HHS Public Access

Author manuscript

J Am Geriatr Soc. Author manuscript; available in PMC 2019 April 01.

Published in final edited form as:

J Am Geriatr Soc. 2018 April ; 66(4): 671–678. doi:10.1111/jgs.15182.

Personality Changes During the Transition from Cognitive Health to Mild Cognitive Impairment

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Abstract

Background/Objectives—Behavioral problems in patients with Alzheimer's disease (AD) impose major management challenges. Current prevention strategies are anchored to cognitive outcomes but behavioral outcomes may provide another, clinically relevant opportunity for pre-emptive therapy. We sought to determine whether personality changes which predispose to behavioral disorders arise during the transition from preclinical AD to mild cognitive impairment (MCI).

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Conflicts of Interest

Blake T. Langlais, BS reports no disclosures.
Amylou C. Dueck, PhD reports no disclosures.
Bruce R. Henslin, BA reports no disclosures.
Travis A. Johnson, BA reports no disclosures.
Charlene Hoffman-Snyder, DNP reports no disclosures.
Dona E. C. Locke, PhD reports no disclosures.

Author Contributions

Richard J. Caselli, MD designed the study, participated in data acquisition, management, and analysis, and drafted the manuscript. Dr. Caselli, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Blake T. Langlais, BS performed the primary statistical analysis under the supervision of Dr. Amylou Dueck, and provided critical revision to the manuscript including drafting the data analysis section.
Amylou C. Dueck, PhD contributed to as well as supervised data analysis that was performed by Blake Langlais, provided the data analytic strategy, and provided critical revision to the manuscript.
Bruce R. Henslin, BA assisted in data acquisition and provided critical revision to the manuscript.
Travis A. Johnson, BA assisted in data acquisition and provided critical revision to the manuscript.
Bryan K. Woodruff, MD assisted in data acquisition and provided critical revision to the manuscript.
Charlene Hoffman-Snyder, DNP assisted in data acquisition and provided critical revision to the manuscript.
Dona E. C. Locke, PhD provided supervision and quality control over all neuropsychological test administration, assisted Dr. Caselli with interpretation of results, and provided critical revisions to the manuscript.

Design—Longitudinal observational cohort study.

Setting—Academic medical center.

Participants—277 members of an apolipoprotein E ε4 (*APOE* ε4) genetically enriched cohort of Maricopa County residents were neuropsychiatrically healthy at entry. Over a mean interval of 7 years 25 developed MCI and had the NEO Personality Inventory-Revised (NEO-PI-R) before and during the MCI transition epoch and were compared with 252 nontransitioners also with serial NEO-PI-R administrations.

Intervention—Longitudinal administration of the NEO-PI-R (and neuropsychological test battery).

Measurements—Change in NEO-PI-R factor scores (Neuroticism, Extraversion, Openness, Agreeableness, and Conscientiousness) from entry to either the epoch of MCI diagnosis or an equivalent followup duration in nontransitioners.

Results—NEO-PI-R Neuroticism T-scores increased significantly more in MCI transitioners than in nontransitioners (mean: +2.9; 95% CI: [0.9, 4.9]) vs 0 [−0.7, 0.7], P=.02), and Openness decreased more in MCI transitioners than in nontransitioners (−4.8 [−7.3, −2.4] vs −1.0 [−1.6, −0.4], P<.001). Concurrent subclinical but statistically significant changes in behavioral scores worsened in MCI transitioners relative to nontransitioners on measures of depression, somatization, irritability, anxiety, and aggressive attitude.

Conclusion—Personality and subclinical behavioral changes begin during the transition from preclinical AD to incident MCI, and qualitatively resemble the clinically manifest behavioral disorders that subsequently arise in patients with frank dementia.

Keywords

Aging; Preclinical Alzheimer’s disease; mild cognitive impairment (MCI); personality change; behavioral disorder; NEO-Personality Inventory-Revised

INTRODUCTION

Cognitive loss is the most widely recognized consequence of Alzheimer’s disease (AD), and constitutes the defining feature of its symptomatic onset at the stage of mild cognitive impairment (MCI)[1] yet behavioral problems may be the most troubling aspect of dementia care[2–5]. Analogous to the mild cognitive decline that heralds the symptomatic onset of AD and anticipates the inexorable intellectual decline that subsequently undermines the functional capacity of its victims, behavioral changes might also begin early, even perhaps with the transition from the presymptomatic to the MCI stage anticipating the disruptive behaviors that overburden caregivers and prompt medical intervention.

