The importance of social relationships in the process of cognitive ageing

Kuiper, Jisca Susanne

CHAPTER 5

A longitudinal study of the impact of social network size and loneliness on cognitive functioning in depressed older persons

Jisca S. Kuiper
Nynke Smidt
Richard C. Oude Voshaar
Sytse U. Zuidema
Hannie C. Comijs
Ronald P. Stolk
Marij Zuidersma

Submitted

ABSTRACT

Background: Poor social functioning predicts cognitive decline in population-based samples. Since late-life depression is associated with both, poor social functioning and cognitive decline, we examined whether poor social functioning also predicts cognitive decline in depressed older persons.

Design: Longitudinal cohort study.

Setting: Primary care and specialized mental health care.

Participants: 378 depressed older persons (60-93 years) according to *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition,* criteria.

Measurements: We examined the association between social functioning (i.e. social network size (Close Person Inventory) and loneliness (de Jong Gierveld Loneliness Scale)) measured at baseline with cognitive functioning measured at baseline as well as two-year follow-up. Cognitive functioning was assessed with the STROOP colored-word test, a modified version of the Auditory Verbal Learning Task and the Digit Span subtest from the Wechsler Adult Intelligence Scale, encompassing four cognitive domains; processing speed, interference control, memory, working memory.

Results: Multiple linear regression analyses adjusted for age, sex, level of education, alcohol use, physical activity and depressive symptom severity showed that neither social network size nor loneliness was associated with baseline cognitive performance nor with cognitive functioning over a two-year follow-up.

Conclusion: Social functioning does not seem to contribute to cognitive decline over and above the presence of a depressive disorder. Since poor social functioning and loneliness as well as depression are common among older persons, the intriguing and complex relationship between these variables deserves more attention in future studies on cognitive decline.

INTRODUCTION

Ageing is inevitably associated with cognitive decline, although the rate of cognitive decline shows large variability in the population. Since cognitive decline places older persons at increased risk of developing disabilities in (instrumental) activities of daily living[1] and dementia[2], knowledge of potentially modifiable determinants, like social functioning, is highly relevant. Recent meta-analyses showed that poor social interactions predict the onset of dementia[3] among older adults in the general population.

Late-life depression is associated with poor social functioning as well as lower cognitive performance and may thereby confound population-based findings. To our knowledge, only three studies have examined the impact of poor social functioning on cognitive decline among depressed older patients[4–6]. One study showed that poor social functioning predicts cognitive decline[4], whereas two other studies did not[5,6]. These mixed results may be explained by differences in the applied methodology and statistics, such as control for confounders like depression severity and lifestyle factors[4], using different outcomes for cognitive functioning (i.e. dichotomous versus continuous outcomes)[5], and differences in power to detect an association (i.e. small sample sizes)[6].

The aim of this study was to examine the association between poor social functioning and four domains of cognitive performance, both at baseline and at two-year follow-up in a well-defined sample of depressed older persons adjusted for potential confounders including depressive symptom severity.

METHODS

Study design

The present study used baseline and two-year follow-up data from the Netherlands Study of Depression in Older persons (NESDO). Briefly, NESDO was designed to examine the course and the consequences of depressive disorders in older persons (≥60 years). Detailed description of the methods of NESDO can be found elsewhere[7]. Inclusion criteria for NESDO were being 60 years and older and having a primary diagnosis of major or minor depression or dysthymia within the last 6 months according to the criteria of *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV) which was determined with the Composite International Diagnostic Interview (CIDI)[8]. Participants were excluded from the study if they had a primary diagnosis of or were suspected for dementia according to the clinician, had a Mini Mental State Examination-score under 18 (out of 30 points), or if they had insufficient command of the Dutch language. All participants signed for informed consent[7]. The study protocol of NESDO has been ap-

proved centrally by the Ethical Review Board of the VU University Medical Center, and subsequently by the local ethical review boards of the participating University Medical Centers.

Of the 378 participants at baseline, 285 (75.4%) participated in the two-year follow-up of which cognitive testing was available in 265 (93.0%) participants[9]. The baseline assessment included self-report questionnaires, structured interviews, cognitive testing, and blood withdrawal, and was performed in the morning by well-trained research assistants. All variables amenable for change were repeated at the two-year follow-up visit. Participants not able to come to the site were interviewed at their homes. If necessary, the assessment was spread over two appointments.

