Associations between memory, depression and wellbeing of an ageing population

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Abstract

Dementia is a major challenge in our aging society. Apart from its health economic impact, cognitive decline may affect the quality of life (QoL) and affective states of individuals. From a measurement perspective, it is of high importance to use quality-assured measurements to derive valid and reliable results. This paper investigates to what extent improved memory metrics can be exploited to investigate the strength of correlation between memory ability, depressive symptoms, and well-being. It also aims to shed light on earlier heterogeneous results through the application of quality-assured measurements. In this paper, we analyzed associations between memory ability, measured by the new and more accurate NeuroMET Memory Metric (NMM), and depressive symptoms and wellbeing of the same individuals measured using the Geriatric Depression Scale (GDS) and the WHOQoL-BREF of older individuals (n=332, ranging from healthy controls to patients with dementia due to suspected Alzheimer's Disease (AD), with a mean age of 72 years). While decreased memory ability was moderately associated with more depressive symptoms (Pearson R = -0.36), it was only negligibly associated with worse well-being (associations with WHOQoL-BREF and subdomains ranging between R = 0.08 and 0.12), which is partly in line with previous studies. A group-wise analysis revealed that these effects were stronger for individuals with subjective cognitive decline (SCD). Our study leveraged measurements scales and models with improved accuracy.

Keywords

Cognition, Memory, Quality of Life, Metrology, Rasch-analysis

1. Main text introduction

Increased life expectancy, thanks to a century of improved education, medical care, and public health (at least in high-income countries) has led to what has been called a third epidemiologic transition where chronic and degenerative diseases (such as dementia) have replaced infectious diseases as the dominant health issues (Aisen et al., 2017; European Brain Council, 2018; Fried & Paccaud, 2010; Langa, 2018; *World Health Statistics 2022*, 2022).

The possible effects of decreased cognition on an individual's daily life, such as impact on quality of life (QoL) aspects, are at least as important as the medical and care challenges, i.e., health-economic challenges (Jing et al., 2016). Importantly, with no cure yet for dementia, ensuring the best possible QOL has received increasing attention from patient organizations, health authorities and policy makers (Raeymaekers & Rogers, 2010). QoL broadly encompasses the 'goodness' of multiple aspects of the life of individuals, ranging from personal well-being to economic power and the living standards of individuals (c.f., Malkina-Pykh & Pykh, 2008; Maricic, 2019; Theofilou, 2013). Thus, QoL comprises both objective and subjective components. Closely related to QoL, and sometimes overlapping, are affective states such as feeling happy, relaxed or depressed (Lischetzke, 2014).

Multiple studies have been conducted, for instance, addressing the relation between cognition, QoL and affective states, both on a general level (Waters, 2014) and more specific in an older population with dementia (González-Salvador et al., 2000; Stites et al., 2018) and cognitive decline on a continuous scale independent of diagnoses (Allerhand et al., 2014; Stavrinou et al., 2022; Veldema & Jansen, 2019; Voros et al., 2020; Wilson et al., 2004). These studies suggested that cognitive complaints may be related to lower QoL and greater depression (Allerhand et al., 2014; Stavrinou et al., 2022; Stites et al., 2018; Veldema & Jansen, 2019; Voros et al., 2020; Wilson et al., 2004), and that depressive symptoms may predict cognitive decline in old age (Wilson et al., 2004). However, the strengths of these associations are still unclear. Furthermore, while the relation between cognition and well-being is seen as dynamic (Allerhand et al., 2014; Veldema & Jansen, 2019), most of the variation in well-being has been explained by depression (Allerhand et al., 2014; Voros et al., 2020).

From a measurement perspective, it is of high importance to use quality-assured measurements, as invalid or unreliable testing might cause errors in QoL or cognition measures which can have far-reaching consequences on the conclusions. A better understanding of the relationship between memory and QoL – including measurements thereof – could create better opportunities to address health- and QoL- issues among the aging population. However, only few of the methods used for the measurement of QoL aspects or cognition have applied metrological quality assurance. Rather they have relied on classical test theory (CTT), which suffers from improper handling of ordinal data and lacks a separation between person and item attributes needed for a proper metrological treatment (cf. Cano & Hobart, 2011; L. Pendrill, 2014).

