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Psychological Distress, Self-Beliefs, and Risk of Cognitive Impairment and Dementia

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Abstract

Depressive symptoms and a history of mental disorders are associated with increased risk for dementia. Less is known about whether other aspects of psychological distress and negative self-beliefs also increase risk. The purpose of this research is to examine (1) whether eight aspects of psychological distress and self-beliefs (anxiety, negative affect, hostility, anger-in, anger-out, hopelessness, pessimism, perceived constraints) are associated with risk of incident dementia and cognitive impairment not dementia (CIND), (2) whether the associations are independent of depressive symptoms and history of a mental health diagnosis, and (3) whether the associations are also independent of behavioral, clinical, and genetic risk factors. A total of 9,913 participants (60% female) from the Health and Retirement Study completed the baseline measures, scored in the non-impaired range of cognition at baseline, and had cognitive status assessed across the 6–8-year follow-up. Baseline measures included eight aspects of psychological distress and self-beliefs, cognitive performance, depressive symptoms, and genetic, clinical, and behavioral risk factors. Participants who scored higher on anxiety, negative affect, hostility, pessimism, hopelessness, and perceived constraints were at a 20–30% increased risk of dementia and a 10–20% increased risk of CIND. The associations held controlling for baseline depressive symptoms, history of a mental health diagnosis, clinical and behavioral risk factors, and genetic risk. Anger-in and anger-out were unrelated to risk of either dementia or CIND. Independent of the core experience of depressed affect, other aspects of negative emotionality and self-beliefs increase risk of mild and severe cognitive impairment, which suggests additional targets of intervention.

Keywords

Alzheimer’s Disease; Dementia; Psychological Distress; Self-Beliefs

Several aspects of psychological functioning have been implicated in risk of Alzheimer’s disease and related dementias [1]. Much of the research on distressful aspects of psychological functioning have focused on depression. And, indeed, there is consistent evidence that a history of depression [2] and symptoms of depression [3] increase dementia

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risk. This focus is understandable, given the high prevalence of depression in the population [4] and the robustness of the association [2, 3]. Depression, however, is only one aspect of psychological distress. A focus on depression, to the neglect of other modifiable aspects of distress, risks missing both identifying who is at risk and potential targets of intervention.

There are many other components to psychological distress that are conceptually and empirically distinct from depression [5]. The present study addresses eight such components, including five aspects of distress and three aspects of negative self-beliefs. The five aspects of distress are anxiety (nervousness, fear, and worry), negative affect (frequency of feeling negative emotions), hostility (antagonism toward others), anger-in (a tendency to internalize anger) and anger-out (a tendency to express anger). The three negative self-beliefs are pessimism (belief that things will go wrong), hopelessness (despair for the future), and perceived constraints (belief that there is little control over what happens in life).

Anxiety has been previously associated with both cognitive decline [6] and risk of dementia [7]. Anxiety is often comorbid with depression [8], but its association with risk of cognitive impairment is independent of depression [9]. Others aspects of state negative emotionality that have greater moment-to-moment fluctuations, such as negative affect, have also been associated with risk of severe cognitive impairment in older adulthood, independent of depression [10]. These findings suggest that various aspects of negative emotionality may harm cognition even when the experience of that negative emotionality does not meet the threshold for depression.

Aggression-related aspects of psychological distress may also be implicated in poor cognitive outcomes. There is some evidence, for example, that hostility is associated with greater declines in cognitive function across long follow-ups [11], although the same pattern is not apparent across shorter intervals [12]. There may be long-term cumulative effects of hostility on cognitive function that are only apparent over longer follow-ups. It may also be the case that hostility is more likely to predict the severe changes in cognition that are associated with dementia rather than more gradual cognitive decline. In addition, although anger tends to be correlated with hostility, its effect on cardiovascular outcomes is independent of the effects of hostility on these outcomes [13]. There may be similar independent effects on cognitive impairment. Anger is also associated with intermediate risk factors for dementia that may put the individual at greater risk over the long term [14].

