Psychological aspects in rehabilitation

Schrier, Ernst

Chapter 3

Subjective cognitive dysfunction in rehabilitation outpatients with musculoskeletal disorders or chronic pain

Schrier E, Geertzen JHB, Dijkstra PU

Eur J Phys Rehabil Med. 2017 Aug;53(4):582-589

Abstract

Background: rehabilitation patients, without brain damage, sometimes complain about poor concentration and problems with their memory. The magnitude and associations, of this cognitive dysfunction, with different factors is unclear.
*Aim***:** To determine the magnitude of cognitive dysfunction in rehabilitation outpatient and to explore its associations with patient characteristics, diagnosis, surgery, pain, stress, anxiety and depression.
Design: Cross sectional.
Setting: Rehabilitation outpatients.
Population: Between July 2009 and January 2012, 274 rehabilitation outpatients were included and divided in 8 different groups through diagnosis.
Methods: Cognitive functioning was assessed using the cognitive failure questionnaire and compared with the general Dutch population. Associations of gender, age, diagnosis, recent surgery, pain and stress coping ability with cognitive function was explored. Mediation of depression and anxiety was explored.
Results: The rehabilitation patients had a significantly higher score on the CFQ (mean (SD) = 35.9 (13.4)) when compared to the general Dutch population (mean (SD) = 31.8 (11.1)). Mean difference is 4.1, 95% 2confidence interval 2.60 to 5.60 In the stepwise linear regression analysis only gender, diagnosis and stress coping ability were significantly associated. A significant mediation effect was found of anxiety (p=<0.001) and depression (p=<0.005) between stress coping ability and cognitive function.
Conclusions: Rehabilitation outpatients experience more cognitive problems in comparison to the general Dutch population. Reported dysfunction of cognition in rehabilitation outpatients are associated with stress coping ability and for a small amount to gender and diagnosis. The association of stress coping ability and cognitive dysfunction is mediated by depression and anxiety. Women tend to report more dysfunctional cognition compared to men. Patient characteristics, surgery and experienced pain have no significant influence on the experienced cognitive dysfunction**.**
Clinical rehabilitation impact: Cognitive problems reported by patients should be addressed by adapting the rehabilitation program, for instance write down instructions, repeat explanations and take more time for instructions. . Cognitive problems in rehabilitation patients without brain damage is probably a stress coping problem and can be addressed by boosting resilience. Targeting depression or anxiety is another option of treatment cognition if those are mediating between stress coping and cognitive problems.

Introduction

In rehabilitation inpatients, without brain injury, cognitive dysfunction does occur.[1, 2] Cognitive dysfunction has been found to be associated with different factors including gender, age, diagnosis, surgery, pain, stress, anxiety and depression.[3-13]

There are many hypotheses regarding the associations between cognitive dysfunction and the factors mentioned above. Some hypotheses are biomedical and describe that anoxia, hypoperfusion or micro-emboli may occur during surgery causing brain damage, resulting in cognitive dysfunction.[1, 14] Other hypotheses are biopsychosocial, and describe more complicated pathways to the cognitive dysfunction.[15-18] In patients suffering from medical unexplained symptoms such as irritable bowel syndrome, chronic pain, fatigue and stress, a complicated interaction between different systems and structures has been described to maintain homeostasis including the hypothalamic-pituitary-adrenal axis, the autonomic nervous system, the immune system and the prefrontal cortex.[3, 19-23] These systems interact with endogenous and exogenous stimuli in a protective and beneficial way but can become deleterious and may cause, among other things, cognitive dysfunction. Rehabilitation outpatients are exposed to stressful circumstances and stress factors like surgery and pain.[24, 25]
Stress, chronic and acute, causes an imbalance of the neural circuitry subserving cognition, anxiety and mood.[26] Therefore according to the hypotheses above it is no surprise that patients may complain, along with a change in mood and anxiety, about cognitive dysfunction. Little is known about the extent of this problem nor is it clear if patient characteristics, diagnosis, surgery, pain, are associated with the cognitive dysfunction and if there is a mediating role of depression and anxiety in rehabilitation outpatients.
When there is no clear cue for cognitive dysfunction like brain damage or old age, it may stay unnoticed during the rehabilitation. Cognitive dysfunction such as poor functioning of memory, concentration or problem solving, has a negative influence on the outcome of rehabilitation programs.[27-29] When cognitive dysfunction is recognized, the rehabilitation program need to be adapted,[30] for instance write down instructions, repeat explanations and take more time for instructions.
The aim of the study is to determine the magnitude of cognitive dysfunction in rehabilitation outpatient and to explore its associations with patient characteristics, diagnosis, surgery, pain, anxiety, stress and depression.

