PAPER

Premorbid proneness to distress and episodic memory impairment in Alzheimer's disease

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Background: Chronic stress has been associated with impaired episodic memory, but the association of premorbidly experienced distress with memory function in Alzheimer's disease is unknown.
Objective: To investigate the link between proneness to distress and Alzheimer's disease.
Methods: Participants were 363 persons with clinically diagnosed Alzheimer's disease. At baseline, a knowledgeable informant rated each person's premorbid personality (that is, before dementia onset) along five dimensions, one of which was the tendency to experience psychological distress. Participants underwent structured clinical evaluations at baseline and then annually for up to four years. Each evaluation included 17 cognitive tests from which previously established measures of episodic memory, visuoconstruction, repetition, and naming were derived.
Results: In a series of random effects models adjusted for age, sex, and education, premorbid distress proneness was associated with baseline impairment in episodic memory but not with impairment in other cognitive domains, or with change in any cognitive domain. No other trait was related to baseline function or rate of decline in any cognitive domain.
Conclusions: The results suggest that premorbid proneness to experience psychological distress is related to level of impairment in episodic memory in persons with Alzheimer's disease, but neither distress proneness nor other personality traits are related to disease progression.

Alzheimer's disease is the leading cause of decline in memory and other forms of cognition in old age. At necropsy examination, however, quantitative indices of Alzheimer's disease pathology (for example, neuritic plaques, neurofibrillary tangles) are only modestly related to the presence of dementia and cognitive impairment near the time of death, suggesting that other neurobiological mechanisms are involved.[1 2]

There is substantial evidence that chronic psychological distress may contribute to memory impairment.[3] In animals, stressful experiences have been shown to impair hippocampally mediated forms of learning and memory[4] and to be related to reduced dendritic arborisation and neurogenesis in selected regions of the hippocampus.[5 6] In humans, hippocampal atrophy has been observed in psychiatric disorders marked by high levels of distress,[7 8] and indicators of stressful experience have been associated with impairment in episodic memory,[9 10] which is primarily mediated by the hippocampal formation.[11] These observations raise the possibility that chronic distress contributes to impaired episodic memory in persons with Alzheimer's disease.[12]

People differ in the tendency to experience negative emotional states like depression, anxiety, anger, shame, and embarrassment.[13] This personality trait—which can be assessed using self report or informant report questionnaires[14 15]—is quite stable through adulthood and old age,[16 17] and longitudinal studies have shown that it is a good indicator of how much psychological distress people experience on a chronic basis.[18 19] The trait is variously referred to as neuroticism, negative affectivity, emotional stability, and distress proneness.[13–15 20] We prefer the latter label because it specifies the central feature of the trait in unambiguous terms.

To investigate the link between distress proneness and Alzheimer's disease, we used data from a four year longitudinal study of more than 300 persons with clinically diagnosed Alzheimer's disease. At baseline, a knowledgeable informant used standard scales, modified for informant report, to rate each person's tendency to experience psychological distress and other stable personality traits before dementia onset. Participants had structured uniform clinical evaluations at baseline and annually thereafter for up to four years. The evaluations included detailed cognitive function testing, from which previously established composite measures of episodic memory and other cognitive functions were derived. We hypothesised that distress proneness would have a negative association with the baseline level of episodic memory function but not with function in other cognitive domains. To evaluate the specificity of this association, we examined the association of other personality traits with baseline level of episodic memory and other cognitive functions. We also tested whether distress proneness or the other traits were related to rate of decline in episodic memory or other cognitive domains.

METHODS

Subjects

Participants were 410 persons recruited from the Rush Alzheimer's Disease Center. Eligibility required a clinical diagnosis of Alzheimer's disease (see below), community residence, and a score of 11 or more on the mini-mental state examination (MMSE[21]). Of 492 persons who met these criteria during a 12 month period, 410 (83%) agreed to participate in the study. The study was approved by the Institutional Review Board of Rush University Medical Center.

