Introduction

Alzheimer’s disease and related dementias (ADRD) represents an increasing burden for patients and caregivers, including physical, emotional, and financial demands for care provision [1-3].

An estimated 5.4 million Americans of all ages had Alzheimer’s disease in 2012, one in eight Americans over age 65, ranging from approximately 53 new cases per 1,000 people aged 65 to 74, to 170 new cases per 1,000 people aged 75 to 84. Global prevalence of dementia is as high as 24 million, and is expected to quadruple by the year 2050. In the US alone, it accounts for an estimate direct health-care costs of $172 billion per year and $210 billion in unpaid care giving [4].

Even when etiological mechanisms underlying this illness remain unknown, both environmental and genetic factors have been proposed as putative causes, beginning years before symptoms became clinically evident. Risk factors for dementia, such as advancing age, family history, genetics, brain reserve, and lifestyle have been proposed [5].

Provided that only modest therapeutic effects have been achieved with currently available pharmacologic disease-modifying treatments for AD, attention has shifted toward prevention or delay of AD onset [6,7].

In a recent systematic review, association of multiple factors with ADRD was assessed, and several potentially modifiable conditions were identified, such as lifestyle, diabetes, hypertension, obesity, smoking, depression, cognitive engagement, physical activity and diet. Surprisingly, personality traits were not addressed [8] despite strong associations between personality and health [9].

Very few studies have evaluated the relationship between premorbid personality, life events and ADRD. For example, early childhood stressful situations could impair elder’s psychosocial adaptation favoring the emergence of ADRD [10].

Previous psychiatric history, including premorbid personality, may predispose subjects to ADRD and its corresponding psychiatric symptoms [11-13] concluding that before Alzheimer’s disease onset, patients were more passive, hostile and less spontaneous. Other authors also reported diminished initiative/growing apathy, relinquishment of hobbies and increased rigidity [14].

Similar results were obtained in studies comparing premorbid and present personality using the NEO-PI instrument [15]. Changes in the five personality domains could be summarized as higher neuroticism, lower extraversion and conscientiousness, and smaller reductions in openness and agreeableness.

In a long term prospective study, higher scores on vulnerability to stress, anxiety, and depression preceded onset of dementia up to 30 years. Those traits were associated with higher ADRD neuropathology at autopsy, and lower resilience to clinical dementia. On the other side, agreeableness, order and competence, as part of a resilient personality, were significantly associated with lower risk or delay of clinical dementia, even when post mortem AD neuropathology was present [16,17]. Those findings were replicated in an independent study [18].

In another research using data from the Religious Orders Study [19] conscientiousness or will and goal directedness were associated with a reduced risk of AD, and to a slower rate of cognitive decline.

Several other studies have acknowledged the association between mid-life personality and incident ADRD [20-24]. Finally, in recent
meta-analysis [25] individuals with high neuroticism and low conscientiousness had a threefold increased risk of incident AD, together with self-discipline and depression. Some studies do not support those previous findings, however, and found no relationship between previous personality and risk of dementia [26].

Some authors, indeed, tend to stress the continuity between pre- and post-morbid personality profiles [27,28]. For those researchers, the personality traits of patients with dementia seemingly reflect adaptive coping models used before onset of dementia. Considering the aforementioned studies, research on personality disorder as a risk factor for dementia usually has been based on psychobiological models [29] or the Five Factor Taxonomy (FFT) of personality [30-32], and examined relatively homogeneous groups [33].

Given the putative role of education and lifestyle as risk factors for ADRD [34], research should also focus in ethnically heterogeneous cohorts and tap on more clinically oriented personality clusters. In that sense, subjects with personality disorders and associated neurobiological vulnerabilities, such as Borderline, Narcissistic or Antisocial Personality Disorder [35,36] could be prone to develop neurodegenerative diseases such as dementia in old age.

However, only few case reports are available to support this hypothesis [37-39] without corresponding epidemiological data. With regard to Narcissistic Personality Disorder, the most consistent findings have been a positive correlation with negative emotionality, aggressiveness, psychoticism and extraversion; a negative correlation with agreeableness and conscientiousness36, and inconsistent correlation with introversion and low positive emotionality.

