Cognition: Not a determinant of health related quality of life in middle to old aged men.

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Samenvatting:

Inleiding: Gezondheidsgerelateerde kwaliteit van leven is een belangrijk onderwerp in d sociale en medische wetenschappen. Het wordt steeds vaker gebruikt als evaluatiecriterium voor interventies. In de literatuur wordt een correlatie tussen algemene cognitie en kwaliteit van leven bij mensen zonder dementie gevonden. Aangezien dit allen dwarsdoorsnedenonderzoeken waren, is het niet duidelijk of cognitie een determinant is van gezondheidsgerelateerde kwaliteit van leven.

Doel: Het doel van dit onderzoek is om te bepalen of cognitie een determinant van kwaliteit van leven is. Daarnaast is een doel om te bepalen of één of meerdere cognitieve domeinen (mentale status, geheugen, snelheid en capaciteit van informatieverwerking, executieve functies en verbale intelligentie) onafhankelijke determinanten van gezondheidsgerelateerde kwaliteit van leven.

Methode: Een analyse van de data van een observationele prospectieve cohort studie van 401 niet-demente mannen van 48 tot 88 jaar werd uitgevoerd. De data werd met behulp van multiple regressie worden geanalyseerd waarbij gecorrigeerd werd voor mogelijke confounders (depressie, functionele achteruitgang en leeftijd).

Resultaat: Zonder correctie voor depressie, functionele achteruitgang en leeftijd is er een significante associatie van zowel cognitie als verandering in cognitie op gezondheidsgerelateerde kwaliteit van leven. Als er wel correctie voor deze factoren plaatsvindt, blijft er geen significante associatie meer over, behalve een kleine associatie van verbale intelligentie op gezondheidsgerelateerde kwaliteit van leven.

Discussie: Cognitie is geen determinant van gezondheidsgerelateerde kwaliteit van leven, De individuele cognitieve domeinen ook niet. Depressie en functionele afhankelijkheid hebben een sterk effect op de relatie tussen cognitie en kwaliteit van leven. Het is niet duidelijk of depressie of functionele achteruitgang confounders of mediators zijn in deze relatie.

Abstract

Introduction: Quality of Life (QoL) is an important topic in social and medical sciences (1). It is increasingly used as an evaluation criterion for interventions. In the literature, a correlation between general cognition and QoL of non-demented adults is found. Since those studies are all cross-sectional studies, it is not known cognition is a determinant of Health related quality of life (HR-QoL).

Objective: The aim of this study is to investigate the relationship between cognition and (HR-QoL) so to know if it is useful to develop interventions aimed at cognition to sustain or improve health related quality of life. A secondary objective is to asses if any of the domains of cognition (mental state, memory, processing capacity and speed, executive function, verbal intelligence) are an independent determinant of HR-QoL.

Method: A analysis of the data of an observational prospective cohort study of 401 non-demented men aged 48-88 was be performed. Data was analysed using multiple regression, correcting for possible confounders (depression, functional decline and age). Cognition was measured by a range of instruments (MMSE)

Result: When not corrected for age, functional dependence and depression there is a significant association of both cognition and change in cognition on HR-QoL. When correction for these factors does take place, no significant association remains, except for a small association of verbal intelligence on HR-QoL.

Discussion: Cognition did not have an effect on HR-QoL, neither did any of the individual cognitive domains. Depression and functional dependence have a strong effect on the relation between cognition and HR-QoL. It is not clear whether depression and functional decline are confounders or mediators.

Cognition: Not a determinant of health related quality of life in middle to old aged men.

Introduction

(1). There is an ongoing discussion about the definition of quality of life, however experts agree that it consists of social, psychological and physiological well-being (2, 3). The World Health Organisation (WHO) defines quality of life as *'… an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns'* (4). There is however a difference between QoL and health related quality of life (HR-QoL). HR-QoL is defined by Ericson and Patric as: *"The value assigned to the duration of life as modified by the impairments, functional states, perceptions and social opportunities that are influenced by disease, injury, treatment or policy* (5). The difference between the two constructs is that in HR-QoL more emphasis is placed on the impact of impairments. HR-QoL is frequently used to asses the effect of a disease or dysfunction (6). Because QoL has a highly individualistic, subjective and multidimensional nature, its is difficult to define and measure (7). QoL is also more influenced by response-shift (6). Therefore HR-QoL is used more regularly in research (8).

