Original Research Article

Personality-Related Determinants of Subtle Cognitive Decline in Old Age: A Population-Based Study

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Key Words

Personality · NEO-Personality Inventory-Revised · Elderly controls · Cognitive decline · Mild cognitive impairment · Openness

Abstract

Background/Aims: Recent studies of cases with mild cognitive impairment (MCI) suggested that besides Alzheimer disease (AD)-related biomarkers, some personality dimensions are associated with progression to AD. To date, there are no studies addressing the psychological determinants of subtle cognitive decline in healthy elderly controls. **Methods:** 488 community-dwelling healthy controls were assessed with a detailed neuropsychological battery at baseline and an 18-month follow-up. Personality factors and facets were investigated at baseline using the NEO-Personality Inventory-Revised (NEO-PI-R). Upon follow-up, there were 264 stable controls (sCON) and 224 deteriorating controls (dCON). Their personality data were compared to those of the 102 MCI cases using one-way analysis of variance and logistic regression models. **Results:** Significantly higher scores of Openness factor (as well as Aesthetics, Ideas and Values facets) were found in sCON than in both dCON and MCI cases. The three groups did not differ in the other NEO-PI-R factor and facet scores. Openness factor (and the same facets) was associated with cognitive preservation in healthy controls (OR: 0.72, 95% CI: 0.59, 0.87). Lower scores in the same factor and facets conferred higher risk to have MCI (OR: 0.61, 95% CI: 0.46, 0.79). **Conclusion:** Higher openness to new experiences and thoughts may be a protective factor against early cognitive decline in brain aging.

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Introduction

Subtle decrease in episodic memory and executive function performances typically occurs in the course of normal aging [1]. Most of these decreases are benign, remain stable over time and do not affect daily living and quality of life. In some cases, cognitive deficits may rapidly progress to pre-mild cognitive impairment (MCI) and MCI states. These constructs correspond to the transitional state between normal cognitive aging and dementia and are based on the presence of subjective concern for and an objective evidence of cognitive decline with the overall preservation of independence and only mild problems with complex functional abilities [2, 3]. Preceding the pre-MCI state, the concept of preclinical Alzheimer disease (AD) was introduced designing elderly controls with progressive installation of clinically silent AD-related molecular and imaging changes [4]. These persons who usually display PiB-positive deposits in positron emission tomography scans and decreased concentration of A β 42 in cerebrospinal fluid (CSF) remain cognitively stable for variable time periods but ultimately display significantly increased risk for AD [5]. Stressing the difficulty to isolate cases at high risk of AD among these persons, a 5-year follow-up showed that more than 60% among them have a stable memory trajectory, 36% display subtle memory decline and only 4% progress to pre-MCI [6]. Markers of A β accumulation (decreased levels of CSF A β 42, positive positron emission tomography amyloid imaging) and neurodegeneration (increased CSF t-tau and p-tau, increased hippocampal atrophy or cortical thinning) as well as functional magnetic resonance imaging and electroencephalographic abnormalities have been shown to be associated with increased rates of cognitive decline in this group [7–10].

Unlike AD-related biomarkers, data regarding the psychological determinants of subtle cognitive deterioration in healthy elders are still scarce [11, 12]. Among them, personality traits have been drawing growing interest since they are associated with MCI status and may modulate independently dementia risk in MCI [13–15]. According to a widely accepted taxonomic approach, there are five major personality traits (i.e. Neuroticism, Extraversion, Openness, Agreeableness and Conscientiousness) that are typically measured with the Neuroticism Extraversion Openness Personality Inventory-Revised (NEO-PI-R), a cross-culturally validated instrument [16, 17]. A few longitudinal studies explored the predictive role of personality factors in AD. Overall, high levels of Neuroticism increase, whereas high levels of Conscientiousness and Openness decrease the dementia risk in MCI cases [18]. To date, there is no longitudinal study addressing this issue in elderly controls.

Using data from a large, population-based study of community-dwelling older adults who have undergone an 18-month follow-up, we aimed to explore whether personality factors and facets were associated with rapid changes in cognitive function before the emergence of MCI. Because sociodemographic characteristics (i.e. age and educational level) [19] and anxiety and depressive symptomatology may influence cognitive performance and decline [20] these were also accounted for in the present analysis.

Materials and Methods

Study Protocol and Participants

Community-dwelling men and women aged 50 years and older, living in the French-speaking part of Switzerland were censed and invited to take part into a prospective cohort study designed to investigate the determinants and trajectories of cognitive function in late life. A telephone screening interview was used to exclude those with self-reported major physical and mental illnesses (including cancer, severe visual impairment, psychiatric and neurologic disorders and alcohol or drug abuse), and with a history of cerebro- and cardio-

vascular diseases. Those under neuro-psychopharmacological treatment (including narcotics, antidepressants and psychostimulants) were excluded. Eligible participants were assessed by board-certified neuropsychologists under the supervision of a senior psychiatrist. Data on age (years), sex and educational level (primary, less than 9 years; secondary, between 9 and 12 years; and tertiary or university level, more than 12 years) were collected at the first visit. All participants provided written informed consent, and standard approval of the study was obtained from the local Ethics Committee of the University Hospitals of Geneva.

