

Research Article

Premorbid personality traits as predictors for incident predementia syndromes: a multistate model approach

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Abstract

Objective: Associations have been found between five-factor model (FFM) personality traits and risk of developing specific predementia syndromes such as subjective cognitive decline (SCD) and mild cognitive impairment (MCI). The aims of this study were to: 1) Compare baseline FFM traits between participants who transitioned from healthy cognition or SCD to amnestic MCI (aMCI) versus non-amnestic MCI (naMCI); and 2) Determine the relationship between FFM traits and risk of transition between predementia cognitive states. Methods: Participants were 562 older adults from the Einstein Aging Study, 378 of which had at least one follow-up assessment. Baseline data collected included levels of FFM personality traits, anxiety and depressive symptoms, medical history, performance on a cognitive battery, and demographics. Follow-up cognitive diagnoses were also recorded. Results: Mann–Whitney U tests revealed no differences in baseline levels of FFM personality traits between participants who developed aMCI compared to those who developed naMCI. A four-state multistate Markov model revealed that higher levels of conscientiousness were protective against developing SCD while higher levels of neuroticism resulted in an increased risk of developing SCD. Further, higher levels of extraversion were protective against developing naMCI. Conclusions: FFM personality traits may be useful in improving predictions of who is at greatest risk for developing specific predementia syndromes. Information on these personality traits could enrich clinical trials by permitting trials to target individuals who are at greatest risk for developing specific forms of cognitive impairment. These results should be replicated in future studies with larger sample sizes and younger participants.

Keywords: personality; mild cognitive impairment; subjective cognitive decline; multistate modeling; cognitive outcomes; Einstein Aging Study

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Introduction

It has been proposed that personality be incorporated into conceptual models of dementia risk as personality assessments have utility as readily available, low-cost measures to predict cognitive impairment (Low et al., 2013) and dementia (Aschwanden et al., 2021). Such measures could then be used in intervention studies targeting those who are at greater risk for cognitive impairment based on personality traits. Because personality traits are generally considered to be stable over the lifespan (Edmonds et al., 2013), they may be used to identify risk during early and middle adulthood (before symptoms of dementia-related cognitive impairment typically manifest) and allow interventions to begin earlier. The predominant model for describing dimensions of personality is the fivefactor model (FFM; Widiger, 2015) which includes openness (the degree to which an individual wants to try new things or go to new places), conscientiousness (the degree to which an individual is hardworking, orderly, and rule-abiding), extraversion (the degree to which an individual is sociable or assertive), agreeableness (the

degree to which an individual maintains positive relationships with others), and neuroticism (the degree to which an individual experiences the world as threatening or unsafe).

Several studies have investigated the relationships between FFM personality traits and the development of specific predementia syndromes. A recent longitudinal study investigating the association between premorbid personality traits and the incidence of specific mild cognitive impairment (MCI) syndromes (i.e., amnestic [aMCI] vs. non-amnestic [naMCI]) in a community sample found that neuroticism was associated with greater risk of developing naMCI while there was no association between personality traits and development of aMCI (Ayers et al., 2020). This suggests that personality traits may differently predict cognitive state transitions depending on whether an individual shows signs of memory impairment specifically.

At the subjective cognitive decline (SCD) stage, those with subjective memory complaints often endorse higher degrees of neuroticism/emotional instability when compared to cognitively

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healthy (CH) peers (Hill et al., 2019b; Luchetti et al., 2016; Muñoz et al., 2020; Pearman & Storandt, 2005; Steinberg et al., 2013). High neuroticism in SCD has also been associated with greater risk of conversion to objective cognitive impairment (Aschwanden et al., 2022) and MCI (of unspecified subtype) over a seven year follow-up period (Bessi et al., 2018). One European cross-sectional study compared the personality profile of SCD to those with aMCI and naMCI in individuals who presented to a memory clinic (Berger-Sieczkowski et al., 2019). It was found that individuals with SCD had significantly higher levels of extraversion and openness compared to those with aMCI and similar personality profiles to those with naMCI. This finding further suggests personality traits may have differential utility in predicting future cognitive impairment depending on whether memory is impacted.

The present study

Sieczkowski and colleagues' (2019) and Ayers and colleagues' (2020) results suggest that certain personality traits may differentiate individuals who develop memory deficits and those who do not. To date, to our knowledge no studies have examined the association between premorbid personality traits and transitions from CH to SCD to MCI (both amnestic and non-amnestic). This information is necessary to make inferences about which personality traits best predict progression to primarily amnestic (e.g., aMCI) versus non-amnestic neurodegenerative disorders (e.g., naMCI). Multistate modeling (MSM) analyses allow for better understanding how various biological and psychosocial factors influence transitions between several cognitive states simultaneously. This methodology has previously been used by Yoneda and colleagues to investigate the role of FFM personality traits on transitions between CH, MCI, dementia, and death states (Yoneda et al., 2023). They found that higher neuroticism and lower conscientiousness were associated with increased risk of transitions from CH to MCI, and higher extraversion was associated with transitioning back to CH from MCI. MSM has also been used to investigate the role of demographic and genetic factors such as age, sex, education, and APOE status on transitions across cognitive states (Robitaille et al., 2018; Salazar et al., 2007). Given the associations between personality and cognitive states, there is precedent to explore FFM personality traits as risk/protective factors for transitions between cognitive states using MSM.