Materials and methods

This study is assessed by the Medical ethics Review Board and they state that it fulfils all the requirements of our University Hospital for publication of patient data on 08-20-2015 (2015/348). All patients signed an informed consent.
Participants
Between July 2009 and January 2012, 327 outpatients (≥18 years) from the Department of Rehabilitation Medicine of the University Medical Centre Groningen were referred to a psychologist with experience in patients undergoing rehabilitation. They were referred by a rehabilitation physician for a psychological assessment and/or treatment. All the referred out clinic patients were included. Medical referral diagnosis were used to form 8 different diagnosis groups. Excluded from this consecutive study sample were patients with possible brain damage or organ failure. Before the first meeting with the psychologist, a set of questionnaires was sent by mail with the request to fill out the questionnaires and bring these to the first

session. An informed consent was sent together with the questionnaires. The following patient characteristics were collected during the intake procedure; gender, education (according to the International Standard Classification of Education)[31], marital status and age. Also the highest and lowest pain intensity, experienced in the last week, assessed on a numeric rating scale from 0 to 10 was collected. From the medical records data regarding recent surgery (< 3 months ago) and the referral diagnosis of the rehabilitation physician was collected.

Questionnaires

This study used questionnaires to assess cognitive functioning, the stress coping ability, depression and anxiety. Self-reported cognitive functioning was assessed using the cognitive failure questionnaire (CFQ).[32, 33] The CFQ is a 25-item self-report questionnaire assessing failures in perception, memory, and motor function in the completion of everyday tasks in the past 6 months. Individuals were asked to rate the frequency of experiences and behaviors on a 5-point scale from 0 (never), to 4 (very often). In this study, the sum score (range 1-100) was used. Higher scores indicate more cognitive failures. The CFQ is shown to have excellent psychometric properties, CFQ reliability (r) over 24 months is 0.71, the inter-item reliability Cronbach's α of the CFQ is 0.92.[34]

The Connor-Davidson Resilience Scale (CD-RISC) was used to estimate the stress coping ability of a patient.[35] The CD-RISC is a 25 item questionnaire. Each item is rated on a 5-pont scale, higher scores reflecting greater resilience. Resilience may be viewed as a measure of stress coping ability.[35] There is no gold standard for resilience yet but in a review of different resilience questionnaires the CD-RISC was 1 of the 3 questionnaires with the best psychometric properties.[36]

The hospital anxiety and depression scale (HADS) was used to assess anxiety and depression.[37] This scale is divided into an anxiety subscale (HADS-A) and a depression subscale (HADS-D), both containing 7 intermingled items. During the development of this scale the 'noise' from somatic disorders on the scores, all symptoms of anxiety or depression also relating to physical disorder, such as dizziness, headaches, insomnia, anergia and fatigue, were excluded.[34] In patients with musculoskeletal disorders the depression subscale is stable. The reported Chronbach alpha was .83 for the anxiety subscale and .84 for the depression subscale, indicating adequate internal consistency.[38]

Statistical procedures

Data was anonymized and analyzed using IBM SPSS Statistics (v.20). P-P and Q-Q plots were used to assess normal distribution of dependent variables. Results are significant at $p \leq 0.05$ unless stated otherwise. To analyze differences in means of the CFQ in rehabilitation outpatients with a general Dutch population the confidence interval (CI) for difference in means was calculated.[30]

