Late-life personality traits, cognitive impairment, and mortality in a population-based cohort

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Abstract

Objectives: We examined longitudinal associations between late-life personality traits and cognitive impairment, dementia, and mortality in the population-based Cardiovascular Risk Factors, Aging and Dementia (CAIDE) Study.

Methods: Anger expression and trait anger (State-Trait Anger Expression Inventory), anxiety (State-Trait Anxiety Inventory), and sense of coherence (Sense of Coherence Scale) were assessed at the 1998 CAIDE visit (1266 cognitively normal individuals, mean age 71.0 years). Totally, 582 participants had complete re-examination in 2005-2008 (105 mild cognitive impairment, MCI; and 29 dementia). National registers data until 2008 were also used for both participants and nonparticipants to ascertain incident dementia (96 cases) and mortality (227 died). Analyses were adjusted for age, sex, education, follow-up time, cardiovascular and lifestyle factors, and depressive symptoms.

Results: Higher anxiety was associated with higher risk of MCI/dementia (OR 1.68, 95% CI 1.07-2.63) and death (HR 1.46, 95% CI 1.08-1.98). High sense of coherence was associated with lower mortality (HR 0.65, 95% CI 0.45-0.93). These associations were attenuated after accounting for depressive symptoms (OR 1.57, 95% CI 0.96-2.58 for anxiety-MCI/dementia; HR 1.35, 95% CI 0.97-1.86 for anxiety-mortality; and HR 0.68, 95% CI 0.45-1.04 for sense of coherence-mortality). Trait anger was associated with higher dementia risk even after adjustments (HR 1.90, 95% CI 1.14-3.18).
1 | INTRODUCTION

Dementia and Alzheimer's disease (AD) are a global health problem. Several modifiable risk factors have been identified, for example, lifestyle-related, metabolic and vascular factors, and depression.\(^1\) Personality-related factors have also been investigated, usually using a five-factor model (agreeableness, conscientiousness, extraversion, neuroticism, and openness to experiences). In general, negative emotion traits such as high neuroticism, low conscientiousness, lower agreeableness, and lower openness to experiences have been linked to higher risk of cognitive impairment and dementia/AD.\(^2\)\(^-\)\(^6\) In addition, psychological distress and anxiety, which can also be seen as components of neuroticism, have been associated with mild cognitive impairment and/or dementia/AD.\(^7\)\(^-\)\(^9\)

These personality-related factors have also been studied regarding longevity. For example, low conscientiousness and high neuroticism have been related to higher mortality as well,\(^10\)\(^,\)\(^11\) while higher extraversion and openness to experiences were reported as protective.\(^12\) Some studies have linked anxiety to mortality, but overall findings are inconclusive.\(^13\) Other factors such as anger suppression,\(^14\)\(^,\)\(^15\) and a weak sense of coherence\(^16\)\(^,\)\(^17\) have also been reported to increase mortality.

Sense of coherence has not been studied regarding cognitive impairment or dementia, although purpose in life has been connected with lower risk of dementia.\(^18\) Furthermore, some anger-related traits such as hostility, pessimism, and cynical distrust have been connected to dementia, but no association with anger expression style was found.\(^19\)\(^,\)\(^20\) On the other hand, emerging irritability has been observed preceding dementia, but whether this is a risk factor or manifestation of already underlying dementia-related pathology, is unclear.\(^21\)

We examined associations between late-life personality-related factors (anger expression, trait anger, anxiety, and sense of coherence) and incident cognitive impairment, dementia, and mortality in the Cardiovascular Risk Factors, Aging and Dementia (CAIDE) Study. Anger and anxiety reflect distinct facets of neuroticism, and the current study aims to further investigate which personality traits connected to negative emotionality affect most detrimentally cognitive health and longevity.

2 | MATERIALS AND METHODS

2.1 | The CAIDE study

The CAIDE study has been previously described in detail. In brief, participants were derived from four independent population-based samples of the North Karelia Project and the FINMONICA study, with midlife examinations in 1972, 1977, 1982, or 1987.\(^22\) In 1998, a random sample of 2000 individuals still alive, aged 65 to 79, and living in the towns or surroundings of Kuopio and Joensuu in Eastern Finland, was invited for the first late-life examination.\(^22\) Of these, 1449 persons (72.5%) participated. In 2005, 1426 of the initial sample of 2000 individuals were still eligible for follow-up (alive and living in the target areas), and 909 (63.7%) attended a second late-life examination during 2005-2008.