Study objectives

Our first aim was to compare baseline FFM personality traits between individuals who develop aMCI versus naMCI before objective cognitive impairment occurs. Based on previous findings (Berger-Sieczkowski et al., 2019), we hypothesized that participants who developed aMCI would report lower levels of openness, conscientiousness, extraversion, and neuroticism at baseline compared to participants who developed naMCI.

Our second aim was to determine the effect of FFM personality traits prior to the development of objective cognitive impairment on transitions across cognitive states (CH, SCD, naMCI, aMCI, and dementia). Based on previous research, we hypothesized that higher levels of neuroticism and lower levels of conscientiousness would be associated with greater risk of transitions from normal cognition to SCD, aMCI or naMCI, and/or dementia, while lower levels of extraversion and openness would be associated with greater risk of transition from either normal cognition or SCD to aMCI.

Methods

Participants

Participants were part of the Einstein Aging Study (EAS) database. The EAS is a large-scale general population-based cohort study based in the United States, examining normal cognitive aging and dementia. The EAS has collected data annually since 1993, with the final follow-up occurring in 2017. The sample size of the EAS study was 2600 participants as of the 2018 (EAS - Maelstrom Research, n.d.). A detailed study description for the EAS can be found elsewhere (Katz et al., 2012). The eligibility for enrollment in the EAS included being at or above the age of 70, being fluent in English, and being cognitively intact at baseline assessment. For the current study, data requested included demographic characteristics (age, sex, years of education, and ethnicity), levels of FFM personality traits, levels of depression and anxiety symptoms, the cognitive assessment battery, and cognitive diagnoses (aMCI, naMCI, and dementia). Baseline assessment for the present study was considered the first year that participants completed a personality questionnaire, meaning that baseline year varied across participants. Because personality assessment was not added until 2005, only 730 of the original EAS sample completed the personality questionnaire (Hill et al., 2019b). The inclusion/ exclusion protocol for this study is summarized in Figure 1. This work was approved by the University of Victoria Research Ethics Board (REB21-0052) and completed in accordance with the Helsinki Declaration.

Specific inclusion criteria for this study included: (1) no objective cognitive impairment (i.e., no dementia or MCI, but could have SCD) at the time of the assessment used as our baseline; and (2) available information regarding FFM personality traits, and cognitive assessment data at their baseline and at least one follow-up visit. Exclusion criteria included: (1) Pathological substance use as these conditions are known to impact cognition (Gould, 2010; Saa et al., 2019); and (2) Incident non-dementia neurological illness during the study that would impair cognition (Multiple Sclerosis, brain tumor, etc.). Individuals with diagnosed cerebrovascular disease prior to baseline were included as this is a requirement for a diagnosis of vascular dementia (World Health Organization, 1992).

Measures

Personality assessment

Levels of FFM personality traits were measured in the EAS using the 50-item International Personality Item Pool (IPIP) version of the NEO-Personality Inventory (Goldberg, 1992; Maples et al., 2014). The IPIP has demonstrated high internal consistency, with Cronbach's α values ranging from .76 to .87 for each of the five factors and .84 to .88 for the full questionnaire (Goldberg, 1992; Ypofanti et al., 2015). The IPIP factors have shown moderate correlation with other FFM personality inventories such as the Ten Item Personality Index (Ypofanti et al., 2015). The internal consistency of the IPIP subscales in our sample were also acceptable (Cronbach's $\alpha=0.70$ –0.76).

Cognitive assessment and outcomes

Participants in the EAS study underwent a comprehensive neuropsychological battery measuring verbal intelligence, attention and processing speed, episodic memory, visuospatial ability, language, and executive function (see Table S1 for a list of cognitive tests).

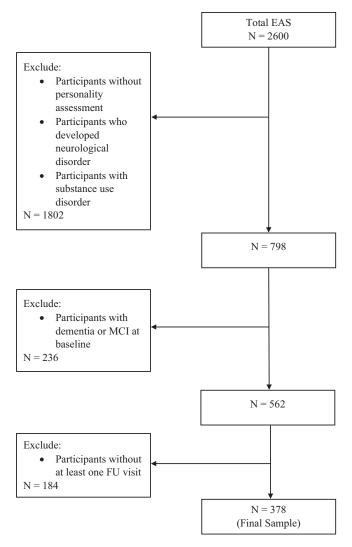


Figure 1. Study eligibility diagram.

Cognitive outcomes (i.e., maintained CH status, SCD, aMCI, naMCI, dementia) were extracted for follow-up visits. The EAS categorized participants as having dementia based on the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV) criteria (American Psychiatric Association, 2013). A diagnosis of MCI was made based on revised criteria from the International Working Group on Mild Cognitive Impairment (Artero et al., 2006; Winblad et al., 2004). MCI participants with memory deficits were classified as aMCI, while those with deficits in cognitive domains other than memory were classified as naMCI.

A binary SCD variable was generated using participants' responses to 17 yes/no items on the Consortium to Establish a Registry for Alzheimer's Disease (CERAD) Self-Report of Memory Questionnaire (Morris et al., 1993). All items were summed and converted to z-scores. Many studies classify SCD when participants endorse at least one item on a subjective cognition scale (e.g., Cherbuin et al., 2015; Schultz et al., 2015). However, because the CERAD questionnaire has not been thoroughly validated for classifying SCD, a more conservative psychometric approach was used (as described elsewhere; Diaz-Galvan et al., 2021), where participants who endorsed a total number of cognitive complaints above one standard deviation (SD) from the mean and did not meet the criteria for a diagnosis of MCI or dementia were classified as SCD.