To determine cognitive abilities, different cognitive domains can be measured through neuropsychological tests. When it comes to the measurement of memory, this can be done with different neuropsychological tests, such as recall of blocks, numbers and words. To respond to the lack of metrological quality assurance for cognition measurements in general and more specifically memory measurements, the NeuroMET Memory Metric (NMM) has recently been developed, including applying the Rasch model to provide separate and linear estimates if person memory ability and memory task difficulty on the same conjoint scale. The NMM, generated from a bank of items carefully selected from legacy short-term memory tests, linking language- and cultural-free items (blocks, digits) to more complex word recalling items, has been demonstrated to have superior accuracy compared with previous memory metrics (Melin et al., 2022b, 2023). The improved accuracy of the NMM, which is exploited in the present study of correlations between memory ability,

depressive symptoms and wellbeing, tackles several of the above-mentioned limitations in CTT thanks to deploying the Rasch-model (cf. Andrich, 2004; Cano & Hobart, 2011).

The NMM, the product of the NeuroMET projects (Quaglia et al., 2019, 2021), is more efficient – including handling of distorted raw scores and ensuring comparability – and has substantially reduced measurement uncertainties compared with traditional legacy memory tests (Melin et al. 2023). Following earlier studies with the new NMM of correlations between memory ability and biomarkers (Melin, Cano, Flöel, et al., 2021; Göschel, Dell'Orco. Fillmer, et al., 2024), the present work aims to investigate to what extent the improved memory metrics can be exploited to investigate strength of correlation between the memory ability of older people and their degree of depressive symptoms and well-being. The paper further aims to shed light on earlier heterogeneous results (c.f., Allerhand et al., 2014; Beerens et al., 2015; González-Salvador et al., 2000; Stavrinou et al., 2022; Stites et al., 2018; Voros et al., 2020) through the application of quality assured measurements.

2. Materials and methods

Study sample

Between 2016 and 2022 a total of 332 individual assessments of the QoL aspects were conducted among 127 participants. The individual assessments comprised visits of healthy controls (HC, n=110, 33%), individuals with subjective cognitive decline (SCD, n=102, 31%) and patients with mild cognitive impairment (MCI, n=55, 17%) and dementia due to suspected Alzheimer's Disease (AD, n=65, 20%), with an equal distribution of individual visits of men (n=164, 49%) and women (n=168, 51%) and a mean age of 72 years (SD=7). Diagnoses were established by a multidisciplinary team of neurologists, neuropsychologists, and researchers based on neuropsychological test outcomes and clinical assessments, incorporating CSF results when available. Inclusion criteria were 55-90 years of age, normal vision with or without aid and ability to consent. Exclusion criteria were stroke, Morbus Parkinson, newly initiated therapy with Acetylcholinesterase (AChE) inhibitors/memantine, pregnancy, other neurological disorders that could potentially affect cognition, history of drug or alcohol abuse, and non-suitability for MRI (e.g., persons with claustrophobia, active or ferromagnetic implants such as pacemakers).

Data came for a two-day assessment, where most of the legacy tests included in the NMM were performed on the first day of each assessment (Corsi block test (CBT) (Corsi, 1972), Digit span test (DST) (Wechsler, 1955), Word Learning List from the CERAD test battery (WLL CERAD) (Morris et al., 1989) and Mini Mental State Examination (MMSE) Folstein, Folstein, & McHugh, 1975), while the German version of Rey's Auditory Verbal Learning Test (German Verbaler Lern- und Merkfähigkeitstest) (Helmstaedter, Lendt, & Lux, 2001)was completed on the second day. The assessment of the Geriatric Depression Scale (GDS) (Yesavage et al., 1982) was done on the first day, while the assessment of the World Health Organization Quality of Life Brief Version (WHOQoL-BREF) (World Health Organization, 1996) was done on the second day. Due to the adjustment for missing data, there are minor differences in the demographics of the respondents of the WHOQoL-BREF and the GDS (see attachments).