Quality of life of people with dementia has been studied in the last few decades; however the studies researching the relation between HR-QoL and normal cognitive aging are limited (9, 10). A correlation between general cognition and HR-QoL of independent living non-demented people has been found in the literature (11, 12). However these studies had a cross-sectional design and were therefore unable to asses the type of relationship between cognitive decline and HR-QoL. One study found an independent contribution of executive functions to HR-QoL in older women (13).

A concept related to HR-QoL is successful aging (7, 14). Successful aging is described by Rowe and Kahn (15) to be composed of the aspects of: freedom from disease, engagement with life, and physical and mental competence.
Because of the aging population there is a growing urge for nurses and other health care providers to promote successful ageing, and therefore HR-QoL.(16, 17)

One of the factors that could influence successful ageing and HR-QoL is cognitive aging (16-19). Cognitive ageing is considered to be a continuum of cognitive changes (20). Several cognitive tasks decline during the adult life span in a more or less linear process (21). These changes differ strongly from person to person. Normal aging affects various aspects of cognition (22). Cognitive aging is a feared aspect of aging (22-24).

Cognition is a multidimensional construct (25) and often separated in different domains. (26). The separation in domains makes it possible to distinguish more precise which part of cognition could play an important role in sustaining quality of life (25). The cognitive domains mental state, memory, executive function, language and visuospatial function are thought to be influenced by aging (22). Insight in the influence of each specific cognitive domain on HR-QoL could give insight in which cognitive domain is the 'key' to sustain or improve HR-QoL.

Insight in the relationship between cognitive decline and HR-QoL can lay a foundation for the development of interventions for sustaining HR-QoL by preventing or stabilising cognitive decline. Some promising interventions have already been developed: Aerobic fitness has shown to reduce brain tissue loss (21). Cognitive training has shown to improve certain cognitive processes (21). Both mental and physical training interventions could sustain cognitition in normal aging persons (21) . Nurses and other healthcare workers, especially those in primary care settings, face the challenge of helping growing numbers of people to age successfully and sustain HR-QoL. By investigating whether cognition is a determinant of HR-QoL, this study can help them face this challenge.

Problem-statement, aim and research question

Problem-statement:
Since there are no longitudinal studies that investigate the nature of the relationship between cognitive decline and HR-QoL, there remains a lack of insight in the nature of this relationship. Is it just a correlation or is there an influence, or even causality of cognition on HR-QoL?

Aim
The aim of this study is to investigate the relationship between cognition and health related quality of life (HR-QoL) so to know if it is useful to develop interventions aimed at cognition to sustain or improve health related quality of life.

Questions
Therefore the following research questions are formulated:
1. Is cognition a determinant of health related quality of life in non-demented adults?
2. Are the specific cognitive domains determinants of health related quality of life in non-demented adults?

Method

Design

To answer the research question an analysis of the data of an observational prospective cohort study, the PROFIEL of the Julius Centre/ UMC Utrecht., was performed. PROFIEL is a study to gain insight in which factors contribute to preservation of functioning and it's aim is to develop interventions to delay functional decline. Due to its data on many measurements of both cognition as well as possible confounding variables and its longitudinal design the dataset could give insight in the relationship of cognition and HR-QoL. In January 2011 the data collection for the male participants had been completed. The data collection for female participants was not completed at the start of this study but will be completed in 2011. Therefore only the data of the male participant has been analysed.

Ethical consideration

The data used in this study has been collected in the PROFIEL study. All participants of the PROFIEL study gave their informed consent and were given an incentive at the value of 25 euro per visit. Also taxi costs were covered when needed. The PROFIEL study was conducted according to the principles of the declaration of Helsinki, version 59, October 2008 and in accordance with the Medical Research Involving Human Subjects Act (WMO).
The PROFIEL study has been approved by the Medical Ethics Committee of the UMC Utrecht. For the current secondary analysis only the anonimized data has been used. Therefore no further approval of a medical ethics committee was needed.