Neuropsychological Assessment

Participants were evaluated at inclusion with an extensive neuropsychological battery, including the Mini-Mental State Examination (MMSE) [21], the Hospital Anxiety and Depression Scale (HAD) [22], and the Lawton Instrumental Activities of Daily Living (IADL) [23]. Cognitive assessment included (a) attention (Digit-Symbol-Coding [24], Trail Making Test A [25]); (b) working memory [verbal: Digit Span Forward [24], visuospatial: Visual Memory Span (Corsi) [24]]; (c) episodic memory (verbal: RI-48 Cued Recall Test [26] or RL/RI-16 Free and Cued Recall Test [27], visual: Shapes Test [28]); (d) executive functions [Trail Making Test B [25], Wisconsin Card Sorting Test (WCST) [29] and Phonemic Verbal Fluency Test [30]]; (e) language (Boston Naming Test [31]); (f) visual gnosis (Ghent Overlapping Figures [32]), and (g) praxis [ideomotor [33], reflexive [34], and constructional (Consortium to Establish a Registry for Alzheimer's Disease, CERAD), figures copy [35]]. All individuals were also evaluated with the Clinical Dementia Rating (CDR) scale [36].

Those who met dementia DSM-IV diagnostic criteria on the basis of the neuropsychological and clinical assessments were excluded. In agreement with the criteria of Petersen et al. [37], participants with a CDR score of 0.5 but no dementia and a score more than 1.5 standard deviations (SD) below the age-appropriate mean in any of the previously mentioned tests were confirmed to have MCI. Participants with neither dementia nor MCI were classified as cognitively healthy older 'controls' and underwent a full neuropsychological assessment at follow-up, on average 18 months later. Participants whose cognitive scores remained stable were classified as stable controls (sCON), and those whose performance at follow-up was at least 0.5 SD lower compared to the first evaluation, in at least two cognitive tests, were classified as deteriorating (dCON) controls. All individuals were clinically assessed independently by two trained neuropsychologists (S.T. and M.A.). The final classification of dCON was made blindly by a board-certified psychologist (C.R., 10 years of experience) who took into account both the neuropsychological scores and clinical assessment [38].

The final sample included 590 participants, of which 264 were classified as sCON [age 71.56 (4.35 SD) years; 160 women], 224 dCON [age 73.12 (4.82 SD) years; 137 women], and 102 met MCI diagnostic criteria [age 71.78 (6.06 SD) years; 37 women].

Personality Assessment

Personality features and dimensions were assessed at baseline using the French version of the NEO-PI-R [16, 17]. Participants were asked to complete the 240-item self-report version of the NEO-PI-R questionnaire using a five-point Likert agreement scale. The NEO-PI-R assesses 30 facets, 6 for each of the following five personality factors: Neuroticism, which is the tendency to feel negative affect including anxiety, hostility and anger; Extraversion, which encapsulates the proneness towards positive emotions and feelings such as warmth and enthusiasm; Openness, which is the personal inclination to experience and the appreciation of new situations and thoughts with a curious, imaginative and creative attitude, which is defined along six facets that cover imagination (or fantasy), sense of aesthetics, emotions and feelings, but also proactive behaviors and actions to explore and experiment beyond habits

and routines, as well as intellectual curiosity, and the disposition to negotiate and discuss social, political and religious values; Agreeableness, which is characterized by trustful, cooperative and altruistic tendencies, and finally Conscientiousness, which is the predisposition to be reliable, resolute and well organized, and unwilling to deviate from rules and moral principles.

Statistical Analysis

Continuous variables at baseline were compared among the 3 groups using one-way ANOVA and categorical variables using the Kruskal-Wallis test. Pairwise comparisons were performed after Bonferroni's correction. Gender differences were assessed using the χ^2 test. The comparison of continuous variables between two groups (neuropsychological differences between sCON and dCON at follow-up), Neuroticism factors and its facets versus a reference population [39] were performed using the unpaired t test.