Measurements

The present study addressing the associations between QoL aspects and memory ability benefits from the improved accuracy of the recently developed NMM mentioned in the Background (Melin, Cano, & Pendrill, 2021; Melin et al., 2022a, 2022b, 2023). The NMM has shown up to a five folded reduction in measurement uncertainty for memory ability compared with individual legacy tests while at the same time not jeopardizing validity (Melin et al., 2022b, 2023).

The test battery used in the NeuroMET studies included several assessments of QoL aspects. To study the relationship between QoL aspects and memory ability, the GDS (Greenberg, 2012) was used to measure depression and the WHOQoL-BREF (WHO, 1998) was used to measure wellbeing. The GDS consists of 15 items and is a shorter form of the GDS Long Form (Greenberg, 2012). The items are questions regarding how the participant has felt over the past week, which can be answered with either yes or no. The WHOQoL-BREF has 26 items and is an abbreviated version of the WHOQOL-100 quality of life assessment. The questionnaire has four domains related to quality of life, which are physical health, psychological, social relationships, and environment (Noerholm et al., 2004; WHO, 1998). Items are typically answered on a 1-5 Likert scale.

Data analysis

The Rasch-analysis was applied, both for the measurements of memory and the QoL aspects. For the NMM, the dichotomous Rasch model using RUMM2030 (Andrich et al., 2009) was applied and the measurement properties have been reported elsewhere (Melin et al., 2023). The analyses of GDS, WHOQoL-BREF, and WHOQoL-BREF domains were performed using the RISEkbmRasch package (Johansson et al., 2023) in R version 4.1.1 (R Core Team, 2019). The complete analysis and measurement properties have been documented in six HTML-files; one for GDS, one for WHOQoL-BREF, and one for each of the four domains of the WHOQoL-BREF, that can be retrieved at the Open Science Foundation website (see Availability of data and materials).

Based on the person measures derived from the Rasch-analyses, associations between person measures of memory ability and depression and well-being were examined through a Pearson correlation analysis using the programming language R (version 4.3.0) and the package Correlation (version 0.8.3). Standard interpretations of Pearson correlation coefficients, *R*, were as follows: 0.90-1.00 = very high, 0.70-0.89 = high, 0.50-0.69 = moderate; 0.26-0.49 = low, and 0.00-0.25 little if any (Munro, 2005). Correlation measures, such as Pearson *R*-coefficients, are in themselves not necessarily signs of causality (Altman & Krzywinski, 2015), where the latter would require longitudinal studies which we have yet to perform.