In both re-examinations, cognitive status was evaluated with a three-step protocol including screening, a clinical phase, and a differential diagnostic phase. In 1998, individuals scoring ≤24 on the Mini-Mental State Examination (MMSE)\(^23\) at screening were referred for further assessments. In 2005-2008, individuals with ≤24 points or decline ≥3 points since 1998 on the MMSE, delayed recall word list test <70% in the CERAD test battery,\(^24\) or an informant expressing concerns about the participant’s cognition, were referred for further assessments. In both re-examinations, the clinical phase included detailed neurological, neuropsychological, and cardiovascular assessments; the differential diagnostic phase included blood tests, brain imaging (MRI/CT), and, if needed, electrocardiogram and cerebrospinal fluid analysis. A review board comprising a senior neurologist, a senior neuropsychologist, the study physician, and the study neurologist, ascertained the final diagnoses based on all available

Conclusions: Anxiety was linked to worse cognitive outcome and mortality and sense of coherence to lower mortality. Depressive symptoms attenuated the associations. As a novel finding, trait anger was connected to dementia risk. These findings emphasize the importance of personality-related risk factors for dementia and mortality.

KEYWORDS
anger, anxiety, cognitive impairment, dementia, epidemiology, sense of coherence

Key Points
- Some personality-related factors have been associated with dementia and mortality, but, for example, trait anger and sense of coherence have not been previously investigated in relation to cognitive impairment or dementia.
- Trait anger was associated with incident dementia, even after adjusting for cardiovascular and lifestyle-related factors and depression.
- Anxiety was linked to worse cognitive outcomes and mortality, and sense of coherence to lower mortality, although depressive symptoms attenuated these associations.
- Findings emphasize the role of personality-related factors as risk factors for cognitive impairment, dementia, and mortality.
information. Dementia was diagnosed according to Diagnostic and Statistical Manual of Mental Disorders fourth edition (DSM-IV) criteria and AD according to National Institute of Neurological and Communicative Disorders and Stroke and Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) criteria. For diagnosing MCI, a modification of the Mayo Clinic AD Research Center criteria was used. These included (a) memory complaint by patient, family, or physician; (b) normal activities of daily living; (c) normal global cognitive function; (d) objective impairment of memory or one other area of cognitive function as evidenced by scores >1.5 SD below the age-appropriate mean; (e) Clinical Dementia Rating (CDR) score of 0.5; and (f) absence of dementia.

2.2 Standard protocol approvals, registrations, and patient consents

The study was approved by the local ethics committee of Kuopio University and Kuopio University Hospital and conforms to Declaration of Helsinki. Written informed consent was obtained from all participants.

2.3 Design of the present study

The present study focused on the 1266 CAIDE participants who were cognitively normal at the 1998 examination (ie, no dementia or MCI) when the personality-related factors were assessed for the first time. Totally, 1014 were eligible for the 2005-2008 re-examination, 747 participated, and 582 had complete data on at least one personality-related factor and cognition (105 with MCI and 29 with dementia) (Figure 1). Dementia diagnoses and mortality until the end of 2008 were also ascertained from national registers for both participants and nonparticipants. In total, 1005 out of 1266 individuals had complete data on at least one personality-related factor. For incident dementia analyses, six individuals who were too close to dementia onset (diagnosis before year 2000) were excluded, leaving a population of 999 individuals including 96 dementia cases (diagnosis either from the second visit or register) for the analyses with the extended population (Figure 1). The validity of dementia diagnoses in the Finnish national registers has been previously reported. Since AD formed the majority of dementia cases (23 of the 29 cases for participants in the 2005-2008 examination and 78 of the 96 cases for extended population including nonparticipants), the present study did not focus on specific dementia types. For mortality analyses, the study population consisted of 1005 individuals, of which 227 died before December 31, 2008 (Figure 1).

