cognitive skills through the regular synthesis and processing of complex information. Behaviorally, persons higher in this trait are dependable and achievement oriented. Having life goals toward which one strives, as well as routines which engage one in daily life may present more opportunities for everyday problem-solving and cognitive activity.

Overall study findings have several implications. From a clinical perspective, older persons prone to distress may require closer monitoring, and/or more aggressive interventions to maintain cognitive function from their 70s onward. The same may be true of those who are more Extraverted, less Open, and/or less Conscientious. Persons with more than one of these dispositional risk factors warrant special attention, as the effects we observed for these traits were independently additive. Brief personality assessments based on the FFM, appropriate

for memory clinics, mental health, or even primary care settings, exist^{43, 44}. Clinically, patients who are low in Openness may require closer monitoring of cognitive function. This could include closer attention by family members to every day cognitive activities, as well as earlier or more frequent specialist evaluations at memory clinics, for instance. Low Openness patients may also represent good candidates for early intervention or prevention efforts aimed at staving off cognitive decline, including cognitive training programs and/or pharmacologic agents. Potential interventions to bolster cognitive function may include both pharmacotherapy and training in compensatory strategies, such as the use of memory aids, schedules, and cognitive exercise⁴⁵. Such training would be best targeted to those at dispositional risk. As well, some habitual tendencies encompassed by personality may be amenable to modification. For instance, antidepressants reduce Neuroticism as well as depression in depressed persons¹³, and behavioral interventions may improve Neuroticism in some non-depressed adults¹⁴. Although cognitive impairment is associated with impaired functioning in all persons, conceivably additional impairment may occur in persons high in Neuroticism, because they may be less likely to seek or receive the assistance of others in compensatory strategies such as collaborative problem solving⁴⁶ due to their tendency toward negative affect.

From a research perspective, our findings echo prior work on the importance of untangling the pathophysiologic and cognitive mechanisms through which Neuroticism speeds cognitive decline. Our findings on Openness, Extraversion, and Conscientiousness indicate that the mechanisms through which these aspects of personality exert their effects—both cognitively and biologically (including possible genetic components)—require additional elucidation to guide interventions. In particular, it would be useful to deploy imaging methods to investigate signs of structural and/or functional changes associated with dispositional risk.

Findings must be interpreted with balanced consideration of study strengths and limitations. Although recent evidence suggests that personality can be shaped via programs early in the life course¹² and during adulthood^{13, 14}, little is known at this point about how and when to attempt intervention, whether to target global Big 5 dimensions, more specific aspects of personality, or behavioral manifestations of personality, or who might be good candidates for such interventions. Further study of these issues is needed. In the mean time, personality phenotype is probably most useful as an index of risk, facilitating the targeting of interventions intended to bolster cognitive function in old age. Although covariate coverage was extensive, the possibility of unmeasured confounders can never be ruled out. Biologic markers of disease may have provided better covariate data, to the extent that diseases were related to both personality and cognitive function.

As depression and possibly other diseases may lie on the causal path between Neuroticism and cognitive decline, our findings (which controlled for depression) may underestimate the total impact of Neuroticism (i.e., through its intervening mechanisms). Although controlling for death during follow-up showed no evidence of healthy survivor bias (selective loss of subjects with specific personality profiles), such effects can never be entirely ruled out. Personality traits cannot be randomized, so despite robust prospective prediction, causal inference must be tentative. Even if they are not directly or indirectly causal, however, personality phenotype would appear relevant in prognosticating the course of cognition among older persons. A related limitation, however, is that we were not able to measure the impact of cognitive decline upon personality, owing to lack of repeated personality measurements. Another limitation is that subjects willing and able to enroll in a long-term dementia prevention project likely have particular dispositional characteristics so the findings may not generalize to other populations of older persons. As well, the 3MSE might

not be optimally sensitive to subtle cognitive changes, and persons with the greatest declines may have failed to come to clinics for assessments.

We also did not examine in detail the longitudinal course of other diseases potentially related to personality, such as heart disease; further work might pursue this. This study was carried out in the context of a clinical trial. This is a limitation in that an intervention was present. However, the intervention was ineffective and showed no differential effectiveness by personality. Thus, there is nothing about the design of the study which precludes inference about personality on the longitudinal course of cognitive function. In this sense, the study is a valuable 7-year longitudinal assessment of a cohort in the latter decades of life. Finally, the 3MSE is a measure of global cognitive function, meaning we were not able to study the effects of personality upon specific components of cognitive function. **The overall stability in mean 3MSE scores may have reflected a combination of practice and healthy survivor effects.** However, as a composite measure of cognitive function, it may hold broad relevance to daily life functioning for older persons.

In the context of these considerations, our findings suggest that not only higher Neuroticism, but also higher Extraversion and lower Openness and Conscientiousness may be important risk factors for worse cognitive function over the long term, in a group of older persons recruited from the community. Further investigation of the pathways that connect personality traits to cognitive decline and/or dementia would appear useful for prevention, intervention and prognostic purposes.