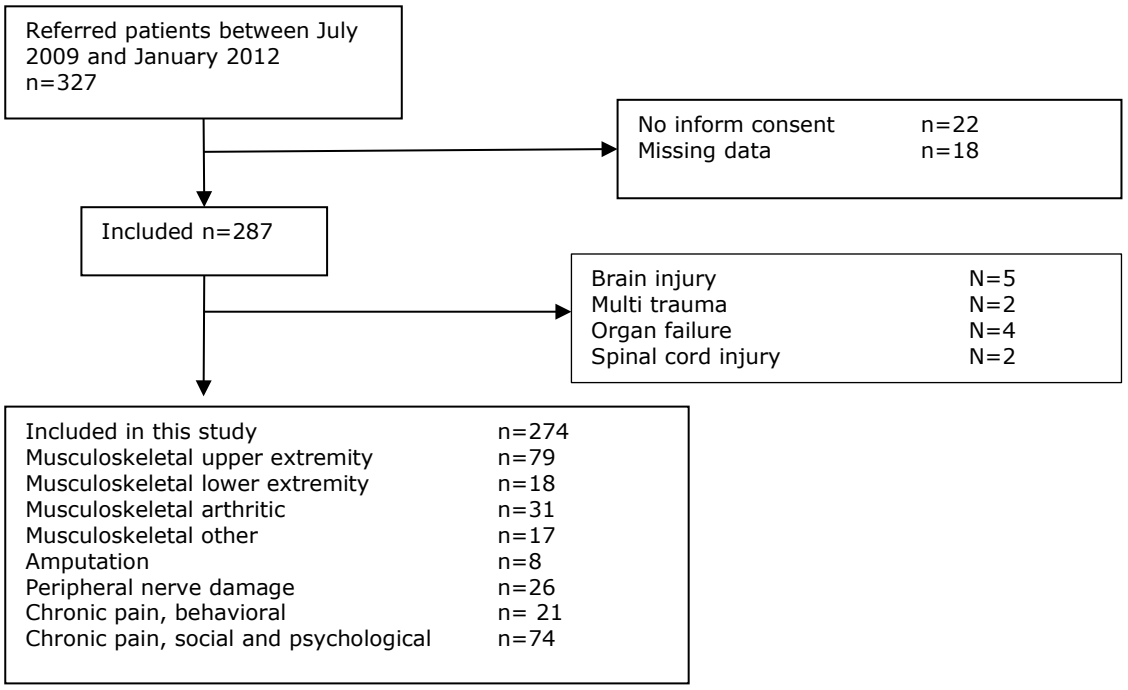
A Pearson Chi-Square test and ANOVA were used to analyze if gender, education, social status, age, HADS-D, HADS-A, pain, CFQ and CD-RISC total score, differed between diagnosis groups. Education was split according to the international Standard Classification of Education (ISCED) 2011; Low education equals the ISCED level 0-4, middle the level 5 and high the level 6-9.[31] For (regression) analyses several dummy variables were computed. Social status was dichotomized into living alone (living alone and living with the family or a partner), diagnosis was

dichotomized into musculoskeletal (upper extremity, lower extremity, arthritic and other) and the other 4 groups (chronic pain complex/not complex, peripheral nerve damage and amputation). To analyze the association between gender, age, diagnosis, surgery, pain and stress coping ability, a hierarchical step wise regression analysis was used with the sum score CFQ as dependent variable. In the first step we entered gender and age, in the second the diagnosis, in the third surgery and pain intensity, in the fourth stress coping ability. Interaction effects were explored and residuals were checked for a normal distribution. Anxiety and depression were added in the fifth step to check mediation. Anxiety and depression were used in a mediation model using stress coping ability as independent variable, cognition as dependent variable and depression and anxiety as mediators. PROCESS v2.16 add on for SPSS by Hayes was used for mediation calculation.[39]

Results

Of all the referred patients (n=327) some did not want to participate (n=22) and some questionnaires contained too much missing data (n=18). Of the remaining 287 patients, 13 patients had an organ failure or a (presumably) central neurologic problem and were excluded. The most common referral diagnosis, of the included 274 patients, was musculoskeletal disorder (53%), followed by chronic pain (35%). The musculoskeletal group was divided in 4 subgroups, 3 depending on the location of their musculoskeletal disorder, upper extremity, lower extremity and other such as spine or trunk, and 1 arthritic disorder group including rheumatoid arthritis. The pain group was divided in 2 subgroups. Social and psychological factors played a substantial role in maintaining the pain in the first chronic pain group (complex) and behavior such as overuse played a substantial role in maintaining the pain in the second chronic pain group (not complex).

Figure 1 Flowchart of inclusion procedure.



The group of peripheral nerve damage (9%) and a small group of patients with an amputation (3%) are the last 2 of the total of 8 groups (Figure 1).
No significant differences were found between the 8 different diagnosis groups with regard to gender, education, social status, age and stress coping ability (Table 1).

Table 1 Characteristics of participants of the total group, the musculoskeletal group, the chronic pain group and subgroups.