2.4 Assessment of personality-related factors

We used personality-related factors assessed at the 1998 CAIDE visit in this study. Anger-related assessments were based on the State-Trait Anger Expression Inventory (STAXI). The STAXI Trait Anger (T-Anger) scale (10 questions) measures individual differences in the frequency of angry feelings, such as annoyance, irritation, fury, or rage, experienced over time. This can also be described as individual differences in anger proneness as a personality trait. Persons with high T-Anger tend to perceive more situations as anger-provoking. The T-Anger scale includes two related subscales (4 questions each) called Angry Temperament and Angry Reaction measuring disposition to experience angry feelings without special provoking factor and disposition to experience angry feelings in situations involving frustration and/or negative evaluations, respectively. The three STAXI anger expression scales (eight questions each) assess the frequency of anger expression toward other people or environment (anger out, AX/Out), anger suppression (anger in, AX/In), or anger control (AX/Con). Each question had a four-point Likert scale answer, coded as 0 = “Almost never,” 1 = “Sometimes,” 2 = “Often,” and 3 = “Almost always.” The number of points ranged from 0 to 30 for the T-Anger scale, a higher score indicating more pronounced trait anger. For each of the AX/Out, AX/In, and AX/Con scales, the number of points

![FIGURE 1](image-url)
ranged from 0 to 24, a higher score indicating more pronounced outward, inward, or controlled, anger expression. STAXI also includes State Anger scale that measures anger as an emotional state varying in intensity.\textsuperscript{29} Separation between state and trait anger factors has shown to be good.\textsuperscript{33} State anger assessment was not included in the CAIDE study questionnaire. In the present study, concerning anger experience, we have thus focused on trait anger, which represents a longer-term personality trait and may be less variable over time.

Anxiety was assessed with a short six-item form of the state scale of the Spielberger State-Trait Anxiety Inventory,\textsuperscript{32} which has shown a good validity and reliability.\textsuperscript{32,33} Thus, only state anxiety, representing feelings of anxiety at the time of answering the questionnaire, was considered in the CAIDE study. This scale includes three anxiety-present items and three anxiety-absent items measured on a four-point Likert scale as described above. The anxiety-absent items were reverse coded, and a total state anxiety score was calculated, ranging from 0 to 18, a higher score indicating higher anxiety level.

Sense of coherence was assessed using a 13-item version of the Antonovys’s Sense of Coherence Scale.\textsuperscript{34} Sense of coherence is a personality characteristic described as a global orientation that expresses the extent to which one has the confidence that what happens in life is reasonable and acceptable; there are resources to deal with different stressors; and these stressors are challenges worth investment.\textsuperscript{34} The scale captures these three dimensions: comprehensibility (five questions), manageability (four questions), and meaningfulness (four questions).\textsuperscript{34} Answers were provided on a seven-point Likert scale. Five of the 13 questions were reverse coded, and a total score was calculated as recommended,\textsuperscript{35} ranging from 0 to 78, a higher score indicating higher sense of coherence. Individuals with a high sense of coherence are more likely to cope successfully with stressors, whereas a low sense of coherence may lead to anxiety and maladaptive responses to stress.\textsuperscript{35,36}

We categorized the scores on each aforementioned scale into tertiles.

2.5 | Other assessments

CAIDE examinations in 1998 and 2005-2008 were similar to baseline surveys, which were standardized and adhered to international guidelines and the World Health Organization (WHO) Multinational Monitoring of trends and determinants in Cardiovascular disease (MONICA) protocol. Surveys involved self-administered questionnaires on medical history, sociodemographic factors, and health-related behaviors. Persons who engaged in physical activity at least twice a week, lasting at least 20 to 30 minutes on each occasion, and causing sweating and breathlessness, were regarded as physically active. For smoking, participants were divided into ever- and never-smokers. Depressive symptoms were evaluated using the Beck Depression Inventory.\textsuperscript{37}

A trained nurse verified the answers and measured height, weight, and blood pressure. A venous blood sample was taken to determine serum high-density lipoprotein and total cholesterol. We calculated a cardiovascular risk score based on the Finnish FINRISK score\textsuperscript{38} for predicting risk of major coronary events and stroke. The score included age, sex, smoking status, systolic blood pressure, serum total cholesterol, serum HDL cholesterol, and diabetes.

2.6 | Statistical analyses

To compare baseline characteristics between the groups (control, MCI, and dementia in the participant population; with and without dementia in the extended population including nonparticipants; and alive vs died in the mortality population), one-way ANOVA, t test, or \( \chi^2 \) test were used as appropriate.