Previous research has found optimism to be protective against dementia [15]. Optimism, however, may either be construed as either a unitary dimension, with pessimism as its opposite pole, or it can be construed as a dimension separate from pessimism [16]. When only the optimism dimension is considered (i.e., without the items that measure pessimism), optimism is unrelated to dementia risk [17]. This pattern suggests that a tendency to expect the worse, rather than an inclination to see the positive in any situation, increases risk of impairment. Hopelessness is a specific aspect of pessimism that reflects a feeling of giving up on the future [18]. This specific facet of negative emotionality related to pessimism may likewise increase risk of cognitive impairment. Hopelessness, like other aspects of psychological distress, has been found to be associated with worse health, independent of depression, including intermediate markers of dementia risk [19].

Finally, another dimension of negative self-related beliefs, perceived constraints, has also been associated with declines in aspects of cognitive functioning over time. Specifically, individuals who perceive that they lack control over their lives tend to show more declines in episodic memory across adulthood [20, 21]. It is possible that this decline in memory culminates in risk of dementia in older adulthood. There is some cross-sectional evidence that the association between perceived constraints and cognition varies by race, with greater perceived constraints mediating the relation for African American participants but not white participants [22]. The relation between perceived constraints and risk of significant cognitive impairment may likewise vary across race.

Despite the strength of the initial evidence, several gaps in this literature remain. No individual study, for example, has taken a comprehensive approach to the relation between multiple aspects of negative affectivity and self-related beliefs and risk of cognitive impairment. Such an approach is needed to be able to compare directly the relative predictive power of each dimension of psychological distress and related self-beliefs on risk of dementia. It also provides a direct test of whether specific aspects of negative emotionality increase risk of cognitive impairment or whether most aspects share a similar risk. In addition, control variables tend to vary across studies that, again, make direct comparisons across constructs difficult. Finally, much of the previous research has also focused on dementia as the outcome. Before dementia, cognitive impairment not dementia (CIND) is a more mild cognitive impairment that has significant consequences for the individual's functioning and well-being [23] and is an intermediate marker of cognitive health [24]. Distress and self-beliefs may likewise increase risk of such impairments.

To that end, the purpose of the present research is to examine whether these eight aspects of psychological distress and self-related beliefs are associated with risk of dementia and risk of CIND. Our first goal is to identify which aspects are associated with increased risk of cognitive impairments. Our second goal is to examine whether these associations are independent of depressive symptoms measured at the same time as the focal predictors and history of emotional or mental disorder, which tend to be correlated with distress and self-beliefs. Our third goal is to examine whether these associations are independent of common clinical (hypertension, diabetes), behavioral (smoking, physical activity), and genetic (APOE risk status, polygenic scores for Alzheimer's disease) risk factors for cognitive impairment. We include these risk factors because they are associated with risk of dementia [25] and most are also associated with the aspects of distress [14]. In supplemental analyses, we further examine the predictive power of the eight aspects combined by identifying the common variance through a principal components analysis. Finally, in sensitivity analyses, we also test whether any of the associations are moderated by demographic (age, sex, education, race, ethnicity) or genetic factors. We test these associations in a large national sample of older adults.

Method

Participants and procedure

Participants were drawn from the Health and Retirement Study (HRS; http://hrsonline.isr.umich.edu). Detailed measures of psychological distress and functioning were

first administered to half of the HRS sample as part of the 2006 Leave-Behind Questionnaire; the other half completed these measures for the first time in 2008. The two subsamples were combined as baseline. Participants were selected into the analytic sample if they had complete data on the eight measures of distress, scored within the normal range of cognition at the 2006/2008 baseline (see below), and had follow-up cognitive data. A total of 9,913 participants had the relevant data to be included in the analysis. The sample was, on average, 65.53 years old (SD=8.61), 61% female, 8% African American, and 5% Hispanic. See Table 1 for complete demographic characteristics of the sample. Over the follow-up, 397 participants developed dementia and 2,392 developed CIND. Of the 637 participants who had complete baseline data but not follow-up cognition, 439 participants died during the follow-up. Compared to participants in the analytic sample, participants who completed the psychological measures, had non-impaired cognition at baseline, no follow-up cognition and had not died (n=198) were more likely to have had a diagnosis of a mental or emotional problem (χ^2=9.40, p=.002). There were no differences in age (d=.03, p=.62), sex (χ^2=.35, p=.56), race (χ^2=.73, p=.69), Hispanic ethnicity (χ^2=.52, p=.46), years of education (d=.06, p=.38), anxiety (d=−.02, p=.86), negative affect (d=−.08, p=.34), hostility (d=−.01, p=.85), anger in (d=−.14, p=.06), anger out (d=.00, p=.90), pessimism (d=−.04, p=.63), hopelessness (d=.04, p=.58), perceived constraints (d=.04, p=.51), or depressive symptoms (d=−.02, p=.51).