To assess the discriminating values of personality factors and facets, we included them, after a z-score transform, as independent variables in univariate and adjusted (for age, education and sex) logistic regression models to predict either the distinction between sCON/dCON or that between sCON/MCI. Z-scores were computed with mean and SD for each factor and facet using the sCON group as the reference population. The coefficient of determination is presented as pseudo- R^2 . All analyses have been conducted using STATA 14.0 (STATA Corp., College Station, Tex., USA, 2015)

Results

Demographic and neuropsychological data in the three diagnostic groups at baseline are presented in table 1. Regarding demographic factors, dCON were older than sCON ($p = 0.001$). More men were present in the MCI groups ($p < 0.001$), and the sCON counted less depressive participants than the MCI group ($p = 0.039$). The educational level was similar among the three groups ($p = 0.157$). There were no significant differences in episodic memory cognitive performances between sCON and dCON at baseline. Slight but still significant group differences were found in Digit-Symbol-Coding ($p < 0.001$), Shapes Test immediate cued recall ($p < 0.001$) and praxis ideomotor test ($p = 0.007$) scores. As expected, significant differences were found at baseline between sCON and MCI as well as between dCON and MCI in MMSE ($p < 0.001$), RI-48 (total immediate cued recall, total cued recall, intrusions; $p < 0.001$), Verbal Fluency ($p < 0.001$), Trail Making Test B time ($p < 0.001$), Trail Making Test B/A ($p < 0.001$), and Shapes Test (total score immediate three recall and delayed recall; $p < 0.001$) scores.

In respect to personality, only Openness factor scores differed between sCON and the two other groups [Openness, $F(2, 587) = 14.71$, $p < 0.001$; table 2]. This also concerned the Openness facets of Aesthetics (O2) [$F(2, 587) = 6.49$, $p = 0.002$], Ideas [$F(2, 587) = 9.12$, $p < 0.001$], and Values (O5) [$F(2, 587) = 11.82$, $p < 0.001$]. Significant differences were evident between the sCON and the MCI group in the Action (O4), [$F(2, 587) = 10.81$, $p < 0.001$] as well as in the Fantasy facet (O1), [$F(2, 587) = 4.86$, $p = 0.008$] scores. In addition, sCON showed significantly higher scores in the Deliberation facet (C5) compared to the MCI group [$F(2, 587) = 4.65$, $p = 0.010$]. Significant differences were also found between the dCON and the MCI group for Gregariousness (E2) [$F(2, 587) = 3.45$, $p = 0.033$], Excitement seeking (E5) [$F(2, 587) = 4.78$, $p = 0.009$] and Action (O4) [$F(2, 587) = 10.81$, $p < 0.001$].

At follow-up, sCON had significantly better performances than dCON in all of the neuropsychological functions except visual gnosis (table 3).

Table 1. Demographic and neuropsychological data in the three diagnostic groups at baseline (sCON dCON and MCI)

	sCON (n = 264)	dCON (n = 224)	MCI (n = 102)	p
Female gender, %	160±60.61	137±61.16	37±36.27	<0.001 ^{b,c}
Age, years	71.56±4.35	73.12±4.82	71.78±6.06	0.001 ^a
Education, %				0.157
<9 years	40±47.62	31±36.90	13±15.48	
9–12 years	107±40.53	118±52.68	45±44.12	
>12 years	117±44.32	75±33.48	236±40.00	
MMSE	28.51±1.23	28.43±1.49	27.38±1.85	<0.001 ^{b,c}
IADL	8.29±0.78	8.25±0.94	8.48±1.02	0.167
HAD Total	5.55±3.26	5.85±3.70	5.91±3.63	0.535
Anxiety	4.23±2.47	4.28±2.72	4.12±2.57	0.877
Depression	1.34±1.47	1.58±1.71	1.79±1.76	0.039 ^b
Digit Span Forward	5.62±1.13	5.81±1.00	5.55±0.99	0.054
Visual Memory Span Forward	5.18±1.00	5.14±0.93	5.14±1.02	0.892
RI-48 Cued Recall Test				
Immediate verbal cued recall	40.05±4.43	39.53±4.88	35.69±5.20	<0.001 ^{b,c}
Delayed cued recall	27.69±5.02	27.20±5.26	16.94±4.96	<0.001 ^{b,c}
Intrusions	2.25±2.53	2.20±2.36	4.74±5.53	<0.001 ^{b,c}
Shapes Test				
Total score (3 immediate recalls)	34.00±3.67	32.91±4.49	29.95±7.20	<0.001 ^{a,b,c}
Delayed recall	11.70±0.71	11.46±1.19	10.16±2.74	<0.001 ^{b,c}
Boston Naming Test	19.36±0.95	19.30±1.76	19.72±3.25	0.214
Digit-Symbol-Coding	56.78±11.73	51.60±11.40	49.50±10.80	<0.001 ^{a,b}
Trail Making Test A				
Time, s	39.70±14.00	41.78±12.35	43.39±13.86	0.040 ^b
Error	0.08±0.28	0.08±0.31	0.07±0.36	0.907
Trail Making Test B				
Time, s	94.59±40.87	103.43±40.22	126.67±67.94	<0.001 ^{b,c}
Error	0.47±0.76	0.49±0.72	0.65±1.04	0.163
Trail Making Test B/A	2.48±0.91	2.58±0.99	2.99±1.31	<0.001 ^{b,c}
Verbal Fluency	22.15±5.83	22.18±6.29	19.35±7.05	<0.001 ^{b,c}
WCST				
Categories completed	4.74±2.08	4.32±2.21	3.97±2.37	0.036 ^b
Failure to maintain set	0.14±0.37	0.14±0.39	0.20±0.51	0.521
Praxis				
Constructional (CERAD)	10.82±0.58	10.73±0.72	10.73±0.76	0.245
Ideomotor transitive	9.44±0.75	9.24±1.02	9.09±1.18	0.007 ^{a,b}
Ideomotor intransitive	19.55±0.94	19.42±0.99	19.45±0.87	0.338
Reflexive	7.06±1.03	6.83±1.15	6.91±1.19	0.074
Visual gnosis (Ghent)	4.99±0.09	5.00±0.07	4.97±0.18	0.129