	Total group **n=274**	**Musculoskeletal** **n= 145**				**Chronic pain** **n= 95**		**Peripheral nerve damage** **n=26**	**Amputation** **n=8**	**P value ***
		Upper extremity n=79	Lower extremity n=18	Other n=17	Arthritic n=31	Complex n=74	Not Complex n=21			
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	
Gender	200 (73.0)	59 (74.7)	15(83.3)	13(76.5)	23(74.2)	49(66.2)	16(76.2)	22(84.6)	3(37.5)	0.192†
Education										0.288†
--Low/lowest	86 (31.3)	22 (27.9)	4(22.2)	4 (22.2)	13(41.9)	28 (37.8)	6 (28.6)	7(26.9)	2(25.0)	
--Medium	121 (44.2)	40 (50.6)	5(27.8)	7(41.2)	11 (35.5)	34 (45.9)	7 (33.3)	13(50.0)	4(50)	
--High	67 (24.5)	17 (21.5)	9(50.0)	6 (35.3)	7 (22.6)	12 (16.2)	8 (38.1)	6(23.1)	2(25)	
Social status										0.234†
--Living alone	61 (22.3)	13 (16.5)	4(22.2)	7 (41.4)	7 (22.6)	17 (23.0)	8 (38.1)	4(15.4)	1(12.5)	
--With person(s)	231 (77.7)	66(83.5)	14(77.8)	10(58.6)	24(77.4)	57 (77)	13(61.9)	22(84.6)	7(87.5)	
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	
Age, mean (sd)	40.6 (14.6)	38.9(14.6)	30.4(15.2)	44.8(14.0)	44.5 (15.2)	41.2(13.0)	40.3(16.9)	41.7(13.2)	36.6(13.9)	0.122‡
HADS-D§	6.9 (4.4)	6.0(4.5)	6.1(4.0)	7.9(4.9)	6.2(4.1)	8.7(4.3)	6.5(3.6)	6.0(4.5)	4.8(4.5)	0.003‡
HADS-A||	8.3 (4.8)	7.3 (4.8)	7.9(3.9)	10.5(5.1)	7.6(4.8)	10.5(4.9)	7.5(3.9)	6.8(4.0)	5.7(4.1)	<0.010‡
Pain-high	5.2(3.5)	5.5(3.2)	5.7(3.3)	2.7(3.5)	4.7(3.7)	6.0(3.2)	5.2(3.6)	4.5(4.3)	2.9(4.2)	0.009‡
Pain-low	3.0(2.7)	3.0(2.5)	3.0(3.0)	1.7(2.4)	3.0(2.9)	3.4(2.4)	2.6(2.9)	2.9(3.2)	1.3(2.6)	0.198‡
CFQ total score	35.9(13.3)	33.7(11.5)	32.8(14.0)	40.3(12.8)	33.4(12.3)	41.2(13.6)	35.9(14.7)	32.5(14.7)	29.3(11.3)	0.003‡
CD-RISC	63.2(14.1)	62.5(14.7)	65.3(15.0)	61.0 (15.9)	65.9(14.1)	60.0(13.3)	62.9(11.5)	67.5(14.0)	73.4(11.6)	0.840‡

Posthoc analysis of the HADS-D showed significant difference between upper extremity and complex chronic pain; Posthoc analysis of the HADS-A showed significant difference between upper extremity and complex chronic pain and between complex chronic pain and peripheral nerve damage; Posthoc analysis of the pain high showed significant difference between upper extremity and other; Posthoc analysis of the CFQ total showed significant difference between complex chronic pain and upper extremity.*Significance differences between groups †: chi square test, ‡: ANOVA CFQ=cognitive failure questionnaire, HADS = hospital anxiety and depression scale §) depression subscale, ||) anxiety subscale

The rehabilitation patients had a significantly higher score on the CFQ (mean (SD) = 35.9 (13.4)) when compared to the general Dutch population (mean (SD) = 31.8 (11.1)). Mean difference 4.1, 95% confidence interval 2.6 to 5.6.
In the stepwise linear regression analysis only gender, diagnosis and stress coping ability were significantly associated, after stress coping ability (CD-RISC) was entered in the fourth step. There were no significant interaction effects (Table 2). The explained variance of the model was 0.159. Residuals were normally distributed.

Table 2 Results of the stepwise regression analyses of the CFQ as dependent variables. With 4 steps of independent variables.

	B	**SE B**	**Sig**	**95%Confidence interval**		**R Square Change**
				Lower bound	**Upper bound**	
Step 1						0.017
Gender/male	-3.532	1.713	.040	-6.905	-.159	
Age	.039	.053	.465	-.066	.144	
Step 2						0.019*
Diagnosis†	-3.304	1.512	.030	-6.281	-.328	
Step 3						0.018
Surgery‡	-3.567	2.253	.115	-8.003	.868	
Pain high§	.110	.339	.747	-.558	.777	
Pain low||	-.342	.444	.442	-1.215	.532	
Step 4						0.106**
CD-RISC	-.311	.054	<.001	-.417	-.205	
Constant	57.632	4.647	<.001	48.482	66.781	

* sig < 0.05. ** <0.001 * . †. Musculosketetal yes, no. ‡. Surgery <3 month before intake, yes, no. §. Highest experienced pain level last week on the numeric rating scale ||. Lowest experienced pain level last week on the numeric rating scale. B = unstandardized coefficients. For gender the reference group was female. for surgery the reference group was no surgery. For was musculoskeletal disorders the reference groups was chronic pain, peripheral nerve damage and amputation combined.