Measures

Psychological distress and self-beliefs.—Eight aspects of psychological distress and self-beliefs were measured in the 2006/2008 assessment and were the focal predictors of the current study: anxiety, negative affect, hostility, anger-in, anger-out, pessimism, hopelessness, and perceived constraints. See Smith and colleagues [26] for detailed information about the reliability, validity, and scoring of each of the distress and self-belief measures described below.

Recent feelings of anxiety were measured with five items from the Beck Anxiety Inventory [27]. Participants were asked, “Please read the statements below. How often did you feel that way during the past week?” Items (e.g., “I had fear of the worst happening.” alpha=.82) were rated on a scale from 1 (*never*) to 4 (*most of the time*).

Participants reported on their experience of negative emotions (e.g., ashamed) felt within the last month. Emotion words were taken primarily from the Positive and Negative Affect Schedule [28]. Participants rated items from 1 (*very much*) to 5 (*not at all*). Ratings were reverse scored such that higher scores reflected more negative affect. The measure used different emotion words in 2006 (6 items) and 2008 (12 items); scale scores were standardized (M=0, SD=1) within wave before combined to account for this difference. For all models, the results were similar if the two measures were tested separately.

Hostility was measured with five items from the Cook Medley Hostility Inventory [29]. Each item (e.g., “I think most people would lie in order to get ahead.” alpha=.88) was rated on a scale from 1 (*strongly disagree*) to 6 (*strongly agree*).

Anger-in and anger-out were measured with the Spielberger Anger Expression Scale [30]. Instructions for this scale were, “Here are some statements that describe how people react or behave when they are feeling angry or mad. Thinking of the times you feel angry, for each statement please indicate how often you react or behave this way.” Four items for anger-in (e.g., “When I am feeling angry or mad, I keep things in.” alpha= .78) and seven items for anger-out (e.g., “When I am feeling angry or mad, I argue with others.” alpha=.88) were rated on a scale from 1 (*almost never*) to 4 (*almost always*).

Pessimism was measured with three items from the revised version of the Life Orientation Test [5]. Items (e.g., “If something can go wrong for me it will.” alpha=.77) were rated on a scale from 1 (*strongly disagree*) to 6 (*strongly agree*).

Participants reported on their degree of hopelessness with four items (e.g., “I feel it is impossible for me to reach the goals that I would like to strive for.” alpha=.85) [18]. Participants rated each item from 1 (*strongly disagree*) to 6 (*strongly agree*).

Perceived constraints was measured with five items from the Perceived Constraints on Personal Control measure [31]. Items (e.g., “What happens in my life is often beyond my control.”; alpha=.87) were rated on a scale from 1 (*strongly disagree*) to 6 (*strongly agree*).

Depressive symptoms and history of an emotional or mental disorder.— Depressive symptoms were measured with an 8-item version of the Center for Epidemiological Studies Depression Scale. History of distress was measured with a question (yes/no) on whether a medical doctor or physicians’ assistant had ever diagnosed them with an emotional or mental disorder (diagnoses by mental health professionals were not assessed). Depressive symptoms and history of distress were measured at the 2006/2008 baseline assessment.