Behavioral problems are often attributed to, or even equated with a change in a patient’s personality, but a distinction should be drawn between them. Personality describes a tendency toward a certain reaction or behavior, not the reaction or behavior itself. While behaviors adapt to varied situations, personality itself remains stable[6]. For example, a stress prone individual may feel highly stressed driving in traffic yet may feel no stress while

watching television whereas an actively depressed person will be depressed regardless of whether they are driving or watching television. Studies seeking to address the way in which AD affects personality have documented an informant's (typically a spousal caregiver) impressions of how personality changed from the premorbid to the dementia state. These studies are limited, however, by reliance on a proxy's recollection of what a dementia patient was like before the onset of dementia, and by confusing the consequence that is the impaired behavior of frankly demented patients with earlier true personality changes that predispose to subsequent behavioral disruption[7–19].

If personality begins to change as early as the preclinical or MCI stage of AD, then personality assessment might be a way to identify patients at risk of future behavioral problems possibly facilitating earlier (and potentially more benign) intervention, but existing data are limited[20,21]. To address this need and overcome prior limitations, we have been prospectively administering the NEO Personality Inventory-Revised (NEO-PI-R)[22] to cognitively normal members of the Arizona *APOE* Cohort who are able to complete their own personality questionnaires to determine whether personality changes during the transition from presymptomatic AD to the earliest symptomatic state, incident MCI.

METHODS

Subjects

From January 1, 1994 through December 31, 2016, cognitively normal residents of Maricopa County age 21 years and older were recruited through local media ads, underwent apolipoprotein E (*APOE*) genotyping and longitudinal neuropsychological assessment every two years. Determination of *APOE* genotype was performed using Taqman Single Nucleotide Polymorphism assays.

All identified ε4 homozygotes (HMZ) were matched by age, sex, and education to one ε4 heterozygote (HTZ; all with the ε3/4 genotype) and two ε4 non-carriers. Many additional heterozygous persons and non-carriers who were otherwise eligible for enrollment were also recruited so that roughly half of the cohort represents matched quartos and the remaining members were not matched but otherwise fulfilled entry criteria. Each participant had screening tests that included a medical history, neurological examination, the Folstein Mini-Mental State Exam (MMSE), Hamilton Depression (Ham-D) Rating Scale, Functional Activities Questionnaire (FAQ), Instrumental Activities of Daily Living (IADL), and Structured Psychiatric Interview for DSM-III-R. We excluded anyone with potentially confounding medical, neurologic, or psychiatric problems (essentially any condition that might adversely affect cognitive abilities such as end stage organ disease, stroke, or active major depression). None met published criteria for MCI[1], AD[23], other forms of dementia or major depressive disorder[24]. Entry criteria included scores of at least 27 on the MMSE (with at least 1 of 3 on the recall subtest), 10 or less on the Ham-D, and perfect scores on the FAQ and IADL. All individuals gave their written, informed consent to participate in the study and have the results of the APOE test withheld from them which was approved by the Mayo Clinic Institutional Review Board.

Data were reviewed at each visit by a neurologist (RJC) and neuropsychologist (DECL) for indications of cognitive impairment. Amnestic MCI was diagnosed in those individuals who endorsed symptoms of memory loss (corroborated by a close informant), exhibited objective decline from previous performance on neuropsychological tests sensitive to memory, and who met published criteria for MCI[1]. MCI was first suspected based on collected study data, and such individuals were then invited to complete a clinical neurological evaluation (RJC) that included standard laboratory and radiological assessments following which a formal diagnosis was made and provided to the patient.

Members of the Arizona *APOE* Cohort with two of more NEO-PI-R administrations were considered for study inclusion. Patients diagnosed with incident amnestic MCI who received the NEO-PI-R prior to developing MCI as well as at the time of MCI diagnosis were identified as MCI transitioners. The youngest MCI transitioner was 54 years old at the time of their first NEO-PI-R administration so a lower age cut-off of 50 years at the time of the initial NEO-PI-R administration was chosen for the control group. Those nontransitioners who received the NEO-PI-R serially but did not develop a cognitive disorder were included as controls. The first and last NEO-PI-R administrations, typically the first and second or third, for each member were used to evaluate change in NEO-PI-R factor and facet scores.