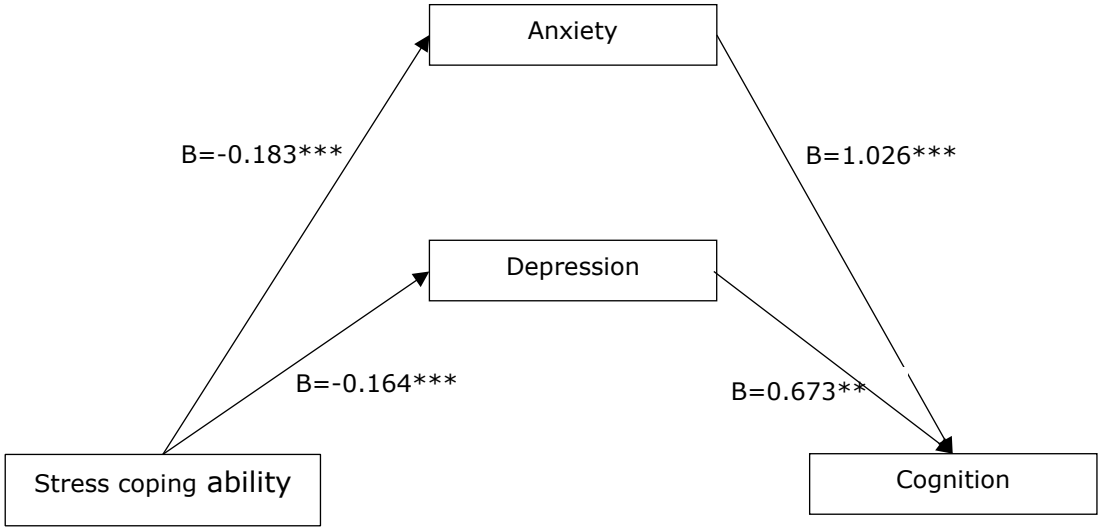
Table 3 Results of the stepwise regression analyses of the CFQ as dependent variables. With 5 steps of independent variables.

	B	**SE B**	**Sig**	**95%Confidence interval**		**R Square Change**
				Lower bound	**Upper bound**	
Step 1						0.017
Gender/male	-3.232	1.498	.032	-6.181	-.282	
Age	-.014	.048	.765	-.108	.080	
Step 2						0.019*
Diagnosis†	-1.554	1.335	.245	-4.182	1.074	
Step 3						0.018
Surgery‡	-2.528	1.977	.202	-6.421	1.365	
Pain high§	.092	.298	.758	-.494	.678	
Pain low||	-.670	.389	.086	-1.437	.096	
Step 4						0.106**
CD-RICS	-.024	.056	.669	-.135	.087	
Step 5						0.204**
HADS-A	.973	.219	<.001	.542	1.404	
HADS-D	.746	.240	.002	.273	1.219	
Constant	34.946	2.421	<.001	30.180	39.712	

* sig =< 0.05. ** sig=<0.001 †. Musculosketetal yes. no. ‡. Surgery <3 month before intake. yes. no. §. Highest experienced pain level last week on the numeric rating scale ||. Lowest experienced pain level last week on the numeric rating scale. B = unstandardized coefficients SE = standard error. For gender the reference group was female. for surgery the reference group was no surgery. For was musculoskeletal disorders the reference groups was chronic pain, peripheral nerve damage and amputation combined.

In a fifth step Anxiety (HADS-A) and depression (HADS-D) were entered. Association between stress coping ability and CFQ was reduced and no longer significant, indicating a strong mediating effect of the HADS-A and HADS-D.
A significant mediation effect was found of anxiety (p=<0.001) and depression (p=0.006) between stress coping ability and cognitive function (Figure 2). Gender and diagnosis did not have any mediation effect.

Figure 2
Mediation model.



Mediation model showing that stress coping ability, (independent variables) on cognition (dependent) is mediated by anxiety and depression. Total effect model B = -0.324, t(272)=-6.037, *p*=<.001 ** p=<0.005 *** p=<0.001

Discussion

Rehabilitation outpatients experience more cognitive problems compared to the general Dutch population. This difference confirms the observation that a proportion of the rehabilitation outpatients complained about cognitive functioning. Of the patient characteristics analyzed in this study gender appeared to be significantly related to the CFQ scores but the effect was small (1.7% explained variance). Diagnosis also had a small effect (1.9% explained variance). Stress coping ability (CD-RISC) had the foremost influence on the model (11% explained variance). Beside the direct effect there was a substantial mediating effect of anxiety and depression on cognition (Table 3). Entering anxiety and depression in the fifth step reduced the association between stress coping ability and cognitive problems. That is a sign of mediation (Figure 2). The presented model is simple and the discussion about a (more complicated) model is going on.[19-21, 40] This model provides the clinician with more possibilities to modify the rehabilitation program. The obvious

solution is to adapt the program as described in the introduction. Other opportunities are strengthening the stress coping ability or treatment of anxiety and depression.[41, 42]

