

Worries about Alzheimer's Disease and Subjective Cognitive Decline in Proxies of AD Patients and Controls

Annika Philipps¹, Stephan Müller¹, Oliver Preische^{1,2} and Christoph Laske^{1,2*}

¹Section for Dementia Research, Hertie Institute for Clinical Brain Research and Department of Psychiatry and Psychotherapy, University of Tübingen, Tübingen, Germany

²German Center for Neurodegenerative Diseases (DZNE), Tübingen, Germany

Abstract

Objective: Subjective Cognitive Decline (SCD) is actually considered to be associated with an increased likelihood of future cognitive impairment and dementia. Much less is known about worries concerning Alzheimer's disease (AD Worry) and their relation to SCD, SCD with worries (SCD+Worry) and objective cognitive performance.

Methods: We examined the prevalence and relation of AD Worry, SCD and SCD+Worry along with cognitive measures (MMSE, DemTect) among 100 proxies of persons with AD and 119 age-, gender- and education-matched controls.

Results: AD Worry, SCD and SCD+Worry were frequently present in proxies of persons with AD (64.0%/47.0%/21.0%) and controls (62.2%/51.3%/16.8%) without significant group differences concerning frequency of occurrence and cognitive measures. Among proxies of AD patients, AD Worry occurred more frequently in first degree relatives (sons/daughters; 76.5%) compared to spouses (45.5%; $p=0.002$). Proxies with AD Worry were significantly younger (58.9 years) than proxies with SCD+Worry (67.4 years; $p=0.012$). Proxies of AD patients with feelings of burden reported SCD (55.6%) significantly more frequently than proxies without feelings of burden (32.4%; $p=0.025$). Controls with AD Worry reported SCD+Worry (23.0%) significantly more frequently compared to controls without AD Worry (6.7%; $p=0.021$). In line with the latter result, there was a significant positive correlation between AD Worry and SCD+Worry ($r=0.211$, $p=0.021$) in the control sample.

Conclusion: AD Worry is a widespread phenomenon within the examined cohorts of proxies of AD patients and controls. It is not associated with objective cognitive impairment. However, the higher presence of SCD+Worry in those controls who reported AD Worry and the higher presence of AD Worry among sons and daughters of AD patients compared to spouses indicate that AD Worry could be an early indicator of future cognitive impairment. Longitudinal studies examining larger samples are needed to further elucidate the potential association between AD Worry, SCD and future cognitive decline.

Keywords: Worries about Alzheimer's disease; Subjective cognitive decline; Alzheimer's disease; Dementia; Proxies; Controls; Burden

Introduction

Subjective cognitive decline (SCD) is actually considered to be associated with an increased likelihood of future cognitive impairment and dementia, especially among those who worry about their memory [1-3]. According to the suggestions made by the Working Group of the Subjective Cognitive Decline Initiative (SCD-I) [4], SCD is defined as personal complaints about one's cognitive state in the absence of objective cognitive impairment. This definition of SCD was also used in the present study.

Much less is known about worries concerning Alzheimer's disease (AD Worry) and their relation to SCD, SCD with worries (SCD+Worry) and objective cognitive performance. Currently, there is no common definition of AD Worry. The term was first established by Cutler and Hodgson (1996) [5] who related this term to the concept of anticipatory dementia. They understand AD Worry as the perceived threat of getting AD [5,6]. This construct brings into focus whether someone believes to be at higher risk of developing dementia and is worried by this. While often assessed by a single question, a recent study used the Dementia Worry Scale developed by Suhr and Isgrigg [7]. This 15-items questionnaire inquires thoughts about developing or getting dementia [8]. Kessler et al. [9] used a more general definition of worries about dementia, combining affective and cognitive components influenced by the perceived threat of developing dementia. Our definition of AD Worry goes beyond the perception of personal dementia risk. The perception of the seriousness of a condition and coping resources apart

from the personal risk perception were found to play a role in worries about a specific condition [10]. AD Worry is a relatively unexplored phenomenon but widespread within the general population, at least in Western societies. Estimates of its community prevalence have ranged from 26% to 76.6% [11-16]. Cultural differences in the presence of AD Worry were reported in a few studies, worries about AD were found to be mostly common in Western cultures [9]. There is evidence that AD is one of the diseases most worried about. A recent survey among 1.697 British respondents found that dementia was the greatest concern about the later years of life for people over the age of 60 [17]. In international and national surveys, the prevalence of respondents reporting that AD is the disease getting which they fear most ranged from 20% in Poland to 47% in France [18,19].