Values are presented as mean ± SD unless otherwise indicated.

^a Significant difference between sCON and dCON. ^b Significant difference between sCON and MCI.

^c Significant difference between dCON and MCI.

Table 2. Personality factor and facet values in the three diagnostic groups at baseline

Personality traits		sCON	dCON	MCI	p
Neuroticism	N	76.34±18.82	76.71±18.24	77.30±18.98	0.904
Anxiety	N1	13.59±5.29	13.88±5.14	14.28±5.30	0.513
Angry hostility	N2	11.93±4.07	12.07±3.98	12.51±4.24	0.471
Depression	N3	12.53±4.68	13.10±4.39	12.59±4.40	0.345
Self-consciousness	N4	14.00±4.15	13.70±3.95	13.59±3.96	0.580
Impulsiveness	N5	14.45±4.23	13.96±3.61	13.70±3.58	0.174
Vulnerability	N6	9.83±3.68	10.00±4.27	10.12±4.54	0.812
Extraversion	E	102.34±16.54	100.06±17.12	102.47±17.15	0.268
Warmth	E1	22.72±4.25	22.42±4.46	22.91±4.05	0.577
Gregariousness	E2	14.17±5.07	13.62±4.93	15.18±4.87	0.033^c
Assertiveness	E3	15.07±4.19	14.93±4.61	14.81±4.64	0.869
Activity	E4	18.04±4.34	17.87±4.55	17.10±4.31	0.182
Excitement seeking	E5	12.70±4.07	12.31±4.06	13.80±4.05	0.009^c
Positive emotion	E6	19.65±4.66	18.92±4.82	18.66±4.81	0.105
Openness	O	115.15±17.80	108.86±17.39	105.31±16.10	<0.001^{a,b}
Fantasy	O1	17.99±4.99	17.24±4.14	16.38±4.30	0.008^b
Aesthetics	O2	19.47±5.26	18.13±5.31	17.60±4.87	0.002^{a,b}
Feelings	O3	19.64±4.18	18.80±3.90	18.75±3.96	0.039
Actions	O4	16.80±3.97	15.98±3.83	14.73±3.71	<0.001^{b,c}
Ideas	O5	20.64±4.33	19.25±4.97	18.69±4.17	<0.001^{a,b}
Values	O6	20.61±3.38	19.46±3.40	18.94±3.28	<0.001^{a,b}
Agreeableness	A	132.27±15.04	130.41±16.75	129.52±15.41	0.233
Trust	A1	21.33±3.93	20.65±4.17	21.00±3.73	0.171
Straightforwardness	A2	23.28±4.26	23.21±4.38	22.68±4.49	0.470
Altruism	A3	23.64±3.29	23.35±3.44	23.45±3.34	0.634
Compliance	A4	20.59±3.99	20.42±4.09	19.89±3.91	0.324
Modesty	A5	21.31±4.19	21.31±4.43	21.44±3.87	0.961
Tender-mindedness	A6	22.11±3.47	21.45±3.87	21.14±3.72	0.036
Conscientiousness	C	120.36±17.33	122.32±16.6	122.46±22.24	0.406
Competence	C1	20.55±3.28	20.25±3.59	20.33±3.37	0.607
Order	C2	18.25±4.28	18.58±4.47	19.16±4.24	0.195
Dutifulness	C3	24.77±3.38	24.94±3.19	24.73±4.15	0.819
Achievement striving	C4	18.69±3.71	19.29±3.50	19.52±3.33	0.067
Self-discipline	C5	19.88±4.50	20.32±4.55	20.59±4.67	0.335
Deliberation	C6	18.22±4.17	18.94±3.73	19.65±5.08	0.010^b

Values are presented as mean ± SD.