Clinical and behavioral risk factors.—Clinical covariates included obesity (BMI≥30; yes/no) and reported physician diagnosis of hypertension (yes/no) and diabetes (yes/no). Behavioral covariates were self-reported current smoking status (yes/no) and self-reported frequency of moderate physical activity (ranging from hardly ever or never to more than once a week). The clinical and behavioral covariates were measured at the 2006/2008 baseline assessment.

Genetic risk.—Genetic information on *APOE* risk status was available for a subset of participants (n=7,966). Any ε4 risk variant (i.e., ε2/ε4, ε3/ε4, ε4/ε4) was contrasted against all other variants. Polygenic risk scores for Alzheimer’s disease [32] were also available for a subset of participants (n=7,050).

Dementia and CIND.—The modified Telephone Interview for Cognitive Status (TICSm [33] is administered to participants every two years in HRS. The total TICSm score (27 possible points) is based on three cognitive tasks: immediate and delayed recall of 10 words (0–20 points), serial 7 subtraction (0–5 points), and backward counting (0–2 points). Dementia was classified as TICSm≤6 and CIND was classified as TICSm >6 and ≤11. These cutoffs have been validated against a comprehensive neuropsychological assessment and

clinical diagnosis of dementia and mild cognitive impairment [33, 34] and used to track national trends in cognitive impairment and dementia [35]. Cognitive data was used from the 2006/2008 baseline assessment and every two years up through the 2014 HRS assessment.

Statistical Approach

To facilitate comparison of effect sizes across the eight dimensions of psychological distress and self-beliefs, each scale was standardized (mean=0, SD=1) before entered into the analysis. We used Cox proportional hazards regression models to test whether each measure of distress was associated with incident dementia and incident CIND over the 6–8 year follow-up. Each measure was entered separately into the model. Time was coded in years from the year of baseline assessment. Participants who remained cognitively normal were censored at the last available follow-up cognitive assessment. Participants who developed dementia were excluded from the analysis of incident CIND. Model 1 included demographic covariates (age, sex, race, ethnicity, education). Model 2 included demographic covariates and depressive symptoms. Model 3 included the demographic covariates, depressive symptoms, and history of a mental disorder. Model 4 controlled for the same covariates as in Model 3 and the clinical and behavioral covariates associated with dementia risk (obesity, diabetes, hypertension, smoking, physical activity). Additional analyses included *APOE* genetic risk and the polygenic risk scores as covariates and tested demographic (age, sex, education, race, ethnicity) and genetic (*APOE* risk status, polygenic risk scores) factors as moderators. To identify the common variance across the eight aspects, we did a principal components analysis (PCA) on the eight scales and extracted one component. We then used that component to predict dementia and CIND, controlling for the demographic factors. Statistical significance was set at $p<.01$.

Results

Descriptive statistics for all study variables are shown in Table 1. Six of the distress measures were associated with increased risk of dementia (Table 2) and increased risk of CIND (Table 3): Participants who reporter higher levels of anxiety, negative emotions, hostility, pessimism, hopelessness, and perceived more external constraints had a 20–30% increased risk of dementia and a 10–20% increased risk of CIND. These associations were independent of depressive symptoms (Model 2). Except for negative affect, the associations remained significant even after accounting for history of an emotional or mental disorder (Model 3) and common clinical and behavioral risk factors (Model 4). The associations were also independent of *APOE* ε4 risk status and the polygenic risk score for Alzheimer's disease (see Supplemental Table 1). For comparison, depressive symptoms measured at the 2006/2008 baseline assessment were associated with a 24% increased risk of dementia (HR=1.24, 95% CI=1.13–1.35) and a 17% increased risk of CIND (HR=1.17, 95% CI=1.13–1.22) in this sample.

We also examined the combined association of these eight constructs on risk of dementia and CIND, using the component extracted from the PCA. For both outcomes, the common component was a stronger predictor than any of the individual measures (HR=1.42, 95% CI=1.20–1.56 and HR=1.24, 95% CI=1.19–1.20, respectively for dementia and CIND).

These associations remained significant after controlling for depressive symptoms, history of an emotional or mental disorder, the clinical and behavioral risk factors, *APOE* ε4 risk status, and polygenic risk score for Alzheimer's disease.

