**Personality Predictors of Dementia Diagnosis and Neuropathic Burden: 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, which may reduce their risk of the onset of dementia. Years or decades of better pre-onset health behaviors, or a more positive outlook pre-onset, may lead to slower cognitive declines that reduce the likelihood of incident dementia diagnoses compared to those without these predisposing factors.

In recent years, two dominant paradigms for understanding personality and well-being have emerged. First, the Big Five (Extraversion, Agreeableness, Conscientiousness, Neuroticism, and Openness to Experience) have risen as parsimonious descriptive and predictive structure of the core personality characteristics within a population. Indeed, there now exists a deep literature describing the extent to which the Big Five have been recovered across cultures (Benet-Martínez & John, 1998; McCrae & Terracciano, 2005), languages (Denissen, Geenen, van Aken, Gosling, & Potter, 2008; Saucier & Ostendorf, 1999), and age categories (Marsh, Nagengast, & Morin, 2012; McCrae et al., 1999). Moreover, the Big Five have strong and replicable predictive utility (Ozer & Benet-Martinez, 2005; Soto, 2019) across ages, studies, countries, covariates, moderators, and decades between personality and outcome measurement (Beck & Jackson, 2020). For well-being, the last two decades have seen the rise of Subjective Well-Being, a tripartite construct consisting of positive affect, negative affect, and satisfaction with life, that captures the core aspects of psychological well-being within a population (Diener, Sapyta, & Suh, 1998; Diener, Suh, Lucas, & Smith, 1999). Like the Big Five, Subjective Well-Being has demonstrated important descriptive and predictive power across cultures (Diener & Suh, 2003; Oishi & Diener, 2009), languages (Jaidka et al., 2020), and age categories (Diener & Suh, 1997).

**Personality, Well-Being, and Dementia**

Previous research has demonstrated that personality and well-being prospectively predict later dementia diagnoses. Conscientiousness and Neuroticism, in particular, have been consistently linked to dementia, with Conscientiousness serving as a protective factor and Neuroticism as a risk factor (Duberstein et al., 2011; Terracciano et al., 2013, 2014; Wilson, Schneider, Arnold, Bienias, & Bennett, 2007). Extraversion has consistently had no relationship to incident dementia diagnoses, while Agreeableness and Openness have been differentially linked to dementia diagnoses across the studies in which they have been examined (Duberstein et al., 2011; Terracciano et al., 2014). Although Subjective Well-Being has largely been examined following – rather than preceding – dementia diagnoses, there is some evidence that satisfaction with life is a protective factor against dementia diagnoses (Peitsch, Tyas, Menec, & St John, 2016).

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. The use of multiple studies is necessary to test the robustness of such associations across samples, measures, and time. Given that different personality and well-being characteristics have been differentially predictive of dementia diagnoses and neuropathic burden across studies, it is critical to examine the consistency of such associations across studies to determine their robustness and examine the study-level properties that may underlie such inconsistencies. Although traditional meta-analyses have investigated such relationships, their reliance on published effect sizes, which reflect the timing of publication and analytic choices made by different investigators, result in less than ideal final estimates of robustness. Even when personality and well-being predictors of dementia have been investigated in samples previously, pooling them together provides a more direct avenue for testing overall and study-specific effects as well as what underlies them.

Second, most studies to date have examined simple personality-dementia relationships, which ignores individual differences in pathology (see Duchek et al., 2019; Terracciano et al., 2013 for exceptions). However, an increasing number of studies, such as the ongoing BLSA 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 and psychological experiences predict specific kinds and degrees of pathology in ways that may provide avenues for early intervention and targeting.

In the proposed study, we ask two questions. First, do personality and well-being predict later dementia diagnoses? Second, do personality and well-being predict different indicators of neuropathic burden? To do so, we will examine whether the Big Five and Subjective Well-Being predict dementia diagnoses in nine studies and neuropathic burden in five studies using an integrated analysis framework. The proposed study is the first of its kind to examine personality and well-being predictors of dementia in a multi-study framework, which will allow us to estimate the overall robustness of personality and well-being predictors of dementia and pathology while preserving real and important heterogeneity in prediction across studies.

**Method**

The proposed study will examine the relationship between baseline personality and dementia diagnosis in eight longitudinal studies and neuropathic burden using five longitudinal studies. Diagnoses will be examined using (1) the RUSH Memory and Aging Project, (2) the RUSH Religious Orders Study, (3) the ADRC Memory and Aging Project, (4) the Einstein Aging Study, (5) the Baltimore Longitudinal Study, (6) The Swedish Adoption Twin Study of Aging, (7) the German Socioeconomic Panel, (8) The Longitudinal Studies for the Social sciences, and (9) The Health and Retirement Study. Neuropathic burden will be examined using the first five studies listed above. These five 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 have been preregistered on the Open Science Framework (https://osf.io/fmjv3), and all code and results (minus data) will be made available for enhanced reproducibility (https://osf.io/dzty7/).

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 regression models, we will predict dementia diagnoses from personality and well-being measures. Doing so will both give us an overall estimate of the personality-dementia relationship and study-specific deviations from that. Third, we will predict neuropathic burden from personality and wellbeing using a series of Bayesian multilevel regression models. All of these models will include age, gender, lifestyle indicators (e.g., smoking) and health markers (e.g., previous diagnoses of other clinical disorders).

We believe that data collected by the BLSA are among just five 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 diagnoses have clear implications for studying risk factors of dementia in early life by offering clear behavioral pathways through which behaviors might change incident dementia risk. Our research team is uniquely suited to running the proposed analyses for three reasons. First, 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). Second, the authors have ongoing relationships with many of the studies we propose to include in project. Third, the authors have strong financial support to carry out the proposed project. The research team is currently working under a five-year NIA grant entitled "Personality prediction of dementia risk and progression" (1R01AG067622).

Based on the documentation available and a survey of the literature that has used BLSA data, we are hoping to gain access to the following categories of data:

**Demographics**:

Participant IDs; date of birth; date of death; gender; race and ethnicity; years of education; marital status

**Personality**:

240 item NEO-PI-R (beginning 1989)

**BLSA cognitive battery:**

- California Verbal Learning Test (List A Total Correct, Free Recall, Short Delay, and Free Recall Long Delay)

- Category Fluency

- Boston Naming Test

- Card Rotation

- Trail-Making Test (Parts A&B)

- Digit Span (Forward and Backward)

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

Self-rated health

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

- Braak stage (0 to 6)

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

- Lewy Body Disease (2-level: 0 = No, 1 = Yes)

- 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)

Note: parenthetical coding reflect final coding used for analyses. Provided data will be recoded as necessary.

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