New Directions in Aging

Personality and Incident Alzheimer's Disease: Theory, Evidence, and Future Directions

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Abstract

Personality, especially the dimensions of neuroticism and conscientiousness, has prospectively predicted the risk of incident Alzheimer's disease (AD). Such a relationship could be explained by personality and AD risk having a *common cause* such as a gene; by personality creating a *predisposition* for AD through health behavior or inflammation; by personality exerting a *pathoplastic* effect on the cognitive consequences of neuropathology; or by AD and personality change existing on a disease *spectrum* that begins up to decades before diagnosis. Using the 5-dimensional taxonomy of personality, the present review describes how these models might arise, the evidence for each, and how they might be distinguished from one another empirically. At present, the evidence is sparse but tends to suggest predisposition and/or pathoplastic relationships. Future studies using noninvasive assessment of neuropathology are needed to distinguish these 2 possibilities.

Keywords: Alzheimer's dementia, Conscientiousness, Health behavior, Neuroticism, Personality

The world population is aging: projections forecast that 22% of the world's population will be aged 60 and older by 2050. Consequently, the number of people with dementia, mostly Alzheimer's disease (AD), is projected to roughly double every 20 years, from a 2010 estimate of 35.6 to 65.7 million in 2030 and 115.4 million in 2050 (Duthey, 2013).

AD is a continuum that begins with pathological changes in the brain, progresses to mild cognitive impairment (typically characterized by memory decline), and ends with dementia and ultimately, death. However, brain pathology accumulation and cognitive decline can dissociate, and new criteria have been proposed that recognize "pre-clinical" AD as pathology in the absence of dementia and apply the term "Alzheimer's dementia" to those with dementia (Alzheimer's Association, 2017). (The present review will use the established terminology, in which AD refers to dementia in the presence of characteristic pathology.) In the brain, pathological changes associated with

AD primarily comprise beta-amyloid (A β) protein plaques and tau protein tangles in and around neurons and gross morphological changes in the brain, especially loss of hippocampal volume (Alzheimer's Association, 2017; Bateman et al., 2012; Martin, Smith, Collins, Schmitt, & Gold, 2010). The pathogenic process underlying the development of AD is still a matter of some contention. Focus on plaques as causal has been called into question considering large, Phase III pharmacological clinical trials in which clinical progression of mild-to-moderate AD was not affected even when the drug reduced A β and tau relative to controls (Doody et al., 2014; Salloway et al., 2014).

The primary risk factors for AD are age, genetic polymorphisms, and family history (Alzheimer's Association, 2017). However, there are other, modifiable risk factors (Barnes & Yaffe, 2011). Therefore, although pharmacological treatment options are currently limited, early identification of risk for AD offers hope of early intervention to prevent or postpone disease progression. Several studies

have now identified personality as a prospective predictor of incident AD diagnosis. The present review summarizes these findings and considers them in light of several possible models of the personality–AD relationship. This consideration suggests approaches for future research in this area that could clarify the nature of the personality–AD relationship and exploit advances in neuroimaging and biomarkers.

Personality and Health

Personality refers to individual differences in thoughts, motivations, affect, behavior, and other psychological processes. The Big 5 and five-factor models (FFM), nomothetic models of the structure of personality, propose that personality can be described along five dimensions: agreeableness; extraversion; conscientiousness; FFM neuroticism or Big 5 emotional stability; and FFM openness to experience or Big 5 intellect (Table 1; John, Naumann, & Soto, 2008).

Although the label “personality” can imply stability over time, personality varies over both the long and short term. Over the long term, personality traits show reasonable interindividual stability. That is, someone who is more agreeable than his or her peers at age 30 is likely to be more agreeable than his or her peers at age 50 (Terracciano, Costa, & McCrae, 2006). Adult development is also accompanied by normative increases in agreeableness, extraversion, conscientiousness, emotional stability, and openness/intellect, with largest increases in early adulthood for openness/intellect and the social dominance aspect of extraversion, mid-life for emotional stability and conscientiousness, and older age for agreeableness (Roberts, Wood, & Caspi, 2008). Differential mortality (i.e., earlier mortality in people with “risky” traits leading to personality differences among age cohorts) cannot fully explain these changes, which occur throughout the adult lifespan and not only during older adulthood (cf. Segerstrom, Combs, Winning, Boehm, & Kubzansky, 2016).

