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ORIGINAL PAPER

Cognitive Differences in Subjective Cognitive Decline with and without Associated Worry

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ABSTRACT

Objectives: *Subjective cognitive decline (SCD) is a heterogenous concept that has been associated with future objective cognitive decline. Our objective was to assess the cognitive function of three groups: one with SCD who claimed to be worried about their symptoms, one with SCD who did not claim to be worried about their symptoms and one without SCD (control group).*

Materials and methods: *We designed a cross-sectional study including people from primary care units and a memory center. We collected socio-demographic and clinical characteristics of all participants who signed informed consent prior to inclusion. Those with current major depression, anxiety disorder and neurocognitive disorder were excluded. Cognitive evaluation was performed using the Mini–Mental State Examination (MMSE), Rey Auditory-Verbal Learning Test, Rey complex figure test, Trail Making Test A and B and Verbal Fluency Test. Descriptive statistics were used to characterize the sample. We used Chi-Square to analyze categorical variables, ANOVA for normally distributed continuous variables and Kruskal-Wallis for non-normally distributed continuous variables. Statistically significance was established at p<0.05.*

Results: *There were 101 patients included in the analysis, of which 49.50% in the "Yes, and it worries me" group (A), 16.83% in the "Yes, but it does not worry me" (B) group and 33.66% in the control group (C) (participants who answered "No"). There was a statistically significant difference regarding age status (p=.048) between groups A and C. Participants who expressed worry regarding their SCD symptoms had an increased negative emotion trait compared to the control group. There were statistically significant differences in attention and immediate memory between groups A and C.*

Conclusions: *Individuals with SCD and associated worry performed worse in auditory and verbal memory testing when compared to the control group. Longitudinal assessment is necessary to establish firm causal relationships between SCD, personality traits and cognitive function.*

Keywords: subjective cognitive decline, cognition, anxiety, worry.

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INTRODUCTION

Subjective cognitive decline (SCD) is generally understood to be the first segment in the pathological continuum of neurodegenerative disorders, before mild cognitive impairment (MCI) and dementia (1). There is a large body of evidence to attest that individuals with SCD are significantly more at risk for developing objective cognitive impairment (2, 3), with SCD preceding objective cognitive decline by around 10 years (4).

However, the utility of treating SCD as a separate disease entity has been often called into question. Most people who experience it never go on to develop objective cognitive impairment (5) and it is present in several non-degenerative psychiatric and somatic conditions as well as in normal aging (6). In a bid for conceptual clarification, Jessen *et al* elaborated several criteria for detecting high risk cases (1), one of which was associated with excessive worry. The feeling of worry can be due to several conditions such as anxiety, depression or personality traits or a combination of these, increasing its heterogeneity. For this reason, Jessen and the SCD-Initiative (SCD-I) advice that research on SCD should include the evaluation of present or past anxiety disorders, major depression and personality traits in order to better control their possible confounding effect on SCD and future cognitive decline. It is known that neuroticism (defined as the personality trait where people perceive negative emotions such as anxiety, depression, anger, regret more often and more intensely than other people) is a risk factor for both developing SCD (7) and further cognitive decline in those already suffering from it. Subsequent research has confirmed that associated worry is indeed a predictor for progression to MCI in individuals with SCD (8).

The aim of our study was to compare the cognitive function of three groups: people with SCD who are worried about it (group A), people with SCD who are not worried about it (group B) and people without SCD (group C). In doing so, we wanted to determine whether worry over cognitive decline is strictly due to higher neuroticism or is a consequence of an actual difference in cognitive performance which may herald a higher risk of future decline.

MATERIAL AND METHODS

We designed a cross-sectional study including patients recruited from practices of their general practitioners (GPs) during routine checkup visits. All participants provided an informed consent prior to inclusion and the study was conducted according to the Declaration of Helsinki (9). The study had the ethics approval from the local institutional review board (IRB).