Of the 410 study participants, premorbid personality data were available for 363 (89%). Descriptive information on these persons is provided in table 1. There were 236 women and 127 men; 57 were black and 306 were white. Women were more apt to be missing personality data than men (14% *v* 7%, p = 0.03), but the subgroups with and without personality data did not differ in age, education, race, or any cognitive function measure. The informant who rated

Table 1 Baseline characteristics of 363 persons with personality data

Characteristic	Mean (SD)
Age (years)	75.3 (7.5)
Education (years)	12.1 (3.4)
MMSE score	18.7 (4.3)
Episodic memory score	0.005 (0.697)
Visuoconstruction score	−0.001 (0.824)
Repetition score	0.005 (0.784)
Naming score	0.012 (0.749)
Global cognition score	0.002 (0.585)

MMSE, mini-mental state examination.

premorbid personality traits was most often the spouse (46%) or child (38%) of the participant (12% other relative, 4% other).

Clinical evaluation

At baseline, each participant had a uniform structured clinical evaluation which included a medical history, neurological examination, cognitive function assessment, informant interview, and standard laboratory tests. A magnetic resonance imaging scan was also done in persons without a brain scan in the past year or if otherwise clinically indicated. The evaluation incorporated the procedures used by the Consortium to Established a Registry for Alzheimer's Disease (CERAD[22]) and conformed to the practice guidelines recommended by the quality standards subcommittee of the American Academy of Neurology.[23] Further information on this evaluation is published elsewhere.[24–27]

On the basis of this evaluation, a board certified neurologist diagnosed dementia and Alzheimer's disease clinically according to the criteria of the joint working group of the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's disease and Related Disorders Association (NINCDS/ADRDA[28]). These criteria require a history of cognitive decline and evidence of impairment in memory and at least one other cognitive domain. Persons who met those criteria but also had another condition judged to contribute to cognitive impairment, termed possible Alzheimer's disease in the NINCDS/ADRDA system, were included in analyses.

The essential details of the baseline evaluation were repeated at annual intervals for up to four years. Examiners were blinded to previously collected data.

Assessment of cognitive function

At each evaluation, a set of 17 cognitive function tests was administered. On the basis of a factor analysis of the tests at baseline,[29] we grouped the tests into four functional domains. Tests of episodic memory included immediate and delayed recall of the East Boston story[30]; a three alternative, forced choice, delayed recognition memory test for 15 previously presented Boston naming test items[31]; and the figural memory test,[29] which tests recognition memory for abstract line drawings in three separate trials. Visuoconstruction was assessed with three tasks: *constructional praxis*, which involves copying geometric designs[22]; the *facial recognition test*, which assesses facial perception in a match-to-sample format[32]; and the *figural recognition test*, which assesses perception of the abstract drawings from the figural memory test in a match-to-sample format.[29]

Repetition was assessed using word repetition, high probability phrase repetition, low probability phrase repetition, and commands from the Boston diagnostic aphasia examination.[33] Naming was assessed with responsive naming and body part identification from the Boston diagnostic aphasia examination[33] and CERAD versions of the Boston naming test and verbal fluency.[22]

Analyses were based on composite measures rather than individual tests, to minimise floor and ceiling artefacts and other forms of measurement error. Measures of episodic memory, visuoconstruction, repetition, and naming were formed by converting raw scores on each individual test to z scores, using the baseline mean and standard deviation in the entire cohort, and then computing the average of the z scores of tests belonging to that domain. A measure of global cognition based on all 17 tests was constructed in the same way. Further information about the 17 individual tests and the derivation of the composite measures is contained in previous reports.[25–27 29 34]

Assessment of premorbid personality

We assessed five personality traits with standard adjective rating scales developed by Goldberg.[35] At baseline, the person with the most daily contact with the participant was asked to indicate whether or not each of 100 adjectives accurately described the participant during their adult life up to five years before the onset of dementia. For each trait, the score was the number of item responses in the direction indicative of that trait out of a possible 20. The five traits (with examples of adjectives describing each) are as follows: distress proneness (for example, tense, emotional); extraversion (talkative, active); intellect (curious, creative); agreeableness (warm, generous); conscientiousness (organised, hardworking).