In addition, over the short term, mean tendencies (e.g., to be agreeable) are accompanied by significant intraindividual variation from hour to hour or day to day (Fleeson,

2001). Almost all people behave agreeably at some times and disagreeably at others. However, some people are more likely to be disagreeable, and others are more likely to be agreeable at any given time. Although personality may have a modest influence on emotions, decisions, behavior, or physiology at any given moment, aggregate effects over longer periods of time may be considerable, making personality particularly relevant for chronic and degenerative diseases (Segerstrom & Smith, 2006). Diseases such as cancer, cardiovascular disease, and AD are more likely to be diagnosed with older age, but the underlying pathology can be found years and even decades earlier (Albert et al., 2014; Friberg & Mattson, 1997; Jack et al., 2010; Strong et al., 1999). Therefore, the long time frame of these disease processes may make them particularly amenable to modification by personality.

In support of a personality–health relationship, people who are higher in agreeableness, extraversion, emotional stability, and especially conscientiousness enjoy lower risk for premature all-cause mortality (Graham et al., 2017; Jokela et al., 2013). The magnitude of these effects resembles that of IQ and exceeds that for socioeconomic status, two variables robustly prognostic for health (Roberts, Kuncel, Shiner, Caspi, & Goldberg, 2007). Personality predicts morbidity as well as mortality, including morbidities such as cardiovascular disease that can accelerate the progression of AD dementia (Esiri, Nagy, Smith, Barnetson, & Smith, 1999; Jokela, Pulkki-Råback, Elovainio, & Kivimäki, 2014). There are qualifications: For example, people who are high in both conscientiousness and neuroticism may be quicker to attend to health threats, seek a remedy for such threats, and consequently enjoy better health (Turiano, Mroczek, Moynihan, & Chapman, 2013).

Personality and Risk of Incident AD

Broad effects of personality on non-AD morbidity and mortality foreshadow correlations between personality and risk of incident AD. Two early retrospective case-control studies yielded conflicting results, with a Swedish study suggesting that personality traits related to neuroticism (hypersensitive, difficulty coping) had a protective effect among men (Hagnell, Franck, Gräsbeck, Öhman, Otterbeck, & Rosman, 1992) and an American study suggesting that personality traits related to introversion and neuroticism were associated with greater AD risk (Malinchoc, Rocca, Colligan, Offord, & Kokmen, 1997). However, in the following decades, multiple studies with larger numbers of cases and average follow-up periods ranging from 6 to 38 years found that higher neuroticism and lower conscientiousness were associated with higher risk of incident AD (Table 2). A meta-analysis of several studies confirmed these individual findings: 1 SD higher scores on neuroticism and conscientiousness were associated with hazard ratios of 1.33 and 0.77, respectively. In addition, although individual studies were inconsistent in

Table 1. Dimensions in the Five-Factor Model and Big Five Personality Taxonomies

I.	<i>Extraversion</i> : energetic, sociable, happy <i>Introversion</i> : shy, inhibited
II.	<i>Agreeable</i> : prosocial, altruistic, cooperative <i>Disagreeable</i> : quarrelsome, aloof
III.	<i>Conscientious</i> : controlled, planful, organized <i>Unconscientious</i> : distractible, inefficient
IV.	<i>Neurotic</i> : anxious, sad, vulnerable <i>Emotionally stable</i> : stable, even-tempered
V.	<i>Intellectual/open to experience</i> : reflective, artistic, adventuresome <i>Closed to experience</i> : concrete, unimaginative, conservative

Table 2. Studies Linking Personality to the Incident AD (1992–2018)