We collected social, demographic and clinical information as well as a comprehensive psychiatric history. We also evaluated the history of physical illness by interviewing the patient and screening GP records. We grouped hypertension and type 2 diabetes separately because these were the most commonly seen somatic diseases, while other somatic disorders were grouped under "Other somatic diseases". We also presented data on the medication status for somatic disease. Participants with current anxiety disorders (HAM-A score over 17) or major depressive disorder (HAM-D score over 12) were excluded. For cognitive evaluation we used MMSE (10), Rey Auditory-Verbal Learning Test (RAVLT) (11), Rey-Osterrieth Complex Figure Test (12), Verbal Fluency and Trail Making Test (TMT) (11). We examined some of the possible confounders for SCD, including personality traits by using the BIG Five Short Form Questionnaire (13) , the level of physical activity by using the International Physical Activity Questionnaire (IPAQ) (14) , and sleep by using Pittsburgh Sleep Quality Index (PSQI) (15) .

Subjective cognitive decline was evaluated according to Jessen *et al* (16) using the question "Do you feel that you are having difficulties with your memory?", with the following possible answers: "Yes, and it worries me", "Yes, but it does not worry me" and "No". Jessen considered that there might be differences between persons who picked one of the two "Yes" responses. More specifically, the presence of anxiety related to the presence of subjective cognitive impairment could represents the highest risk category for further cognitive decline.

Hachinski Ischaemia Score (17) evaluates the probability that a patient has either vascular dementia, degenerative dementia or a mixed form. A score above 4 increases the probability of vascular etiology.

Mini-Mental State Examination (10) is a short test which evaluates attention, memory, calcula-

tion, visuo-spatial ability and executive functioning. A score over 24 generally represents a lack of cognitive impairment. The Romanian adaptation of MMSE-2 Standard Version (18) presents a cut-off of 25.6 (±1.8) for MCI. The mean score was 24.75 (±3) for a general population sample aged between 60-64 years, who had 5-8 years of education, and 28.6 (±2.25) for participants with over 16 years of education.

The RAVLT is designed to evaluate verbal memory. During the first five trials, the patient has to learn a list of 15 words that are read to him/her before each trial. Then, the participant is asked to recall the words from the first list (Trial 6) after being distracted by another verbal memorizing task. Trial 7 (Delay) is done after a five-minute break and the patient is asked to recall as many words as possible without hearing the list. During the last examination of RAVLT (Recognition), the participant has to recognize the 15 words from a text.

The Rey-Osterreith Complex Figure Test consists of two trials which examine memory, visuo-spatial ability and executive function. It involves a copying trial and a memorizing trial. The maximum score for each trial is 36.

The verbal fluency test (VFT) examines patients' verbal ability and executive function. We conducted three trials using the same three letters in the same order for all patients. In our analysis we summed all the correct words from all three trials into a single score (VFT Total).

The trail making test (TMT) examines a variety of cognitive functions such as attention, visual and spatial ability, sequencing and shifting, psychomotor speed, abstraction, flexibility and executive function (11). It consists of two trials which are timed, with trial B having an increased difficulty compared to trial A. The cutoff for trial A is considered 78 seconds and for trial B, 273 seconds.(19)

The BIG FIVE Short Version is a questionnaire that evaluates personality across five domains: Extraversion, Agreeableness, Conscientiousness, Negative Emotionality and Open-Mindedness. Continuous scores are computed according to scoring instructions for each domain, with increased scores representing more prominent personality traits.

The International Physical Activity Questionnaire (IPAQ) evaluates health-related physical activity performed in the prior week. Scores for each domain are calculated in multiples of resting metabolic rates (METs) performed for minutes (MET-minutes).

The Pittsburgh Sleep Quality Index (PSQI) is a self-administered questionnaire which examines sleep quality over the last month. Patients with total scores over 5 are considered to have poor sleep quality.

Statistical analysis

All analyses were performed using SPSS Statistics v26 (IBM). We presented the sample characteristics using descriptive statistics. We used Chi-Square to analyze categorical variables such as gender, locative status, presence of hypertension or type 2 diabetes and ANOVA (for normally distributed data) or Kruskall-Wallis (for non-parametric data) to analyze continuous data such as age, education and questionnaire scores, using pair comparison. Categorical data was presented with number of participants (%) and continuous data as mean (standard deviation) for normally distributed data and median (inter-quartile range) for non-parametric data. Statistical significance was defined as p below .05, 2-sided.