Few of the associations between the eight constructs and the cognitive outcomes were moderated by the demographic factors. The association between negative affect and dementia risk was stronger among men than women ($HR_{interaction}$=.76, 95% CI=.62-.92). The association between pessimism and hopelessness and dementia was stronger among relatively more educated than less educated participants ($HR_{interaction}$=1.11, 95% CI=1.03–1.20 and $HR_{interaction}$=1.14, 95% CI=1.06–1.22, respectively). The association was stronger among non-Hispanic than Hispanic participants for hopelessness ($HR_{interaction}$=.68, 95% CI=.52-.89). The association between hostility ($HR_{interaction}$=.92, 89-.96), pessimism ($HR_{interaction}$=.95, 95% CI=.91-.98), hopelessness ($HR_{interaction}$=.95, 95% CI=.92-.98), anxiety ($HR_{interaction}$=.94, 95% CI=.90-.97), and anger out ($HR_{interaction}$=.93, 95% CI=.90-.97) and risk of CIND was stronger among relatively younger than older participants. The association between hopelessness and CIND risk was stronger for participants with relatively more than less education ($HR_{interaction}$=1.04, 95% CI=1.01–1.07) and in non-Hispanic than Hispanic participants ($HR_{interaction}$=.86, 95% CI=.76-.96).

Finally, fewer interactions emerged for the genetic factors. There was one interaction with *APOE*: The association between hostility and risk of CIND was only apparent among participants without the ε4 risk allele; hostility was unrelated to CIND among those with the risk allele ($HR_{interaction}$=.79, 95% CI=.72-.87). There were two interactions with the polygenic risk scores: both pessimism and hopelessness were associated with increased risk of dementia for participants across the range of polygenic risk scores, but the association was stronger among those with greater genetic risk ($HR_{interaction}$=1.16, 95% CI=1.04–1.30 and $HR_{interaction}$=1.18, 95% CI=1.07–1.31 for pessimism and hopelessness, respectively). There were no significant interactions between any of the psychological dimensions and polygenic scores on risk of CIND.

Discussion

Independent of depressive symptoms and history of a clinical diagnosis of a mental or emotional disorder, six aspects of psychological distress and self-related beliefs were associated with increased risk of dementia and CIND: anxiety, negative affect, hostility, pessimism, hopelessness, and perceived constraints. The magnitude of the effect size for each of these dimensions was fairly consistent with each other and of similar magnitude to the association between depressive symptoms and risk of dementia and CIND. Further, the common variance among the eight measures was a stronger predictor of risk of dementia and CIND than any of the individual constructs. The present findings suggest that multiple aspects of psychological distress and self-beliefs increase risk of cognitive impairment in older adulthood.

Similar to symptoms of depression, anxiety is commonly implicated in risk of dementia [9]. Given the high comorbidity between symptoms of depression and anxiety [8], it is of note that anxiety remained a significant predictor of cognitive impairment even after controlling

for depression. The pathological processes that damage the brain, however, could drive the association between anxiety and dementia; that is, the reverse causality hypothesis suggests that the relation between anxiety and risk of impairment is due to increasing anxiety from the brain changes that occur with dementia. Contrary to expectations from this hypothesis, however, a long-term prospective study found no evidence for increases in trait anxiety during the preclinical phase of Alzheimer's disease [36]. Other long-term prospective studies have found that anxiety increases risk even when measured 20 to 30 years before dementia, which presumably is prior to the development of significant neuropathology [7, 37]. There is also evidence for bidirectional associations between anxiety and cognitive functioning in adulthood, such that anxiety is associated with subsequent declines in cognition and poor cognitive performance predicts subsequent increases in anxiety [6]. Thus, it is possible that both processes contribute to the association with dementia: anxiety is both a risk factor for dementia and anxiety may increase with the progression of neurodegeneration underlying the emergence of cognitive impairment.