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The study sponsor had no role in designing or conducting the study analyses or in preparing the manuscript.

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Appendix

GEM Study Personnel

Project Office

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Clinical Centers

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Schwabe Pharmaceuticals

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Cognitive Diagnostic Center

Steven DeKosky, MD, Judith Saxton, PhD, Oscar Lopez, MD, Beth Snitz PhD, M. Ilyas Kamboh PhD, Diane Ives, MPH, Leslie Dunn, MPH, University of Pittsburgh

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MRI Reading Center

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Data Safety Monitoring Board

Richard Grimm, MD, PhD (Chair), University of Minnesota; Jonathan Berman, MD, PhD (Executive Secretary), National Center for Complementary and Alternative Medicine; Hannah Bradford, M.Ac., L.Ac., MBA, Carlo Calabrese, ND MPH, Bastyr University Research Institute; Rick Chappell, PhD, University of Wisconsin Medical School; Kathryn Connor, MD, Duke University Medical Center; Gail Geller, ScD, Johns Hopkins Medical Institute; Boris Iglewicz, Ph.D, Temple University; Richard S. Panush, MD, Department of Medicine Saint Barnabas Medical Center; Richard Shader, PhD, Tufts University.

Table 1

Sample Characteristics

	Mean/N	SD/%
<u>Baseline Characteristics</u>		
Age (years)	75	6.6
Male	188	38%
Female	309	62%
Education (years)	14.3	2.4
Neuroticism	44.8	10
Extraversion	51.3	10
Openness	49.9	9.8
Agreeableness	54.6	9.6
Conscientiousness	49.5	9.9
No History of Alcohol/Substance Abuse/Dependence		
No History of Alcohol/Substance Abuse/Dependence		
Never Smoker	294	39%
Current Smoker	65	9%
Former Smoker	390	52%
Normal Tensive History	138	28%
History of Hypertension	359	72%
<u>Time-Varying Characteristics</u>		
<u>HDRS Affective Symptoms</u>		
Wave 1 (Baseline)	2.8	3.8
Wave 2 (12 Month Follow-up)	2.6	3.3
Wave 3 (24 Month Follow-up)	2.2	2.9
Wave 4 (36 Month Follow-up)	2.4	3.1
Wave 5 (48 Month Follow-up)	2.5	2.8
<u>Fasting Cholesterol</u>		
Wave 1 (Baseline)	195.0	36.4
Wave 2 (12 Month Follow-up)	190.3	36.4
Wave 3 (24 Month Follow-up)	186.4	38.9
Wave 4 (36 Month Follow-up)	180.7	39.2
Wave 5 (48 Month Follow-up)	183.7	39.8
<u>Cumulative Illness Rating Scale</u>		
Wave 1 (Baseline)	7.4	2.9
Wave 2 (12 Month Follow-up)	8.6	3.1
Wave 3 (24 Month Follow-up)	9.3	3
Wave 4 (36 Month Follow-up)	9.9	3.2
Wave 5 (48 Month Follow-up)	11	2.6

Note: HDRS = Hamilton Depression Rating Scale

Table 2

Predictor	Hypothesis Tested	
	Personality Predicts <i>Average Levels Of Illness Burden Over Follow-up</i>	Personality Predicts <i>Rate of Illness Burden Accumulation Over Follow-up</i>
<u>Fixed Effects</u>		
Neuroticism	0.62 ***	0.63 ***
	(0.16)	(0.16)
Extraversion	−0.16	−0.16
	(0.16)	(0.17)
Openness	−0.06	−0.06
	(0.18)	(0.18)
Agreeableness	−0.13	0.03
	(0.18)	(0.19)
Conscientiousness	−0.43 **	−0.44 **
	(0.16)	(0.16)
Time: Years	1.28 ***	1.37 ***
	(0.06)	(0.07)
Time: Years ²	−0.11 *	−0.11 *
	(0.05)	(0.05)
Time: Years ³	0.06	0.06 *
	(0.03)	(0.03)
Baseline Age (Years)	0.13 ***	0.13 ***
	(0.02)	(0.02)
Education (Years)	−0.07	−0.07
	(0.06)	(0.06)
Female Gender	−0.48	−0.49
	(0.28)	(0.28)
Agreeableness * Time		−0.18 **
		(0.05)
Intercept (Average CIRS at Wave 3)	9.72 ***	9.73 ***
	(0.22)	(0.22)
<u>Random Effects</u>		
Linear Time Variance	0.53 ***	0.51 ***
	(0.07)	(0.07)
Quadratic Time Variance		
	.08 ***	.08 ***
	(0.03)	(0.03)
Cubic Time Variance		

Predictor	Hypothesis Tested	
	Personality Predicts <u>Average Levels</u> Of Illness Burden Over Follow-up	Personality Predicts <u>Rate of Illness Burden Accumulation</u> Over Follow-up
	.05 ***	.05 ***
	(0.02)	(0.02)
Intercept Variance		
	7.09 ***	7.11 ***
	(0.49)	(0.49)
Residual Variance		
	.59 ***	.59 ***
	(0.06)	(0.05)
<i>N</i>	1453	1453
<i>AIC</i>	5714	5709
<i>BIC</i>	5804	5804

Notes. Entries are parameter estimates (change in CIRS scores per unit increase in predictor), beneath which standard errors are in parentheses.