Study	Personality assessment	Length of follow-up	N (men/women)	AD cases	Findings
Hagnell and colleagues (1992)	Sjöbring personality taxonomy (capacity, validity, solidity, stability)	15 years	526 (244/282)	41	Lower capacity (intelligence) and neuroticism-like traits associated with higher risk
Malinchoc and colleagues (1997)	Minnesota Multiphasic Personality Inventory	20 years ^a	29 (12/17)	13	Higher introversion and pessimism associated with higher risk
Wilson and colleagues (2003)	Neuroticism (NEO Five-Factor Inventory)	4.9 years	797 (252/545)	140	Higher N associated with higher risk as well as faster decline in cognition
Wilson, Schneider, Arnold, Bienias, and Bennett (2007)	Five-factor model (NEO Five-Factor Inventory)	12 years ^b	904 (284/620)	176	Higher N, lower C associated with higher risk
Wang and colleagues (2009)	Neuroticism and extraversion (Eysenck Personality Inventory)	6 years ^c	506 (144/362)	144	Low N with high E (but not either trait alone) associated with lower risk; other combinations associated with higher risk
Duberstein and colleagues (2011)	Five-factor model (NEO Five-Factor Inventory)	7.3 years	767 (446/321)	116	Higher N, lower O, lower C associated with higher risk
Dar-Nimrod and colleagues (2012) ^d	Five-factor model (NEO Five-Factor Inventory)	7.3 years	602 (353/249)	76	APOE ε4 genotype more strongly associated with risk of AD for people higher in N and E
Johansson and colleagues (2014)	Neuroticism and extraversion (Eysenck Personality Inventory)	38 years	800 (0/800)	104 (153 with any dementia)	Higher N associated with higher risk of AD dementia only
Terracciano and colleagues (2014)	Five-factor model (NEO-PI-R)	22 years ^e	1,671 (846/825)	90	Higher N, lower C associated with higher risk
Sutin, Stephan, and Terracciano (2018)	Conscientiousness (HRS Psychosocial and Lifestyle Questionnaire 2006–2010)	4–6 years	11,181 (4,361/6,820)	278 (based on telephone assessment)	Lower C facets of self-control, industriousness, and responsibility associated with higher risk

Note. AD = Alzheimer's disease; C = conscientiousness; E = extraversion; HRS = Health and Retirement Survey; N = neuroticism; O = openness to experience.

^aCases identified within 5 years of personality assessment excluded from analysis.

^bTime between personality assessment and AD diagnosis ranged from 0.4 to 11.5 years.

^cResults held when excluding cases diagnosed in the first 3 years after personality assessment.

^dGenotyped subsample of the sample reported in Duberstein and colleagues (2011).

^eTime between personality assessment and AD diagnosis ranged from 1 to 22 years; results held when excluding cases diagnosed within 2 years of personality assessment.

the effects of openness and agreeableness, meta-analytic estimates indicated that higher openness and agreeableness may also reduce the risk of AD (although the magnitude of the effects was smaller, with hazard ratios of 0.86 and 0.88, respectively; Terracciano et al., 2014). Calculation of population-attributable risk suggested that 10% of incident AD cases could be attributed to neuroticism and 10% to conscientiousness (Terracciano et al., 2014).

A question that remains largely unanswered is *why* personality correlates with AD risk. The modal attribution is that personality exerts a causal effect, but there are other plausible models for this relationship. Borrowing from

models of the relationship between personality and psychopathology (Klein, Wonderlich, & Shea, 1993), personality and AD may have *common cause*; personality may be a *predisposition* for AD; personality may have a *pathoplastic* effect on the appearance or severity of AD; personality may be a *spectrum* effect of AD; or some combination thereof (Table 3). Most of these models remain to be subjected to strong empirical tests.