Neuropsychological Assessment

A previously described comprehensive neuropsychological battery was administered every two years[25], and is summarized in Table 1. Personality was assessed with the NEO-PI-R which defines personality according to five factors: Neuroticism, Extraversion, Openness, Agreeableness, and Conscientiousness[22]. It was added to our battery in 2006, and repeated on alternate visits (roughly every four years). Brief operational definitions of these five factors are as follows (adapted from ref. 26): Neuroticism is a tendency to feel anxiety and other negative emotions, Extraversion is a tendency to be outgoing and lead in social contexts, Openness is a tendency to be receptive to new ideas and experiences, Agreeableness is a tendency to be trusting and deferential, and Conscientiousness is a tendency to be organized and rule abiding. Each factor is comprised of six facets. For example, the six facets of the Neuroticism factor all reflect reactivity to stress and include the tendency to experience anxiety, anger, depression, and self-consciousness; the ability to resist temptations and cravings (impulsivity), and a general ability to cope with stress (vulnerability)[22]..

The NEO-PI-R is designed to measure personality traits and not psychological abnormality. The scores on the domain and facet scales represent how much of that particular trait an individual holds and does not imply clinical diagnosis or disorder. Therefore, our neuropsychological battery also includes measures of psychopathology (Table 1) including (in addition to the Ham-D which we use as a screening measure) the Beck Depression Inventory, Geriatric Depression Scale (GDS), and Personality Assessment Inventory (PAI). In contrast to the NEO-PI-R, the PAI is designed to measure clinically significant levels of symptomatology related to “clinical diagnosis, treatment planning and screening for psychopathology” (PAI manual page 5). It was not designed to measure the domains of normal personality[27].

Statistical Analysis

Baseline demographics, NEO-PI-R scores, and other neuropsychological scores at the time of the first NEO-PI-R administration were summarized within the groups using means and 95% confidence intervals (CI) or relative frequencies and compared between groups using t-tests and chi-squared tests. NEO-PI-R change scores were computed as the score at last NEO-PI-R administration minus the score at the first administration. Personality Assessment Inventory (PAI) change scores were similarly computed and were derived from the same administrations as the first and last NEO-PI-R administrations. NEO-PI-R and PAI change scores were compared between groups using t-tests. To assess within-subject change, the percentage of subjects meeting various thresholds for meaningful change (5-point increase in Neuroticism or 5-point decline in Openness) were compared between groups using chi-squared tests. In a subsequent analysis to adjust for potential differences between groups in time between administrations, scores at the last visit were compared between groups adjusting for score at the first visit and time interval between administrations using analysis of covariance (ANCOVA). To supplement primary univariate and multivariate statistical testing, a novel graphical approach utilizing a multi-sectional 'fishbone' plot displays NEO-PI-R domain- and subdomain-specific effect sizes. *P* values ≤ .05 were considered statistically significant.. Statistical analysis was carried out using SAS software (SAS Version 9, SAS Institute, Cary, NC).

RESULTS

277 members of the Arizona *APOE* Cohort met inclusion criteria, of which 25 were incident MCI cases and 252 were nontransitioning controls. Subject characteristics at baseline are summarized in Table 2. There was a higher rate of *APOE* e4 carrier status (80 vs 38.1%, *P*<. 001) among MCI transitioners compared to nontransitioners, but there was no difference in mean age (mean: 62.9; 95% CI: [62.1, 63.8] years), education (16.1 [15.8, 16.3] years), race/ethnicity (83.4% non-Hispanic white), sex (67.9% female), mean number of NEO-PI-R administrations (2.3 [2.3, 2.4]) or interval between first and last NEO-PI-R administration (78.9 [76.2, 81.7] months) (Table 2). Baseline scores did not differ between MCI transitioners and nontransitioners on any personality (NEO-PI-R factor and facet scores) or behavioral (PAI, Ham-D, Beck, GDS) measure. Neuropsychological and behavioral test performances at baseline, summarized in Supplementary Tables S1 and S2, were normal but characterized by lower scores in the MCI transitioner group on memory related measures such as the Auditory Verbal Learning Test Long Term Memory score (7.0 [5.8, 8.2] vs 9.9 [9.5, 10.3], *P*<.001).

Longitudinally, MCI transitioners exhibited greater decline on multiple neuropsychological measures (as expected) particularly in the domains of memory and executive skills than nontransitioners (Supplementary Table S1). NEO-PI-R changes are summarized in figure 1 and table 3. At the group level Neuroticism T-scores increased more in MCI transitioners than in nontransitioners (+2.9 [0.9, 4.9] vs 0 [−0.7, 0.7], *P*=.02), and Openness decreased more in MCI transitioners than in nontransitioners (−4.8 [−7.3, −2.4] vs −1.0 [−1.6, −0.4], *P*<.001). Facet scores that worsened more in MCI transitioners than nontransitioners included the Neuroticism facet score of depression (+4.6 [1.7, 7.4] vs −0.2 [−1.1, 0.6], *P*<.