Associations between personality-related factors and cognitive outcomes were examined using ordinal logistic regression (ordinal outcome with three categories: control-MCI-dementia, participant population) and Cox proportional hazard regression models (outcome dementia, extended population including also nonparticipants; censoring was done at the date of dementia diagnosis, death, or 31 December 2008). Associations between personality-related factors and mortality were investigated using Cox proportional hazard regression models (censored at the date of death or 31 December 2008). In all analyses, Model 1 was adjusted for age, sex, education, and follow-up time. Model 2 was additionally adjusted for cardiovascular risk (FINRISK score) and physical activity. Model 3 was additionally adjusted for Beck Depression Inventory score. Analyses were carried out using SPSS Statistics 23 for Windows (IBM Corp., Armonk, NY) and Stata software, version 12 (StataCorp.). The level of statistical significance was \( P < .05 \).

3 | RESULTS

3.1 | Population characteristics

Baseline characteristics of the study population are shown in Table 1. Of the 582 participants in both late-life examinations, individuals who later developed dementia were older and had lower systolic blood pressure level and more pronounced depressive symptoms. In addition, individuals who developed MCI had lower education level (Table 1).

In the extended population including both participants and nonparticipants, individuals who developed dementia were older (Table 1). Individuals who died before the end of 2008 were older and had lower education, lower total and HDL cholesterol, higher FINRISK score, and higher Beck Depression Inventory score. They were also more likely to be men, smokers, physically inactive, and diabetic. Their anger control capacity and sense of coherence scores were lower (Table 1).

Individuals with incomplete data on all personality-related factors (N = 261) were older, more likely to be women, physically inactive, with lower education, higher HDL-cholesterol, and lower level of anger expression outward (data not shown). They were also more likely to develop dementia compared with the population included in analyses (N = 1005): 43 (16.6%) vs 96 (9.6%) incident dementia, \( P = .002 \).
| Baseline characteristics (1998 examination) | Participants in 2005-2008 examination | Extended population including nonparticipants |
|--------------------------------------------|--------------------------------------|---------------------------------------------|
|                                            | Control (N = 448) | MCI (N = 105) | Dementia (N = 29) | No dementia (N = 903) | Dementia (N = 96) | Alive (N = 778) | Died (N = 227) |
| Age (y)                                    | 69.6 (3.4)  | 70.8 (3.3)  | 71.8 (4.3)**  | 70.6 (3.8)  | 72.4 (4.0)**  | 70.3 (3.6)  | 72.6 (4.2)**  |
| Gender                                     | 37.5  | 41.0  | 27.6  | 41.4  | 36.5  | 36.2  | 56.4**  |
| Men (%)                                    | 62.5  | 59.0  | 72.4  | 58.6  | 63.5  | 63.8  | 43.6  |
| Women (%)                                  | 9.8 (3.6)  | 8.4 (3.0)  | 10.0 (4.4)*  | 9.1 (3.5)  | 9.2 (4.2)  | 9.3 (3.6)  | 8.3 (3.4)**  |
| Education (y)                              | 8.3 (1.1)  | 8.6 (1.1)  | 8.2 (1.1)*  | 8.3 (22)  | 6.8 (2.2)**  | 10.0 (0.0)  | 5.8 (3.1)**  |
| Smoking                                    | 63.2  | 69.5  | 72.4  | 61.4  | 64.6  | 65.7  | 48.0**  |
| Never (%)                                  | 36.8  | 30.5  | 27.6  | 38.6  | 35.4  | 34.3  | 52.0  |
| Ever (%)                                   | 82.4  | 80.0  | 75.9  | 78.4  | 70.8  | 79.6  | 71.4*  |
| Physical activity                          | 17.6  | 20.0  | 24.1  | 21.6  | 29.2  | 20.4  | 28.6  |
| Active (%)                                  | 5.85 (1.00)  | 5.72 (0.93)  | 5.61 (1.12)  | 5.78 (1.02)  | 5.86 (1.03)  | 5.86 (1.00)  | 5.56 (1.05)**  |
| Total cholesterol (mmol/L)                 | 1.43 (0.34)  | 1.42 (0.32)  | 1.45 (0.39)  | 1.41 (0.35)  | 1.47 (0.38)  | 1.44 (0.35)  | 1.36 (0.39)*  |
| HDL cholesterol (mmol/L)                   | 150 (23)  | 154 (21)  | 140 (20)*  | 152 (23)  | 152 (26)  | 151 (23)  | 153 (26)  |
| Systolic blood pressure (mm Hg)            |                      |                      |                  |                      |                      |                  |                      |
| Diabetes                                   | 92.4  | 94.3  | 82.8  | 90.7  | 84.4  | 91.8  | 84.1*  |
| No (%)                                     | 7.6  | 5.7  | 17.2  | 9.3  | 15.6  | 8.2  | 15.9  |
| Yes (%)                                    | 21.66 (17.86)  | 24.17 (19.15)  | 23.20 (21.53)  | 25.60 (20.91)  | 29.16 (25.05)  | 22.73 (18.82)  | 36.74 (25.49)**  |
| FINRISK score                              | 8.86 (6.04)  | 10.68 (7.03)  | 10.31 (7.31)*  | 9.49 (6.41)  | 10.18 (7.09)  | 9.33 (6.38)  | 10.40 (6.77)*  |
| Beck Depression Inventory                   | 4.76 (2.58)  | 4.84 (3.01)  | 4.16 (2.34)  | 4.79 (2.84)  | 4.68 (2.94)  | 4.78 (2.76)  | 4.75 (3.17)  |
| Anger expression outward*                  | 8.68 (3.20)  | 8.88 (3.53)  | 9.73 (3.54)  | 8.48 (3.24)  | 9.16 (3.71)  | 8.54 (3.27)  | 8.59 (3.39)  |
| Anger control capacitya                     | 17.88 (4.20)  | 17.80 (4.39)  | 18.16 (3.56)  | 17.77 (4.34)  | 17.43 (4.21)  | 17.88 (4.20)  | 17.16 (4.73)*  |
| Trait angerc                               | 6.94 (3.98)  | 6.65 (4.01)  | 7.19 (4.42)  | 6.58 (4.01)  | 7.38 (4.43)  | 6.67 (4.00)  | 6.59 (4.31)  |
| Anxietyc                                   | 3.82 (2.28)  | 4.22 (2.48)  | 4.52 (3.38)  | 4.03 (2.37)  | 4.63 (3.05)  | 4.00 (2.42)  | 4.35 (2.51)  |
| Sense of coherencec                         | 56.91 (10.81)  | 54.78 (12.27)  | 57.15 (11.75)  | 56.35 (11.15)  | 55.90 (11.44)  | 56.87 (11.06)  | 54.00 (11.45)*  |