About two thirds of persons suffering from dementia live in private households and are cared for by family and friends [20,21]. As the

***Corresponding author:** Christoph Laske, Section for Dementia Research, Department of Psychiatry and Psychotherapy, Calwer Street 14, D-72076 Tübingen, Germany, Tel: +4970712983444; E-mail: christoph.laske@med.uni-tuebingen.de

Received January 23, 2017; **Accepted** January 27, 2017; **Published** February 04, 2017

Citation: Philipps A, Müller S, Preische O, Laske C (2017) Worries about Alzheimer's Disease and Subjective Cognitive Decline in Proxies of AD Patients and Controls. J Alzheimers Dis Parkinsonism 7: 302. doi: [10.4172/2161-0460.1000302](https://doi.org/10.4172/2161-0460.1000302)

Copyright: © 2017 Philipps A, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

prevalence of dementia is expected to increase in the next decades [21,22], the number of needed caregivers will also highly increase in the future. This underlines the need for deeper investigation of the influence of caregiving for people with dementia on long-term effects.

The aim of the present study was to examine the prevalence and relation of AD Worry, SCD and SCD+Worry along with cognitive measures (Mini-Mental-State Examination [MMSE], Dem-Tect) among 100 proxies of persons with AD and 119 age-, gender- and education-matched controls.

Materials and Methods

Subjects

100 proxies of persons with AD and 119 age-, gender- and education- matched control subjects without a family history of AD or other types of dementia were included in the study (Table 1). This study was cross-sectional and performed in the Memory Clinic Tübingen or in the participants' home.

AD Worry was defined as present if participants stated to be worried about AD in general. SCD was defined as present if participants were cognitively unimpaired and stated to have decline in cognitive functioning unrelated to an event or condition explaining the cognitive deficits according to recent research criteria [4]. SCD+Worry were defined as present if participants had worries concerning their memory in addition to the presence of SCD.

The regional ethical committee approved the study and written informed consent was obtained from each individual.

Performed tests

All participants underwent clinical assessment of cognitive status by means of the scores on MMSE [23] and Dem-Tect [24]. Caregiver burden was assessed by the Zarit Burden Interview (ZBI) [25].

Data analysis

The statistical analysis was conducted with the software packages Excel (Microsoft Inc.) and SPSS-22. Parametric/non-parametric and correlation analyses were applied. For all tests, a probability of less than 0.05 was considered significant. We used the Kolmogorow-Smirnoff Test and Shapiro-Wilk Test to test for normality. Differences of normally distributed, interval and ratio data were assessed using the Independent Samples T-Test (Age, Years of Education). Levene's test was used to assess the homogeneity of variance. For detecting group differences of metric, not normally distributed or ordinal data we applied the nonparametric Mann-Whitney U test (MMSE score, Dem-Tect score, ZBI score). The Pearson's chi-squared test was used for

Feature	Proxies (N=100)	Controls (N=119)	P-Value
Gender (m/f) (%)	35.0/65.0	42.0/58.0	0.29
Age ^a	61.0 (13.0)	60.6 (9.5)	0.78
Education ^a (years)	14.6 (3.5)	14.6 (3.4)	0.94
MMSE ^b	29.0 (1.0)	29.0 (1.3)	0.84
Dem-Tect ^b	17.0 (2.5)	17.0 (2.1)	0.97
AD Worry (%)	64.0	62.2	0.78
SCD (%)	47.0	51.3	0.53
SCD + Worry (%)	21.0	16.8	0.43

^aData as mean; standard deviation in breaks; ^bdata as median; standard deviation in breaks

Table 1: Descriptive statistics for relevant study variables in proxies and controls.

detecting group differences of nominal data (Gender, AD Worry, SCD, SCD+Worry, Caregiver Burden).

Correlations between AD Worry, SCD+Worry and measures on demographics, anxiety, memory and depression were computed for controls and proxies. We calculated the phi coefficient to measure the association of two binary variables and Cramer's V for nominal variables having two or more levels.

Results

All study participants

All demographic and neuropsychological parameters are displayed in (Table 1). AD Worry, SCD and SCD+Worry were frequently present in proxies of persons with AD (64.0%/47.0%/21.0%) and controls (62.2%/51.3%/16.8%) without significant group differences concerning frequency of occurrence and cognitive measures.