Although the difference with the general Dutch population was clinically small, it is relevant in rehabilitation because cognition is one important determinant of rehabilitation outcome.[27, 28]

The expected association with, surgery or pain was not found. Other studies did find a significant association between surgery and pain and cognition.[1, 2, 6, 7] One explanation of this difference in outcomes is that in previous studies, stress coping ability, depression and anxiety was not included into the analyses.[43] Another explanation for this difference is that in our study, patients were included up to 3 months after surgery. Cognitive decline was found to be most distinct in the first 2 weeks after surgery.[14]

In a study including patients with chronic pain, an association was found between pain and cognitive dysfunction but depression made the strongest unique contribution to the cognitive dysfunction.[3] A study in fibromyalgia patients found that pain played an important role in cognitive dysfunction.[44] Sleep disturbance and depression were referred to as factors influencing cognition.[45] All mentioned studies acknowledge the role of depression in disrupting cognition.[1-3, 6, 7, 14, 15, 44, 45] In our study depression, anxiety mediated cognitive problems. Although the pathway is not yet revealed, our study suggests that perceived cognitive dysfunction may be an indicator of an imbalance of the neural circuitry resulting in cognitive problems, anxiety or depressive symptoms. This imbalance is caused by acute and chronic stress as experienced by rehabilitation patients.[24]

It is safe to assume that the patients in this study experienced stress.[24, 46] This is stress for example about their health, the pain they experience, and frustration about the things they can't do, like work or hobby, due to their disorder. Stress is linked to dysfunctional cognitions, major depression and anxiety in several studies.[19, 47]

The strength of this study is that it included different diagnoses within the rehabilitation outpatients, included different possible causes of the cognitive problem and the mediating factors.

Study limitations

The weakness of this study is the use of one screening instrument for cognitive dysfunction. The CFQ is a subjective measure of cognitive functioning. A study about cognitive functioning in bipolar disorders showed no association between cognitive complaints and objective cognitive functioning, but cognitive complaints were strongly related to depressive symptoms.[48] Other studies found a relationship between objective testing and subjective questionnaire as the CFQ and even that perceived cognitive problems predict cognitive decline at an earlier stage than objective tests.[49] Whereas another study concluded white matter lesions were associated with subjective cognitive failures, even in the absence of objective cognitive impairment.[50]

Conclusions
Rehabilitation outpatients experience more cognitive problems in comparison to the general Dutch population. Reported dysfunction of cognition in rehabilitation outpatients are associated with stress coping ability and for a small amount to gender and diagnosis. The association of stress coping ability and cognitive dysfunction is mediated by depression and anxiety. Women tend to report more dysfunctional cognition compared to men.

Declaration of interest
The authors declare no conflicts of interests.
This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Acknowledgements
The authors wish to thank V. Leseman, MSc, psychologist for helping with the start of the study.

References

1. Purohit M, Goldstein R, Nadler D, Mathews K, Slocum C, Gerrard P, et al. Cognition in patients with burn injury in the inpatient rehabilitation population. Arch Phys Med Rehabil 2014; 95: 1342-9.
2. Woods AJ, Mark VW, Pitts AC and Mennemeier M. Pervasive cognitive impairment in acute rehabilitation inpatients without brain injury. PM R 2011; 3: 426-32.
3. Roth RS, Geisser ME, Theisen-Goodvich M and Dixon PJ. Cognitive complaints are associated with depression, fatigue, female sex, and pain catastrophizing in patients with chronic pain. Arch Phys Med Rehabil 2005; 86: 1147-54.
4. Keizer AM, Hijman R, van Dijk D, Kalkman CJ and Kahn RS. Cognitive self-assessment one year after on-pump and off-pump coronary artery bypass grafting. Ann Thorac Surg 2003; 75: 835-8; discussion 838-9.
5. Pechtel P and Pizzagalli DA. Effects of early life stress on cognitive and affective function: an integrated review of human literature. Psychopharmacology (Berl) 2011; 214: 55-70.
6. Berryman C, Stanton TR, Jane Bowering K, Tabor A, McFarlane A and Lorimer Moseley G. Evidence for working memory deficits in chronic pain: a systematic review and meta-analysis. Pain 2013; 154: 1181-96.
7. Rudolph JL, Schreiber KA, Culley DJ, McGlinchey RE, Crosby G, Levitsky S, et al. Measurement of post-operative cognitive dysfunction after cardiac surgery: a systematic review. Acta Anaesthesiol Scand 2010; 54: 663-77.
8. Vardy J, Rourke S and Tannock IF. Evaluation of cognitive function associated with chemotherapy: a review of published studies and recommendations for future research. J Clin Oncol 2007; 25: 2455-63.
9. Wu CL, Hsu W, Richman JM and Raja SN. Postoperative cognitive function as an outcome of regional anesthesia and analgesia. Reg Anesth Pain Med 2004; 29: 257-68.