The different models have different public health implications. Depending on the nature of the relationship—and multiple relationships are possible (e.g., both pathoplastic and spectrum relationships may hold)—personality might

Table 3. Models of the Relationship Between Personality and AD

Model	Implication	Example of evidence that would support the model
Common cause	Personality and AD have a common cause but are not causally related to each other	Genes that affect personality phenotype also affect risk for AD
Predisposition	Personality affects risk for AD through some plausible pathway	Personality affects health behaviors that modify risk for AD
Pathoplastic	Personality affects the appearance or severity of AD	The cognitive or behavioral consequence of a particular level of pathological burden is determined by personality
Spectrum	Personality is part of the spectrum of AD symptoms	Personality differences associated with AD risk are prodromal symptoms of AD

Note. AD = Alzheimer's disease.

be exploited to improve outcomes and decrease the impact of AD on public health. For example, people who are conscientious behave in healthier ways. If conscientiousness is a predisposition for AD via these healthier behaviors, then behavior change makes an appealing therapeutic target. Personality change *per se* may also be affected by relatively brief (≥ 8 weeks) psychotherapy, resulting in relatively long-lasting (≥ 1 year) personality change (Roberts et al., 2017). However, if personality and AD relate to each other through a common cause, then the behaviors of conscientious people or phenotypic change in personality as a result of therapy may be irrelevant to AD risk.

Common Cause

The common cause model specifies that personality and AD have a shared etiology. One possibility is that genetic polymorphisms provide a “common core liability” (Klein et al., 1993, p. 5) that results in individual differences in both personality and AD risk. Polymorphisms in the *APOE* gene, which regulates cholesterol, are the most common genetic predictors of AD risk. Carriers of 2 *APOE* $\epsilon 4$ alleles have 8–12 times the risk for AD compared with carriers of no $\epsilon 4$ alleles (Alzheimer's Association, 2017). Among young and midlife adults ($n = 502$, age range = 17–52), *APOE* genotype (2/3 vs 3/3 vs 3/4) was unrelated to any of the dimensions of the FFM (Montag et al., 2014). The article further reported a personal communication that *APOE* genotype was unrelated to any of the dimensions of the FFM among older adults ($n = 602$, age range = 72–91; Dar-Nimrod et al., 2012). Studies that controlled for *APOE* $\epsilon 4$ genotype also demonstrated the relative independence of personality and *APOE* genotype, finding that statistical control did not substantially affect the relationship between personality and AD risk (Johansson et al., 2014; Terracciano et al., 2014; Wang et al., 2009; Wilson et al., 2007).

Although *APOE* is the best-studied gene with regard to AD risk (Andrews, Das, Anstey, & Eastale, 2017), other genes are being identified that associate with increased risk. For example, gene polymorphisms affecting proneness to inflammation have been implicated in AD and may also be associated with personality. Further research assessing the

overlap between total genetic risk for AD and premorbid personality phenotype is needed to further test the common cause model.

Of course, genes account for only a third to a half of the personality phenotype, with experience accounting for the rest (Vukasović & Bratko, 2015). Therefore, if life experiences modify personality and AD risk independently, a common cause model would be supported. In male rats, early life stress was associated with late-life memory deficits and differences in hippocampal synaptic physiology (Brunson et al., 2005). Early life stress in humans likewise might be associated with differences in personality development and with AD risk.

Predisposition

The predisposition model specifies that personality is a risk or protective factor for the development of AD. If this is true, the critical question is how personality gets “under the skull” to affect risk for AD. The strongest empirical case can be made for mediation via health behavior. Approximately half of AD cases are attributable to seven risk factors related to health behavior, including diabetes, hypertension, obesity, smoking, depression, cognitive inactivity, and physical inactivity (Barnes & Yaffe, 2011). Personality, especially conscientiousness, is correlated with all of these risk factors (Booth-Kewley & Vickers, 1994; Bogg & Roberts, 2004), supporting a predisposition model in which personality affects health behavior that in turn promotes or prevents AD.

High conscientiousness predisposes to healthier behavior in multiple domains including alcohol and drug use, diet, physical activity, and tobacco use (Bogg & Roberts, 2004). Health behaviors partially—although not entirely—explained the increased longevity associated with both childhood and adult conscientiousness (Friedman et al., 1995; Turiano, Chapman, Gruenewald, & Mroczek, 2015). Conscientiousness is also associated with higher educational attainment, which may imply higher cognitive activity. Education partially mediated the relationship between childhood conscientiousness and adult health (Hampson, Goldberg, Vogt, & Dubanoski, 2007).