Proxies

Table 2 compares the demographic and neuropsychological measures in proxies who reported AD Worry and among those who did not worry about AD.

Among proxies of AD patients, AD Worry occurred more frequently among first degree relatives (sons/daughters; 76.5%) than among spouses (45.5%; p=0.002). Proxies with AD Worry were significantly younger (58.9 years) than proxies with SCD+Worry (67.4 years; p=0.012). Among proxies of AD patients who reported feelings of burden SCD was more frequent (55.6%) than among proxies without feelings of burden (32.4%; p=0.025).

Controls

Table 3 represents the comparison of controls who reported

Feature	PW ¹ (N=64)	PNW ² (N=46)	P-Value
Gender (m/f) (%)	34.4/65.6	36.1/63.9	0.86
Age ^a	58.9 (12.3)	64.9 (13.3)	0.03
Education ^a (years)	14.5 (3.6)	14.8 (3.4)	0.60
MMSE ^b	29.0 (1.0)	30.0 (1.2)	0.13
Dem-Tect ^b	17.0 (2.4)	17.0 (2.7)	0.56
SCD (%)	51.6	38.9	0.22
SCD+Worry (%)	26.6	11.1	0.07

¹Proxies who reported to worry about AD; ²proxies who reported not to worry about AD; ^adata as mean; standard deviation in breaks; ^bdata as median; standard deviation in breaks

Table 2: Descriptive statistics for relevant study variables in proxies who reported to worry about AD and proxies without AD worry.

Feature	CW ¹ (N=74)	CNW ² (N=45)	P-Value
Gender (m/f) (%)	36.5/63.5	51.1/48.9	0.12
Age ^a	60.3 (10.0)	61.1 (8.6)	0.67
Education ^a (years)	14.4 (3.2)	14.9 (3.7)	0.62
MMSE ^b	29.0 (1.4)	29.0 (0.9)	0.91
Dem-Tect ^b	17.0 (2.2)	17.0 (2.1)	0.58
SCD (%)	55.4	44.4	0.25
SCD+Worry (%)	23.0	6.7	0.021

¹Proxies who reported to worry about AD; ²proxies who reported not to worry about AD; ^adata as mean; standard deviation in breaks; ^bdata as median; standard deviation in breaks

Table 3: Descriptive statistics for relevant study variables in controls who reported to worry about AD and controls without AD worry.

AD Worry with those who did not worry about AD. Controls with AD Worry reported SCD+Worry (23.0%) significantly more often compared to controls without AD Worry (6.7%; $p=0.021$). In line with the latter result, there was a significant positive correlation between AD Worry and SCD+Worry ($r=0.211$, $p=0.021$) in the control sample.

Discussion

In the present study, we investigated AD Worry and SCD among proxies of AD patients versus an age-, education- and gender-matched random sample. Thus, we were able to compare individuals familiar with the character and course of AD due to their family history with individuals of a random sample whose knowledge of AD is rather tenuous.

The main findings of the present study are: 1) SCD and AD Worry were equally frequent among both, proxies of AD patients and random controls. 2) Cognitive performance of individuals with AD Worry, SCD and SCD+Worry was comparable to those without AD Worry, SCD and SCD+Worry within the normal range. 3) SCD+Worry was more frequent in controls with AD Worry than in those without AD Worry 4) Among proxies of AD patients, AD Worry occurred more often in first degree relatives (sons/daughters; 76.5%) compared to spouses (45.5%; $p=0.002$). 5) Proxies of AD patients with feelings of caregiver burden reported SCD more often than individuals without such feelings.

AD Worry is a frequent phenomenon occurring in more than two thirds of each examined sample which underlines the need to understand AD Worry within the general population. Though multifactorial, AD Worry does not seem to be associated with objective cognitive impairment. SCD is widely considered to be associated with future cognitive impairment and is therefore used as a screening tool for detecting preclinical stages of dementia [1,26-29]. Our finding of a higher frequency of SCD+Worry in controls with AD Worry compared to those without AD Worry indicates that AD Worry could be an early indicator of future cognitive impairment. Our additional finding that AD Worry occurred more frequently in first degree relatives - bearing a genetically driven increased risk of future AD development [30-32] compared to spouses points in the same direction. The finding that proxies of AD patients with feelings of caregiver burden reported SCD more often than individuals without such feelings and data from a previous study [33] suggests that proxies of AD patients experiencing caregiver burden might be at higher risk of future cognitive impairment. If caregiver stress was proven to increase personal dementia risk this would have serious consequences for our society as the majority of persons with dementia is cared for by their friends or family [20,21].