Population

The target population of this study are non-demented males aged 40-88. For this study the data of 401 male participants has been analysed. At the time of the baseline measurement in 2001-2002, they were between 40-80 years of age, were independent living and had not been diagnosed with dementia. The follow-up measurement took place in 2009-2010, when the participants were 48-88 years of age. The recruitment of the men at the time of the first measurement took place in two different ways: First female participants of a similar study were asked if they knew any possible interested male volunteers of the appropriate age. Two hundred forty volunteers responded. Secondly a random sample of 1230 men of the appropriate age from the municipal register of a large sized town in the centre of the Netherlands were send an invitation letter of which 390 responded positively. Sixteen men were excluded, because they did not live independent or were mentally or physically unable to visit the study centre on there own. Of the remaining 614 men 401 men, spread across the included ages, were randomly selected to participate. Of this 401 participants 267 participated in the follow up measurement. The number of follow-up participants gives enough power to detect correlation coefficients of 0.25 or larger (27).

Variables

Dependent variable: Health related quality of life.
The dependent variable in this study was HR-QoL at the follow-up measurement. HR-QoL is measured with the Dutch language version of the RAND-36 health survey. (28). RAND-36 is a frequently used instrument in the research of HR-QoL in relation to aging (6). The RAND-36 measures the perception of health on eight dimensions: physical functioning, social functioning, role limitations because of physical problems, role limitations because of emotional problems, mental health, vitality, bodily pain and general health perception (29). The scores are converted to a 0 to 100 scale, higher scores indicate higher levels of well-being or functioning (29).
The RAND-36 has a high internal consistency, with alpha values of .71-.92. (28). TRT reliability for the different scales is .58-.82 after two months. (28). The RAND-36 has proven to have a good validity (28).

Independent variables
The main independent variable is the total cognition at the follow up measurement. Because cognition is a multidimensional construct (25) many measurements are taken into account. These measurements are divided in the following domains: **Mental state:** MMSE (30), **memory:** Rey Auditory Verbal Learning Test (RAVLT) (31), Doors test (32) and the Digital Span Test (33), **processing capacity and spee**d: Verbal Fluency (34) and Digit Symbol Substitution Test (33), **executive** functions: Trail Making Test A1, A2 and B37 (33), **verbal intelligence:** measured with a Dutch version of the National Adult Reading Test (NART), the Dutch Adult Reading Test (35). For each domain one or more instruments have been used. In table 1 the psychometric properties of the used instruments are presented.

<put table 1 here>

A total cognition global composite measure was calculated by combining all the cognitive domains (see figure 1). The change in total cognition was calculated by subtracting the scores of baseline (t1) measurements from the scores in the follow up measurement (t2).
In this way a decline in cognition will result in a negative score. In the analysis these change scores were standardized. The individual cognitive domains where calculated in the same way.

Possible confounders

Variables which were considered possible confounders of the relationship between cognition and HR-QoL, and which needed to be corrected for, were depression, functional dependence and age (36). Depression has been measured with the Patient Health Questionnaire (PHQ-9) (37). Functional dependence has been measured with the KATZ 15-questionaire (38)

Demographic measurements

Demographic measurements which are being used to describe the study population are: Age, marital status, living situation and education level, MMSE scores and HR-QoL scores.

Data analysis

The data were analysed with the SPSS 16 computer program. (SPSS Inc., Chicago, IL). Missing values where deleted pair wise. Prior to the data analysis the data were visually screened for outliers and linearity was analysed by using scatter plots.

The value of each of the individual cognitive domains (mental state, memory, processing capacity and speed, executive functions and verbal intelligence) were calculated by pooling the z-scores of the individual values included in that particular domain. The domain 'total cognition' was calculated by pooling the z-scores of all the individual domains together.

First the crude association of the total cognition on HR-QoL was analysed in simple regression models. The same was done for the individual cognitive domains.
Secondly the association of the total cognition on HR-QoL when corrected for the confounders (age, functional dependence, depression) was analysed in multiple regression models. The same was done for each of the individual cognitive domains, where correction took place for the confounders as well as for the other cognitive domains.

To test if there is an effect of change in cognition on quality of life, the change of total cognition between the baseline and the follow-up measurement was calculated. This value was analysed in a simple regression model to get a crude association of the effect of this cognitive change. In a multiple regression model the association of cognitive change was analysed while correcting for confounders. The same was done for the change in each of the individual cognitive domains while correcting for the confounders as well as correcting for the effects of the other cognitive domains.