Neuroticism is strongly associated with higher risk for depression (Klein, Wonderlich, & Shea, 1993). People higher in neuroticism are also more likely to smoke, which partially accounts for their higher all-cause mortality risk (Lahey, 2009; Mroczek, Spiro, & Turiano, 2009).

Openness to experience (five-factor model) or intellect (Big 5) may predispose people to engage in more cognitive activity. Children higher in Big 5 intellect achieved higher education, with positive health consequences in adulthood (Hampson et al., 2007). Among cognitively normal adults, people higher in openness engaged in more cognitively demanding activities in daily life, but activities did not mediate between openness and crystallized or fluid cognitive function (Soubelet & Salthouse, 2010). It is possible that the correlation between cognitive activity and openness arises from the effects of cognitive activity on openness and not vice versa, although any such effects may be relatively short-lived, limited to certain kinds of cognitive activity, or both (Jackson, Hill, Payne, Roberts, & Stine-Morrow, 2012; Sander, Schmiedek, Brose, Wagner, & Specht, 2017).

Inflammation could also mediate between personality and AD risk. Higher levels of peripheral inflammatory markers may indicate proneness to inflammation in the brain that could promote AD pathological processes (Akiyama et al., 2000). Personality, particularly lower conscientiousness and lower openness/intellect, correlates with higher peripheral inflammatory markers such as C-reactive protein (Allen & Laborde, 2017; Luchetti, Barkley, Stephan, Terracciano, & Sutin, 2014). Neuroticism's relationship with inflammatory markers may depend on age, socioeconomic status, and other personality traits (Luchetti et al., 2014; Millar et al., 2013; Turiano et al., 2013). The relevance for AD of personality's relationship with peripheral inflammation requires further investigation. First, peripheral inflammation as measured in blood might imply central nervous system inflammation but is not equivalent, and central nervous system inflammation is probably most important for AD pathology (Akiyama et al., 2000). Second, personality and inflammatory markers may themselves have a common cause relationship through genetic polymorphisms (see *Common cause*, above). Finally, because personality affects health behavior, inflammatory markers may be adding a link of unknown significance in the causal chain from personality to AD.

A point that applies not only to inflammation but to other potential links in the causal chain is that risk factors may also influence personality. For example, the experience of depression may increase neuroticism (Klein et al., 1993). Therefore, personality (e.g., neuroticism or conscientiousness) might influence the AD risk factor (e.g., depression or inflammation), the risk factor might influence personality, or personality might be associated with AD through the risk factor. Longitudinal studies with multiple, repeated measurements can establish the temporal precedence of personality, risk factors, and AD. Such studies avoid problems in inferring precedence that arises when personality and

putative mediators are measured at the same time. Another advantage of such studies is they can provide evidence of correlated change; cross-sectional tests of mediation can be inaccurate (cf. Lindenberger, von Oertzen, Ghisletta, & Hertzog, 2011).

Finally, to the degree that the predisposition model relies on a causal chain, investigators will need to distinguish between covariates that reduce excess error variance and those that are linked in the causal chain. For example, if personality affects AD risk through health behaviors, then studies that uniformly covary out health behavior rather than systematically testing a mediational pathway will underestimate the effect of personality.

Pathoplastic

In a pathoplastic model, personality “influences the presentation, course, or outcome” (Klein et al., 1993, p. 5) of AD. AD neuropathology (e.g., the extent of plaques and tangles) is not perfectly related to neuropsychology (e.g., the extent of memory dysfunction), suggesting the presence of pathoplastic effects (Jack et al., 2014). One possibility is that resilience to neuropathology is associated with personality.

Differentiation between the predisposition and pathoplastic models requires knowledge of the amount of neuropathological burden. If personality is associated with lesser burden, that association would favor the predisposition model because personality directly reduces risk; if personality is associated with better function despite burden, that association would favor the pathoplastic model because personality affects the presentation of the disease. Until recently, it would have been difficult to acquire knowledge of the amount of burden. However, recent advances have made it possible to quantify A β in the brain noninvasively. Supporting a pathoplastic model, older adults who had AD neuropathology on autopsy but were historically cognitively intact (mean age at death = 85) were less neurotic and more conscientious than those with AD (mean age at death = 89), even controlling for pathology burden (A β plaques and tau tangles; Terracciano et al., 2013). Older adults (mean age 81) lower in neuroticism appeared to be protected from the effects of A β deposition on memory complaints, but no such relationship was found for conscientiousness (Snitz et al., 2015). Conversely, a predisposition model was not supported for neuroticism insofar as a relationship with AD pathology at autopsy was not found (Wilson et al., 2003).