Note: Values are means (SD) unless otherwise specified. Analyses included individuals with complete data on at least one personality trait. Missing data: 40 anger expression outward, 45 anger expression inward, 48 anger control capacity, 38 trait anger, 19 anxiety, 46 sense of coherence (participants population N = 582); 80 anger expression outward, 100 anger expression inward, 95 anger control capacity, 76 trait anger, 35 anxiety, 94 sense of coherence (extended population including nonparticipants N = 1005).

aHigher value indicates more pronounced personality trait.

*P < .05.

**P < .001.
3.2 Associations between personality-related factors and cognitive outcomes

Table 2 shows the associations between personality-related factors and cognitive outcomes (control-MCI-dementia) in participants in both late-life examinations. High anxiety level was related to higher risk of worse cognitive outcome, with OR (95% CI) 1.68 (1.07-2.63) after adjusting for age, sex, education, and follow-up time (Model 1). This association remained after further adjustment for cardiovascular and lifestyle-related risk factors: 1.70 (1.08-2.67), Model 2. However, it was somewhat attenuated after adjusting for depressive symptoms: 1.57 (0.96-2.58), Model 3.

Table 3 shows the associations between personality-related factors and dementia in the extended study population including also nonparticipants at the second late-life examination. Individuals with higher level of trait anger had a nearly 2-fold risk of dementia, with HR (95% CI) 1.91 (1.15-3.16) in Model 1. This association was not affected by further adjustments for cardiovascular and lifestyle-related risk factors (HR 1.90, 95% CI 1.15-3.14, Model 2) and depressive symptoms (HR 1.90, 95% CI 1.14-3.18, Model 3). The results were essentially the same for both trait anger subscales, that is, angry temperament and angry reaction (data not shown).

3.3 Associations between personality-related factors and mortality

Table 4 shows the associations between personality-related factors and mortality. People with higher level of anxiety had an increased risk of death: HR (95% CI) was 1.46 (1.03-2.06) for intermediate and 1.46 (1.08-1.98) for high compared with low anxiety level in Model 1. This association was not affected by cardiovascular and lifestyle-related risk factors (HR 1.44 (1.04-2.01) and 1.46 (1.08-1.95), respectively, Model 2).