Results

Demographic data

<put table 2 here>

In table 2 the demographic data of the participant who were measured at the follow-up ('completers') measurement are compared with the drop-out participants. The drop-out rate was approximately one-third of the participants. The completers had a lower age, lived independently more frequently and had a higher baseline MMSE score.

Regression analysis

<put table 3 here>
In table 3 the results of the different (multiple) regression analyses are presented.
Both total cognition and *change* of total cognition (models one and two) have a significant crude association with HR-QoL. When corrected for age, functional dependence and depression, the relation between total cognition and change in total cognition on HR-QoL does not remain significant (beta -.009 and -.063 respectively).

In the model that describes the crude association of the individual cognitive domains (model three), all the domains except verbal intelligence had a significant association with HR-QoL. When the cognitive domains were corrected for each other, only the association of mental state on quality of life remains significant (beta .247). After correcting for age, depression and functional dependence no significant effect remained.

In the model of the crude association of the *change* between measurement one and measurement two of the individual cognitive domains (model four), all cognitive domains except verbal intelligence have an effect on HR-QoL. When corrected for other cognitive domains, the effect of mental state and executive functions were found to be significant (beta.152 and .182 respectively). When correction for age, depression and functional dependence took place, no significant effect remained except for the domain of verbal intelligence (beta .108).

Subgroup analysis

A comparison was made between persons with and without cognitive decline (defined as a drop of one point or more in cognition) in relation with the presence of depression and functional dependence.

Significantly (p.009) more persons with cognitive decline also had a functional dependence (defined as a KATZ score one or higher). There was no statistical difference in the presence of depression (defined as a PHQ-9) score of 10 or higher(39) between the cognitive decline versus the non-cognitive decline subgroup.

Discussion

Cognition did not have an effect on HR-QoL, neither did any of the individual cognitive domains except for a small effect of the verbal intelligence domain in the longitudinal model.

. A mayor limitation of this study was the high drop-out rate. In this study only anonimized data, without information of reasons for drop-out was provided. The data about reasons for drop out could not be obtained. Since a large part of the study-population consists of older adults one reasonable explanation for the high drop-out rate is that some of the participants have died. This assumption is supported by the fact that the mean age of the drop-outs is higher than that of the completers. Since no data about mortality is available, this however, is a speculation.

A mayor strongpoint of this study is its longitudinal design. Because of its longitudinal design the effect change of cognition in time was taken into account in the analysis. Earlier studies of the effect of cognition on HR-QoL were mostly cross-sectional (40). In this study the number of participants provided enough power to detect small effect-sizes.

A high proportion of the participants had a higher education. This is also seen in other QoL-studies (11, 12). Because the sample is population based it is more representative of the general population than clinical populations used in other studies. This study included a broad spectrum of measurements of cognition instead of using just one instrument as the MMSE. Therefore a reliable representation of cognitive state of each of the participants was taken into account in the analyses. Also measurement of possible confounding and mediating factors as age, depression and functional dependence were taken into account, making it possible to compare the crude association of cognition on HR-QoL with the corrected association.

In the relation between the independent variables and HR-QoL no pattern of non-linearity could be found, therefore multiple linear was an appropriate technique to use. Some discrepancies from normality of residues where observed, this could have led to an overestimation of the effects (41). However, since no effects of cognition on quality of life were found this overestimation does not lead to a different conclusion.

When not corrected for age, functional dependence and depression there is a significant association of both cognition and change in cognition on HR-QoL. When correction for these factors does take place, no significant association remains, except for a small association of verbal intelligence on HR-QoL. The threshold of discriminating a minimal change in HR-QoL has been reported to be a half standard deviation (SD) (42). The significant but small (beta .108) association of verbal intelligence on HR-QoL therefore seems clinically not-relevant. Both depression and functional dependence have an effect on the relation between cognition and HR-QoL. In another study of 1620 community dwelling older adults, a strong association between depressive symptoms and functional status on life satisfaction, a concept that resembles QoL, was found (43). In the literature depression has been described as an effect of cognitive decline (37) but a decline in cognition also can be a symptom of a depression (44). Therefore it is unclear whether depression is a confounder or a mediator of the effect of cognition on quality of life. No statistical difference in the presence of depression in the cognitive decline or non-decline subgroups was found. Therefore it could be hypothesised that is not a mediating effect (persons with cognitive decline did not have more depressions) but a true confounder. However the data analysis done in this study does not give a conclusive insight in this relation so more research is needed.