OUTCOMES

There were 101 patients included in our analysis, of which 49.50% (N=50) were included in the "Yes, and it worries me" group (A), 16.83% (N=17) in the "Yes, but it does not worry me" (B) group, and 33.66% (N=34) in the control group (participants who answered "No" (group C). Patients who answered with "Yes" are considered to have subjective cognitive decline (either "Yes, and it worries me" or "Yes, but it does not worry me").

There were statistically significant differences between the worried and control groups regarding age (p=.048), with worried participants being slightly older than controls (63.5 IQR 56-69 compared to 59.5 IQR 52-67). The same groups presented statistically significant differences in Hachinski score (p=.028) and negative emotion personality trait (p=.017). The worried group had a higher median HAM-D score (2 IQR 0-3) but the difference did not reach statistical significance (p=.05). Details are presented in Table 1.

There were no differences in MMSE score between the three groups. The worried group performed significantly worse than controls on RAVLT Trial 1 (p=.044), RAVLT Trial 5 (p=.047), RAVLT Total (p=.017) and TMT A (p=.035).

TABLE 1. Social, demographic and clinical characteristics of the sample

	Yes and it worries me (A) N=50	Yes but it does not worry me (B) N=17	No (C) N=34	A vs B	A vs C	B vs C
Gender	39 (78%)	11 (64.7%)	21 (61.8%)	.239		
Age	63.5 (56-69)	63 (54.5-67)	59.5 (52-67)	.676	**.048**	.288
Education (years)	13 (12-15.25)	13 (11-16.5)	15 (12-17)	.815	.184	.580
Urban area	29 (59.2%)	12 (70.6%)	22 (64.7%)	.681		
BMI	27.65 (24.19-31.16)	27.34 (24.19-35.32)	26.69 (24.56-30.54)	.579	.665	.497
Hypertension	29 (58%)	6 (35.3%)	13 (38.2%)	.111		
Type II Diabetes	9 (18%)	3 (17.6%)	4 (11.8%)	.726		
Other somatic disorders	19 (38%)	4 (23.5%)	7 (20.6%)	.191		
Currently on treatment for somatic disorders	35 (70%)	9 (52.9%)	16 (47.1%)	.092		
Hachinski score	2 (1-3)	2 (1-2)	2 (1-2)	.145	**.028**	.679
FAQ	2 (1-2)	2 (0-2)	2 (1-2)	.478	.447	.874
HAM-D	2 (0-3)	1 (0-2)	1 (0-3)	**.050**	.625	.167
HAM-A	2 (0-4)	1 (0-2.5)	2 (0-5)	.083	.639	.332
BIG FIVE						
Extraversion*	16.86 (±4.39)	18.41 (±4.39)	17.85 (±3.36)	.213	.269	.616
Agreeableness*	19.68 (±3.13)	18.47 (±2.04)	19.18 (±3.05)	.142	.466	.393
Conscientiousness	22 (19-25)	20 (17-25)	21 (19.75-24)	.389	.708	.469
Negative Emotion*	14.82 (±4.23)	13.06 (±3.7)	12.65 (±3.68)	.131	**.017**	.708
Open-Mindedness*	17.04 (±4.13)	18.71 (±5.01)	17.21 (±4.24)	.178	.858	.268
IPAQ Total	3772.5 (1694.25-6444.75)	3997.56 (1183.75-6892)	3093.5 (1690-6264)	.420	.778	.363
PSQI	5 (3-8.25)	4 (2-8)	4 (2.75-7)	.276	.262	.763

The SCD group which is not concerned about their subjective impairments performed significantly worse compared to controls on RAVLT Trial 1 (p=.047) and TMT A (p=.020). There were no statistically significant differences regarding cognitive status within the SCD groups. The full results are presented in Table 2.

DISCUSSION

The goal of the present study was to compare cognitive function in individuals with SCD with and without associated worry. Multiple assessment tools where utilized, evaluating several key cognitive domains such as verbal and auditory memory and visuo-spatial memory. Additionally, we collected data on socio-demographic and clinical characteristics as well as personality traits as to account for their confounding effect.