001), and the Openness facet scores of activity (−4.6 [−7.5, −1.7] vs −1.1 [−2.0, −0.2], *P*=.02), aesthetics (−3.8 [−7.0, −0.6] vs −0.6 [−1.4, 0.1], *P*=.01), ideas (−3.6 [−6.2, −1.0] vs −0.8 [−1.5, 0.0], *P*=.03), and values (−5.1 [−7.3, −2.8] vs −0.5 [−1.4, 0.3], *P*=.002). Adjusting for the length of time between NEO-PI-R administrations did not change these results. At the individual level, Neuroticism T-scores increased by more than 5 points in 40% of transitioners and 18.3% of nontransitioners (P=.01) while Openness T-score declined by more than 5 points in 48% of transitioners and 21.4% of nontransitioners (P=.003).

Concurrent clinically insignificant but statistically significant changes in behavioral scores revealed worsening in MCI transitioners relative to nontransitioners including measures of depression (PAI-CSc-DEP [+4.2 (1.3, 7.1) vs +0.3 (−0.8, 1.3), *P*=.04], GDS [+3.8 (1.1, 6.5) vs +0.1 (−0.5, 0.8), *P*=.003), somatization (PAI-CSc-SOM [+5.4 (0.4, 10.3) vs +1.0 (0.2, 1.8), *P*=.008]), irritability (PAI-BOR-I [+4.6 (0.4, 8.9) vs −0.2 (−1.1, 0.8), *P*=.008]), affective anxiety (PAI-ANX-A [+4.4 (1.1, 7.6) vs +0.5 (−0.6, 1.5), *P*=.05]), and aggressive attitude (PAI-AGG-A [+4.8 (0.3, 9.3) vs −0.7 (−1.7, 0.4), *P*=.005]) (Supplementary Table S2). No transitioner experienced the new onset of depression, anxiety, or other psychiatric disorder although one transitioner's husband died during this time prior to MCI transition. This individual had 3 study epochs, and showed transient elevation of depression scores during the second epoch that declined again by the third epoch (HamD 0-9-0, Beck 1-18-14, GDS 11-15-13, and PAI-CSc-DEP T-scores 55-63-57) without commensurate NEO-PI-R T-score changes (Neuroticism 50-49-47, Openness 64-64-61).

DISCUSSION

This is the first study to demonstrate that changes in personality, including increasing Neuroticism and decreasing Openness, coincide with the transition from preclinical AD to incident MCI, with concomitant subclinical changes in behavioral measures of somatization, depression, anxiety, irritability, and aggression. Our findings are based upon longitudinal observations over more than seven years prior to the transition point of incident MCI utilizing the gold standard personality measure, the NEO-PI-R, and are derived directly from patient responses rather than proxy estimates. There were no differences in baseline personality or behavioral scores that might otherwise have suggested a predisposition to these negative changes consistent with the hypothesis that these changes were intrinsic to the disease process itself. These changes were identified at the same time that neuropsychological performance declined to the MCI level yet documented prior to communicating a diagnosis of MCI to the patients so that they do not represent a reaction to diagnosis or a complication of treatment.

All previous studies have relied upon informant recollections of the patient's premorbid personality, and only about half have utilized the five factor model. With few exceptions, patients have had established dementia which risks biasing retrospective estimates of presymptomatic functioning and possibly overestimating the degree of personality (vs frank behavioral) change. Only two studies have looked at a similar period of transition. Copeland et al employed a semi-structured interview and found no differences between patients and controls in 10 patients transitioning from normal to MCI over the course of 3 years[20] while Balsis et al found that individuals with preclinical AD did experience more personality

changes than normal nontransitioners based on the Blessed Dementia Scale including increased rigidity, apathy, egocentricity, and impaired emotional control[21]. Six previous studies utilized the NEO-PI[9,11,14,16] or NEO-PI-R[19], all in established dementia patients, and all concluded that compared to pre-dementia estimates Neuroticism increased while Extraversion, Openness, and Conscientiousness decreased with dementia. One study[11] found Agreeableness declined as well. Another 4 studies[7,8,15,18] utilized the Brooks McKinlay Personality Inventory[28] in which informants rate 18 dichotomized descriptors, and these also found a high frequency of change from the pre-dementia to the post-dementia state. Studies[10,17,21] in which informants utilized the Blessed Dementia Scale[29] or CAMDEX[30] also found changes related to reduced interest, activity, and cognitive flexibility.