Previous research on hostility and cognition has been mixed. Hostility, for example, is associated with worse cognitive function from young to middle adulthood [11], yet in older adulthood it is unrelated to declines in cognition over short follow-ups [12]. There may be a long cumulative effect of hostility on cognition that unfolds over decades and culminates quickly in dementia rather than in gradual cognitive decline. This long-term association may be due, in part, to worse cardiovascular outcomes. Those who are more hostile tend to have higher blood pressure, greater risk of a cardiovascular event (e.g., stroke, heart attack), and greater risk of cardiovascular mortality [38]. Hostility may confer similar risk for cognitive outcomes [37], given that many physiological processes apply to cognition as to cardiovascular outcomes. It is of note that hostility, but not anger, was associated with cognitive impairment. Although anger often co-occurs with hostility, they are separate aspects of psychological functioning that have independent associations with health outcomes [39], a pattern that extends to cognition.

Our results are consistent with previous research that has found perceived constraints to be associated with greater decline in episodic memory across both middle [20] and older [21] adulthood. This decline in memory appears to culminate in greater risk of severe cognitive impairment. Previous research has suggested that perceived constraints contribute to health disparities in cognitive functioning: African Americans perceive more constraints than white participants that, in turn, are associated with worse cognitive health [22]. The present research addressed whether the harmful effect of these self perceptions on dementia risk varied by race. In contrast to previous research on cognitive function, this association was equally harmful across both race (African American and white participants) and ethnicity (Hispanic and non-Hispanic participants).

Less research has addressed whether other self-related beliefs are associated with cognition and risk of cognitive impairment. Previous research using the HRS sample indicated that optimism is associated with decreased risk of dementia [15]. The present research, which considered the dimension of pessimism without the optimism items, suggests that the negative self-beliefs drive the association with cognitive impairment. Thus, as with other health outcomes, optimism and pessimism have differential associations with important

outcomes when conceptualized as two separate dimensions [16].Hopelessness is another aspect of negative self-beliefs that is considered a dimension of pessimism that measures the extent to which the individual is giving up on the future [18]. Hopelessness is most often implicated in depression and other mental disorders [40]. There is growing evidence, however, that hopelessness is also a long-term predictor of poor physical health status, independent of depression [19]. The present study indicates that this association extends to risk of dementia.

In addition to being independent of depression, nearly all of the associations between the measures of psychological distress and self-beliefs and risk of dementia and CIND were independent of common clinical and behavioral risk factors for cognitive impairment. It is estimated that up to one-third of cases of AD are attributable to modifiable risk factors such as diabetes, hypertension, obesity, physical inactivity, and smoking, as well as depression and education [41]. Psychological distress and self-beliefs are also regularly associated with these risk factors (e.g., [14]). And yet, the associations were only reduced slightly when these covariates were accounted for in the model. This pattern indicates that these common risk factors do not account for all of the relation between distress and risk of cognitive impairment.

The mechanistic pathways that explain how these aspects of psychological distress and self-beliefs lead to an increased risk of dementia thus remain unclear. There are likely to be other pathways, in addition to common modifiable risk factors, that contribute to this pathway. Other physiological pathways could include greater activation of the hypothalamic-pituitary-adrenal (HPA) system. Greater concentrations of cortisol have been found to be associated with faster cognitive decline in dementia [42]. In addition, psychological distress and negative self-beliefs may lead an individual to disengage from their social environment or distanced from loved ones that may also harm cognitive function over time [43]. Finally, lack of cognitive engagement could likewise lead to greater declines in cognition [44]. Future work could address these potential mechanistic pathways to better understand how psychological distress and negative self-beliefs increase risk of dementia.

There was relatively little evidence that risk was moderated by demographic or genetic factors. In general, what little moderation did emerge suggested that the psychological factor was a stronger risk factor in the less vulnerable group. For example, pessimism and hopelessness were stronger risk factors for dementia among relatively more than less educated participants and five of the eight dimensions were stronger risk factors for CIND among relatively younger than older participants. This pattern suggests that the risk associated with the demographic/genetic factor accounts for most of the risk posed by the psychological distress for vulnerable groups.