10. Schwabe L, Joels M, Roozendaal B, Wolf OT and Oitzl MS. Stress effects on memory: An update and integration. Neurosci Biobehav Rev 2012; 36: 1740-9.
11. Paleacu D, Shutzman A, Giladi N, Herman T, Simon ES and Hausdorff JM. Effects of pharmacological therapy on gait and cognitive function in depressed patients. Clin Neuropharmacol 2007; 30: 63-71.
12. Wessels AM, Pouwer F, Geelhoed-Duijvestijn PH, Snel M, Kostense PJ, Scheltens P, et al. No evidence for increased self-reported cognitive failure in Type 1 and Type 2 diabetes: a cross-sectional study. Diabet Med 2007; 24: 735-40.
13. Lucassen PJ, Pruessner J, Sousa N, Almeida OFX, Van Dam AM, Rajkowska G, et al. Neuropathology of stress. Acta Neuropathol 2014; 127: 109-35.
14. Cormack F, Shipolini A, Awad WI, Richardson C, McCormack DJ, Colleoni L, et al. A meta-analysis of cognitive outcome following coronary artery bypass graft surgery. Neurosci Biobehav Rev 2012; 36: 2118-29.
15. van Hoogmoed D, Fransen J, Bleijenberg G and van Riel P. Physical and psychosocial correlates of severe fatigue in rheumatoid arthritis. Rheumatology (Oxford) 2010; 49: 1294-302.
16. Hutchison M, Comper P, Mainwaring L and Richards D. The influence of musculoskeletal injury on cognition: implications for concussion research. Am J Sports Med 2011; 39: 2331-7.
17. Burnes DP and Burnette D. Broadening the etiological discourse on Alzheimer's disease to include trauma and posttraumatic stress disorder as psychosocial risk factors. J Aging Stud 2013; 27: 218-24.
18. Whittaker R, Kemp S and House A. Illness perceptions and outcome in mild head injury: a longitudinal study. J Neurol Neurosurg Psychiatry 2007; 78: 644-6.
19. Kennedy PJ, Clarke G, Quigley EMM, Groeger JA, Dinan TG and Cryan JF. Gut memories: Towards a cognitive neurobiology of irritable bowel syndrome. Neurosci Biobehav Rev 2012; 36: 310-40.
20. Hennig-Fast K, Werner NS, Lermer R, Latscha K, Meister F, Reiser M, et al. After facing traumatic stress: brain activation, cognition and stress coping in policemen. J Psychiatr Res 2009; 43: 1146-55.
21. Sandstrom A, Peterson J, Sandstrom E, Lundberg M, Nystrom IL, Nyberg L, et al. Cognitive deficits in relation to personality type and hypothalamic-pituitary-adrenal (HPA) axis dysfunction in women with stress-related exhaustion. Scand J Psychol 2011; 52: 71-82.
22. Bol Y, Duits AA, Lousberg R, Hupperts RM, Lacroix MH, Verhey FR, et al. Fatigue and physical disability in patients with multiple sclerosis: a structural equation modeling approach. J Behav Med 2010; 33: 355-63.
23. Sarzi-Puttini P, Atzeni F and Mease PJ. Chronic widespread pain: from peripheral to central evolution. Best Pract Res Clin Rheumatol 2011; 25: 133-9.
24. Vincent HK, Horodyski M, Vincent KR, Brisbane ST and Sadasivan KK. Psychological Distress After Orthopedic Trauma: Prevalence in Patients and Implications for Rehabilitation. PM R 2015; 7: 978-89.
25. Putukian M. The psychological response to injury in student athletes: a narrative review with a focus on mental health. Br J Sports Med 2016; 50: 145-8.