^a Significant difference between sCON and dCON. ^b Significant difference between sCON and MCI;

^c Significant difference between dCON and MCI.

Regression data on the association between NEO-PI factors and facets (independent variables) and the risk to experience subtle cognitive deterioration (dCON) as compared to sCON are summarized in table 4. Only Openness was significantly associated with a 42.8% ($1.428 = 1/0.70$; OR = 0.70; 95% CI 0.58–0.84) risk reduction of being in the dCON group for 1 z-score of this factor. After adjusting for age, sex and educational level (OR_{adjusted} = 0.72; 95% CI 0.59–0.87), this factor explained almost 5% of the sCON/dCON variance. Amongst the Openness facets, Aesthetics, Feelings, Ideas and Values are always significantly reducing the risk of deterioration, with and without adjustment, with OR_{adjusted} ranging from 0.76 to 0.81 (table 4).

Table 3. Neuropsychological differences between sCON and dCON at follow-up

	sCON (n = 264)	dCON (n = 224)	p (t test)
Age, years	71.56±4.35	73.12±4.82	<0.001
MMSE	28.59±1.18	28.05±1.50	<0.001
IADL	8.19±0.58	8.29±0.88	0.147
HAD Total	5.77±3.45	6.17±3.96	0.228
Anxiety	4.24±2.64	4.51±3.03	0.299
Depression	1.53±1.48	1.67±1.75	0.350
Digit Span Forward	5.85±1.06	5.53±1.03	0.001
Visual Memory Span Forward	5.45±0.93	5.06±0.97	<0.001
RI-48 Cued Recall Test			
Immediate verbal cued recall	41.11±4.49	39.31±0.96	<0.001
Delayed cued recall	29.66±29.66	26.17±6.19	<0.001
Intrusions	2.11±2.53	3.40±3.32	<0.001
Shapes test			
Total score			
(3 immediate recalls)	34.46±3.03	32.98±4.17	<0.001
Delayed recall	11.83±1.75	11.13±1.54	<0.001
Boston Naming Test	19.68±1.99	19.16±1.92	0.003
Digit-Symbol-Coding	56.61±11.64	51.25±11.89	<0.001
Trail Making Test A			
Time, s	39.28±12.86	43.42±12.92	0.001
Error	0.07±0.29	0.13±0.42	0.083
Trail Making Test B			
Time, s	86.08±33.17	115.26±47.71	<0.001
Error	0.21±0.59	0.70±0.95	<0.001
Trail Making Test B/A	2.27±0.78	2.73±0.98	<0.001
Verbal Fluency	21.25±6.01	18.82±6.08	<0.001
WCST			
Categories completed	5.04±1.87	4.00±2.33	<0.001
Failure to maintain set	0.13±0.41	0.28±0.57	0.001
Praxis	10.84±0.49	10.70±0.72	0.015
Constructional (CERAD)			
Ideomotor transitive	9.66±0.71	9.46±0.82	0.003
Ideomotor intransitive	19.66±0.79	19.33±0.97	<0.001
Reflexive	7.37±0.87	7.15±1.06	0.012
Visual gnosis (Ghent)	5.00±0.00	5.00±0.00	0.318

Values are presented as mean ± SD.

The associations of personality factors and facets with the risk of being in the MCI group as compared to sCON are shown in table 5. Only Openness was significantly associated with a 65.0% ($1.650 = 1/0.606$; $OR_{adjusted} = 0.61$; 95% CI 0.46–0.79) risk reduction of being in the MCI group for 1 z-score of this factor. The adjusted regression model explained 8% of the sCON/MCI variance. All but one of the Openness facets showed similar associations and effect sizes (table 5).

In order to further explore the absence of association between Neuroticism and cognitive decline observed in our cohort, an additional analysis was conducted to compare mean factors of Neuroticism of the whole study population (n = 590) with a reference population [39]. Neuroticism factor (and its facets Angry hostility, Depression and Vulnerability) scores were significantly lower in our series as compared to the group of reference (table 6).

Table 4. Association between personality factors and facets, expressed as z-scores, and the risk of being in the dCON versus the sCON group

