**Personality Predictors of Dementia Onset and Progression: An Integrated Data Analysis**

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Personality traits are relatively stable, dispositional patterns that differentiate people from one another (Roberts, Wood, & Caspi, 2008). Personality traits are robust predictors of many life outcomes (Beck & Jackson, 2020), including health outcomes such as disease onset (Weston et al., 2015), terminal cognitive decline (Wilson et al., 2015) and mortality risk (Mroczek & Spiro, 2007, Graham et al., 2017). They also are critical predictors of important factors that lead to later disease or early mortality, most notably health behaviors (Turiano et al., 2014) and physician adherence (Hill & Roberts, 2011). In fact, this is one mechanism by which psychological dimensions such as well-being or personality influence more distal health outcomes: via mediating factors such as lifestyle factors. Those with particular personality- or wellbeing-based predisposing factors, may have slower rates of decline, meaning less impairment and better functioning for a longer length of time even after the onset of dementia. Just as those with higher Conscientiousness have longer survival times, along with better health during that time, people higher in conscientiousness may have slower progression of decline in the post-diagnosis period. Years or decades of better (pre-onset) health behaviors, or a more positive outlook (pre- or post-onset), may lead to slower declines compared to those without these predisposing factors. Indeed, work on older adults where pathology diagnosis was not known has indicated conscientiousness predicts terminal cognitive decline (Wilson et al., 2015).

Despite important advances of personality predictors of dementia, previous research leaves an incomplete picture of personality-dementia relationships. First, personality predictors of dementia onset and progression have not been investigated in a multi-study format. However, the use of multiple studies is necessary to test the robustness of such associations across samples, measures, and time. Second, most studies (see Duchek et al., 2019 for an exception) to date have examined simple personality-dementia relationships, which ignores individual differences in pathology. However, an increasing number of studies, such as the ongoing ADRC studies, are beginning to collect post-mortem autopsy data using criteria set forth by the joint working group of the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer’s Disease and Related Disorders Association. Such an endeavor provides a number of neuropathological measures that capture the degree and type of Alzheimer’s disease. Examining-personality-neuropathology relationships may reveal important pathways through which lifestyle behaviors predict specific kinds and degrees of pathology in ways that may provide avenues for early intervention and targeting.

The proposed study will examine the relationship between baseline personality and dementia onset, progression, and neuropathic burden using six longitudinal studies: the RUSH Memory and Aging Project, the RUSH Religious Orders Study, the Swedish Adoption Twin Study of Aging, the Health and Retirement Study, the ADRC Memory and Aging Project, and the Baltimore Longitudinal Study. These six studies are unique in that they include personality, well-being, cognitive ability, dementia diagnoses and indicators, and background variables longitudinally, which allows for important extensions of previously addressed questions. Moreover, all analyses will be preregistered on the Open Science Framework, and all code and results (minus data) will be made available for enhanced reproducibility.

The analyses of these data will proceed in several parts. First, prior to any analyses, data will be cleaned according to preregistered criteria to harmonize data across studies. Second, using Bayesian multilevel logistic cross-classified random slope regression models, we will predict AD onset from personality and well-being measures. Doing so will both give us an overall estimate of the personality-AD relationship and study-specific deviations from that. Third, we will predict neuropathic burden from personality and wellbeing using a series of Bayesian multilevel cross-classified random slope regression models. Fourth, we will predict whether personality predicts cognitive decline (measured as changes in cognitive ability measures longitudinally) after AD onset. To do so, we will use Bayesian multilevel piecewise cross-classified random slope growth models to test whether personality does moderate the relationship between AD onset and cognitive decline. All of these models will include age, gender, and socioeconomic status indicators, but we will also test whether these moderate the relationship between personality and AD onset and progression.

We believe that data collected by the ADRC are among just six studies in the world who have the requisite data needed to test the proposed questions. Moreover, we believe that understanding linkages between personality and dementia onset and progression have clear implications for studying risk factors of AD in early life by offering clear behavioral pathways through which behaviors might change incident AD risk. Our research team is uniquely suited to running the proposed analyses as we have become experts in conducting large-scale integrated and coordinated analyses of many large studies (e.g., Beck & Jackson, 2020; Graham et al, 2017, 2020).

Having corresponded with core leaders, we are hoping to use the following resources from the ADRC. Because we will be using personality data already provided (see below), we are happy to send a list of MAPIDs of the subjects for whom we have those data:

Demographics:

MAP ID; date of birth; date of death; gender; race and ethnicity; years of education; marital status

Psychometrics Core:

Free and Cued Selective Reminding Test total and free recall scores; animal naming test; trailmaking tests part a & b; number span (forward and backward); WAIS Block Design; WAIS Information; WAIS Digit Symbol

Clinical Core:

MMSE, CDR-global, CDR-SB, diagnoses 1 and 2 (Dx1 and Dx2), Geriatric Depression Scale (as well as dates for each)

Health history: previous diagnoses of other illnesses (e.g., stroke, diabetes, cancer, etc.)

Self-rated health

Biomarker Core:

dates of all CSF collections; for each CSF collection—CSF Aβ42, Aβ40, total tau and ptau by Lumipulse once available; CSF Aβ42, total tau and ptau by Elecsys; CSF Aβ42, total tau and ptau by INNOTEST; NfL

Neuropathology/Biostatistics Core:

based on the National Alzheimer's Coordinating Center's Neuropathology Data Form:

- Braak stage (0 to 6)

- CERAD (1 = definite to 4 = no AD)

- Overall Amyloid Beta Score (average cross-region percent area of cortex oocupied by amyloid beta)

- Diffuse plaque burden (average of scaled regional counts)

- Neuritic plaque burden (average of scaled regional counts)

- Neuronal neurofibrillary tangle density (mean density across regions per mm2)

- Neuronal neurofibrillary tangle burden (average of scaled regional counts)

- Lewy Body Disease (4 level; 0 = none, 1 = nigral-predominant; 2 = limbic-type; 3 = neocortical-type)

- Gross Cerebral Infarcts (0 = No, 1 = Yes)

- Gross Cerebral Microinfarcts (0 = No, 1 = Yes)

- Cerebral Atherosclerosis (0 = none to 3 = severe)

- Cerebral Amyloid Angiopathy (0 = none to 3 = severe)

- Arteriolosclerosis (0 = none to 3 = severe)

- Hippocampal Sclerosis (0 = No, 1 = Yes)

Personality (already received from Dave Balota, Jan Duchek, and Andrew Aschenbrenner):

NEO-FFI

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