Follow up participation

Of 363 persons with personality data at baseline, 16 died before the first follow up evaluation. Of the remaining 347 persons, follow up data were available on 328 (94.5%), with an average of three to four annual evaluations per individual.

Data analysis

We computed Cronbach's coefficient α to assess the internal consistency of each trait scale, and Pearson correlation coefficients to assess the associations among the trait measures.

We used random effects regression models to test whether each trait was associated with baseline level of function or annual rate of change in each cognitive domain.[36] In this approach, between person variation in baseline cognition and in rate of cognitive change can be estimated from a single model. Other advantages of this approach are that persons need not have the same number of observations and that the time between observations is not assumed to be constant between or within persons. Further information on these models and their application to cognitive data is published elsewhere.[29 34 37]

In the core analysis, the composite measure of episodic memory was the outcome, and the model included terms for distress proneness (centred at or near the median), time in years since baseline, and their interaction. The model also included terms to control for the effects of age, sex, and education on baseline level and rate of change of episodic memory. The term for distress proneness indicates the average effect of 1 point on the distress proneness scale upon the baseline episodic memory score of a typical participant. The term for time indicates the average annual change in episodic memory for a typical participant. The interaction tests whether distress proneness is related to rate of episodic memory decline.

We conducted additional analyses to see if the informant's relationship to the participant affected results. We first repeated the core model with terms added for informant relationship (spouse versus other) and its interaction with

time. We then repeated the latter model with terms for the interaction of distress proneness with relationship and for the triple interaction of distress proneness, relationship, and time.

We repeated the core model separately for each of the remaining three composite measures of cognition. We then repeated this set of analyses for each of the other four premorbid personality traits. Model assumptions were examined graphically and analytically and found to be adequately met. Analyses were carried out in SAS.[38]

RESULTS

Premorbid personality measures

Scores on each premorbid personality trait measure ranged from 0 to 20, with higher scores indicating a higher level of the trait (table 2). The distributions of distress proneness, extraversion, and intellect were approximately symmetrical, whereas the distributions of agreeableness and conscientiousness were negatively skewed, with most persons reported to have had high levels of these traits before dementia onset. Cronbach's coefficient α ranged from 0.85 to 0.92, indicating a high degree of internal consistency for each trait scale. Correlations between traits were of modest size and similar in pattern to those found with self report measures of these traits,[14] supporting the validity of the current measures. On average, ratings by spouses, compared with observers other than the spouse, were lower for distress proneness ($t_{[357]} = 2.60$, $p = 0.010$), higher for agreeableness ($t_{[353]} = 3.07$, $p = 0.002$), and did not differ for the other three traits (all $p > 0.50$).

Distress proneness, cognitive impairment, and cognitive decline

We began the analyses with the composite measure of episodic memory. At baseline, it ranged from −1.521 to 1.863, with higher scores indicating better memory function (table 1). We examined the relation of distress proneness to baseline level of episodic memory and to annual rate of episodic memory decline in a random effects model which also included terms to control for the potentially confounding effects of age, sex, and education (table 3). Distress proneness was inversely related to episodic memory at baseline, as shown by the term for distress proneness in the table. There was an average reduction of 0.019 unit in the baseline memory score (95% confidence interval (CI), −0.003 to −0.035) for each point on the distress proneness scale. Thus a person with a low level of distress proneness (score = 3, 25th centile) had a predicted baseline episodic memory score of 0.193, which was more than three times the score of 0.060 predicted for a person with a high level of distress proneness (score = 10, 75th centile).

The episodic memory score declined an average of 0.275 unit per year (95% CI, −0.338 to −0.212) in a typical participant, as shown by the term for time in table 3. Distress proneness was unrelated to rate of episodic memory decline, however, as shown by the lack of an interaction between distress proneness and time.