The interaction between *APOE* genotype and personality may also represent a form of pathoplastic relationship, a relationship tested by some of the studies in Table 2. An interaction was found for neuroticism: People carrying *APOE* ϵ 4 and high in neuroticism had a hazard ratio for AD of 8.68, whereas those low in neuroticism had a hazard ratio of 1.80. Neuroticism had little effect on those without the *APOE* ϵ 4 gene (hazard ratios of 0.90 for those high in

neuroticism and 1.10 for those low.) No interaction was found for conscientiousness (Dar-Nimrod et al., 2012).

However, when Wang and colleagues (2009) stratified their sample on APOE $\epsilon 4$ status, no differences in the risk for neuroticism and extraversion were found. Likewise, Terracciano and colleagues (2014) only found interactions between APOE $\epsilon 4$ status and personality for the dimensions of openness (higher openness was protective only among APOE $\epsilon 4$ carriers) and agreeableness (higher agreeableness was protective only among noncarriers). Further investigating the interactions among personality, pathology, and function is an important direction for research.

Personality may contribute to other variables that have pathoplastic effects on AD. Cerebrovascular disease (CVD), in particular, can arise from health behavior and inflammation and may have a pathoplastic effect on AD severity: when CVD is present, the presentation of AD is worse, and the course may be accelerated. Most older people (>80 years) with AD also had CVD (Schneider, Arvanitakis, Bang, & Bennett, 2007). The combined presence of CVD and hippocampal sclerosis or AD pathology may predict the worst cognitive function (Esiri et al., 1999; Schneider et al., 2007).

Finally, cognitive reserve refers to the pathoplastic effect of variables such as educational and occupational attainment and cognitive activity on AD risk (Stern, 2012). People with more cognitive reserve can bear more neuropathology without experiencing symptoms. For example, conscientiousness and openness/intellect likely contribute to higher cognitive reserve through their effects on educational attainment (see under *Pathoplastic*, above; Hampson et al., 2007). Other personality dimensions may also build reserve through physical and social activity (Fratiglioni & Wang, 2007).

Spectrum

Spectrum models specify that personality is a prodrome or other subclinical manifestation of AD. Personality change commonly occurs in AD. A review of retrospective informant reports of personality change in AD patients indicated marked decreases in conscientiousness, moderate increases in neuroticism, and additional decreases in extraversion, agreeableness, and openness. Notably, the average normed T scores for the premorbid reports were typically close to 50, suggesting that retrospective personality change was not a function of rosy memories of premorbid personality (Robins Wahlin & Byrne, 2011). Personality differences between people with and without AD, particularly in neuroticism, conscientiousness, and openness, might be detectable even in the earliest stages of the disease either by self-report or informant report (Duchek, Balota, Storandt, & Larsen, 2007). Initially, nondemented older adults were more likely to be diagnosed with AD if informants indicated personality change over a ~4-year interval. Decreased emotional control and increased egocentricity and apathy

were commonly reported for eventual cases but not those who remained nondemented (Balsis, Carpenter, & Storandt, 2005). However, a large case-control study found no differences in the rate of change in self-reported personality between cognitively normal people at baseline who eventually developed mild cognitive impairment or dementia and those who did not during a follow-up of 1–36 years (Terracciano, An, Sutin, Thambisetty, & Resnick, 2017). This study, which prospectively assessed premorbid personality, suggests that retrospective informant reports may not be reliable when assessed after AD onset.