We have previously shown that memory decline is detectable preclinically, roughly ten to fifteen years before expected symptomatic onset[25,31], and that that personality impacts longitudinal cognitive trajectories in a normal aging population[32]. Neuroticism and other personality factors do not change simply as a function of aging, but instead are detectable within the context of symptomatic AD at its earliest clinical stage, and unlike preclinical memory decline, there is no preclinical escalation in depression scores prior to the symptomatic transition to MCI[33]. Thus our current findings are consistent with a model in which personality changes follow memory decline during the transitional period, and precede clinically symptomatic behavioral disorders that do not (usually) emerge until later in the MCI and early dementia stages.

Behavioral symptoms pose major therapeutic challenges during the course of disease progression, and those that are severe enough to prompt pharmacotherapeutic intervention are not rare. For example, in a large Veterans Administration study, 17.7% of dementia patients in 1999 were taking antipsychotic drugs, and although their use has been declining in the U.S. and elsewhere since a 2006 FDA black box warning[34], the prevalence of psychotropic use in Finland in 2011 was 45.0–47.9%[35]. In France, antidepressant use in dementia patients increased from 26% in 2010 to 31% in 2014[36]. Despite their widespread use, psychotropic agents have been found to be of either inconsistent or no benefit in patients with dementia[37], and associated with significant adverse outcomes[38]. Gilley et al have previously reported that Neuroticism, as estimated from informant ratings of patients with AD, was predictive of depressive symptoms in a cohort or 410 AD patients followed over four years[39]. If we can correlate early stage personality changes with behavioral outcomes it may be possible to prevent adverse behavioral outcomes. Caregivers and even patients at these early stages may be alerted to impending behavioral risks allowing for earlier life plans (medical proxies, wills, and so forth), and well as potential prevention strategies. Clinical trials will be needed to assess the efficacy of any prevention therapies that may include both pharmacological and nonpharmacological interventions.

The neurobiology of personality is poorly understood. Both structural[40] and functional[41] MRI studies of MCI patients have shown alterations in frontotemporal cortices that have been associated with behavioral disturbances, and we found concomitant cognitive changes in not only memory but in executive skills as well (which are not seen prior to MCI transition[42]) during the MCI transition referable to these anatomical regions. Further work is needed to determine whether greater executive decline portends future behavioral

impairment, as both share similar anatomical substrates. Chronic stress has itself been associated with reduced functional integration of limbic networks[43], reduced gray matter volumes in frontostriatal regions[44], and a variety of functional and structural changes in prefrontal and hippocampal regions[45] possibly predisposing stress prone individuals to earlier personality changes and subsequent behavioral disturbances. Previous work has shown that personality factors influence cognitive aging trajectories[32], and the risk for MCI and AD[46] and support the hypothesis that lifestyle choices that are influenced by personality can impact cognitive outcomes, plausibly through modifiable cerebrovascular components of cognitive decline and dementia[47]. It is less clear if there is an independent effect of personality on AD itself, but whether or not personality impacts neuropathology, it is clear that neuropathology can impact personality. Even at the earliest stage of symptomatic transition illustrated in this study, personality factors start to change in a way that one could expect to foster behavioral problems. Indeed, behavioral symptoms have been shown to be highly prevalent among patients with established MCI and have included, congruent with our findings, depression, apathy, irritability, and anxiety most frequently[48].

A limitation of our study is the lack of neuropathological or biomarker evidence of AD neuropathology as the underlying cause of MCI in our patients. To address this we utilized *APOE* ε4 as a proxy and infer that MCI in *APOE* ε4 carriers reflects underlying AD as previous research has shown that e4 is a strong predictor of clinical progression to AD in MCI patients[49] and the positive predictive value of *APOE* ε4 for AD in a neuropathological series was 97%[50]. Another limitation is the relatively small number of MCI transitioners who received the NEO-PI-R serially. Before our findings can be generalized, replication in other cohorts will be needed, although as our study progresses we will be able to add to these numbers as well as identify behavioral outcomes to correlate with NEO-PI-R scores.