Cognitive measures

Three well-known tests of cognitive functioning were performed: a modified version (10 instead of 15 words) of the Auditory Verbal Learning Test[10,11], the subtest Digit Span (both forward and backward) from the Wechsler Adult Intelligence Scale (WAIS)[12], and the Stroop Color-word test[13]. Previous analyses on the NESDO study showed that the scores of the three tasks represent four cognitive domains: memory, working memory, information processing speed, and interference control[14]. *The memory domain* comprises the total score (i.e. sum of the scores on the five tasks) and the delayed recall score of the modified version of the Auditory Verbal Learning Test. *Working memory* comprises the sum of the forward and backward scores of the Digit Span subtest from the WAIS. *Information processing speed* comprises the sum of the time in seconds needed to complete Stroop card I and Stroop card II tasks. The information processing speed variable was transformed by the formula 1/x to make it normally distributed. *Interference control* comprises the interference score of the Stroop task. The STROOP interference score is computed with the formula: (tIII - .5 * (tI + tII)) / (.5 * (tI + tII)) * 100%[14]. The interference control variable was transformed by taking the natural log to make it normally distributed (after 50 was added to the original variable to ensure no log of negative value was taken) and it was multiplied by -1 to make higher scores represent better performance. So for all domains, higher scores represented better cognitive functioning.

Social functioning

Social functioning was operationalized as either social network size or loneliness. Social network size was assessed with the first question of the Close Person Inventory[15]. Participants were asked to indicate how many family members, friends and good acquaintances, over the age of 18, they had regular and important contact with, disregarding roommates. Responses to this question were classified as 1 (0 to 1 contacts), 2 (2 to 5 contacts), 3 (6 to 10 contacts), 4 (11 to 15 contacts), 5 (16 to 20 contacts) or 6 (more than

20 contacts). This classification (range 1 through 6) can be considered as a dimensional measure of social network size.

Loneliness was measured with the De Jong Gierveld loneliness scale[16], which is shown to be a valid and reliable instrument[17]. The questionnaire consists of eleven items that have to be answered with yes or no, resulting in a sum score (range 0 – 11) with higher scores indicative of a more severe level of loneliness.

Covariates

Demographic data were collected on age, sex, and years of education, as well as lifestyle and disease-related characteristics that are potentially associated with social or cognitive functioning. Alcohol use was classified as no drinking, moderate alcohol use and problematic alcohol use, based on the first two questions of the Alcohol Use Disorders Identification Test (AUDIT)[18]. Problematic alcohol use was defined as taking 5 or more units on a typical drinking day irrespective of the frequency of drinking, or 3 or more units on a typical drinking day at least 4 or more days a week. Physical activity was classified into low, moderate and high physical activity according to the International Physical Activities Questionnaire (IPAQ)[19]. Finally, depressive symptom severity was measured with the 30-item Inventory of Depressive Symptoms (IDS)[20], a valid and reliable self-report instrument with higher scores indicating more severe levels of depressive symptoms.

Statistical analysis

Multiple imputation was applied, using the fully conditional specification approach[21]. Since 27% of cases had at least one missing value, 27 datasets were created with 100 iterations for each dataset[22]. As using the outcomes for imputation of missing predictor values gives more reliable results[23], the imputation model included all variables that were used in the analyses, including the outcomes. Missing values on the outcomes themselves were not imputed, because this introduces noise to the estimates[22,24]. Therefore, analyses were performed in the subset of cases with complete data on the cognitive outcomes.

Descriptive characteristics are presented for the total group of participants and separate for participants with follow-up data and those lost to follow-up. Groups were compared with independent t-tests for normally distributed variables, Mann-Whitney U tests for not normally distributed variables, and Chi Square tests for categorical variables.

Linear regression analyses were performed to examine the relation between social functioning (independent variable) and each of the four cognitive domains (dependent variable) in separate models. In case cognitive functioning at 2-year follow-up was examined, the model was additionally adjusted for baseline cognitive functioning.

Separate models were performed for social network size and loneliness. Furthermore, we present both, univariate as well as fully adjusted models (see covariates).

All the analyses were performed on the imputed datasets, pooling the results from the different datasets using Rubin's rules[21]. IBM SPSS statistics software version 22 was used for the statistical analysis. Significance levels were set at $p<0.05$ and all tests were two-tailed.

RESULTS

The sample consisted of 378 depressed older persons, of whom 250 (66%) were female and 99% had the Dutch nationality. The mean age was 70.7 years (SD: 7.4; range 60-93). Compared to those lost to follow-up, those still available for follow-up were younger and had more years of education at baseline. They also had less severe depressive symptoms, performed more in moderate of high physical activity, and had better baseline cognitive functioning (except for interference control) (see Table 1).

Table 2 shows the results of the uni- and multivariable linear regression analyses on the association of social network size as well as loneliness with cognitive functioning in the four cognitive domains. Neither social network size nor loneliness was significantly associated with baseline measures of any of the cognitive functioning domains (all $p>0.05$). Similarly, neither social network size nor loneliness predicted cognitive functioning at 2-year follow-up in any of the four domains tested in the fully adjusted models.