A difference in functional dependence was found between cognitive-decline and the non-cognitive-decline subgroups. In the cognitive decline subgroup more persons had a functional dependence. In literature cognitive decline has been described as a determinant of functional dependence (45). Therefore functional dependence could be a mediator of the effect of cognition on HR-QoL rather than a confounder. However more research should be done to really understand this relationship.

Conclusion

Cognition is not a determinant of HR-QoL of middle to old aged non-demented men , nor are any of the individual cognitive domains. Depression and functional dependence have a strong effect on the relation between cognition and HR-QoL and could be confouders or mediators of this relation.

Recommendations

More research should be done about how depression and functional decline influences the relation between cognition and HR-QoL so it can be determined whether these factors are mediators or confounders.

In clinical practice, nurses and other health-care workers should put their effort in preventing depression to help people sustain their HR-QoL. In people with cognitive decline nurses and other healthcare workers should put their effort in preventing functional dependence and depression as this is an important factor in the relation between cognition and HR-QoL

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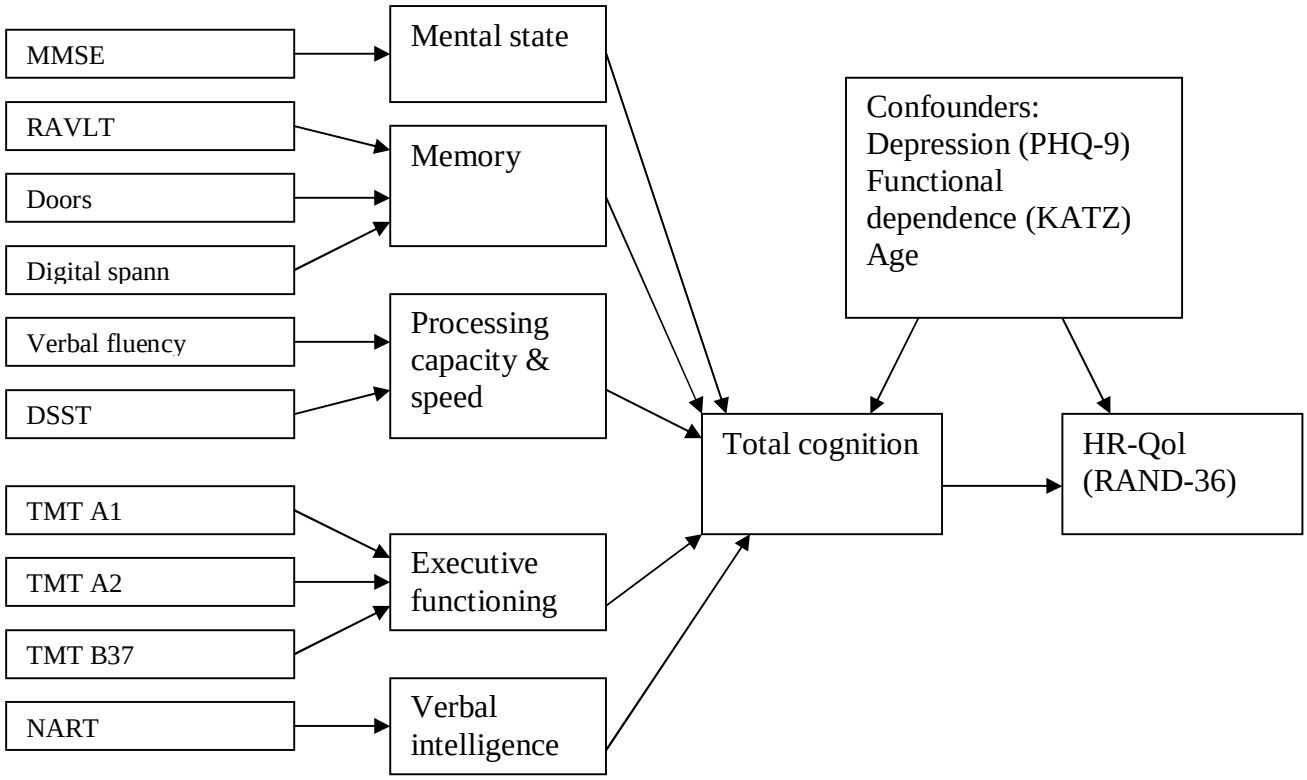