A substantial degree of variability in convergence between measures of narcissism grandiosity and vulnerability and the domains of the FFT still persist [40], suggesting that narcissistic personality as risk factor for dementia should be studied in its own, and not simply associating it with the FFT results [41]. As most of the evidence on risk factors for ADRD has been based on case-control studies, longitudinal studies may represent a better design to identify risk factors for development of ADRD of affected individuals. They avoid the need to obtain exposure data from proxy respondents as individuals affected with ADRD may be unable to provide reliable data.

In conclusion, the objective of this research was to investigate the role of previous pathological narcissistic personality disorder as a risk factor for ADRD in a Spanish-speaking population using a longitudinal study. Ultimately, we hope that these data could aid in two ways: first, developing clinically useful risk markers for predicting ADRD, which, in turn, would pave the way for dementia prevention strategies; second, studying the risk posed by personality could yield insights about the etiology of ADRD [42-44].

Materials and Methods

Sample size

Based on an age-standardized prevalence for ADRD of 4.4% [45-47], a relative risk (RR) of 1.19 in relation to premorbid health status, an alpha risk of 5%, a power of 95% and an expected drop-out rate of 20% over 36 months, 452 patients were selected.

Study design

The research was based on a prospective cohort study of Spanish-speaking subjects with personality disorders who resided in the community, and received psychiatric treatment at a community mental health center. Inclusion criteria included age 65-75 years, availability of a proxy respondent, preserved ability to complete clinical and neuropsychological evaluations, sign informed consent, and exhibit normal cognitive performance and no significant morbidity. Exclusion criteria included severe visual or hearing impairment, dementia, idiopathic Parkinson’s disease, liver disease, alcoholism, known terminal illness, hospitalization for depression within the last year or having received electroconvulsive therapy within the prior decade, current treatment with cholinesterase inhibitors, anti-Parkinson medications, tricyclic antidepressants, antipsychotics or other medications with significant psychotropic or central cholinergic effects. Patients were enrolled and interviewed from March 2009 to March 2010. At baseline, patients underwent a clinical, neuropsychological and psychiatric examination, and a brain MRI. Patients were followed up over a period of 36 months, at 6 months intervals. Informed written consent was obtained from subject and caregiver at enrollment and before baseline assessment took place. The study protocol was reviewed and approved by the local institutional review board. All procedures were in accordance with the declaration of Helsinki. The sample was middle-class, most subjects were female (63 percent). Only 2 subjects with missing data, and 7 subjects who moved or declined to return for follow-up were excluded. After that, 452 subjects remained available for the study.

Measures

Cognitive impairment was assessed using the Modified Mini-Mental State Exam (normal values ≥78) [48]. The 3MSE is based on the Mini-Mental State Exam and offers a more graded scoring.

Depression was assessed using the Geriatric Depression Scale (Short Form) [49] which has shown good psychometric properties. A score of 0 to 5 is normal. A score greater than 5 suggests depression.

Diagnosis of dementia was made using the informant/subject structured interview based on the Clinical Dementia Rating Scale (CDR) (normal values ≤ 0.5) [50] and the Blessed Information Memory Concentration scale (normal values ≤ 4) [51]. This last test exhibits a high test–retest reliability (0.86), and correlate closely with the stages of Alzheimer’s disease [52].

Narcissistic Pathological Personality was assessed with the Pathological Narcissism Inventory (PNI) [53] which is a 52-item multidimensional self-report measure of pathological narcissism. Respondents are asked to use a 6-point scale ranging from 0 (not at all like me) to 5 (very much like me) to rate each item. It consists of seven subscales that measure different characteristics of pathological narcissism: Contingent Self-Esteem (CSE), Exploitativeness (EXP), Self-Sacrificing Self-Enhancement (SSSE), Hiding the Self (HS), Grandiose Fantasy (GF), Devaluing (DEV), and Entitlement Rage (ER). Because of the variability in scale length, mean scores are used instead of sums to allow for easy comparison across scales. Two higher order factors encompassing these 7 subscales, Narcissistic Grandiosity and Narcissistic Vulnerability are also scored.
from enrollment to the date when a diagnosis of dementia was issued. Censoring was based on study ending, time of death or follow-up refusal. All multivariate models included following covariates: age at enrollment, sex, educational level (high school vs. college-level education) and base-line scores of 3MSE and geriatric depression scale. Graphical (log-log plots) and analytical (Schoenfeld residuals) methods were used to test the proportional hazards assumption for each analysis; the assumption was supported in every case. Analyses also examined interactions between each of the PNI subscales and other covariates in the model. Finally, analyses explored curvilinear relationships between the PNI subscales and dementia risk, by including each factor together with a squared term for each factor.