Table 1. Descriptive statistics of sample characteristics at baseline and two-year follow-up.

	Total sample	Available for follow-up	Dropped out at follow-up	p-value
	(n=378)	(n=265)	(n=113)	
Demographics:				
Age, mean (SD) years	70.7 (7.4)	70.1 (7.3)	72.0 (7.6)	0.03
Sex, n (%) female	250 (66%)	170 (64%)	80 (71%)	0.24
Education, mean (SD) years	10.4 (3.4)	10.7 (3.4)	9.8 (3.4)	0.01
Depression characteristics:				
Depressive symptom severity, mean (SD) IDS score	30.1 (13.0)	29.3 (12.7)	32.2 (13.6)	0.05
Lifestyle characteristics:				
Alcohol use, n (%)				0.11
No drinking	153 (40%)	99 (37%)	54 (48%)	
Moderate alcohol use	191 (51%)	143 (54%)	48 (42%)	
Problematic alcohol use	34 (9%)	23 (9%)	11 (10%)	
Physical activity, n (%)				<0.001
Low physical activity	120 (32%)	69 (26%)	51 (45%)	
Moderate physical activity	139 (37%)	104 (39%)	35 (31%)	
High physical activity	119 (31%)	92 (35%)	27 (24%)	
Social functioning:				
Social network size[a], mean (SD)	2.5 (1.1)	2.5 (1.1)	2.4 (1.0)	0.59
Loneliness (total score), median (IQR)	7 (4-10)	7 (3-10)	8 (4-10)	0.34
Cognitive performance:				
Processing speed (transformed)[b], mean (SD)	22.0 (4.4)	22.7 (4.2)	20.6 (4.9)	<0.001
Interference control (transformed)[c], mean (SD)	-5.2 (0.4)	-5.2 (0.4)	-5.2 (0.4)	0.38
Memory, mean (SD)	37.2 (8.9)	38.4 (8.7)	34.3 (8.7)	<0.001
Working memory, mean (SD)	13.2 (3.2)	13.5 (3.2)	12.4 (2.9)	<0.001

SD: standard deviation; IDS: Inventory of Depressive Symptomatology; IQR: interquartile range.

[a] Categorized as: 0-1 (1), 2-5 (2), 6-10 (3), 11-15 (4), 16-20 (5) >20 (6)

[b] The processing speed (transformed) score is computed with the formula: 1/x to make it normally distributed

[c] The STROOP interference control score is computed with the formula: ((tIII - .5 * (tI + tII)) / (.5 * (tI + tII)) * 100%). The scores were transformed by taking the natural log to make it normally distributed (after 50 was added to the original variable to ensure no log of negative value was taken) and is multiplied by -1 so that higher scores represented better scores for all cognitive domains

Table 2. Multiple Linear Regression Models Showing Cross-Sectional and Longitudinal Associations Between Social Functioning and Cognitive Functioning (N=378 for baseline correlations; N=265 for longitudinal associations)[a,b]

	Processing speed[c]	Interference control	Memory	Working memory
	Unstandardized B (95% CI)	Unstandardized B (95% CI)	Unstandardized B (95% CI)	Unstandardized B (95% CI)
Baseline correlations				
Social network size:				
Univariate	0.03 (-0.40 to 0.45)	-0.03 (-0.07 to 0.00)	0.16 (-0.68 to 1.00)	0.08 (-0.22 to 0.39)
Adjusted model[d]	0.02 (-0.38 to 0.42)	-0.03 (-0.06 to 0.01)	0.17 (-0.62 to 0.97)	0.01 (-0.27 to 0.29)
Loneliness:				
Univariate	-0.11 (-0.24 to 0.03)	0.00 (-0.01 to 0.01)	-0.17 (-0.44 to 0.09)	-0.04 (-0.13 to 0.06)
Adjusted model[d]	-0.03 (-0.16 to 0.10)	0.00 (-0.01 to 0.01)	-0.03 (-0.29 to 0.23)	0.04 (-0.05 to 0.14)
Longitudinal associations:				
Social network size:				
Univariate[e]	-0.10 (-0.40 to 0.21)	0.00 (-0.04 to 0.04)	-0.46 (-1.22 to 0.29)	-0.01 (-0.27 to 0.24)
Adjusted model[f]	0.00 (-0.30 to 0.30)	0.01 (-0.03 to 0.04)	-0.16 (-0.91 to 0.59)	-0.02 (-0.28 to 0.24)
Loneliness:				
Univariate[e]	-0.01 (-0.11 to 0.09)	0.00 (-0.01 to 0.01)	-0.03 (-0.28 to 0.23)	-0.08 (-0.17 to 0.00)*
Adjusted model[f]	-0.02 (-0.12 to 0.08)	0.00 (-0.01 to 0.01)	-0.06 (-0.32 to 0.20)	-0.07 (-0.16 to 0.01)

CI: confidence interval; B: Beta; CI: confidence interval. * p<0.05.