### Table 2

| Personality-related factors                                  | OR (95% CI)                  |
|--------------------------------------------------------------|------------------------------|
|                                                               | Model 1                      | Model 2                      | Model 3                      |
| **Anger expression outward**                                 |                              |                              |                              |
| Low                                                          | Reference                    |                              |                              |
| Intermediate                                                | 0.72 (0.43-1.21)             | 0.72 (0.43-1.21)             | 0.70 (0.42-1.17)             |
| High                                                        | 0.92 (0.57-1.49)             | 0.92 (0.57-1.49)             | 0.86 (0.52-1.40)             |
| **Anger expression inward**                                  |                              |                              |                              |
| Low                                                         | Reference                    |                              |                              |
| Intermediate                                                | 0.72 (0.41-1.25)             | 0.72 (0.41-1.25)             | 0.68 (0.38-1.20)             |
| High                                                        | 1.10 (0.69-1.76)             | 1.10 (0.69-1.76)             | 0.99 (0.60-1.65)             |
| **Anger control capacity**                                  |                              |                              |                              |
| Low                                                         | Reference                    |                              |                              |
| Intermediate                                                | 0.74 (0.44-1.25)             | 0.74 (0.44-1.24)             | 0.75 (0.45-1.26)             |
| High                                                        | 0.86 (0.53-1.40)             | 0.83 (0.51-1.37)             | 0.89 (0.54-1.47)             |
| **Trait anger**                                             |                              |                              |                              |
| Low                                                         | Reference                    |                              |                              |
| Intermediate                                                | 1.10 (0.66-1.81)             | 1.10 (0.66-1.82)             | 1.05 (0.63-1.75)             |
| High                                                        | 0.83 (0.51-1.38)             | 0.84 (0.51-1.39)             | 0.77 (0.46-1.29)             |
| **Anxiety**                                                 |                              |                              |                              |
| Low                                                         | Reference                    |                              |                              |
| Intermediate                                                | 0.79 (0.45-1.41)             | 0.78 (0.44-1.39)             | 0.76 (0.42-1.35)             |
| High                                                        | 1.68 (1.07-2.63)             | 1.70 (1.08-2.67)             | 1.57 (0.96-2.58)             |
| **Sense of coherence**                                      |                              |                              |                              |
| Low                                                         | Reference                    |                              |                              |
| Intermediate                                                | 0.77 (0.46-1.29)             | 0.77 (0.46-1.30)             | 0.88 (0.51-1.54)             |
| High                                                        | 0.93 (0.57-1.52)             | 0.93 (0.57-1.53)             | 1.16 (0.64-2.09)             |

*Note: Values are odds ratios (OR) and 95% confidence intervals (CI) from ordinal logistic regressions (ordered outcome control-MCI-dementia) with personality-related factors categorized by tertiles.

*Model 1 is adjusted for age, sex, education, and follow-up time.

*Model 2 is additionally adjusted for cardiovascular and lifestyle-related risk factors (FINRISK score based on age, sex, smoking status, systolic blood pressure, serum total cholesterol, serum HDL cholesterol, and diabetes) and physical activity.

*Model 3 is additionally adjusted for depressive symptoms (Beck depression Inventory).

*P < .05.
related factors (Table 4, Model 2), but was slightly attenuated after adjusting for depressive symptoms: HR (95% CI) was 1.41 (0.99-2.00) for intermediate anxiety level and 1.35 (0.97-1.86) for high anxiety level in Model 3 (Table 4). Individuals with the highest sense of coherence had lower risk of death (HR 0.65, 95% CI 0.45-0.93, Model 1). Effect size was similar after cardiovascular and lifestyle-related adjustments (HR 0.69, 95% CI 0.48-0.93, Model 2) and also after adjusting for depressive symptoms, although with slightly broader confidence interval (HR 0.68, 95% CI 0.45-1.04, Model 3).