Personality traits		Crude		Adjusted	
		OR (95% CI)	p value	OR (95% CI)	p value
Neuroticism	N	1.02 (0.85, 1.22)	0.825	1.00 (0.83, 1.12)	0.975
Anxiety	N1	1.06 (0.88, 1.27)	0.542	1.06 (0.88, 1.28)	0.526
Angry hostility	N2	1.04 (0.87, 1.24)	0.695	1.03 (0.85, 1.23)	0.793
Depression	N3	1.14 (0.95, 1.37)	0.164	1.10 (0.91, 1.33)	0.334
Self-consciousness	N4	0.93 (0.77, 1.11)	0.404	0.91 (0.75, 1.09)	0.307
Impulsiveness	N5	0.88 (0.72, 1.06)	0.173	0.88 (0.73, 1.08)	0.218
Vulnerability	N6	1.04 (0.88, 1.23)	0.652	0.99 (0.83, 1.18)	0.945
Extraversion	E	0.87 (0.73, 1.04)	0.135	0.89 (0.74, 1.07)	0.212
Warmth	E1	0.93 (0.78, 1.11)	0.446	0.93 (0.77, 1.11)	0.416
Gregariousness	E2	0.89 (0.75, 1.07)	0.226	0.91 (0.75, 1.09)	0.303
Assertiveness	E3	0.97 (0.82, 1.15)	0.727	0.99 (0.83, 1.19)	0.939
Activity	E4	0.96 (0.81, 1.15)	0.671	0.99 (0.83, 1.19)	0.948
Excitement seeking	E5	0.91 (0.76, 1.09)	0.292	0.89 (0.74, 1.07)	0.214
Positive emotion	E6	0.86 (0.72, 1.02)	0.088	0.87 (0.72, 1.05)	0.147
Openness	O	0.70 (0.58, 0.84)	<0.001	0.72 (0.59, 0.87)	0.001
Fantasy	O1	0.84 (0.69, 1.02)	0.074	0.85 (0.70, 1.04)	0.106
Aesthetics	O2	0.78 (0.65, 0.93)	0.006	0.77 (0.64, 0.93)	0.008
Feelings	O3	0.81 (0.67, 0.97)	0.023	0.82 (0.68, 1.00)	0.045
Actions	O4	0.81 (0.67, 0.97)	0.022	0.84 (0.69, 1.02)	0.076
Ideas	O5	0.76 (0.64, 0.90)	0.001	0.77 (0.65, 0.93)	0.005
Values	O6	0.71 (0.59, 0.86)	<0.001	0.76 (0.62, 0.92)	0.005
Agreeableness	A	0.89 (0.75, 1.06)	0.196	0.89 (0.74, 1.07)	0.213
Trust	A1	0.85 (0.71, 1.01)	0.065	0.85 (0.71, 1.02)	0.087
Straightforwardness	A2	0.98 (0.83, 1.17)	0.858	1.03 (0.86, 1.24)	0.769
Altruism	A3	0.92 (0.77, 1.10)	0.346	0.92 (0.76, 1.10)	0.362
Compliance	A4	0.96 (0.80, 1.14)	0.641	0.94 (0.78, 1.13)	0.521
Modesty	A5	1.00 (0.84, 1.19)	0.996	0.98 (0.82, 1.18)	0.865
Tender-mindedness	A6	0.84 (0.71, 1.00)	0.049	0.83 (0.70, 1.00)	0.047
Conscientiousness	C	1.13 (0.94, 1.35)	0.205	1.14 (0.94, 1.38)	0.173
Competence	C1	0.92 (0.77, 1.09)	0.330	0.95 (1.03, 1.13)	0.546
Order	C2	1.08 (0.91, 1.29)	0.393	1.08 (0.90, 1.29)	0.418
Dutifulness	C3	1.05 (0.88, 1.27)	0.571	1.07 (0.88, 1.29)	0.496
Achievement striving	C4	1.19 (0.99, 1.43)	0.071	1.21 (1.00, 1.46)	0.055
Self-discipline	C5	1.10 (0.92, 1.32)	0.282	1.12 (0.94, 1.35)	0.210
Deliberation	C6	1.21 (1.00, 1.46)	0.049	1.19 (0.98, 1.44)	0.090

Total: n = 488; dCON: n = 224 (45.9%). Logistic regression models adjusted for: sex, educational level and age at the time of cognitive assessment.

Discussion

Our findings in a community-based sample reveal that elderly controls with higher openness were less likely to experience subtle decline in cognitive function over an 18-month follow-up. Pointing to the relevance of these data in respect to AD progress, the same analysis in MCI compared to control cases led to similar associations in respect to personality factors and facets.

The association between personality 'Big Five' factors and facets and cognitive impairment is still a matter of debate. There is wide agreement that extraversion and agreeableness are

Table 5. Association between personality factors and facets, expressed as z-scores, and the risk of being in the MCI versus the sCON group