[a] None of the associations were statistically significant (i.e. p>0.05 for all associations, except for the association between loneliness and working memory at follow-up in univariate analysis).

[b] Results were obtained by using the transformed and imputed data.

[c] Results of the Processing Speed variable were multiplied by a constant of 1000 to make the presentation of the results more informative.

[d] Adjusted for age, sex, years of education, alcohol use, physical activity, and depressive symptom severity.

[e] Adjusted for baseline cognitive functioning

[f] Adjusted for baseline cognitive functioning, age, sex, years of education, alcohol use, physical activity, and depressive symptom severity

DISCUSSION

In contrast to population-based findings, poor social functioning, operationalized as either social network size or loneliness, were neither associated with actual cognitive functioning nor with cognitive decline over a two-year follow-up within a large sample of depressed older persons taken potential confounders and especially depressive symptom severity into account.

Our findings are in contrast to previous findings of the Neurocognitive Outcomes of Depression in the Elderly (NCODE) study, reporting that poor social functioning is associated with cognitive decline[4]. However, social functioning in the NCODE study was operationalized as change in social support over a one-year period, using four subscales including change in a) subjective social support; b) instrumental social support; c) social network size; and d) social interaction. Whereas a decrease in instrumental social support and in social interaction were associated with cognitive decline among a total sample of 213 older persons (of which 112 were depressed), a decrease in subjective social support and in social network size were not[4]. The significant findings, however, might be caused by the lack of adjustment for lifestyle factors and depression severity. Furthermore, since cognitive decline in itself is associated with social withdrawal[25], these results may have been driven by reverse causality (i.e. cognitive decline may not be the consequence but rather the cause of poor social functioning). Interestingly, a subsequent paper on the same NCODE study but extended with additional patients up to 299 depressed older patients, showed that poor social support (i.e. based on the same four subscales, measured at baseline as well as one-year change) did not predict conversion to a cognitive disorder over a seven year follow-up when adjusted for depressive symptom severity[5]. These results are in line with a smaller (n=130) and probably underpowered study with a two-year follow-up[6].

Strengths of the present study are the large sample size, structured psychiatric diagnostic interviews, assessment of cognitive functioning across four different domains, and adjustment for all relevant covariates including depressive symptom severity. Moreover, we distinguished between social network size and loneliness instead of using a composite score for the measurement of social factors as many other studies do[26]. Nonetheless, our measure of social network size did not specify the social network composition, while a relatively higher proportion of friends might protect against cognitive impairments, whereas a relatively higher proportion of family contacts might be associated with impairments in cognitive functioning[25]. Furthermore, the dropout rate in our study was higher among patients with relatively poorer cognitive functioning which might represented accelerated cognitive decline among the dropouts. However,

as no selection occurred with respect to social functioning at baseline, it is unlikely that this selective dropout has contributed to our (negative) findings.

Three explanations can be put forward for the lack of any impact of poor social functioning on cognitive decline among depressed older patients. Firstly, inherently associated with this research question, is the reliability of the social and cognitive measures. Depressed patients suffer from negative cognitive biases[27], which might affect self-report measures of social functioning. Secondly, depression itself is strongly associated with cognitive deficits[27]. Therefore, social functioning may not contribute to cognitive functioning over and above the presence of a depressive disorder. If true, the presence of depressive disorder or depressive symptom severity may explain the relation between social and cognitive functioning, which is often found in population samples[26,28]. Furthermore, depressed patients might perform worse on cognitive tests due to problems with motivation or concentration difficulties, implying that at least part of the cognitive problems may disappear when depression is successfully treated. Although the impact of these mechanisms is rather limited, noise due to these limitations may have obscured any relationship between social functioning and cognitive decline. Therefore, controlling for the presence of depressive disorder is important in future studies. Finally, worse scores on both social and cognitive function in the present sample may limit the possibility to find a relation between the two. Indeed, patients in our sample performed worse on social network size, loneliness and cognitive functioning compared to older adults from the general population. Participants in the present study had a substantially smaller social network and higher loneliness scores compared to community-dwelling older persons in the Dutch population[29,30]. Additionally, participants from the present study performed below norm scores and worse than older adults from the general population on cognitive performance[11,13]. Nonetheless, taken into account the level of variance between patients, it is unlikely that this can explain the absence of any relationship.

Since poor social functioning and loneliness as well as depression are common among older persons, the intriguing and complex relationship between these variables deserves more attention in future studies on cognitive decline. Especially since both, depression and social functioning are amenable to change, but require different interventions.

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