As to limitations of the study: the examined sample size was rather small ($n=219$), underlining the necessity of studies with larger samples. In order to broadly examine the factors related to SCD and AD Worry among proxies, we have chosen a cross-sectional study design. A drawback of this design is that it is not possible to investigate the association of SCD or AD Worry to future cognitive impairment. This suggests the need for longitudinal studies examining larger samples. Furthermore, the neuropsychological assessment used in the present study was based on MMSE and Dem-Tect, which may have been not sensitive enough to detect very early signs of cognitive impairment in the examined individuals. In addition, there is currently no general definition of AD Worry, making comparison of results from different working groups rather difficult. In this context, a next step should be to develop a common definition of worries about AD as this has been done for SCD by the SCD-I [4]. In the context of recent neurophysiological data, the application of non-invasive brain stimulation techniques

such as transcranial magnetic stimulation (TMS) seems to be useful to identify those individuals in whom cholinergic degeneration has occurred [34]. Thus, such diagnostic measures should be included in future studies.

Conclusion

AD Worry is a widespread phenomenon within the examined cohorts of proxies of AD patients and controls and is not associated with objective cognitive impairment. However, the higher presence of SCD+Worry in those controls with AD Worry and the higher presence of AD Worry in first degree relatives of AD patients compared to spouses indicate that AD Worry could be an early indicator of future cognitive impairment. Longitudinal studies examining larger samples are needed to further elucidate the potential association between AD Worry, SCD and future cognitive decline.

Acknowledgement

We acknowledge support by Deutsche Forschungsgemeinschaft and Open Access Publishing Fund of University of Tübingen.

References

1. Jessen F, Wiese B, Bachmann C, Eifflaender-Gorfer S, Haller F, et al. (2010) Prediction of dementia by subjective memory impairment: Effects of severity and temporal association with cognitive impairment. *Arch Gen Psychiatry* 67: 414-422.
2. Reisberg B, Gauthier S (2008) Current evidence for subjective cognitive impairment (SCI) as the pre-mild cognitive impairment (MCI) stage of subsequently manifest Alzheimer's disease. *Int Psychogeriatr* 20: 1-16.
3. van Oijen M, de Jong FJ, Hofman A, Koudstaal PJ, Breteler MM (2007) Subjective memory complaints, education, and risk of Alzheimer's disease. *Alzheimers Dement* 3: 92-97.
4. Jessen F, Wolfgruber S, Wiese B, Bickel H, Mösch E, et al. (2014) AD dementia risk in late MCI, in early MCI, and in subjective memory impairment. *Alzheimers Dement* 10: 76-83.
5. Cutler SJ, Hodgson LG (1996) Anticipatory dementia: A link between memory appraisals and concerns about developing Alzheimer's disease. *Gerontologist* 36: 657-664.
6. Cutler SJ, Hodgson LG (2001) Correlates of personal concerns about developing Alzheimer's disease among middle-aged persons. *Am J Alzheimer's Dis Other Dement* 16: 335-343.
7. Suhr JA, Isgrigg A (2011) Development and initial validation of an Alzheimer's disease worry scale. Annual meeting of the International Neuropsychological Society, Boston, MA.
8. Kinzer A, Suhr JA (2016) Dementia worry and its relationship to dementia exposure, psychological factors and subjective memory concerns. *Appl Neuropsychol Adult* 23: 196-204.
9. Kessler EM, Bowen CE, Baer M, Froelich L, Wahl HW (2012) Dementia worry: A psychological examination of an unexplored phenomenon. *Eur J Ageing* 9: 275-284.
10. Rosenstock IM (1974) Historical origins of the health belief model. *Health Education and Behavior* 2: 328-335.
11. Connell CM, Scott Roberts J, McLaughlin SJ (2007) Public opinion about Alzheimer disease among blacks, Hispanics and whites: Results from a national survey. *Alzheimer Dis Assoc Disord* 21: 232-240.
12. Cantegreil-Kallen I, Pin S (2012) Fear of Alzheimer's disease in the French population: Impact of age and proximity to the disease. *Int Psychogeriatr* 24: 108-116.
13. Roberts JS, McLaughlin SJ, Connell CM (2014) Public beliefs and knowledge about risk and protective factors for Alzheimer's disease. *Alzheimers Dement* 10: S381-389.
14. Zeng F, Xie WT, Wang YJ, Luo HB, Shi XQ, et al. (2015) General public perceptions and attitudes toward Alzheimer's disease from five cities in China. *J Alzheimers Dis* 43: 511-518.