Personality traits		Crude		Adjusted	
		OR (95% CI)	p value	OR (95% CI)	p value
Neuroticism	N	1.05 (0.84, 1.32)	0.660	1.12 (0.88, 1.42)	0.350
Anxiety	N1	1.14 (0.91, 1.43)	0.261	1.20 (0.95, 1.53)	0.129
Angry hostility	N2	1.15 (0.92, 1.44)	0.226	1.11 (0.88, 1.39)	0.395
Depression	N3	1.01 (0.80, 1.28)	0.908	1.09 (0.85, 1.39)	0.493
Self-consciousness	N4	0.90 (0.71, 1.14)	0.384	0.94 (0.74, 1.20)	0.635
Impulsiveness	N5	0.82 (0.64, 1.05)	0.110	0.85 (0.66, 1.09)	0.191
Vulnerability	N6	1.07 (0.86, 1.32)	0.535	1.17 (0.93, 1.46)	0.175
Extraversion	E	1.01 (0.80, 1.26)	0.948	1.01 (0.80, 1.27)	0.921
Warmth	E1	1.05 (0.83, 1.33)	0.688	1.14 (0.89, 1.46)	0.302
Gregariousness	E2	1.23 (0.97, 1.56)	0.086	1.24 (0.98, 1.59)	0.078
Assertiveness	E3	0.94 (0.76, 1.18)	0.607	0.89 (0.70, 1.12)	0.317
Activity	E4	0.80 (0.64, 1.01)	0.063	0.79 (0.62, 1.01)	0.059
Excitement seeking	E5	1.31 (1.04, 1.65)	0.021	1.24 (1.07, 1.58)	0.089
Positive emotion	E6	0.81 (0.30, 0.48)	0.072	0.86 (0.68, 1.09)	0.210
Openness	O	0.55 (0.43, 0.71)	0.000	0.61 (0.46, 0.79)	0.000
Fantasy	O1	0.70 (0.55, 0.90)	0.005	0.74 (0.58, 0.96)	0.022
Aesthetics	O2	0.69 (0.55, 0.88)	0.002	0.78 (0.61, 0.99)	0.043
Feelings	O3	0.81 (0.64, 1.02)	0.067	0.88 (0.69, 1.12)	0.296
Actions	O4	0.59 (0.46, 0.75)	0.000	0.63 (0.49, 0.81)	0.000
Ideas	O5	0.63 (0.50, 0.80)	0.000	0.63 (0.49, 0.81)	0.000
Values	O6	0.61 (0.48, 0.77)	0.000	0.64 (0.50, 0.83)	0.001
Agreeableness	A	0.84 (0.67, 1.05)	0.120	0.91 (0.72, 1.16)	0.467
Trust	A1	0.92 (0.73, 1.16)	0.460	0.97 (0.76, 1.23)	0.791
Straightforwardness	A2	0.87 (0.70, 1.09)	0.229	0.96 (0.76, 1.22)	0.739
Altruism	A3	0.94 (0.75, 1.19)	0.623	1.02 (0.80, 1.29)	0.892
Compliance	A4	0.84 (0.67, 1.05)	0.130	0.89 (0.70, 1.13)	0.328
Modesty	A5	1.03 (0.82, 1.31)	0.784	1.07 (0.84, 1.37)	0.578
Tender-mindedness	A6	0.76 (0.61, 0.96)	0.020	0.80 (0.63, 1.02)	0.069
Conscientiousness	C	1.11 (0.90, 1.38)	0.339	1.02 (0.82, 1.27)	0.877
Competence	C1	0.94 (0.75, 1.17)	0.568	0.86 (0.68, 1.10)	0.227
Order	C2	1.24 (0.98, 1.58)	0.069	1.20 (0.94, 1.52)	0.146
Dutifulness	C3	0.99 (0.80, 1.22)	0.910	0.96 (0.77, 1.19)	0.687
Achievement striving	C4	1.27 (1.00, 1.61)	0.050	1.18 (0.92, 1.51)	0.188
Self-discipline	C5	1.17 (0.93, 1.48)	0.182	1.10 (0.87, 1.39)	0.434
Deliberation	C6	1.35 (1.08, 1.68)	0.008	1.23 (0.99, 1.54)	0.065

Total: n = 366; MCI participants: n = 102 (27.87%). Logistic regression models adjusted for sex, educational level and age at the time of cognitive assessment.

not related to the dementing process [18], a viewpoint that is further supported by the present results. In contrast, data on Neuroticism, Conscientiousness and Openness are less conclusive. Cross-sectional observations pointed to the presence of high levels of Neuroticism and low levels of consciousness both in AD [40] and MCI cases [41]. Previous longitudinal studies supported the association between higher levels of Neuroticism both in midlife and old age and dementia as well as MCI risk [14, 42, 43]. In contrast, higher conscientiousness conferred protection against dementia and MCI, but this effect was marginal in most of the previous studies [18] and absent in the present series. More recent data challenged the association

Table 6. Comparison of Neuroticism factor and facet scores between NEO-PI reference and the present series

		NEO-PI standards	Current sample	p (t test)
Neuroticism	N	92.7±8.2	76.6±18.6	0.010
Anxiety	N1	17.0±4.2	13.8±5.2	0.070
Angry hostility	N2	16.2±3.0	12.1±4.1	0.003
Depression	N3	15.9±3.0	12.8±4.5	0.039
Self-consciousness	N4	15.0±3.0	13.8±4.0	0.381
Impulsiveness	N5	15.6±2.9	14.1±3.9	0.276
Vulnerability	N6	13.0±4.1	9.9±4.1	0.026

Values are presented as mean ± SD.

between high Neuroticism scores and dementia risk. In their 6-year longitudinal study based on the Dutch personality questionnaire, Ramakers et al. [13] showed that, although neuroticism scores showed negative correlation with mental speed in MCI, there was no significant association between this variable and MCI conversion to AD.