26. McEwen BS, Eiland L, Hunter RG and Miller MM. Stress and anxiety: structural plasticity and epigenetic regulation as a consequence of stress. Neuropharmacology 2012; 62: 3-12.
27. Seematter-Bagnoud L, Lecureux E, Rochat S, Monod S, Lenoble-Hoskovec C and Bula CJ. Predictors of functional recovery in patients admitted to geriatric postacute rehabilitation. Arch Phys Med Rehabil 2013; 94: 2373-80.
28. O'Neill BF and Evans JJ. Memory and executive function predict mobility rehabilitation outcome after lower-limb amputation. Disabil Rehabil 2009; 31: 1083-91.
29. Bellelli G, Frisoni GB, Pagani M, Magnifico F and Trabucchi M. Does cognitive performance affect physical therapy regimen after hip fracture surgery?. Aging Clin Exp Res 2007; 19: 119-24.
30. Coutu MF, Durand MJ, Marchand A, Labrecque ME, Berbiche D and Cadieux G. Factors associated with generalized anxiety in workers undergoing work rehabilitation for persistent musculoskeletal pain. Disabil Rehabil 2013; 35: 1599-607.
31. Anonymous ISCED (2019, accessed https://www.cbs.nl/nl-nl/onze-diensten/methoden/classificaties/onderwijs-en-beroepen/isced/isced-f-2013-richting.
32. Broadbent DE, Cooper PF, FitzGerald P and Parkes KR. The Cognitive Failures Questionnaire (CFQ) and its correlates. Br J Clin Psychol 1982; 21 (Pt 1): 1-16.
33. Wallace JC, Kass SJ and Stanny CJ. The cognitive failures questionnaire revisited: dimensions and correlates. J Gen Psychol 2002; 129: 238-56.
34. Bridger RS, Johnsen SA and Brasher K. Psychometric properties of the Cognitive Failures Questionnaire. Ergonomics 2013; 56: 1515-24.
35. Connor KM and Davidson JR. Development of a new resilience scale: the Connor-Davidson Resilience Scale (CD-RISC). Depress Anxiety 2003; 18: 76-82.
36. Windle G, Bennett KM and Noyes J. A methodological review of resilience measurement scales. Health Qual Life Outcomes 2011; 9: 8,7525-9-8.
37. Zigmond AS and Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand 1983; 67: 361-70.
38. Pallant JF and Bailey CM. Assessment of the structure of the Hospital Anxiety and Depression Scale in musculoskeletal patients. Health Qual Life Outcomes 2005; 3: 82.
39. Hayes AF. part 2 mediation analysis. In: Anonymous *Introduction to Mediation, Moderation, and Conditional Process Analysis: A Regression-Based Approach*, 2013, p.83.
40. Rutten BPF, Hammels C, Geschwind N, Menne-Lothmann C, Pishva E, Schruers K, et al. Resilience in mental health: linking psychological and neurobiological perspectives. Acta Psychiatr Scand 2013; 128: 3-20.
41. Leppin AL, Gionfriddo MR, Sood A, Montori VM, Erwin PJ, Zeballos-Palacios C, et al. The efficacy of resilience training programs: a systematic review protocol. Syst Rev 2014; 3: 20,4053-3-20.
42. Apostolo J, Bobrowicz-Campos E, Rodrigues M, Castro I and Cardoso D. The effectiveness of non-pharmacological interventions in older adults with depressive disorders: A systematic review. Int J Nurs Stud 2016; 58: 59-70.

43. Dick BD and Pillai Riddell R. Cognitive and school functioning in children and adolescents with chronic pain: a critical review. Pain Res Manag 2010; 15: 238-44.
44. Dick BD, Verrier MJ, Harker KT and Rashiq S. Disruption of cognitive function in fibromyalgia syndrome. Pain 2008; 139: 610-6.
45. Naismith SL, Rogers NL, Lewis SJ, Terpening Z, Ip T, Diamond K, et al. Sleep disturbance relates to neuropsychological functioning in late-life depression. J Affect Disord 2011; 132: 139-45.
46. Haverkamp GL, Torensma B, Vergouwen AC and Honig A. Psychological Distress in the Hospital Setting: A Comparison between Native Dutch and Immigrant Patients. PLoS One 2015; 10: e0130961.
47. Beck AT. The evolution of the cognitive model of depression and its neurobiological correlates. Am J Psychiatry.2008 Aug;165(8):969-77.
48. van der Werf-Eldering MJ, Schouws S, Arts B and Jabben N. Cognitive dysfunction in bipolar disorder: determinants and functional outcome. Tijdschr Psychiatr 2012; 54: 709-18.
49. Dufouil C, Fuhrer R and Alperovitch A. Subjective cognitive complaints and cognitive decline: consequence or predictor? The epidemiology of vascular aging study. J Am Geriatr Soc 2005; 53: 616-21.
50. de Groot JC, de Leeuw FE, Oudkerk M, Hofman A, Jolles J and Breteler MM. Cerebral white matter lesions and subjective cognitive dysfunction: the Rotterdam Scan Study. Neurology 2001; 56: 1539-45.