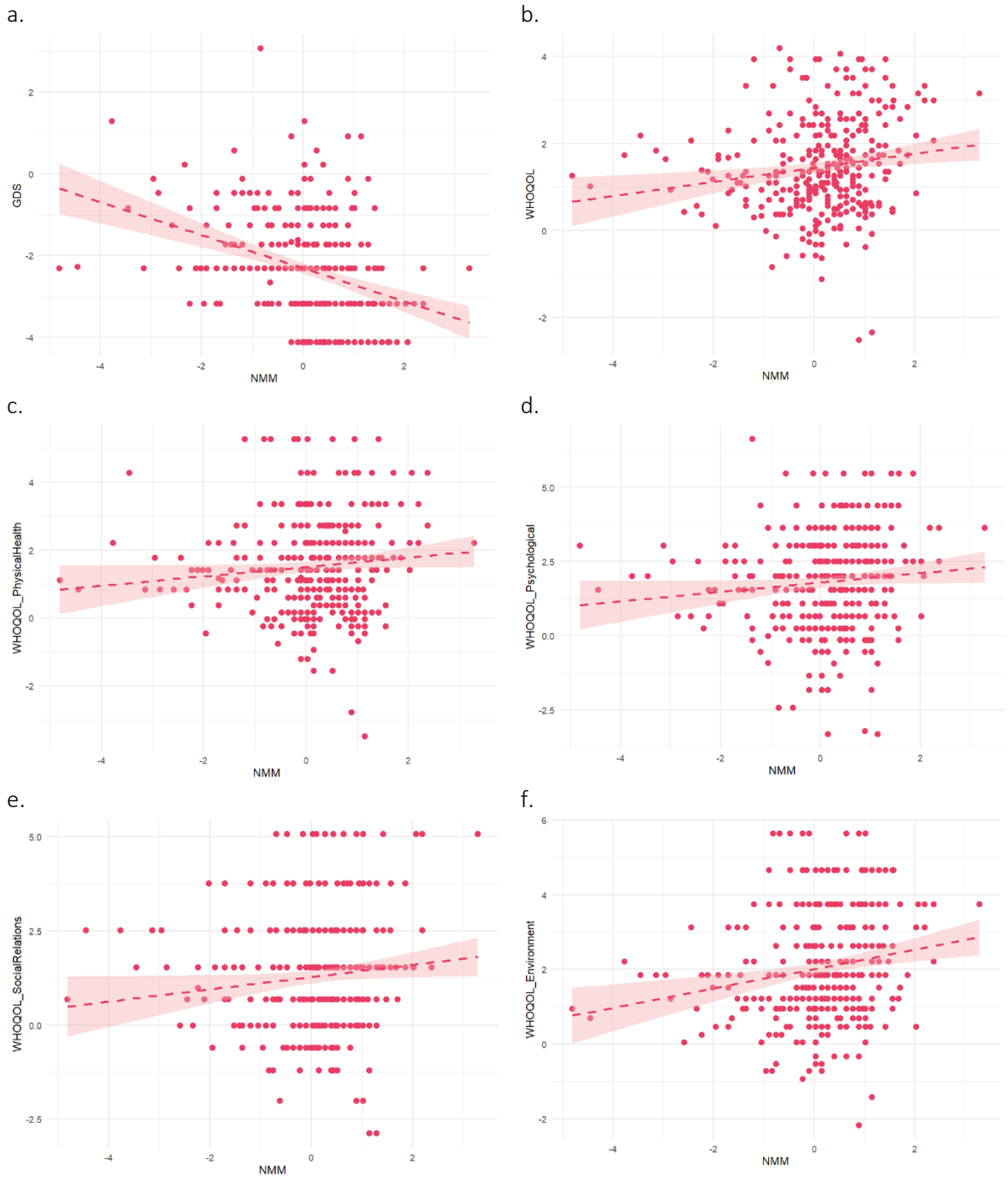
3. RESULTS

The person measures used, derived from the Rasch-analyses, are on a logit interval scale, i.e., not summarised raw scores, which compensates for potential scale distortion and ensures comparability within the cohort members. A higher person measure derived from NMM indicates better memory ability, a higher person measure derived from GDS indicates more severe depressive symptoms, and a higher person measure derived from WHOQoL-BREF and its domains indicates better wellbeing.

Figure 1a-f shows associations between person measures of memory ability and each of the outcome measures with further associations in Table 1 (full cohort and for each diagnostic group). The degree of correlation between memory ability and depressive symptoms, when measured with GDS, was low and negative (Figure 1a and Table 1). This implies that in the full cohort, most persons with better memory showed fewer depressive symptoms and vice versa. We observed little, if any, correlation between memory ability and well-being when measured with the full WHOQoL-BREF or WHOQoL-BREF domains (Figure 1b-f and Table 1).

Furthermore, Table 1 also includes coefficients of correlation between the selected person measures for all QoL aspects, separated into groups of HC, SCD, MCI and AD based on participant diagnosis. When it comes to the strength of correlation between person measures for memory ability and wellbeing measured with WHOQoL-BREF and its subscales, this correlation appears to be differentiated for the participants with SCD. In most cases, as shown in Table 1, the correlation coefficients were stronger among the participants with SCD compared to the other groups. A further

important note is that among the participants with MCI, there was a negative correlation (R = -0.375) between person measures for memory ability and the WHOQoL-BREF psychological domain, i.e., patients with MCI showed worse psychological wellbeing with better memory ability.