In summary, personality changes occur very early in the clinical course of AD, are characterized by increased Neuroticism and decreased Openness, and coincide with subtle, clinically insignificant behavioral changes that qualitatively mirror and anticipate the clinically severe behavioral problems that often complicate dementia care. Further research is needed to determine whether earlier identification of predisposing personality changes might facilitate earlier, safer and more effective treatment or even prevention of behavioral disorders in patients with AD.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Richard J. Caselli, MD receives research funding from NIA, Merck, Novartis, and the Arizona Alzheimer's Consortium, and serves as an advisory medical editor for Clinical Neurology News.

Bryan K. Woodruff, MD receives research funding from Genentech.

Funding Sources: NIA R01AG031581, P30AG19610, and the Arizona Alzheimer's Research Consortium.

Sponsor's Role

The funding sources including the National Institute on Aging and the Arizona Alzheimer's Research Consortium had no role in any aspect of this study including concept and design, acquisition of subjects and data, analysis and interpretation of data, and preparation of the manuscript.

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Impact

We certify that this work is novel. The potential impact of this research on clinical care includes the following: recognizing that even as early as the transition to MCI personality begins to change putting patients at risk for behavioral problems. Further research is needed to correlate specific personality and cognitive profiles during the MCI stage with behavioral outcomes.