Psychosocial assessment

Baseline and follow-up levels of depression and anxiety were evaluated using raw scores on the 15-item Geriatric Depression Scale (GDS; Sheikh & Yesavage, 1986) and Beck Anxiety Inventory (BAI; Beck et al., 1988) respectively. The GDS is scored on a scale from 0 to 15 with higher scores indicating more depressive symptoms. The internal consistency of the GDS in our sample was acceptable (Cronbach's $\alpha = 0.75$). The BAI is a 21-item self-report scale with scores ranging from 0 to 63 (higher scores indicate more significant symptoms). The internal consistency of the BAI in our sample was also acceptable (Cronbach's $\alpha = 0.84$).

Demographics and clinical information

Demographic information including age, sex, years of education, and ethnicity were extracted for each participant at baseline. Additionally, a summary multimorbidity index (MMI) score (0–9) was derived by summing the following nine physician-diagnosed conditions: angina, arrhythmia, coronary artery bypass, diabetes, chronic heart failure, hypertension, myocardial infarction, Parkinson's disease, and stroke.

Statistical analyses

Prior to running primary analyses, the normality of all continuous variables was examined using Shapiro–Wilk tests and normal probability plots. All continuous variables were non-normally distributed (Shapiro–Wilk < 0.001), so nonparametric tests were used for this study. All analyses were performed using SPSS version 27.0 and R.

Independent samples Mann–Whitney U tests were performed to compare baseline FFM personality traits as well as demographic and clinical variables between participants who developed aMCI or developed naMCI. As the intention of these analyses were to compare baseline personality traits between individuals who developed memory impairment versus non-memory impairment, participants who transitioned between aMCI and naMCI were coded as aMCI for these analyses. Effect sizes for between group comparisons are reported as Cohen's r, where 0.1, 0.3, and 0.5 are considered small, medium, and large, respectively (Cohen, 2013).

MSM was used to model the transition of participants across cognitive states, using FFM personality traits at baseline as covariates. Due to insufficient numbers of participants who transitioned to dementia in the final sample (n=12), only transitions across predementia syndromes were modeled for this study. Thus, a four-state model was generated with State 1 defined as CH, State 2 defined as SCD, State 3 defined as aMCI, and State 4 defined as naMCI. Forward and backward transitions to each state from each other state were allowed. A pictorial representation of this model is shown in Figure 2. Each personality trait was explored in a separate model. Goodness of fit for each model was assessed using Pearson-type χ^2 test which compares the observed number of each transition to the expected number of transitions (Titman & Sharples, 2010). These analyses were performed using the MSM package for R (Jackson, 2011).

Spearman rho correlations were also used in supplementary analyses to examine relationships in the EAS data between FFM personality traits, demographics, health related variables, and scores on cognitive tests. These correlations were also run separately for those classified as CH versus SCD at baseline. Standardized test scores were used for these analyses (see Supplementary Tables \$2-85 for related results).

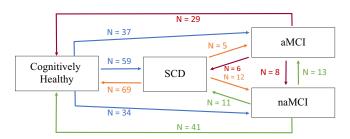


Figure 2. Four-state model and frequencies for transitions across predementia cognitive states. *Note*. CH = State 1; SCD = State 2; aMCI = State 3; naMCI = State 4. The models were adjusted for FFM personality traits (openness, conscientiousness, extraversion, agreeableness, and neuroticism) in separate models.

Results

Sample descriptive analyses

Of the 2600 participants enrolled in the EAS, 1802 participants were removed because they did not complete a personality assessment, self-disclosed a substance use disorder, or developed a neurological disorder over the course of the study. An additional 236 participants were removed due to being classified as having MCI or dementia at baseline assessment resulting in 562 participants. For between group comparisons and MSM, only participants with at least one follow-up visit after baseline were included in analyses, resulting in a sample size of 378 for our main analyses. All 562 participants were retained for supplemental correlational analyses. The number of participants for each follow-up visit are presented in Table 1.

Over the course of the study, 37 participants made at least one transition to aMCI (and were classified as aMCI for between group comparisons), while 29 participants made at least one transition to naMCI without ever developing aMCI (and were classified as naMCI for between group comparisons). Comparisons between participants who were classified as CH (n = 325) and participants who were classified as SCD (n = 53) at baseline are presented in Table 2 and descriptive statistics for all variables of interest for the overall sample as well as participants who developed aMCI and naMCI are presented in Table 3. The overall sample was primarily white (66.40%), with African Americans comprising 27.20% of the sample, Hispanic White Americans comprising 4.50% of the sample, Hispanic Black Americans comprising 1.10% of the sample, and 1% reporting "other" ethnicity. The demographic characteristics of our subsample were similar to the demographics of the full EAS cognitively unimpaired sample reported previously (Katz et al., 2012).

The full sample was relatively healthy with an average of only 1.26 physician diagnosed health conditions on the MMI (SD = 1.05). Similarly, levels of mood disturbances were low with mean scores of 3.75 (SD = 4.42) and 1.67 (SD = 1.83) on the BAI and GDS, respectively. These values fall well below the cutoff values of 8–15 for mild anxiety on the BAI and 5–8 for mild depression on the GDS. Participants who were classified as being CH at baseline reported fewer depressive symptoms, higher levels of openness to experience, conscientiousness, and extraversion, and lower levels of neuroticism compared to those classified as SCD at baseline.