Because the relationship between the informant and participant was associated with distress proneness score, we repeated the analysis with terms added for informant relationship (that is, spouse *v* non-spouse) and its interaction with time. The association of distress proneness with baseline episodic memory score was unchanged in this model (mean (SE) estimate, −0.018 (−0.008), $p = 0.024$). In a subsequent model, we found no evidence that the association of distress proneness with baseline episodic memory varied according to informant relationship ($p = 0.761$ for interaction of distress proneness with relation).

We examined the association of distress proneness with composite measures of visuoconstruction, repetition, and naming in similar analyses (table 3). The average annual rate of decline in each of these cognitive domains was substantial, as shown by the term for time in each model. Distress proneness was not significantly related to initial level of function or rate of decline in these other cognitive domains or in a measure of global cognition based on tests from all four functional domains.

Other traits, cognitive impairment, and cognitive decline

We examined the association of each of the remaining four traits (that is, extraversion, intellect, agreeableness, conscientiousness) with baseline level of function and rate of change in each of the four specific cognitive measures (episodic memory, visuoconstruction, repetition, naming) and the measure of global cognition in separate random effects models. Each analysis controlled for the effects of age, sex, and education. None of the four premorbid personality traits was significantly related to initial level of or rate of decline in any of the five cognitive function measures (all $p > 0.05$, data not shown).

DISCUSSION

In this cohort of more than 300 persons with clinically diagnosed Alzheimer's disease, we asked knowledgeable informants to describe persons before dementia onset using standard measures of five personality traits. We found that the tendency to experience negative emotional states was associated with episodic memory impairment at baseline but not with impairment in other cognitive domains, nor with decline in episodic memory or other cognitive domains. The results suggest that premorbid proneness to experience psychological distress may contribute to episodic memory impairment in persons with mild to moderate Alzheimer's disease.

We are not aware of previous studies of the relation of distress proneness to impairment of or decline in memory in Alzheimer's disease. There is evidence, however, that distress proneness is related to episodic memory impairment in older persons without dementia.[39] Our findings suggest that this

Table 2 Psychometric information on measures of premorbid personality traits

				Correlations*				
Trait	Mean (SD)	Range	α†	Distress proneness	Extraversion	Intellect	Agreeableness	Conscientiousness
Distress proneness	7.0 (4.8)	0 to 20	0.89	–	−0.05	−0.09	−0.44	−0.29
Extraversion	11.7 (4.7)	0 to 20	0.87		–	0.30	0.12	0.05
Intellect	12.1 (4.4)	1 to 20	0.85			–	0.19	0.24
Agreeableness	17.5 (3.8)	0 to 20	0.90				–	0.43
Conscientiousness	17.1 (4.1)	0 to 20	0.92					–

*$p < 0.05$ for correlations with an absolute value of 0.12 or more.
†Cronbach's coefficient α, a measure of internal consistency.

Table 3 Association of distress proneness with baseline level of function and annual rate of change in different cognitive domains, based on separate random effects models*

Cognitive domain	Model term	Estimate	SE	p Value
Episodic memory	Distress proneness	−0.019	0.008	0.021
	Time	−0.275	0.032	<0.001
	Distress proneness × time	−0.001	0.003	0.795
Visuoconstruction	Distress proneness	−0.011	0.010	0.264
	Time	−0.524	0.071	<0.001
	Distress proneness × time	−0.011	0.008	0.128
Repetition	Distress proneness	−0.012	0.010	0.240
	Time	−0.615	0.068	<0.001
	Distress proneness × time	0.004	0.007	0.541
Naming	Distress proneness	0.003	0.011	0.793
	Time	−0.768	0.084	<0.001
	Distress proneness × time	−0.005	0.009	0.552
Global cognition	Distress proneness	−0.010	0.008	0.172
	Time	−0.547	0.054	<0.001
	Distress proneness × time	<0.001	0.006	0.983

*Results show the effect of a 1 unit change in the distress proneness score. Age, sex, and education and their interactions with time (measured in years) were also adjusted for in each model.

association between distress proneness and episodic memory impairment is still discernable among persons with mild to moderately severe Alzheimer's disease. We found no evidence, however, that premorbid proneness to distress affected disease progression.