It is of note that the pattern of associations was similar across risk of dementia and risk of CIND, with slightly stronger associations for the former outcome. Still, the results suggest that negative affectivity and self-related beliefs are implicated in more moderate forms of cognitive impairment. Although most individuals with mild cognitive impairments do not go on to develop dementia, it is a meaningful outcome in its own right. Mild impairments, for

example, are associated with subsequent declines in cognition that do not pass the threshold for dementia [45], limit function in daily life [23], and increase burden on loved ones [46].

This research has several strengths, including a large and relatively diverse sample, multiple measures of psychological distress and functioning, and measures of common clinical, behavioral, and genetic risk factors. The present study also had limitations that could be addressed in future research. First, the assessment of dementia was limited. HRS used a brief performance-based measures (the TICSm) rather than a clinical diagnosis of dementia. Thus, some participants may have been misclassified based on their performance. It is worth noting, however, that previous research has found similar associations between psychological factors and risk of dementia using the TICSm as for dementia diagnosed by clinical consensus [37, 47]. Still, it would be worthwhile to replicate these associations with a clinical diagnosis of dementia, especially to be able to separate different etiologies of dementia (e.g., Alzheimer's disease versus frontotemporal dementia). Second, we had a relatively short follow-up of 6–8 years. The short follow up increases the risk that the associations might be due to reverse causation. As discussed above, the associations could be due to the preclinical disease process rather than true risk factors for dementia. While all participants scored in the range of normal cognitive functioning at the baseline assessment, we could not disentangle these two possibilities (risk factor vs. reverse causation). Future research could address the issue of reverse causality and examine changes in psychological distress as individuals transition from the preclinical to the overt clinical phases of dementia. All participants, however, scored in the range of normal cognitive functioning at the baseline assessment. Finally, the behavioral risk factors were self-reported. Future research would benefit from more objective assessments. Despite these limitations, the present study indicates that in addition to a core of depressed affect, multiple, conceptually distinct aspects of psychological distress and self-beliefs increase risk of dementia and CIND.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Baseline Demographic Characteristics and APOE ε4 Risk Status of the Full Sample and by Cognitive status at Follow-up

	Non-impaired *N*=7124	**CIND *N*=2392**	**Dementia *N*=397**	**Total *N*=9913**
Age (years)	65.53 (8.61)	70.50 (9.40)	73.03 (9.20)	67.03 (9.16)
Education (years)	13.64 (2.44)	12.24 (2.82)	11.87 (2.85)	13.23 (2.64)
Gender (female)	61%	58%	63%	60%
Race (African American)	8%	15%	17%	10%
Race (other or unknown)	2%	3%	3%	2%
Race (white)	90%	82%	80%	88%
Ethnicity (Hispanic)	5%	9%	10%	6%
APOE ε4 risk status[a]	24%	28%	24%	26%
Depressive symptoms at baseline	1.05 (1.68)	1.47 (1.95)	1.69 (2.09)	1.18 (1.78)
History of mental disorder	15%	17%	21%	16%
Obesity	41%	39%	38%	40%
Hypertension	54%	64%	63%	56%
Diabetes	16%	22%	28%	18%
Current smoker	12%	13%	12%	12%
Moderate physical activity	3.35 (1.22)	3.16 (1.34)	3.00 (1.69)	3.29 (1.26)
Psychological dimensions				
Anxiety	1.48 (.51)	1.62 (.59)	1.69 (.63)	1.52 (.54)
Negative affect[b]	−.14 (.87)	−.02 (.97)	.12 (1.04)	−.10 (.91)
Hostility	2.80 (1.07)	3.01 (1.13)	3.11 (1.17)	2.86 (1.10)
Anger in	2.20 (.67)	2.14 (.67)	2.14 (.73)	2.18 (.67)
Anger out	1.48 (.47)	1.49 (.50)	1.51 (.57)	1.49 (.48)
Pessimism	2.32 (1.20)	2.73 (1.29)	2.96 (1.31)	2.45 (1.24)
Hopelessness	2.08 (1.13)	2.48 (1.30)	2.74 (1.38)	2.20 (1.20)
Perceived constraints	1.96 (1.05)	2.28 (1.18)	2.52 (1.22)	2.06 (1.10)

Note. Total *N*=9913. CIND=cognitive impairment not dementia.