Figures 1a-f. Correlation plots of person measures of memory ability measured with the NMM and (a) depression measured with GDS, (b) well-being measured with WHOQoL-BREF, (c-f) domains of well-being measured with WHOQoL-BREF sub-scales. A higher person measure on NMM indicates better memory ability, a higher person measure on GDS indicates more severe depression symptoms, and a higher person measure on WHOQoL-BREF and its sub-scales indicates better wellbeing.

Table 1, Correlation matrix of person measures of memory ability, well-being, and depression for the full cohort and based on the participant's diagnosis.

		NMM	GDS	WHOQoL-BREF	WHOQoL-BREF domains			
					Physical health	Psychological	Social relationships	Environment
NMM								
GDS		Total: -0.341 HC: -0.131 SCD: -0.223 MCI: 0.133 AD: -0.068						
WHOQoL-BREF		Total: 0.158 HC: -0.028 SCD: 0.380 MCI: -0.298 AD: -0.081	Total: -0.507 HC: -0.393 SCD: -0.538 MCI: -0.439 AD: -0.420					
WHOQoL-BREF domains	Physical health	Total: 0.106 HC: 0.016 SCD: 0.252 MCI: -0.375 AD: -0.026	Total: -0.380 HC: -0.174 SCD: -0.492 MCI: -0.320 AD: -0.276	Total: 0.837 HC: 0.776 SCD: 0.846 MCI: 0.857 AD: 0.848				
	Psychological	Total: 0.106 HC: 0.055 SCD: 0.289 MCI: -0.376 AD: -0.238	Total: -0.584 HC: -0.517 SCD: -0.622 MCI: -0.503 AD: -0.487	Total: 0.856 HC: 0.773 SCD: 0.884 MCI: 0.860 AD: 0.898	Total: 0.605 HC: 0.416 SCD: 0.665 MCI: 0.615 AD: 0.669			
	Social relationships	Total: 0.112 HC: -0.002 SCD: 0.438 MCI: -0.019 AD: -0.018	Total: -0.300 HC: -0.417 SCD: -0.232 MCI: -0.368 AD: -0.162	Total: 0.679 HC: 0.756 SCD: 0.714 MCI: 0.623 AD: 0.519	Total: 0.420 HC: 0.412 SCD: 0.457 MCI: 0.418 AD: 0.282	Total: 0.544 HC: 0.647 SCD: 0.557 MCI: 0.530 AD: 0.296		
	Environment	Total: 0.188 HC: -0.060 SCD: 0.369 MCI: 0.072 AD: 0.083	Total: -0.373 HC: -0.275 SCD: -0.375 MCI: -0.300 AD: -0.350	Total: 0.843 HC: 0.787 SCD: 0.851 MCI: 0.860 AD: 0.894	Total: 0.577 HC: 0.438 SCD: 0.584 MCI: 0.616 AD: 0.686	Total: 0.656 HC: 0.525 SCD: 0.707 MCI: 0.669 AD: 0.722	Total: 0.515 HC: 0.508 SCD: 0.594 MCI: 0.436 AD: 0.420	

AD = Alzheimer Disease; GDS = Geriatric Depression Scale; HC = Health controls; SCD = Subjective Cognitive Decline; MCI = Mild Cognitive Impairment; NMM = NeuroMET Memory Metric; WHOQoL-BREF World Health Organization Quality of Life Brefie Version

4. DISCUSSION

This is the first study examining the relationship between memory ability measured with the new NMM, and depressive symptoms and wellbeing. It is also, to our best knowledge, the first study applying the Rasch model when ascertaining such correlations. The results reported here show a low correlation between memory ability and depressive symptoms but no relations between memory ability and well-being. Lower memory ability was, however, associated with lower well-being (i.e., the person measure from WHOQoL-BREF and its subscales) primarily in participants with SCD but not for those with more advanced stages of cognitive decline. This specific group could be particularly sensitive due to their increased perceived cognitive decline.