Results

During 1104 person-years of follow-up (median follow-up, 2.7 years), dementia developed in 159 participants (Alzheimer’s disease in 112 (70%), vascular dementia in 37 (23%), mixed dementia in 9 (1.5%), and other types of dementia in 1 (0.5%). By the end of the study period, no subjects had died and 7 participants had dropped out (follow-up, 2.7±1.1 years). On average, participants in whom dementia developed were mostly female (t=3.7, p<.02), slightly older (t=4.9, p<.04), had lower levels of education (t=5.2, p<.03), lower scores on cognitive test (t=4.9, p<.01), higher scores on narcissistic vulnerability scores (t=8.7, p<.01); but no differences in depression score (Table 1).

The covariates between pathological narcissistic personality subscales along with depression and cognitive scores are observed in Table 2. More robust correlations were observed between depression scores and narcissistic vulnerability and devaluing the self. Also correlations between other covariates were found, such as narcissistic vulnerability and hiding and devaluing the self.

Table 2 shows the adjusted hazard ratios (AHR) and 95% confidence intervals (CI) for AD for each of the subscales of PNI. Each subscale is first reported when entered alone in the model, and then associated with the other subscales. Of the confounders, only age and education were independently associated with AD risk. Older participants [AHR (95% CI) =1.32 (1.18-1.36)] were at greater risk of developing AD over the follow-up period. In addition, AD risk was greater among participants with higher scores in HS, DEV and NV

### Table 1: Baseline Demographic Characteristics of Participants by final dementia status.

<table>
<thead>
<tr>
<th>Variable</th>
<th>no incident dementia (n=259)</th>
<th>incident dementia (n=159)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs.)</td>
<td>73.2±2.9</td>
<td>75.1±3.0</td>
<td>.04</td>
</tr>
<tr>
<td>Gender (female) (%)</td>
<td>149 (57%)</td>
<td>135 (85%)</td>
<td>.02</td>
</tr>
<tr>
<td>Duration of follow up (months)</td>
<td>32.1±4.1</td>
<td>33.8±3.9</td>
<td>.50</td>
</tr>
<tr>
<td>High school education (n%)</td>
<td>220 (85%)</td>
<td>112 (71%)</td>
<td>.03</td>
</tr>
<tr>
<td>3MSE</td>
<td>2.45±0.3</td>
<td>1.02±0.4</td>
<td>.01</td>
</tr>
<tr>
<td>GDS</td>
<td>5.33±2.1</td>
<td>5.71±1.8</td>
<td>.35</td>
</tr>
<tr>
<td>Narcissistic grandiosity</td>
<td>3.21±1.1</td>
<td>2.87±1.9</td>
<td>.09</td>
</tr>
<tr>
<td>Narcissistic vulnerability</td>
<td>2.08±1.5</td>
<td>4.56±2.1</td>
<td>.01</td>
</tr>
<tr>
<td>CSE</td>
<td>2.91±0.3</td>
<td>2.07±0.6</td>
<td>.57</td>
</tr>
<tr>
<td>EXP</td>
<td>2.76±0.5</td>
<td>2.79±0.4</td>
<td>.04</td>
</tr>
<tr>
<td>SSSE</td>
<td>2.19±1.0</td>
<td>3.16±1.1</td>
<td>.05</td>
</tr>
<tr>
<td>HS</td>
<td>1.87±0.3</td>
<td>4.01±1.7</td>
<td>.01</td>
</tr>
<tr>
<td>GF</td>
<td>2.08±0.9</td>
<td>2.33±1.6</td>
<td>.23</td>
</tr>
<tr>
<td>DEV</td>
<td>1.26±1.5</td>
<td>4.07±2.3</td>
<td>.01</td>
</tr>
<tr>
<td>ER</td>
<td>2.03±1.8</td>
<td>3.47±1.5</td>
<td>.02</td>
</tr>
</tbody>
</table>

Plus–minus values are means ±SD. P values for scales and tests were calculated by the Mann–Whitney U test. 3MSE rating range from 1 to 3, with higher scores indicating better cognitive function; scores on the GDS (Geriatric Depression Scale) range from 0 to 15, with higher scores indicating greater depression; scores on the 3MSE rating range from 1 to 3, with higher scores indicating better cognitive function; scores on the GDS (Geriatric Depression Scale) range from 0 to 15, with higher scores indicating greater depression.