[a] *n*=7,966.

[b] Scores for negative affect were standardized within wave (2006, 2008) before combined.

Table 2

Psychological Distress and Self-Beliefs and Risk of Incident Dementia

Construct	Model 1	Model 2	Model 3	Model 4
Anxiety	1.26 (1.15–1.37)*	1.19 (1.08–1.32)*	1.16 (1.05–1.29)*	1.16 (1.04–1.28)*
Negative Affect	1.30 (1.18–1.43)*	1.20 (1.06–1.36)*	1.17 (1.03–1.32)	1.17 (1.03–1.33)
Hostility	1.22 (1.10–1.35)*	1.19 (1.07–1.32)*	1.19 (1.08–1.32)*	1.18 (1.06–1.32)*
Anger In	1.03 (.93–1.14)	.96 (.87–1.07)	.95 (.86–1.06)	.94 (.84–1.05)
Anger Out	1.12 (1.02–1.23)	1.08 (.98–1.19)	1.08 (.98–1.19)	1.08 (.97–1.02)
Pessimism	1.34 (1.22–1.48)*	1.29 (1.17–1.43)*	1.28 (1.16–1.42)*	1.28 (1.16–1.42)*
Hopelessness	1.32 (1.21–1.44)*	1.26 (1.15–1.39)*	1.25 (1.14–1.38)*	1.24 (1.12–1.36)*
Perceived constraints	1.30 (1.19–1.41)*	1.23 (1.12–1.35)*	1.21 (1.10–1.34)*	1.22 (1.11–1.34)*

Note. *N*=9913. Incident dementia=397. Coefficients are hazard ratios (95% confidence intervals) from Cox regression. Model 1 controls for demographic characteristics (age, gender, race, ethnicity, education). Model 2 controls for Model 1 covariates and depressive symptoms. Model 3 control for Model 2 covariates and history of a diagnosis of an emotional or mental disorder. Model 4 controls for Model 3 covariates and the clinical and behavioral risk factors.

*$p<.01$.

Table 3

Psychological Distress and Self-Beliefs and Risk of Incident Cognitive Impairment Not Dementia (CIND)

Construct	Model 1	Model 2	Model 3	Model 4
Anxiety	1.17 (1.13–1.21)*	1.11 (1.06–1.16)*	1.10 (1.06–1.15)*	1.09 (1.05–1.14)*
Negative Affect	1.15 (1.11–1.20)*	1.06 (1.002–1.12)	1.05 (.99–1.11)	1.05 (.99–1.11)
Hostility	1.11 (1.07–1.16)*	1.08 (1.04–1.13)*	1.08 (1.03–1.13)*	1.08 (1.03–1.12)*
Anger In	1.00 (.96–1.04)	.96 (.92–1.01)	.96 (.92–1.01)	.97 (.92–1.01)
Anger Out	1.04 (1.00–1.08)	1.01 (.97–1.06)	1.01 (.97–1.05)	1.01 (.97–1.06)
Pessimism	1.20 (1.15–1.25)*	1.16 (1.12–1.21)*	1.16 (1.11–1.21)*	1.15 (1.10–1.20)*
Hopelessness	1.17 (1.13–1.22)*	1.13 (1.08–1.17)*	1.12 (1.08–1.17)*	1.11 (1.06–1.16)*
Perceived Constraints	1.16 (1.12–1.20)*	1.11 (1.07–1.16)*	1.11 (1.06–1.15)*	1.10 (1.06–1.15)*

Note. *N*=9,516. Incident CIND=2392. Coefficients are hazard ratios (95% confidence intervals) from Cox regression. Model 1 controls for demographic characteristics (age, gender, race, ethnicity, education). Model 2 controls for Model 1 covariates and depressive symptoms. Model 3 control for Model 2 covariates and history of a diagnosis of an emotional or mental disorder. Model 4 controls for Model 3 covariates and the clinical and behavioral risk factors.

*$p<.01$.