15. Low LF, Anstey KJ (2009) Dementia literacy: Recognition and beliefs on dementia of the Australian public. *Alzheimers Dement* 5: 43-49.
16. New survey shows African-Americans are concerned with heart health but unaware of link to brain health (2008) Alzheimer's Association, Chicago.
17. Jordan W, Dahlgreen W (2015) YouGov: Alzheimer's the greatest concern for over-60s. YouGov: What the world thinks.
18. Harvard School of Public Health/Alzheimer Europe (2011) Five-country Alzheimer's disease survey. Alzheimer's Association, Chicago.
19. Alzheimer's Research UK (2011) The Alzheimer's Research Trust became Alzheimer's research UK at the House of Commons.
20. Schulz R, Martire LM (2004) Family caregiving of persons with dementia: Prevalence, health effects and support strategies. *Am J Geriatr Psychiatry* 12: 240-249.
21. Sütterlin S, Hoßmann I, Klingholz R (2011) Berlin-Institut für Bevölkerung und Entwicklung. Demenz-Report.
22. Ferri CP, Prince M, Brayne C, Brodaty H, Fratiglioni L, et al. (2005) Global prevalence of dementia: A delphi consensus study. *Lancet* 366: 2112-2117.
23. Folstein MF, Folstein SE, McHugh PR (1975) Mini-mental state. A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 12: 189-198.
24. Kalbe E, Kessler J, Calabrese P, Smith R, Passmore AP, et al. (2004) Dem tect: A new, sensitive cognitive screening test to support the diagnosis of mild cognitive impairment and early dementia. *Int J Geriatr Psychiatry* 19: 136-143.
25. Zarit SH, Orr NK, Arit JM (1985) The hidden victims of Alzheimer's disease: Families under stress. New York University Press.
26. Koppa A, Riedel-Heller S, Weyerer S, Bickel H, Pentzek M, et al. (2013) Subjective memory impairment in healthy elderly specifically predicts decline in episodic memory over 8 years. *Alzheimers Dement* 9: 782.
27. Kryscio RJ, Abner EL, Cooper GE, Fardo DW, Jicha GA, et al. (2014) Self-reported memory complaints: Implications from a longitudinal cohort with autopsies. *Neurology* 83: 1359-1365.
28. Stone J, Pal S, Blackburn D, Reuber M, et al. (2015) Functional (Psychogenic) cognitive disorders: A perspective from the neurology clinic. *J Alzheimers Dis* 48 Suppl 1: S5-S17.
29. Amariglio R (2013) Subjective cognitive concerns as an early indicator of Alzheimer's disease pathology. *Alzheimers Dement* 9: 824-825.
30. Farrer LA, O'Sullivan DM, Cupples LA, Growdon JH, Myers RH (1989) Assessment of genetic risk for alzheimer's disease among first-degree relatives. *Ann Neurol* 25: 485-493.
31. Silverman JM, Li G, Zaccario ML, Smith CJ, Schmeidler J, et al. (1994) Patterns of risk in first-degree relatives of patients with Alzheimer's disease. *Arch Gen Psychiatry* 51: 577-586.
32. Green RC, Cupples LA, Go R, Benke KS, Edeki T, et al. (2002) Risk of dementia among white and African American relatives of patients with alzheimer disease. *JAMA* 287: 329-336.
33. Norton MC, Smith KR, Østbye T, Tschanz JT, Corcoran C, et al. (2010) Greater risk of dementia when spouse has dementia? The cache county study. *J Am Geriatr Soc* 58: 895-900.
34. Bella R, Cantone M, Lanza G, Ferri R, Vinciguerra L, et al. (2016) Cholinergic circuitry functioning in patients with vascular cognitive impairment--no dementia. *Brain Stimul* 9: 225-233.