How might distress proneness contribute to episodic memory impairment in Alzheimer's disease yet not be related to progressive decline in memory and cognition, the distinguishing feature of the disease? One possibility is that distress proneness contributes to episodic memory impairment independently of Alzheimer's disease. This possibility is supported by two observations. First, because distress proneness is remarkably stable throughout adulthood[16 17] and strongly related to the levels of psychological distress that people actually experience,[18 19] it is an indicator in older persons of the level of negative emotional states experienced during the life span. Second, as noted above, the hippocampal formation—by virtue of its central role in regulation of the hypothalamic–pituitary–adrenal stress axis[40]—is especially vulnerable to chronic stress,[3] with resulting structural changes[5–8] and impairment of forms of learning and memory mediated by the hippocampus.[4 9 10] An implication of this hypothesis is that persons who are relatively more prone to experiencing psychological distress may be at increased risk of developing Alzheimer's disease compared with those who are less distress-prone because less Alzheimer's disease pathology would be needed to cause clinical dementia.

Consistent with this hypothesis is the observation that depressive symptomatology—a common form of psychological distress—is related to risk of Alzheimer's disease[41 42] and to decline in cognitive function,[42–45] especially episodic memory.[42] Among persons with manifest dementia, we found that distress proneness was not related to cognitive decline, but such a finding is not uncommon for Alzheimer's disease risk factors (for example, age, apolipoprotein Eε4).

We also assessed premorbid levels of four other traits: extraversion, intellect, agreeableness, and conscientiousness. None of those traits was related to baseline level of function or rate of decline in memory or other cognitive domains. Overall, therefore, these results suggest that individual differences in personality before dementia onset are not related to individual differences in the rate at which memory and cognitive decline progresses in affected persons.

Confidence in these findings is strengthened by several factors. The clinical diagnosis of Alzheimer's disease was based on a uniform structured evaluation and widely accepted criteria applied by a board certified neurologist, and it has been confirmed in a high proportion of cases at necropsy,[29] reducing the likelihood of diagnostic misclassification. We used previously established composite measures of episodic memory and other cognitive functions, reducing the possibility that floor or ceiling artefacts, or other forms of measurement error, affected the results. The availability of an average of about four annual observations per person with a high rate of follow up participation enhanced our ability to model individual patterns of change in memory and cognition reliably and to test the association of each trait with initial level of function and rate of change.

An important limitation of this study is that we assessed premorbid personality traits retrospectively by asking an informant to describe the person before dementia onset. It is possible, therefore, that the informant's ratings were somehow biased by the participant's condition at baseline, especially by dementia severity. However, such a bias does not explain the differential association of distress proneness with episodic memory compared with other cognitive functions. In addition, because more severe cognitive impairment at baseline was associated with more rapid cognitive decline in this cohort,[29] such a bias should result in an association between a negative trait like distress proneness and cognitive decline, but no such association was observed. Nonetheless, a more secure understanding of the relation of distress proneness with Alzheimer's disease will require longitudinal prospective studies in which personality traits are measured before dementia onset.

Another limitation is that participants were selected from a memory disorders clinic. Because many persons with Alzheimer's disease do not come to medical attention, it is unlikely that the full range of personality and disease severity is represented in this study. Longitudinal studies of population based samples are needed.