Personality traits scaled by interquartile range, so that 1 unit corresponds to difference between a person at 75th v. 25th percentile.

*
p .05

**
p .01

p .001. Random effect standard errors smaller than .001 are reported as zero. P-values are from z-statistics.

Table 3

Effects of Covariate Adjustment on Personality Estimates

Predictor	Covariates Tested to Explain Personality Effects			
	HDRS Affective	Alcohol/Substance	Smoking	Hyper-Tension
Fixed Effects				
Neuroticism	0.59 *** (0.17)	0.62 *** (0.16)	0.62 *** (0.16)	0.61 *** (0.16)
Extraversion	-0.15 (0.16)	-0.17 (0.17)	-0.16 (0.16)	-0.21 (0.16)
Openness	-0.07 (0.18)	-0.07 (0.18)	-0.06 (0.18)	-0.09 (0.18)
Agreeableness	-0.23 (0.18)	-0.19 (0.18)	-0.43 (0.18)	-0.19 (0.18)
Conscientiousness	-0.43 ** (0.16)	-0.43 ** (0.16)	-0.43 ** (0.16)	-0.42 ** (0.16)
Time: Years	1.28 *** (0.06)	1.25 *** (0.07)	1.33 *** (0.09)	1.34 *** (0.10)
Time: Years ²	-0.11 * (0.05)	-0.11 * (0.05)	-0.11 * (0.05)	-0.11 * (0.05)
Time: Years ³	0.06 (0.03)	0.06 * (0.03)	0.06 * (0.03)	0.06 * (0.03)
Baseline Age (Years)	0.13 *** (0.02)	0.13 *** (0.02)	0.13 *** (0.02)	0.12 *** (0.02)
Education (Years)	-0.07 (0.06)	-0.07 (0.06)	-0.07 (0.06)	-0.05 (0.06)
Female Gender	-0.49 (0.28)	-0.42 (0.29)	-0.49 (0.28)	-0.48 (0.28)
Agreeableness * Time	-0.18 ** (0.07)	-0.16 * (0.07)	-0.19 ** (0.05)	-0.19 ** (0.05)
HDRS Affective (Time varying)	0.09 (0.07)			
HDRS Affective * Time	0.03 (0.06)			
History of Alcohol/Substance Abuse/Dependence		0.42 (0.33)		
History of Alcohol/Substance Abuse/Dependence * Time		0.15 (0.11)		
Current Smoker			-0.13 (0.51)	
Current Smoker * Time			-0.16 (0.19)	
Former Smoker			-0.01 (0.27)	
Former Smoker * Time			-0.08 (0.10)	
History of Hypertension				1.02 *** (0.28)
History of Hypertension * Time				-0.08 (0.11)
Fasting Cholesterol (Time Varying)				-0.00 (0.00)
Fasting Cholesterol * Time				-0.00 (0.00)

Predictor	Covariates Tested to Explain Personality Effects				
	HDRS Affective	Alcohol/Substance	Smoking	Hyper-Tension	Fasting Cholesterol
Intercept (Average CIRS at Year 3)	9.59 *** (0.25)	9.59 *** (0.25)	9.75 *** (0.28)	9.00 *** (0.30)	9.70 *** (0.23)
Random Effects					
Linear Time Variance	0.50 *** (0.06)	0.50 *** (0.06)	-0.51 *** (0.07)	-0.50 *** (0.07)	0.50 *** (0.08)
Quadratic Time Variance	.08 *** (0.02)	.08 *** (0.02)	.08 *** (0.03)	.08 *** (0.03)	.08 *** (0.03)
Cubic Time Variance	.05 *** (0.02)	-.05 *** (0.02)	.05 *** (0.02)	.05 *** (0.02)	.05 *** (0.02)
Intercept Variance	7.11 *** (0.49)	7.11 *** (0.49)	7.10 *** (0.49)	6.89 *** (0.48)	6.95 *** (0.48)
Residual Variance	.59 *** (0.06)	.59 *** (0.06)	.59 *** (0.49)	0.59 *** (0.06)	.60 *** (0.06)
<i>N</i>	1453	1453	1453	1453	1414
<i>AIC</i>	5710	5709	5715	5697	4856
<i>BIC</i>	5816	5815	5831	5803	4958

Notes. Entries are parameter estimates (change in CIRS scores per unit increase in predictor), beneath which standard errors are in parentheses. HDRS = Hamilton Depression Rating Scale. Personality traits and HDRS affective scores scaled by interquartile range, so that 1 unit corresponds to difference between a person at 75th v. 25th percentile.

* p .05

** p .01

*** p .001. P-values are from z-statistics.