Between group analyses

There were no significant differences between aMCI and naMCI groups with regards to demographic, physical or mental health, or

Table 1. Number of participants included in this study who completed each annual follow-up visit

Follow-up visit	N	%
Baseline	562	100
FU-1	378	67.30
FU-2	268	47.70
FU-3	199	35.40
FU-4	123	21.90
FU-5	77	13.70
FU-6	47	8.40
FU-7	26	4.60
FU-8	12	2.10
FU-9	4	0.70

Note: Baseline represents the first year a participant completed a personality assessment. Follow-up assessments are the number of years since baseline assessment in this study, accounting for differences in baseline start year.

personality variables (p > 0.05), contrary to our hypotheses. Only small effect sizes were achieved for comparisons between personality traits (r: 0.10–0.18). Due to the small sample sizes of aMCI and naMCI participants, and to reduce multiple comparisons, data between the two MCI subgroups and CH and SCD participants were not statistically compared.

Transitions across predementia cognitive states

The transition matrix (Q), or the frequency of the possible moves across each of the four states, is summarized in Table 4. Across the study, there were 59 transitions from CH to SCD, 37 transitions from CH to aMCI, and 34 transitions from CH to naMCI.

The 5-year transition probabilities between states (probability of transitioning from one state to another after five years) are presented in Table 5. After five years, the probability of a CH participant: remaining CH was approximately 79%; transitioning to SCD was approximately 10%; transitioning to aMCI was approximately 6%; and transitioning to naMCI was approximately 5%.

Effects of covariates

The effects of FFM personality traits on transitions between different states were computed using MSM. The model that included openness as a covariate failed to converge. A Pearson-type goodness of fit test revealed a high degree of discrepancy in the number of observed and expected transitions at various timepoints throughout the study, resulting in a poor model fit ($\chi^2(96) = 120.15$, p = 0.005). While the exact cause of convergence failure and poor model fit for this trait is unclear, it is possibly due to the larger number of missing values for the openness subscale on the IPIP than the other subscales (as shown in Table 3). Hazard ratios and confidence intervals, as well as goodness of fit metrics, for the effect of the remaining four personality traits on transitions across cognitive states are shown in Table 6. All four models achieved acceptable fit based on Pearson-type goodness of fit χ^2 tests (p > 0.05).

Conscientiousness. As expected, higher levels of baseline conscientiousness were marginally associated with a decreased risk of transitioning from CH to SCD (HR = 0.94, CI: 0.88–1.00). Contrary to our hypotheses, no other significant associations were found between conscientiousness and risk of transitions across cognitive states (Figure 3A).

Extraversion. Contrary to our hypotheses, higher levels of baseline extraversion were associated with a decreased risk of transitioning

Table 2. Comparisons between participants classified as CH versus SCD at baseline

Variables	Group	N	Mean (SD) or %	Range	U/χ^2 (CH vs. SCD)	p (CH vs. SCD)	r (CH vs. SCD)
Demographics:							
Age	CH	325	78.56 (4.91)	69-93	9001.50	0.527	0.03
	SCD	53	78.86 (4.66)	71-89			
Sex (%F)	CH	325	60.69%	-	1.30	0.290	-
	SCD	53	68.92%				
Ethnicity (%White)	CH	325	65.23%	-	9.00	0.173	-
	SCD	53	73.58%				
Education (y)	CH	325	14.85 (3.21)	3-20	8041.00	0.434	0.04
	SCD	53	14.62 (3.26)	8-20			
Physical/mental healt	:h:						
MMI	CH	320	1.27 (1.05)	0-5	8185.00	0.844	0.01
	SCD	52	1.25 (1.06)	0-4			
BAI	CH	284	3.68 (4.12)	0-21	4809.500	0.752	0.02
	SCD	35	4.31 (6.40)	0-27			
GDS	CH	325	1.50 (1.64)	0-12	11716.50	< 0.001	0.22
	SCD	53	2.75 (2.50)	0-12			
Personality traits:							
Openness	CH	299	37.64 (6.46)	20-50	5962.00	0.037	0.11
	SCD	49	35.41 (6.93)	20-48			
Conscientiousness	CH	309	38.90 (6.39)	10-50	5150.50	< 0.001	0.21
	SCD	51	35.02 (5.97)	20-47			
Extraversion	CH	315	34.00 (6.21)	12-49	6230.50	0.010	0.13
	SCD	51	31.63 (5.62)	15-47			
Agreeableness	CH	311	40.99 (5.25)	23-50	6917.00	0.061	0.10
-	SCD	53	39.68 (4.99)	26-48			
Neuroticism	CH	312	19.66 (5.81)	10-38	9807.50	0.001	0.17
	SCD	49	22.61 (6.20)	12-39			

Note: CH = Cognitively Healthy; SCD = Subjective Cognitive Decline; naMCI = Non-amnestic cognitive impairment; MMI = Multimorbidity index; BAI = Beck Anxiety Inventory; GDS = Geriatric Depression Scale.

from CH to naMCI (HR = 0.91, CI: 0.83-0.99), but not aMCI (HR = 1.01, CI: 0.93-1.09). No other significant associations were found between extraversion and risk of transitions across cognitive states (Figure 3B).

Agreeableness. No significant associations were found between levels of agreeableness at baseline and risk of transition between any of the predementia cognitive states. This is consistent with our hypotheses.