The studies in Table 2 assessed personality 6–38 years before AD diagnosis. However, AD neuropathology may begin decades before the onset of disease, which calls for a critical examination of whether personality differences at baseline could have been prodromal manifestations of AD. Cognitive changes such as a decline in episodic memory tend to lag behind neuropathological changes but can nonetheless occur years before disease onset (Bateman et al., 2012). Among people with mild cognitive impairment, anxiety, and agitation were correlated with AD biomarkers in cerebrospinal fluid, potentially supporting a spectrum model for neuroticism-related traits (Ramakers et al., 2013).

On the other hand, the absence of substantial correlations between APOE genotype and personality across the life course (see *Common cause* above) suggests that any prodromal personality change due to neuropathological changes may be subtle. Repeated measurement of personality during the preclinical phase as well as studies with longer follow-up periods (e.g., Johanssen et al., 2014; Terracciano et al., 2017) also suggest that baseline personality reflected more than prodromal personality change. Together, these findings favor predisposition or pathoplastic over spectrum models. However, it is important to consider studies with short follow-up periods in light of the possibility that some personality change, which is part of the spectrum of AD symptoms, may occur before formal AD diagnosis. More studies across the course of preclinical change, MCI, and AD are needed to establish the course of personality change associated with AD and its relationship with changes in biomarkers and cognition.

Conclusions

Substantial evidence links “premorbid” personality characteristics, especially conscientiousness and neuroticism, to AD risk. However, there are several models that could account for such risk: common cause (e.g., through a common gene); predisposition (e.g., through health behavior); pathoplastic (e.g., conferring resistance to the effects of neuropathology); and spectrum (e.g., reflecting an early symptom). It seems likely that personality has a predisposing or pathoplastic relationship to the incident AD, given the strong role of behavioral and psychological risk factors in disease development and the influence of personality on

these risk factors in early adulthood. Even with the long prodromal period of AD, personality may set in place habits or physiology (e.g., vascular changes) that make one more or less likely to get AD later. If later evidence reveals that the relationship is strictly prodromal, personality could provide another prognostic sign for clinical care.

Currently, the empirical evidence currently cannot distinguish among several of the models. First, the magnitude of the relationship and the specific dimensions identified in empirical studies may be influenced by prodromal personality change. Second, absent A β and/or tau imaging, the predisposition and pathoplastic models cannot be distinguished from each other. Current evidence suggests a pathoplastic effect of neuroticism and a predisposing effect of conscientiousness, but much more study is needed.

Given the possibility of intervening to change personality itself (Roberts et al., 2017) or the modifiable mediators of personality effects (Barnes & Yaffe, 2011), understanding the nature of personality as a risk factor for AD could shape public health efforts at prevention. Prospective relationships between personality and AD risk, mediated by neuropathology, and absent evidence that baseline personality was a prodromal symptom, would provide support for the predisposition model. Prospective relationships between personality and AD risk, moderated by neuropathology, and absent evidence that baseline personality was a prodromal symptom, would provide support for the pathoplastic model. These distinctions can only be made in long-term longitudinal studies with repeated measures of personality, neuropathology, and cognition as well as AD diagnosis. Further study of the relationship between genetic polymorphisms associated with AD and premorbid personality can determine whether a common cause model also contributes. However, such a contribution may be minor in light of evidence that personality is not affected by the major risk polymorphism in APOE.

This review focused on the FFM/Big 5 taxonomy of personality, but other personality traits such as dispositional optimism and purpose in life are not clear parallels to any of the FFM/Big 5 dimensions and are worthy of further study. Higher purpose in life has been linked to lower AD risk (Boyle, Buchman, Barnes, & Bennett, 2010). In addition, the five personality dimensions are themselves composites of more narrowly defined traits, and only some of these narrower constructs may be responsible for relationships with AD (Sutin et al., 2018). Finally, only a few studies have examined interactions between personality traits (e.g., neuroticism and conscientiousness). Although the FFM/Big 5 framework is nomothetic, individuals have idiographic profiles of personality traits. If each of the five dimensions had only 10 levels, there would be 100,000 possible personality profiles. Of course, depending on the assessment method, there are exponentially more combinations. Interactions among dimensions may be important; if so, the main effects of dimensions have underestimated the potential predictive power of personality.

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Conflict of Interest

The authors declared no conflicts of interest.

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