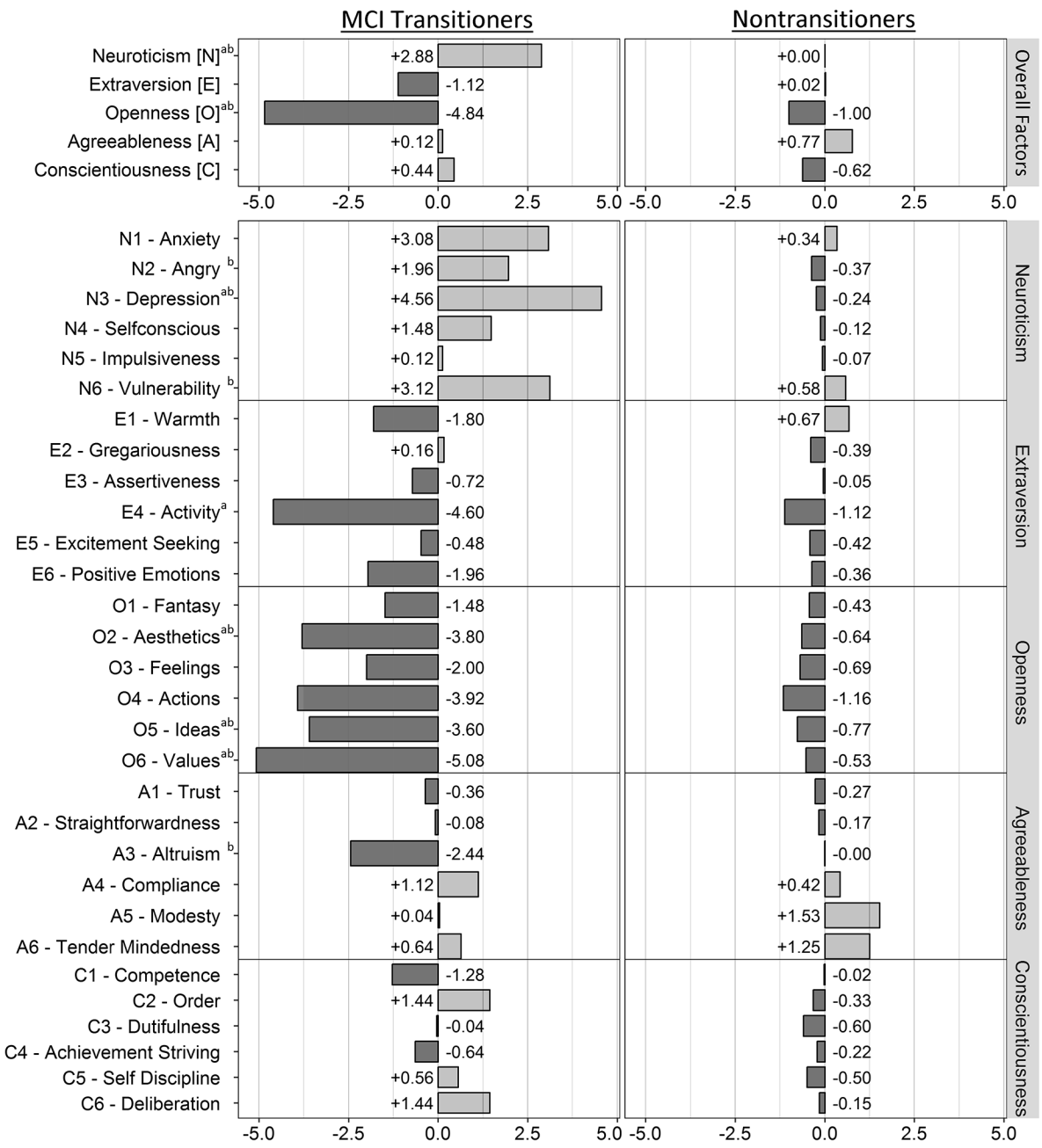

Figure 1. Mean Changes in NEO-PI-R Scores by MCI Transition Status

Fishbone plot of NEO-PI-R changes in MCI transitioners (left) and nontransitioners (right). [a] Unadjusted T-test $P \leq .05$; [b] ANCOVA adjusted for first NEO-PI-R score and time interval $P \leq .05$. Note that all significant differences indicate greater "worsening" in the MCI transitioners relative to the nontransitioners.

Table 1

Neuropsychology Battery

Test	Scores Used
Memory	
Auditory Verbal Learning Test [AVLT]	Total Learning [TL], Long Term Memory [LTM]
Buschke Free and Cued Selective Reminding Test	Total free [SRT-free] recall
Rey-Osterrieth Complex Figure Test [CFT]	Total recall [CFT-recall]
Benton Visual Retention Test [VRT]	Total correct
Executive	
Wisconsin Card Sorting Test [WCST]	Categories completed
Paced Auditory Serial Attention Task 3 [PASAT-3] and 2 [PASAT-2] second versions	Total correct for each
Wechsler Adult Intelligence Scale-Revised [WAIS-R] Digit Symbol Substitution [DSS]	Age-scaled score
Controlled Oral Word Association Test [COWAT]	Total words raw score
Language	
Boston Naming Test [BNT] 60 item	Total correct
Token Test	Total correct
WAIS-R Vocabulary	Age-scaled score
WAIS-R Similarities	Age-scaled score
Visuospatial	
Judgment of Line Orientation [JLO]	Total Correct
Facial Recognition Test	Corrected long form score
Rey-Osterrieth CFT	Copy score
WAIS-R Block Design	Age-scaled score
Behavior	
Personality Assessment Inventory [PAI]	Clinical (CSc), Treatment (TSc), and Interpersonal (ISc) scale T-scores
Beck Depression Inventory [BDI]	Total score
Hamilton Depression Scale [Ham-D]	Total Score
Geriatric Depression Scale [GDS]	Total Score

Neuropsychological tests administered and the scores used in this study.

Table 2

Group Characteristics at First NEO-PI-R Epoch

	MCI Transitioners	Nontransitioners	*P* Value
n	25	252	
Age in years, mean (95% CI)	65.5 (63.1, 67.9)	62.7 (61.8, 63.6)	.06[a]
Female, n (%)	13 (52.0%)	175 (69.4%)	.07[b]
APOE e4 carriers, n (%)	20 (80.0%)	96 (38.31%)	<.001[b]
Non-Hispanic White, n (%)	22 (88.0%)	209 (82.9%)	.64[b]
Education years, mean (95% CI)	16.4 (15.3, 17.5)	16.0 (15.8, 16.3)	.46[a]
Inter-NEO Interval in months, mean (95% CI)	83.8 (73.6, 93.9)	78.5 (75.6, 81.3)	.28[a]
Number of NEO Administrations, n (%)			.24[b]
2	15 (60.0%)	177 (70.2%)	
3	9 (36.0%)	73 (29.0%)	
4	1 (4.0%)	2 (0.8%)	
Neuroticism Factor, mean (95% CI)	41.9 (38.7, 45.1)	42.6 (41.5, 43.7)	.68[a]
Extraversion Factor, mean (95% CI)	50.8 (47.0, 54.6)	49.0 (47.9, 50.1)	.34[a]
Openness Factor, mean (95% CI)	53.1 (49.0, 57.1)	52.3 (51.0, 53.5)	.70[a]
Agreeableness Factor. mean (95% CI)	53.3 (49.6, 56.9)	53.6 (52.6, 54.7)	.84[a]
Conscientiousness Factor, mean (95% CI)	49.0 (45.5, 52.4)	51.6 (50.5, 52.7)	.15[a]

[a] T-test;