Neuroticism. As expected, higher levels of neuroticism were associated with increased risk of transitioning from CH to SCD. Contrary to our hypotheses, neuroticism was not associated with risk of developing either aMCI or naMCI from either CH status or SCD. No other significant associations were found between neuroticism and risk of transitions across cognitive states (Figure 3C).

Sensitivity analyses

Due to the small number of transitions to aMCI and naMCI, sensitivity analyses were performed with the MCI groups combined. These results are presented in Table 7. All five models achieved acceptable fit based on Pearson-type goodness of fit χ^2 tests (p > 0.05). The results of these analyses were remarkably like our initial MSM analyses, however there were no longer any significant transitions in the extraversion model, and openness was associated with increased risk of transitioning from CH to MCI.

Discussion

This study sought to: 1) compare personality profiles of individuals who develop amnestic versus non-amnestic cognitive impairment; and 2) examine the effects of personality traits on transitions across

predementia cognitive states. As the aims of our study centered around the assumption that personality traits are generally stable across the lifespan, we used self-reported personality traits prior to the onset of objective cognitive impairment in our analyses. Only some of our hypotheses were supported.

Between group comparisons: aMCI versus naMCI

Contrary to our hypotheses that participants who transitioned to aMCI would report lower levels of baseline openness, conscientiousness, extraversion, and neuroticism compared to those who developed naMCI, the two groups did not differ on any baseline personality traits. These findings contradict those of Berger-Sieczkowski and colleagues who found that individuals with aMCI displayed lower levels of openness, conscientiousness, and extraversion compared to those with naMCI (Berger-Sieczkowski et al., 2019). Methodological differences may account for these different findings. While Berger-Sieczkowski and colleagues compared personality traits between groups who had already been diagnosed with their respective MCI subtype, this study compared aMCI and naMCI participants' levels of each FFM personality trait measured prior to the onset of objective cognitive impairment. As such, it is possible that the significant differences in personality traits between aMCI and naMCI participants in Berger-Sieczkowski et al.'s (2019) study may reflect changes in personality after the onset of cognitive impairment rather than differences in stable premorbid personality traits across the lifespan between groups, particularly in light of findings that older adults often show changes in levels of FFM personality traits after transitioning to impaired cognitive states (Islam et al., 2019; Terracciano et al., 2017). Although Ayers et al. (2020) found greater neuroticism to be a risk factor for naMCI only, this was not reflected in between group analyses. Finally, as expected,

Table 3. Baseline characteristics of overall sample, participants who progressed to aMCI, and participants who progressed to naMCI

Variables	Group	N	Mean (SD) or %	Range	U/χ^2 (aMCI vs. naMCI)	p (aMCI vs. naMCI)	r (aMCI vs. naMCI)
Demographics:							
Age	Overall	378	78.60 (4.87)	69-93	559.00	0.771	0.04
	aMCI	37	79.66 (4.57)	72-87			
	naMCI	29	79.85 (5.51)	69-88			
Sex (%F)	Overall	378	60.85%	-	.43	0.513	-
	aMCI	37	54.05%				
	naMCI	29	62.07%				
Ethnicity (%White)	Overall	378	66.40%	-	2.16	0.340	-
	aMCI	37	59.46%				
	naMCI	29	41.38%				
Education (y)	Overall	378	14.82 (3.21)	3-20	459.00	0.312	0.12
•	aMCI	37	14.84 (3.16)	8-20			
	naMCI	29	14.14 (3.22)	8-20			
Physical/mental health:			, ,				
MMI	Overall	372	1.26 (1.05)	0-5	559.00	0.771	0.06
	aMCI	37	1.03 (1.01)	0-4			
	naMCI	29	1.10 (0.82)	0–3			
BAI	Overall	319	3.75 (4.42)	0-27	288.00	0.667	0.05
	aMCI	31	3.87 (4.35)	0-21			
	naMCI	20	3.50 (4.05)	0-14			
GDS	Overall	378	1.67 (1.83)	0-12	610.50	0.320	0.12
	aMCI	37	1.57 (1.69)	0–8			
	naMCI	29	1.76 (1.41)	0–6			
Personality traits:			, , ,				
Openness	Overall	348	37.33 (6.57)	20-50	348.50	0.181	0.17
	aMCI	35	36.91 (7.39)	20-48			
	naMCI	25	34.84 (6.26)	26-49			
Conscientiousness	Overall	360	38.35 (6.46)	10-50	385.50	0.162	0.18
	aMCI	36	39.86 (7.07)	21–50			
	naMCI	27	38.04 (5.95)	26-47			
Extraversion	Overall	366	33.67 (6.18)	12-49	437.00	0.198	0.16
	aMCI	37	33.22 (5.72)	21-44		0.200	0.20
	naMCI	29	31.00 (6.32)	15-42			
Agreeableness	Overall	364	40.80 (5.22)	23-50	563.50	0.419	0.10
0	aMCI	36	41.36 (3.59)	31–47	300.00	025	0.20
	naMCI	28	41.64 (5.71)	26-49			
Neuroticism	Overall	361	20.06 (5.95)	10-39	497.50	0.280	0.16
	aMCI	35	18.91 (4.71)	11-31	.555	0.200	0.20
	naMCI	24	20.42 (5.23)	12-30			

Note: The overall sample consists of all participants who met the inclusion criteria for Aims 1 and 2. aMCI = amnestic mild cognitive impairment; naMCI = non-amnestic cognitive impairment; MMI = Multimorbidity index; BAI = Beck Anxiety Inventory; GDS = Geriatric Depression Scale.