Our main finding was that individuals with SCD and associated worry were significantly more likely to be differentiated from healthy controls by cognitive psychometric testing than those without associated worry, suggesting that concern over cognitive decline reflected a quantifiable difference in functioning in people with SCD. Previous studies have consistently reported that associated worry was a predictor for conversion to MCI and

	Yes, and it worries me (A)	Yes, but it does not worry me (B)	No (C)	A vs B	A vs C	B vs C
MMSE	28.5 (27-29.25)	29 (27-30)	29 (28-30)	.875	.187	.320
RAVLT 1	4.5 (3-6)	4 (3-5.5)	5 (4-6)	.644	**.044**	**.047**
RAVLT 5	9 (7-12)	11 (7.5-12.5)	11 (9-13)	.442	**.047**	.532
RAVLT Total*	36.5 (±19.79)	39.12 (±10.71)	42.44 (±11.16)	.390	**.017**	.315
RAVLT 6*	7.64 (±2.8)	8.47 (±4.14)	8.94 (±3.28)	.356	.054	.660
RAVLT Delay*	7.28 (±2.87)	8.41 (±3.66)	8.47 (±3.7)	.196	.101	.957
RAVLT Recognition	14 (12-15)	14 (12.5-15)	14 (12-15)	.367	.735	.567
Rey Copying	36 (34-36)	36 (34-36)	36 (34-36)	.560	.946	.650
Rey Memory	20 (13.75-23.13)	25 (14.5-29)	22.75 (12.75-29.25)	.276	.276	.810
TMT A	55 (45.5-90)	63 (48.5-79)	47 (40.75-59.25)	.751	**.035**	**.020**
TMT B	131.5 (97-168.5)	129 (96-208.5)	113 (82.25-173.25)	.660	.247	.112
VFT*	32.3 (±13.11)	30.82 (±10.7)	32.97 (±11.06)	.677	.544	.338

TABLE 2. Cognitive evaluation of the sample

dementia (20), with one such study reporting a nearly twofold risk (8). Imaging and biomarker studies have found an association between amyloid-pathology and associated worry in SCD (21, 22), lending further credibility towards its role in detecting high risk cases.

Negative emotionality was significantly higher in individuals with SCD and associated worry than in controls. This poses an important question on chain of causality: are higher levels of negative emotionality the cause of poorer performance in cognitive testing or is the concern over declining cognitive function the cause for higher scores in negative emotionality? It seems likely that this relationship is bidirectional - elderly individuals with higher neuroticism experience higher levels of stress (23), which may impact their performance in psychometric testing. Moreover, symptoms of anxiety and depression are very common in the early cognitive decline and tend to decrease in the later stages (24). Another possible explanation for this phenomenon is that concern about developing a neurocognitive disorder could manifest in ruminative thoughts that affect performance in cognitive tests. This resembles the pattern of functional neurological disorders leading some authors to categorize SCD as one such disorder (25). In this case, it is important for clinicians to keep track of these persons and make appropriate interventions when needed, due to lack of current evidence on interventions for SCD.

Of note is the statistical trend towards the differentiation of groups A and B in several personality traits such as Open-mindedness, Agreeableness and Negative Emotionality, hinting at the fact that the former two may have a small beneficial effect on cognitive ability in individuals with SCD. This is in line with previous research, which found that Openness and Agreeableness are associated with better performance in all cognitive domains, except numerical reasoning (26). However, as with Negative Emotionality, it is difficult to say whether this reflects a real difference in cognition or simply a difference in test performance.

Limitations of our study include its cross-sectional design, which is not as well suited as a longitudinal observation for evaluating a degenerative condition and significantly limits our ability to infer causal chains. The number of participants is relatively small, which may hamper our ability to detect more subtle inter-group differences. Strong points include our accounting for socio-demographic and clinical confounders as well as the extensive evaluation of multiple cognitive domains.

CONCLUSION

Individuals with SCD and associated worry performed worse in auditory and verbal memory testing when compared to healthy subjects than those with SCD and without associated worry and exhibited significantly higher negative emotionality. Longitudinal assessment is necessary to establish firm causal relationships between these parameters. ❑

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