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REFERENCES

1 **Grober E**, Dickson D, Sliwinski MJ, *et al*. Memory and mental status correlates of modified Braak staging. *Neurobiol Aging* 1999;**20**:573–9.
2 **Riley KP**, Snowdon DA, Markesbery WR. Alzheimer's neurofibrillary pathology and the spectrum of cognitive function: findings from the Nun study. *Ann Neurol* 2002;**51**:567–77.
3 **Sapolsky RM**. Glucocorticoids and hippocampal atrophy in neuropsychiatric disorders. *Arch Gen Psychiatry* 2000;**57**:925–35.
4 **Baker KB**, Kim JJ. Effects of stress and hippocampal NMDA receptor antagonism on recognition memory in rats. *Learn Mem* 2002;**9**:58–65.
5 **Gould E**, Tanapat P, McEwen BS, *et al*. Proliferation of granule cell precursors in the dentate gyrus of adult monkeys is diminished by stress. *Proc Natl Acad Sci USA* 1998;**95**:3168–71.
6 **Magarinos AM**, Verdugo JMG, McEwen BS. Chronic stress alters synaptic terminal structure in hippocampus. *Proc Natl Acad Sci USA* 1997;**94**:14002–8.
7 **Frodl T**, Meisenzahl EM, Zetzche T, *et al*. Hippocampal changes in patients with a first episodic of major depression. *Am J Psychiatry* 2002;**159**:1112–18.
8 **Sheline YI**, Wang PW, Gado MH, *et al*. Hippocampal atrophy in recurrent major depression. *Proc Natl Acad Sci USA* 1996;**93**:3908–13.
9 **Lupien SJ**, Gaudreau S, Tchiteya BM, *et al*. Stress-induced declarative memory impairment in healthy elderly subjects: relationship to cortisol reactivity. *J Clin Endocrinol Metab* 1997;**82**:2070–5.
10 **Payne JD**, Nadel L, Allen JJ, *et al*. The effects of experimentally induced stress on false recognition. *Memory* 2002;**10**:1–6.
11 **Squire LR**. Memory and the hippocampus: a synthesis from findings with rats, monkeys, and humans. *Psychol Rev* 1992;**99**:195–231.
12 **Rasmusson AM**, Shi L, Duman R. Downregulation of BDNF and mRNA in the hippocampal dentate gyrus after re-exposure to cues previously associated with footshock. *Neuropsychopharmacology* 2002;**27**:133–42.
13 **Watson D**, Clark LA. Negative affectivity: the disposition to experience aversive emotional states. *Psych Bull* 1984;**96**:465–90.
14 **Costa PT**, McCrae RR. *Revised NEO personality inventory (NEO-PI-R) and NEO five-factor inventory (NEO-FFI) professional manual*. Odessa, FL: Psychological Assessment Resources, 1992.
15 **Goldberg LR**. An alternative ''description of personality'': the big-five structure. *J Pers Soc Psychol* 1990;**59**:1216–29.
16 **Hultsch D**, Hertzog C, Small B, *et al*. Use it or lose it: engaged lifestyle as a buffer of cognitive decline in aging? *Psychol Aging* 1999;**14**:245–63.
17 **Costa PT**, McCrae RR. Personality in adulthood: a six-year longitudinal study of self-reports and spouse ratings on the NEO personality inventory. *J Pers Soc Psychol* 1988;**54**:853–63.
18 **Magnus K**, Diener E, Fujita F, *et al*. Extraversion and neuroticism as predictors of objective life event: a longitudinal analysis. *J Pers Soc Psychol* 1993;**65**:1046–53.
19 **Ormel J**, Wohlfarth T. How neuroticism, long-term difficulties, and life situation change influence psychological distress: a longitudinal model. *J Pers Soc Psychol* 1991;**60**:744–55.
20 **Depue RA**, Monroe SM. Conceptualization and measurement of human disorder in life stress research: the problem of chronic disturbance. *Psychol Bull* 1986;**99**:36–51.
21 **Folstein M**, Folstein S, McHugh P. Mini-Mental State: a practical method for grading the mental state of patients for the clinician. *J Psychiatric Res* 1975;**12**:189–98.