Table 4. Frequency of possible moves across each of the four predementia cognitive states

То	СН	SCD	aMCI	naMCI
From				
CH	873%	59%	37%	34%
SCD	69%	47%	5%	12%
aMCI	29%	6%	24%	8%
naMCI	41%	11%	13%	17%

Note: Transitions in all directions were possible. CH = cognitively healthy; SCD = subjective cognitive decline; aMCI = amnestic mild cognitive impairment; naMCI = non-amnestic mild cognitive impairment.

agreeableness did not differ between groups in this study. Our analyses did not appear to be influenced by age, sex, years of education, or ethnicity, or clinical variables including the multimorbidity index, or levels of anxiety and depression.

It is possible that small sample sizes of aMCI and naMCI participants resulted in insufficient power to detect differences. Indeed, post hoc power analyses using an achieved effect size of 0.15 (the average effect size achieved across comparisons between naMCI and aMCI participants on the five FFM personality traits) revealed weak power (1 – β = 0.09). Future studies with larger samples sizes will be needed to confirm the findings of this study.

Table 5. Five-year transition probabilities between four predementia states

То	СН	SCD	aMCI	naMCI
From				
CH	79.23%	9.96%	6.36%	5.31%
SCD	78.56%	9.44%	6.53%	5.46%
aMCI	77.82%	9.45%	7.07%	5.65%
naMCI	78.25%	9.39%	6.81%	5.54%

Note: CH = cognitively healthy; SCD = subjective cognitive decline; aMCI = amnestic mild cognitive impairment; naMCI = non-amnestic mild cognitive impairment.

Multistate model findings

Consistent with previous studies, we found that higher levels of neuroticism were associated with increased risk of transitioning from being CH to experiencing SCD (Hill et al., 2019b; Luchetti et al., 2016; Muñoz et al., 2020; Pearman & Storandt, 2005; Steinberg et al., 2013). This may represent the tendency for individuals with high levels of neuroticism to be hyperaware and concerned about age-related changes in cognition and thus report higher degrees of memory complaints on self-report scales. Contrary to our hypotheses, neuroticism was not found

Table 6. Hazard ratios and 95% confidence intervals for the effect of personality traits on transitions between predementia cognitive states

			Go	Goodness of fit		
	Hazard					
Transition	ratio	95% CI	χ^2	df_{upper}	р	
Conscientiousness			88.52	102	0.587	
State 1 – State 2	0.94**	0.88-1.00	00.02		0.00.	
State 1 – State 3	1.04	0.95-1.15				
State 1 – State 4	0.95	0.86-1.06				
State 2 – State 1	1.01	0.95-1.08				
State 2 - State 3	1.51	0.99-2.32				
State 2 – State 4	0.88	0.76-1.03				
State 3 – State 1	1.06	0.95-1.17				
State 3 – State 2	1.01	0.78-1.30				
State 3 – State 4	0.98	0.86-1.11				
State 4 – State 1	0.96	0.89-1.04				
State 4 – State 2	0.92	0.77-1.06				
State 4 – State 3	0.97	0.87-1.07				
Extraversion	0.0.	0.0. 1.0.	91.91	99	0.339	
State 1 – State 2	0.97	0.91-1.04	31.31	33	0.555	
State 1 – State 3	1.01	0.93-1.09				
State 1 - State 4	0.91*	0.83-0.99				
State 2 – State 1	1.04	0.98-1.10				
State 2 – State 3	1.23	0.67-2.29				
State 2 – State 4	0.93	0.85-1.03				
State 3 – State 1	0.93	0.82-1.05				
State 3 – State 2	1.40	1.08-1.81				
State 3 – State 4	1.08	0.92-1.27				
State 4 – State 1	0.98	0.91-1.06				
State 4 – State 2	1.00	0.82-1.22				
State 4 – State 3	0.99	0.88-1.11				
Agreeableness	0.55	0.00 1.11	84.64	96	0.451	
State 1 – State 2	0.96	0.90-1.02	04.04	30	0.431	
State 1 – State 2 State 1 – State 3	1.06	0.96-1.18				
State 1 – State 4	1.12	0.99-1.27				
State 2 – State 1	1.04	0.95, 1.13				
State 2 – State 1	1.36	0.81-2.27				
State 2 – State 3	0.99	0.78, 1.25				
State 3 – State 1	1.18	0.76, 1.23				
State 3 – State 1	1.10	0.83-1.46				
State 3 – State 2	0.90	0.76-1.07				
State 4 – State 1	0.97	0.70-1.07				
State 4 – State 1 State 2	1.05	0.92-1.03				
State 4 – State 2 State 4 – State 3	1.04	0.92-1.21				
Neuroticism	1.04	0.32 1.17	63.38	93	0.900	
State 1 – State 2	1.06**	1.00-1.12	03.30	93	0.300	
State 1 – State 2 State 1 – State 3	0.99	0.91-1.08				
State 1 – State 3	1.02	0.93-1.11				
State 2 – State 1	0.97	0.93-1.11				
State 2 – State 1 State 2 – State 3	0.75	0.42-1.33				
State 2 – State 3	0.73	0.42-1.33				
State 3 – State 1	1.00	0.83-1.13				
State 3 – State 1	0.91	0.70-1.19				
State 3 – State 2 State 3 – State 4	0.91	0.70-1.19				
State 4 – State 1	0.97	0.85-1.11				
State 4 – State 1 State 4 – State 2	1.09	0.92-1.03				
State 4 – State 2 State 4 – State 3	0.95	0.85-1.06				
State 7 State 3	0.55	0.05-1.00				