4 | DISCUSSION

In this study, more pronounced trait anger was associated with higher dementia risk, even after all adjustments. This association has not been previously reported in the literature, but is in line with the previous findings connecting the related personality trait hostility to higher dementia risk.\textsuperscript{19,20} Trait anger was related to dementia in the extended CAIDE population including also individuals who died or dropped out after the first late-life examination, but not in the smaller main population who participated in both late-life examinations. This may be explained by the size of population and different outcomes, given that in the main population both MCI and dementia were considered. It has been hypothesized that hostility may be more predictive for the severe cognitive decline connected to dementia than more gradual cognitive decline.\textsuperscript{19} Similar pattern could explain the current findings with trait anger.

Higher level of anxiety was associated with increased risk of worse cognitive outcomes and mortality, even after cardiovascular and lifestyle-related adjustments. The associations were somewhat...
attenuated after considering depressive symptoms, most likely due to correlations between anxiety and depression. Moreover, a high sense of coherence was related to lower mortality. Effect size was stable across all models, although the relation became nonsignificant after adjusting for depressive symptoms.

Previous studies of personality-related factors and dementia risk have mainly focused on a five-factor model of personality, with most consistent evidence linking high neuroticism and low conscientiousness to dementia.2-6 Anxiety and anger were investigated with state-trait-based scales in this study, but these characteristics can be seen reflecting different facets of neuroticism.39 A meta-analysis has previously connected anxiety to incident MCI.9 Consistent with this finding, an association with worse cognitive outcome was found in the present study as well. However, significant heterogeneity was reported across studies investigating anxiety in relation to dementia, that is, an association was found primarily in older populations (80 years and above).9 In the present study with a mean population age of 71 years, we did not find a significant association between anxiety and dementia when MCI was not considered as an outcome. It has been suggested that causal pathways may explain the relation to cognitive impairment,9 for example, the effect of anxiety-related chronic stress on the hypothalamic-pituitary-adrenal (HPA) axis, leading to structural brain damage in areas involved in cognitive functioning.40 In contrast, the association with dementia observed at older (but not younger) ages may reflect anxiety as a prodromal dementia symptom.9 The other factors considered in this study (anger expression, trait anger, and sense of coherence) have been investigated primarily in relation to other health conditions, disability, or mortality, but rarely or not at all to dementia or cognition.

Studies examining associations between anxiety and mortality have also reported conflicting results and noted confounding effect of

| Table 4 | Associations between personality-related factors and mortality |
|----------------------|---------------------|---------------------|
| **Personality-related factors** | **N total (dead)** | **HR (95% CI)** |
| **Anger expression outward** | | |
| Low | 329 (82) | Reference |
| Intermediate | 260 (54) | 0.89 (0.63-1.26) | 0.89 (0.63-1.26) | 0.88 (0.63-1.25) |
| High | 336 (70) | 0.81 (0.59-1.12) | 0.78 (0.56-1.07) | 0.76 (0.55-1.06) |
| **Anger expression inward** | | |
| Low | 324 (66) | Reference |
| Intermediate | 239 (48) | 0.97 (0.67-1.41) | 0.96 (0.66-1.39) | 0.94 (0.65-1.37) |
| High | 342 (79) | 1.14 (0.82-1.59) | 1.11 (0.80-1.54) | 1.06 (0.74-1.51) |
| **Anger control capacity** | | |
| Low | 360 (80) | Reference |
| Intermediate | 271 (60) | 0.97 (0.69-1.35) | 0.97 (0.69-1.36) | 0.98 (0.70-1.38) |
| High | 279 (61) | 0.97 (0.70-1.36) | 0.99 (0.71-1.39) | 1.01 (0.72-1.42) |
| **Trait anger** | | |
| Low | 308 (71) | Reference |
| Intermediate | 278 (56) | 0.92 (0.65-1.31) | 0.92 (0.65-1.31) | 0.90 (0.63-1.28) |
| High | 343 (75) | 0.99 (0.71-1.37) | 0.95 (0.68-1.32) | 0.91 (0.65-1.28) |
| **Anxiety** | | |
| Low | 401 (77) | Reference |
| Intermediate | 217 (54) | 1.46 (1.03-2.06)* | 1.43 (1.01-2.03)* | 1.41 (0.99-2.00) |
| High | 352 (90) | 1.46 (1.08-1.98)* | 1.41 (1.04-1.91)* | 1.35 (0.97-1.86) |
| **Sense of coherence** | | |
| Low | 293 (79) | Reference |
| Intermediate | 327 (75) | 0.86 (0.63-1.19) | 0.90 (0.65-1.24) | 0.89 (0.63-1.27) |
| High | 291 (48) | 0.65 (0.45-0.93)* | 0.69 (0.48-0.99)* | 0.68 (0.45-1.04) |

Note: Values are hazard ratios (HR) and 95% confidence intervals (CI) from Cox proportional hazards model (outcome death) with personality-related factors categorized by tertiles.