### Statistical analysis

Data were analyzed using Stata (Stata Statistical Software: Release 13. College Station, TX: StataCorp LP). Continuous variables were compared with use of either an independent-samples t-test or the Mann–Whitney U test, and categorical variables were compared with use of the Pearson chi-square test. The association between personality and risk of dementia was assessed using cox proportional-hazards regression analysis to estimate hazard ratios, with 95 percent confidence intervals. The time to an event was defined as time evolved since enrollment to the date when a diagnosis of dementia was issued.
Table 3: Adjusted Hazard Ratios (AHR) for Alzheimer’s disease (N=159).

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Fixed Model</th>
<th>Model 2</th>
<th>Model 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, gender, education</td>
<td>1.14 (1.09-1.19)</td>
<td>1.16 (1.11-1.24)</td>
<td>1.27 (1.20-1.32)</td>
</tr>
<tr>
<td>CSE-PNI</td>
<td>1.06 (1.01-1.14)</td>
<td>1.05 (1.01-1.11)</td>
<td>1.12 (1.04-1.20)</td>
</tr>
<tr>
<td>EXP</td>
<td>.98 (.73-1.12)</td>
<td>.92 (.85-1.21)</td>
<td>.93 (.67-1.1)</td>
</tr>
<tr>
<td>EXP-PNI</td>
<td>.90 (.86-1.17)</td>
<td>.87 (.85-1.13)</td>
<td>.89 (.56-1.21)</td>
</tr>
<tr>
<td>SSSE</td>
<td>1.00 (1.78-1.09)</td>
<td>1.01 (1.87-1.10)</td>
<td>1.03 (1.73-1.14)</td>
</tr>
<tr>
<td>SSSE-PNI</td>
<td>.96 (1.67-1.13)</td>
<td>.96 (.56-1.16)</td>
<td>.87 (1.78-1.16)</td>
</tr>
<tr>
<td>HS</td>
<td>1.34 (1.18-1.39)</td>
<td>1.45 (1.07-1.49)</td>
<td>1.42 (1.36-1.49)</td>
</tr>
<tr>
<td>HS-PNI</td>
<td>1.44 (1.40-1.49)</td>
<td>1.53 (1.48-1.59)</td>
<td>1.58 (1.53-1.62)</td>
</tr>
<tr>
<td>NF</td>
<td>1.01 (.84-1.12)</td>
<td>0.98 (.76-1.09)</td>
<td>1.02 (.89-1.10)</td>
</tr>
<tr>
<td>NF-PNI</td>
<td>.97 (.86-1.13)</td>
<td>.87 (.75-1.15)</td>
<td>.86 (.56-1.08)</td>
</tr>
<tr>
<td>DEV</td>
<td>1.35 (1.21-1.57)</td>
<td>1.43 (1.31-1.56)</td>
<td>1.53 (1.32-1.78)</td>
</tr>
<tr>
<td>DEV-PNI</td>
<td>1.32 (1.23-1.48)</td>
<td>1.21 (1.15-1.37)</td>
<td>1.31 (1.24-1.57)</td>
</tr>
<tr>
<td>ER</td>
<td>1.02 (1.85-1.15)</td>
<td>.98 (.56-1.12)</td>
<td>1.03 (.89-1.10)</td>
</tr>
<tr>
<td>ER-PNI</td>
<td>1.21 (1.16-1.31)</td>
<td>1.12 (1.03-1.26)</td>
<td>1.10 (1.01-1.21)</td>
</tr>
<tr>
<td>NV</td>
<td>1.43 (1.34-1.69)</td>
<td>1.52 (1.34-1.68)</td>
<td>1.78 (1.56-1.97)</td>
</tr>
<tr>
<td>NV-PNI</td>
<td>1.45 (1.32-1.59)</td>
<td>1.64 (1.45-1.87)</td>
<td>1.67 (1.40-1.81)</td>
</tr>
<tr>
<td>NG</td>
<td>.98 (.67-1.10)</td>
<td>.76 (.53-99)</td>
<td>.86 (.56-1.03)</td>
</tr>
<tr>
<td>NG-PNI</td>
<td>.95 (.78-1.18)</td>
<td>.87 (.56-1.16)</td>
<td>.79 (.45-1.00)</td>
</tr>
</tbody>
</table>