Note: State 1 = CH; State 2 = subjective cognitive decline; State 3 = amnestic mild cognitive impairment; State 4 = non-amnestic cognitive impairment. *Significant hazard ratio. **Significant hazard ratio before rounding.

to increase the risk of transitions to aMCI or naMCI from CH or SCD despite previous studies finding neuroticism to be a predictor of cognitive decline in older adults (Ayers et al., 2020; Luchetti et al., 2016; Terracciano et al., 2017; Yoneda et al., 2023). The addition of SCD as a cognitive state may have influenced these discrepant results by allowing a greater number of transitions to occur over the study period. By treating SCD as distinct from CH in the model, there were fewer transitions between CH and the MCI states than would have been detected had the SCD and CH states

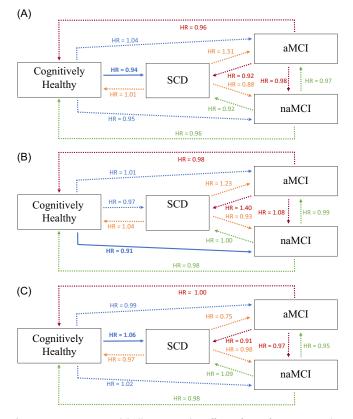


Figure 3. Four-state model illustrating the effect of significant personality covariates on transitions across predementia states. *Note.* Models depict the effects of: Conscientiousness (A); Extraversion; (B); and Neuroticism (C) on transitions across states. Solid arrows represent significant hazard ratios before rounding. SCD = subjective cognitive decline; aMCI = amnestic mild cognitive impairment; naMCI = non-amnestic mild cognitive impairment; HR = hazard ratio.

been treated as a single state. However, given our findings that neuroticism and conscientiousness were significant risk/protective factors respectively for transitioning from CH to SCD, the decision to treat these states as separate in the model is justified.

In direct contrast to our hypotheses, lower levels of extraversion were associated with an increased risk of transitions from being CH to naMCI but not aMCI. The basis for this hypothesis was a previous finding of cross-sectional differences in levels of extraversion between aMCI and naMCI participants (Berger-Sieczkowski et al., 2019), so it remains possible that changes in extraversion may occur after the onset of cognitive symptoms in aMCI. It is unclear why higher levels of extraversion were associated with reduced risk of naMCI in this study but not in previous research (Ayers et al., 2020). However, higher levels of extraversion have been shown to be associated with preserved cognitive status on the MMSE (Luchetti et al., 2016) despite poorer performance on tasks of intelligence, language, and executive function (although these tasks are likely more robust and reliable than the MMSE; Simon et al., 2020; Soubelet & Salthouse, 2011; Williams et al., 2010). Unlike Yoneda & colleagues (2023) who utilized Rush Memory and Aging Project data, we did not find a relationship between extraversion and reverse transitions from MCI to CH in the EAS data, even when the MCI groups were combined. This may be due to the addition of SCD in our model, which meant there were likely fewer direct transitions from MCI to CH. The relationship between levels of extraversion and risk of transition to MCI (both amnestic and non-amnestic) merits further research given these

Table 7. Sensitivity analyses (aMCI & naMCI combined): hazard ratios and 95% confidence intervals for the effect of personality traits on transitions between predementia cognitive states

			Go	Goodness of fit	
Transition	Hazard ratio	95% CIs	χ^2	df_{upper}	р
Openness			49.62	74	0.951
CH - SCD	0.94	0.89 - 1.00			
CH – MCI	0.95**	0.90 - 1.00			
SCD - CH	1.05	0.99-1.08			
SCD - MCI	0.97	0.88 - 1.07			
MCI – CH	0.98	0.94-1.03			
MCI – SCD	1.09	0.97-1.23			
Conscientiousness			53.45	78	0.945
CH – SCD	0.92*	0.88-0.98			
CH – MCI	1.01	0.96 - 1.06			
SCD – CH	1.01	0.95 - 1.07			
SCD - MCI	0.94	0.83-1.06			
MCI – CH	1.00	0.95 - 1.05			
MCI – SCD	0.96	0.88 - 1.05			
Extraversion			72.51	76	0.404
CH – SCD	0.97	0.91 - 1.02			
CH – MCI	0.96	0.91 - 1.01			
SCD – CH	1.03	0.98-1.09			
SCD - MCI	0.96	0.87 - 1.05			
MCI – CH	0.97	0.91 - 1.02			
MCI – SCD	1.16	1.02 - 1.32			
Agreeableness			63.74	76	0.656
CH – SCD	0.97	0.90 - 1.03			
CH – MCI	1.06	1.00-1.13			
SCD – CH	1.04	0.97, 1.12			
SCD - MCI	1.03	0.89 - 1.20			
MCI – CH	1.00	0.95 - 1.05			
MCI - SCD	1.07	0.95-1.20			
Neuroticism			51.10	72	0.887
CH - SCD	1.06**	1.00-1.11			
CH - MCI	1.01	0.96-1.06			
SCD - CH	0.97	0.92-1.02			
SCD - MCI	0.93	0.81-1.07			
MCI – CH	0.99	0.94-1.03			
MCI – SCD	1.05	0.93-1.17			

Note: CH = cognitively healthy; SCD = subjective cognitive decline; MCI = mild cognitive impairment. *Significant hazard ratio. **Significant hazard ratio before rounding.