*aModel 1 is adjusted for age, sex, education, and follow-up time.

bModel 2 is additionally adjusted for cardiovascular risk (FINRISK score based on age, sex, smoking status, systolic blood pressure, serum total cholesterol, serum HDL cholesterol, and diabetes) and physical activity.

*cModel 3 is additionally adjusted for depressive symptoms (Beck depression Inventory).

*P < .05.
depression. A recent meta-analysis showed that positive associations were related to studies with smaller samples and participants with comorbid depression; no association was found in studies that were adjusted for depression. Anxiety often co-occurs with depression, and depression has been shown to increase both dementia risk and mortality. Consistently, in this study, the associations of anxiety with cognitive impairment and mortality were attenuated after adjusting for depressive symptoms, and this may reflect the interplay between anxiety and depression.

Possible mechanisms for the associations between trait anger and dementia may include the effects of anger on cardiovascular risk factors. Anger has been associated with many adverse cardiovascular outcomes, such as coronary heart disease and risk of type 2 diabetes. Cardiovascular factors have in turn been linked to increased risk of cognitive decline and dementia. However, in this study, the associations remained after cardiovascular risk factors were adjusted for. Like anxiety, anger has also been suggested to have an influence on HPA axis function. Further, inflammation has been connected to both anger and Alzheimer’s disease. Anger could also affect dementia risk through adverse health behaviors, such as smoking, sedentary lifestyle, and unhealthy diet.

A high sense of coherence has also previously been associated with lower mortality. One possible explanation may be that a weak sense of coherence may cause more distress, and psychological distress has been associated with higher mortality. Higher sense of coherence has also been connected to healthier lifestyle, which may contribute to lower mortality. Furthermore, a weak sense of coherence has been linked to higher risk of depression and depression to higher mortality.

The main strengths of this study are the longitudinal population-based design, inclusion of both men and women, and thorough assessments of MCI and dementia diagnoses at the CAIDE examinations. However, the study has several limitations as well. The associations between the studied personality-related factors, incident dementia, and mortality may have been underestimated due to missing data and/or nonparticipation in the 1998 CAIDE examination. People with missing data were more likely to develop dementia, compared with people included in the analyses. Further, nonparticipation is usually associated with higher dementia incidence and dementia with higher mortality. To address limitations related to loss to follow-up, dementia diagnoses for individuals who died after 1998 or did not return to the 2005-2008 CAIDE examination were ascertained from Finnish national registers. Although registers tend to underreport dementia cases, diagnoses in Finnish registers were shown to be accurate.

Participants with dementia or MCI at the 1998 CAIDE examination were excluded from this study, thus minimizing the potential impact of cognitive impairment on answers to the personality-related questionnaires. The screening procedure for mild cognitive impairment in 1998 was based on MMSE and thus less extensive compared with later examinations, that is, we cannot fully exclude the possibility that some cases may have been missed. However, the prevalence of MCI in the CAIDE 1998 examination was similar to another population-based study among individuals of similar age living in the same region. Because of the long preclinical phase of dementia-related diseases such as AD, the possibility of reverse causality affecting the results cannot be entirely dismissed. To address this, we excluded individuals who were too close to dementia onset. Another limitation is that no data were available on the participants’ history of psychiatric conditions or treatments.

In conclusion, our findings emphasize the role of personality-related factors as risk factors for cognitive impairment and dementia, as well as mortality. Considering anxiety and anger-prone personality, as well as depression, as part of multifactorial dementia risk scores, especially those designed for older populations, could help identify people at risk for cognitive impairment and dementia. Taking personality-related factors into account may also be useful for future lifestyle-based intervention trials and dementia prevention strategies.

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CONFLICT OF INTEREST
Hilkka Soininen has served in advisory boards for ACImmune and MERCK. Other authors report no conflict of interests.

DATA AVAILABILITY STATEMENT
Data are not publicly available due to ethical requirements. Data generated during and/or analyzed during the present study, and study materials can be made available from author Alina Solomon provided that approval is obtained from the CAIDE Study Steering Committee (contact alina.solomon@uef.fi).

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