Figure 1: variables

Table 1: measurements

Variable	Measure	Psychometric properties
HR-QoL	Rand 36	TRT reliability for the different scales is .58-.82 after two months. The scales have a high internal consistency with alpha values of .71-.92. (19)
Metal state	Mini Mental State Exam (MMSE) (46)	a frequently used instrument to measure cognition (21)
Memory	Rey's Aditory Verbal Learning Test (RAVLT) (28)	*"TRT reliability is good for total recall over 5 trials, .60–.70 over 1y. Internal reliability of total score is high (coefficients .90)*".(30) *"Extensive literature regarding good validity, including construct, criterion, and predictive."* (22)
Memory	Doors test(31)	
Memory	Digital span test(47).	*"TRT stability coefficient is .83. Average reliability coefficient across age is* .90." (47)
Processing capacity and speed	Verbal Fluency(32)	
Processing capacity and speed	Digital symbol substitution test (33).	"TRT stability coefficient is .83. Average reliability coefficient across age is .90." (47)
Executive functions	Trail making test A1, A2, B37(34)	A test-retest correlation of 0.79 of part A and 0.89 for part B has been found" (33) *"Parts A and B are moderately intercorrelated (r_.31–.36), suggesting they measure similar, but somewhat different, functions"* (47) The test is sensitive to effects of age (33).
Verbal intelligence	Dutch Adult Reading Test (47)(47) Is a Dutch version of the National adult reading test (NART)	The test-retest correlation of the NART is 0.98 (48). The inter-rater correlation is between 0.96 and 0.98 (35).
Depression	PHQ-9(36).	The 48 hour test-retest reliability of the PHQ-9 is reported to be 0.84 (49). The internal consistency has a crombachs alpha of 0.89 (49).
Functional dependence	Katz-15(38)	The KATZ questionnaire is considered reliable in one study (50).

Table 2 demographic data:

(measurements at baseline)		**Completers**	**Drop-outs**	**Sig**
N		267	124	
Age #		58,64	63,49	.000
Marital status &	Living together (married or otherwise)	87.6%	91.0%	.386
Living situation &	Independent	98.9%	95.5%	.014
	Home-care	0%	3.8%	
	Service-apartment	.7%	.8%	
	other	.4%	0%	
Education level &	Low	14.6%	20.3	.481
	Middle	28.5%	26.6	
	High	36.0%	33.8	
	University	21.0%	17.3	
MMSE #		28.08	27.67	.012
RAND #		81.98	80.56	.383
Measurements at T2				
MMSE at t2		28.64	-	
RAND at t2		79.99	-	

#= indep. t test &= Pearsons chi square

Table 3: Results of the different regression models.

		Crude associations (bivariate regressions)		Corrected for other cognitive domains.		Associations when corrected for age, depression and functional dependence	
		beta	p	beta	P	beta	p
1. Total cognition at t2	Total cognition	.231	.000*			-.009	.828
2. Change of total cognition	Change of total cognition Age Functional dependence Depression	.184	.005*			-.063	.148
3. All cognitive domains together at t2:	Mental state Memory Processing cap. and speed Executive functions Verbal intelligence	.302 .194 .266 .265 .081	.000* .002* .000* .000* .188	.247 .022 .138 .096 -.121	.001* .788 .134 .274 .096	.053 -.051 -.104 -.035 .108	,253 ,323 ,078 ,542 ,027*
4. change of individual domains	Change mental status Change memory Change pross. Cap & speed Change exec. functions Change verbal intelligence	.196 .180 .136 .263 -.010	.001* .004* .030* .000* .870	.152 .119 .022 .182 -.072	.026* .091 .754 .010* .268	.066 .004 -.043 -.042 -.050	.120 .936 .317 .403 .211

Method=ENTER *= significant at the 0.05 level