Longitudinal studies addressing the association between NEO-PI patterns and cognitive decline in community-dwelling samples of healthy controls are still very rare. In a German population-based study including 222 elderly individuals followed up at three examination waves during a 10-year observation period [42], a decrease of neuroticism and extraversion scores over time was reported. A 2.24-higher risk of developing MCI at 10 years was observed in healthy controls with higher baseline neuroticism. In the same line, the Baltimore Epidemiologic Catchment Area study indicated a small but still significant negative association between neuroticism and MMSE scores. Higher levels of Consciousness were associated with a slight improvement in general cognitive function measures in this cohort [44]. Our data do not confirm the negative effect of higher Neuroticism levels on cognitive fate in normal aging. There are several explanations for this discrepancy. The German study had a significantly longer follow-up period focusing on the transition to MCI status. Since we focused our analysis on rapid cognitive changes, the length of our follow-up was of 18 months that allowed for observing subtle cognitive deficits at the pre-MCI stage. It is thus possible that, although higher Neuroticism scores increase the long-term risk for MCI transition, it does not impact on short-term cognitive changes in healthy controls. Unlike the present study, the Baltimore survey involved adult cases with a mean age of 45 at the time of personality assessment. A 10-point increase in neuroticism score values was associated with only 0.15-point decrease in MMSE score at the 10-year follow-up. Paralleling the findings of Ramakers et al. [13], the absence of difference in Neuroticism factor and facet scores also concerned the sCON/MCI comparison in our series. It is possible that the very low levels of Neuroticism observed in our sample (compared to age-adjusted normative data) reflect an over-representation of elderly persons with better mental health who are a priori less exposed to the deleterious effect of Neuroticism on cognition.

The most intriguing result of this study is the strong association between Openness factor levels and preservation of cognitive functions in elderly controls. In addition, Aesthetics, Feelings, Ideas and Values facet scores were all positively associated with sCON status at follow-up. Moreover, similar results for both Openness factor and facets were found when the distinction sCON/MCI was used as dependent variable in regression analyses. This observation goes beyond the weak positive effect reported in previous studies in MCI cohorts [18], implying that this personality parameter may have a protective effect on cognition that is mostly expressed in very early stages of cognitive impairment. Openness to experience refers

to the breadth, depth, originality, and complexity of an individual's mental and experiential life. People with high scores in this factor (and corresponding facets) are more curious, open to changes, have richer internal lives and better coping abilities. Our findings suggest that these characteristics may represent a significant advantage to preserve cognitive performances in old age. Interestingly, higher openness to experience is also known to be associated with better quality of life both in younger non clinical samples and elderly cohorts [45–47].

Strengths of the present study include the large community-based sample, which may be seen as representative of the elderly population in the Geneva catchment area, exhaustive neuropsychological analysis at inclusion and follow-up, as well as careful exclusion of physical and mental conditions that may act as confounding factors in regression analyses. Some limitations of the present study are worth noting. The lack of a long prospective design poses some potential issues of directionality in the observed associations between personality traits and subtle cognitive impairment and causality cannot be implied. However, reverse causality (that is, subtle cognitive impairment leading to a biased over-reporting of openness) seems unlikely because there were no differences in the other four NEO-PI factors. Consistent with recent core clinical criteria for MCI [2], the identification of dCON was based on the objective decline in cognitive functions measured using serial, comprehensive neuropsychological assessments. However, in the absence of a longer follow-up, the cognitive fate of these cases remains uncertain so that they cannot be a priori considered as incipient AD cases. Although we adjusted for sociodemographic characteristics depressive and anxious symptomatology, the potential residual confounding effect of unmeasured lifestyles and health behaviors associated with both personality and cognitive impairment cannot be excluded [48]. When interpreting the present observations, one should keep in mind that multivariate regression models including the best predictors, openness facets, explain a mere 8% of the cognitive variability. The present analysis focuses on personality and does not take into account AD-related biomarkers (i.e. structural MRI parameters, amyloid burden, apolipoprotein E genotype) that could certainly increase the performance of our regression models. Future studies in community-based cohorts of healthy elders including longer follow-up periods, assessment of lifestyle measures and AD-related biomarkers are warranted to explore the relative contribution of personality in the prediction of cognitive decline.

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