Contingent Self-Esteem (CSE), Exploitativeness (EXP), Self-Sacrificing Self-Enhancement (SSSE), Hiding the Self (HS), Grandiose Fantasy (GF), Devaluing (DEV), and Entitlement Rage (ER), Pathological Narcissistic Inventory (PNI)

and lower in GF and NG. When the 3MSE was added to the fixed model, participants higher in NV, DEV and HS remained at greater risk. The AHRs for NV, DEV AND HS were slightly greater than corresponding values for fixed model. Whereas the figures for NV were unaffected by adding other subscales to the model, NG was no longer statistically significant. People who scored lower on the 3MSE at study entry were more likely to develop AD, AHR (95% CI) = 1.84 (1.71-1.90). When GDS was added to the model, NV, HS and DEV remained associated with higher AD risk, and AHRs scores were slightly greater than those in the fixed model. The positive association between GDS scores and AD risk was not as large as the effect of 3MSE [AHR (95%CI) = 1.84 (1.12-2.13)].

The Kaplan-Meier probability of developing AD over the follow-up period is presented in Figure 1. Relative to the low risk group, the AD HR for high risk group was 2.12 (95% CI = 1.79-3.89), and with full adjustment, including age, gender, education level, GDS and 3MSE, HR was 2.07 (95% CI = 1.18-3.75). Supplementary and sensitivity analyses revealed a significant interaction between NV subscale and DEV, HS and SSSE covariates. No gender differences were found in the relationship between NV and AD risk. Only squared NV subscale scores were significant.

Discussion

In this study a clear association was disclosed between elders with high scores in pathological narcissism and greater risk for AD. For NV, HS and MOV, findings were somewhat comparable when entered alone or in conjunction with the other NPI subscales. Results remained significant even after depression was inserted in the model, and the same could be said regarding cognitive function. The predictive value of NG was not apparent when all subscales were entered simultaneously, suggesting that NV is an independent risk factor for AD. Some authors [54] further distinguish between grandiosity and vulnerability narcissism, the first associated with overt expressions of grandiose fantasies, arrogance and self-entitlement, the latter with themes of fragility, depletion and feelings of inadequacy. Although patients may exhibit both aspects of narcissistic personality, others could probably express only one of those facets much of the time, for example narcissistic vulnerability, being more at risk.

Results for pathological narcissism appear quite robust; however the influence of other variables which probably intervene in the pathway from pathological narcissism to AD, such as comorbid pathological conditions, should be taken into account in future investigations, as they may alter the present results. These findings must be added to the growing literature acknowledging the deleterious effects on cognitive function of dysfunctional coping mechanisms observed in pathological narcissistic personality together with HPA axis dysregulation [55-57]. It is also likely that poor decision making due to perceived high self-efficacy and risk taking [58], and compromised self-care with excessive dieting and over-exercising [59,60] increase risk for AD together with other adverse health outcomes [61]. It is also worth to examine the association between personality disorders, particularly vulnerable narcissism, and cognitive deterioration [62], suggesting that pathological narcissists should benefit from socially embedded, spontaneous cognitive activities with varied content, such as daydreams, fantasies and games [63]. However, data provided in the present study do not allow us to draw any conclusions regarding which type of cognitive activity could play a protective role for dementia risk. In this study a sound relationship was observed between low education and high risk for dementia, which has been mentioned in several studies [64,65]. Given that personality disorders, such as narcissism, have been tied to low education and social outcomes [66,67], pathological narcissism traits could play a mediating role in this association. In that sense, reducing the influence of narcissistic vulnerability and exposing the subject to more stimulant and healthy cognitive and social activities could aid in reducing the risk of AD. Some limitations to this study must be acknowledged: first, selective loss of subjects with specific personality profiles may have influenced the observed relationships. As pathological personality traits are...
associated with lower health outcomes and greater mortality rates [68], healthy survivor effects would underestimate the associations between those traits and dementia. Second, given that changes in personality may predate clinical onset of dementia [69], it is possible that at time of recruitment the presence of incipient Alzheimer’s disease may alter personality diagnosis. Third, as availability of proxy respondents was set as an inclusion criterion, lack of them may pose implications for the cohort’s sampling strategy.

**Conclusion**

Our findings suggest that elevated scores in narcissistic vulnerability traits may be an important risk factor for dementia. These findings have importance on the design and implementation of preventive strategies for dementia, and in the conceptualization of the multifactorial etiology of Alzheimer’s disease.

**References**


39. Saulsman LM, Page AC. The five-factor model and personality disorder