22 **Morris J**, Heyman A, Mohs R, *et al*. The consortium to establish a registry for Alzheimer's Disease (CERAD), part I: clinical and neuropsychological assessment of Alzheimer's disease. *Neurology* 1989;**39**:1159–65.
23 **Quality Standards Subcommittee, American Academy of Neurology**. Practice parameter for diagnosis and evaluation of dementia (summary statement). *Neurology* 1994;**44**:2203–6.
24 **Wilson RS**, Bennett DA, Gilley DW, *et al*. Progression of parkinsonian signs in Alzheimer's disease. *Neurology* 2000;**54**:1284–9.
25 **Wilson RS**, Bennett DA, Gilley DW, *et al*. Progression of parkinsonism and loss of cognitive function in Alzheimer's disease. *Arch Neurol* 2000;**57**:855–900.
26 **Wilson RS**, Gilley DW, Bennett DA, *et al*. Hallucinations, delusions and cognition decline in Alzheimer's disease. *J Neurol Neurosurg Psychiatry* 2000;**69**:172–7.
27 **Wilson RS**, Bennett DA, Gilley DW, *et al*. Premorbid reading activity and patterns of cognitive decline in Alzheimer's disease. *Arch Neurol* 2000;**57**:1718–23.
28 **McKhann G**, Drachman D, Folstein M, *et al*. Clinical diagnosis of Alzheimer's disease: report of the NINCDS/ADRDA work group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. *Neurology* 1984;**34**:939–44.
29 **Wilson RS**, Gilley DW, Bennett DA, *et al*. Person-specific paths of cognitive decline in Alzheimer's disease and their relation to age. *Psychol Aging* 2000;**15**:18–28.
30 **Albert M**, Smith L, Scherr P, *et al*. Use of brief cognitive tests to identify individuals in the community with clinically diagnosed Alzheimer's disease. *Int J Neurosci* 1991;**57**:167–78.
31 **Kaplan EF**, Goodglass H, Weintraub S. *The Boston naming test*. Philadelphia: Lea and Febiger, 1983.
32 **Benton AL**, Sivan AB, Hamsher K, *et al*. *Contributions to neuropsychological assessment*, 2nd ed. New York: Oxford University Press, 1994.
33 **Goodlass H**, Kaplan D. *The assessment of aphasia and related disorders*, 2nd ed. Philadelphia: Lea and Febiger, 1983.
34 **Hebert LE**, Wilson RS, Gilley DW, *et al*. Decline of language among women and men with Alzheimer's disease. *J Gerontol Psychol Sci* 2000;**55B**:354–60.
35 **Goldberg LR**. The development of markers for the big-five factor structure. *Psychol Assess* 1992;**4**:26–42.
36 **Laird N**, Ware J. Random-effects models for longitudinal data. *Biometrics* 1982;**38**:963–73.
37 **Wilson RS**, Beckett LA, Barnes LL, *et al*. Individual differences in rates of change in cognitive abilities of older persons. *Psychol Aging* 2002;**17**:179–93.
38 **SAS Institute Inc**. *SAS/STAT ® user's guide, version 8*. Cary, NC: SAS Institute, 2000.
39 **Meier B**, Perrig-Chiello P, Perrig W. Personality and memory in old age. *Aging Neuropsychol Cognit* 2002;**9**:135–44.
40 **McEwen BS**. Effects of adverse experiences for brain structure and function. *Biol Psychiatry* 2000;**48**:721–31.
41 **Devanand DP**, Sano M, Tang M-X, *et al*. Depressed mood and the incidence of Alzheimer's disease in the elderly living in the community. *Arch Gen Psychiatry* 1996;**53**:175–82.
42 **Wilson RS**, Barnes LL, Mendes de Leon CF, *et al*. Depressive symptoms, cognitive decline, and risk of AD in older persons. *Neurology* 2002;**59**:364–70.
43 **Bassuk SS**, Berkman LF, Wypij D. Depressive symptomatology and incident cognitive decline in an elderly community sample. *Arch Gen Psychiatry* 1998;**55**:1073–81.
44 **Yaffe K**, Blackwell T, Gore R, *et al*. Depressive symptoms and cognitive decline in nondemented elderly women. *Arch Gen Psychiatry* 1999;**56**:425–30.
45 **Paterniti S**, Verdier-Taillefer MH, Dufouil C, *et al*. Depressive symptoms and cognitive decline in elderly people. *Br J Psychiatry* 2002;**181**:406–10.