[b] Chi-squared test

Table 3

NEO-PI-R Change Scores

	MCI Transitioners [mean (95%CI)]	Nontransitioners [mean (95%CI)]	*P* Value[a]	*P* Value[b]
Neuroticism [N]	+2.9 (0.9, 4.9)	0.0 (−0.7, 0.7)	.02	.02
Extraversion [E]	−1.1 (−3.4, 1.1)	+0.0 (−0.6, 0.7)	.30	.49
Openness [O]	−4.8 (−7.3, −2.4)	−1.0 (−1.6, −0.4)	<.001	<.001
Agreeableness [A]	+0.1 (−2.5, 2.8)	+0.8 (0.0, 1.5)	.60	.57
Conscientiousness [C]	+0.4 (−2.5, 3.4)	−0.6 (−1.2, 0.0)	.33	.59
N1-Anxiety	+3.1 (−0.0, 6.2)	+0.3 (−0.6, 1.3)	.08	.10
N2-Anger	+2.0 (−1.4, 5.3)	−0.4 (−1.2, 0.4)	.09	.05
N3-Depression	+4.6 (1.7, 7.4)	−0.2 (−1.1, 0.6)	<.001	<.001
N4-Selfconsciousness	+1.5 (−1.2, 4.2)	−0.1 (−0.9, 0.7)	.24	.13
N5-Impulsiveness	+0.1 (−2.5, 2.7)	−0.1 (−1.0, 0.9)	.90	.79
N6-Vulnerability	+3.1 (1.0, 5.3)	+0.6 (−0.3, 1.4)	.07	.05
E1-Warmth	−1.8 (−5.0, 1.4)	+0.7 (−0.1, 1.4)	.05	.06
E2-Gregariousness	+0.2 (−2.6, 2.9)	−0.4 (−1.3, 0.5)	.71	.58
E3-Assertiveness	−0.7 (−3.3, 1.9)	0.0 (−0.8, 0.7)	.60	.76
E4-Activity	−4.6 (−7.5, −1.7)	−1.1 (−2.0, −0.2)	.02	.07
E5-Excitement seeking	−0.5 (−2.7, 1.7)	−0.4 (−1.2, 0.3)	.96	.95
E6-Positive emotions	−2.0 (−4.5, 0.6)	−0.4 (−1.3, 0.5)	.29	.66
O1-Fantasy	−1.5 (−4.3, 1.4)	−0.4 (−1.3, 0.5)	.49	.23
O2-Aesthetics	−3.8 (−7.0, −0.6)	−0.6 (−1.4, 0.1)	.01	.01
O3-Feelings	−2.0 (−5.5, 1.5)	−0.7 (−1.5, 0.1)	.37	.35
O4-Actions	−3.9 (−7.6, −0.3)	−1.2 (−2.1, −0.2)	.08	.24
O5-Ideas	−3.6 (−6.2, −1.0)	−0.8 (−1.5, 0.0)	.03	.03
O6-Values	−5.1 (−7.3, −2.8)	−0.5 (−1.4, 0.3)	.002	.003
A1-Trust	−0.4 (−3.0, 2.3)	−0.3 (−1.1, 0.5)	.95	.90
A2-Straightforwardness	−0.1 (−3.4, 3.2)	−0.2 (−1.1, 0.7)	.96	.71
A3-Altruism	−2.4 (−6.8, 1.9)	0.0 (−0.8, 0.8)	.10	.04
A4-Compliance	+1.1 (−1.8, 4.1)	+0.4 (−0.4, 1.3)	.63	.61
A5-Modesty	0.0 (−2.7, 2.8)	+1.5 (0.7, 2.4)	.30	.35
A6-Tender Mindedness	+0.6 (−3.4, 4.7)	+1.3 (0.2, 2.3)	.73	.61
C1-Competence	−1.3 (−4.7, 2.1)	0.0 (−0.9, 0.8)	.4	.32
C2-Order	+1.4 (−1.7, 4.6)	−0.3 (−1.1, 0.5)	.21	.47
C3-Dutifulness	0.0 (−3.5, 3.4)	−0.6 (−1.4, 0.2)	.69	.80
C4-Achievement striving	−0.6 (−3.8, 2.5)	−0.2 (−1.1, 0.6)	.77	.65
C5-Self discipline	+0.6 (−3.4, 4.5)	−0.5 (−1.3, 0.3)	.47	.65
C6-Deliberation	+1.4 (−0.8, 3.7)	−0.2 (−0.9, 0.6)	.22	.52

[a]Unadjusted T-test;

[b] ANCOVA adjusted for first NEO-PI-R score and time interval