inconsistent findings. Higher levels of conscientiousness were associated with decreased risk of transitioning from CH to SCD, which is consistent with previous findings that individuals high in conscientiousness tend to report fewer memory complaints on self-report measures (Hill et al., 2019a; Luchetti et al., 2016; Pearman & Storandt, 2004; Steinberg et al., 2013). Finally, our finding that higher levels of openness were associated with decreased risk of transitioning to MCI from CH in our sensitivity analyses was consistent with previous findings indicating that openness is protective against cognitive impairment (Aiken-Morgan et al., 2012; Booth et al., 2006; Soubelet & Salthouse, 2011; Sutin et al., 2019; Williams et al., 2010). Significant findings in the MSM models but not in the between-group comparisons may partly be due to MSM accounting for transitions between SCD, aMCI, and naMCI states simultaneously.

There were few transitions between SCD, aMCI, and naMCI, resulting in large confidence intervals for these transitions. However, large confidence intervals for transition intensities between these states is not uncommon in MSM (e.g., Robitaille et al., 2018) perhaps suggesting a general difficulty of Markov Models to accurately capture transition intensities across states with low conversion rates. Confidence intervals were notably smaller in sensitivity analyses where the MCI groups were

combined. Overall, our findings suggest that high levels of neuroticism and low levels of extraversion may be risk factors for developing SCD and naMCI, respectively, and there may be value to considering these variables in future risk reduction clinical trials for cognitive decline in later life.

Strengths and limitations

Strengths of this study included using data from a large national database with several years of longitudinal data. An advantage of using MSM over cox proportional hazards models was the ability to observe transitions across multiple different cognitive states simultaneously (including reverse transitions from an impaired state to an unimpaired/less impaired state). Additionally, MSM does not make assumptions about time spent in states and allows for skipping states (e.g., skipping SCD and going straight from CH to MCI). The addition of SCD as a cognitive state in this model represents another strength given that SCD is becoming recognized as a distinct stage between healthy cognitive aging and MCI (Jessen et al., 2014).

This study is not without limitations, the primary one being the drastically reduced sample size after removing EAS participants who did not meet the eligibility criteria for the present study. Most participants were removed due to having not completed the IPIP. We may have lacked power to detect medium effect sizes. We explored the potential impacts of cell size and power limitations by conducting follow-up sensitivity analyses that combined the MCI subgroups characterized by the fewest transitions; the results were consistent with the initial findings. Additionally, as culture and upbringing are known to influence the expression of personality (Costa & McCrae, 1988; Terracciano & McCrae, 2006), the generalizability of these results is primarily restricted to older adults within North America. Finally, given findings that personality traits may influence the decision to participate in research studies (Saliba & Ostojic, 2014), it is possible that the personality profiles of study participants are not representative of the greater population.

Although this study sought to explore "premorbid" personality traits as predictors of specific predementia syndromes, the directionality of the relationship between personality and cognition remains unclear. While changes in personality may occur as result of changes in cognition, it is also possible that changes in personality occur prior to the onset of cognitive impairment, a concept known as 'Mild Behavioural Impairment' (Ismail et al., 2017). The advanced age of the study sample was a limitation to drawing conclusions about this issue. At baseline, the average age for both the overall study sample and the subgroups of participants who developed MCI was just under 80, which is close to the average age of onset of MCI (Kremen et al., 2014). It has been well established that the pathological sequalae of dementia such as changes in brain structure and accumulation of amyloid plaques are known to begin up to two decades before the onset of cognitive disturbances (Bateman et al., 2012). Additionally, recent studies have found associations between FFM personality traits and Alzheimer's neuropathology (Aschenbrenner et al., 2020; Yoon et al., 2020). Therefore, we cannot make strong conclusions regarding the directionality of the relationship between personality and cognitive status based on the results of this study.

Future directions

Future longitudinal studies which observe the relationship between personality and cognitive aging many years before the pathological sequalae of dementia is known to begin are warranted to flesh out causal relationships between personality traits and transitions across cognitive states. The Canadian Longitudinal Study on Aging (CLSA), a large Canadian-based study including adults ages 45-85 (Raina et al., 2009), may be a good candidate for addressing these questions as personality questionnaires have been added to the CLSA study protocol. Studies with both in vivo biomarker data such as neuroimaging and pathological diagnoses at autopsy would also be useful in exploring the relationship between personality traits and the biological conduits of specific cognitive syndromes. Studies that employ MSM but treat personality as a timedependent covariate (a covariate which changes over time rather than remaining constant) may also be conducted to explore relationships between changes in personality and transitions across cognitive states. Finally, while our study was underpowered to explore the effects of race/ethnicity on the relationship between personality and transitions across states, this should be investigated in future studies as a two-fold increased risk of naMCI among Blacks compared to Whites has been previously reported (Katz et al., 2012).

Conclusions

This study adds to the literature exploring the relationship between personality traits and transitions across cognitive states. We found support for the hypothesis that higher levels of neuroticism would be associated with increased risk of developing SCD, and unexpectedly found that lower levels of extraversion were related with increased risk of developing naMCI. Overall, findings suggest that premorbid personality traits may play a predictive role in the risk for, or protection against, specific predementia syndromes. Such knowledge could be used to identify individuals who are at greater risk for developing specific predementia syndromes.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S1355617723011505.

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Competing interests. The authors have no competing interests to declare.

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