Compared to earlier work using CTT, our results are in part in agreement and in part in disagreement with earlier studies (Allerhand et al., 2014; Beerens et al., 2015; González-Salvador et al., 2000;

Stavrinou et al., 2022; Stites et al., 2018; Veldema & Jansen, 2019; Wilson et al., 2004). Several factors may explain the divergent results between studies: In short, the differences between earlier studies and our study may be summarised in terms of different cohort compositions and variation of the scales and constructs. Firstly, the cohort compositions vary: For instance, the population included in the study by Stavrinou et al (2022) was older than ours (age 80.6 ± 8.2 years), the proportion of participants suffering from dementia or MCI was greater in the study by Stites et al (2018) compared to ours and Beerens et al (2015); and Conzáles-Salvador et al (2000) included only persons resident in long term facilities. The SCD group in our study also differed from the cohorts of the other studies. Consequently, the differences in results might be attributable to these different subgroups of older people. Second, this study specifically focused on the construct memory ability, and its correlation with depressive symptoms. While other studies used "higher-order measures" for cognition covering several different constructs, e.g., the MMSE as a global cognitive measure (Allerhand et al., 2014; González-Salvador et al., 2000; Stavrinou et al., 2022), our study used NMM to derive person measures focusing specifically on memory ability. Similarly, another study (Stites et al., 2018) used QOL-AD and DEM-QOL compared to WHOQoL-BREF used here. In summary, differences in the associations between cognition and QoL might be due to differences in specific assessments used across studies.

Moreover, previous studies did not comprehensively address the issues of measurement and psychometric properties as discussed above. For instance, relying on raw data on an ordinal scale, systematically underestimates measurements of person attributes at the upper end of the scale and underestimates measurements of person attributes at the lower end of the scale (cf. Cano & Hobart, 2011; Pendrill, 2014). These over- and underestimates will distort correlation studies (Pendrill, 2018). Thus, compensating for ordinality in this work with the psychometric Rasch model might have overcome some of the biases from previous studies.

With questionable measurement practices highlighted by amongst others (Flake et al., 2022; Flake & Fried, 2020; L. Pendrill, 2019) there is "*a risk of ongoing unintentional research misconduct and prolonged problems with non-comparable and unreplicable research results"* (Johansson et al., 2023). The development of the NMM – to respond to the lack of metrological quality assurance for memory measurements – is a result of a research collaboration with a particular focus on improving the measurement quality (Quaglia et al., 2019). The same rigorous and comprehensive work needs to be carried out for measurements based on GDS or WHOQoL-BREF and remains to be done. Although beyond the scope of the present study, we would like to highlight that there are critical issues with the measurement properties of all those measurements. We have documented these in a HTML-file that can be retrieved at the Zenodo website (see Availability of data and materials). Overall, compensating for the ordinality and using person measures separated from the item difficulty rather than raw scores are necessary steps towards improved measurement quality assurance.

While measurements of memory ability rely on observations, e.g., if the test person either passes or fails on recall tasks, measurements of QoL aspects are typically based on self-reports. In these self-reports, an individual's perception of their experience rather than an objective report of an observable event is used. While this approach has the advantage to better reflect the patient perspective, this poses specific challenges for people with cognitive impairment, such as MCI or dementia. For instance, they may have difficulties with memory and attention, which in turn can lead to limitations in recalling and reporting consistently through a questionnaire (Smith, 2023). As a response to this, the DEMQOL and DEMQOL-proxy (disease-specific questionnaires for health-related quality of life in people with dementia) have been developed based on principles for measurement quality assurance with a possibility for equating self- and proxy-reporting (Hendriks et al., 2017; Hughes et al., 2019; Smith,

2023). The work with DEMQOL and DEMQOL-proxy provides unique possibilities to measure some QoL aspects through the AD spectrum to be used longitudinally. Although the understanding and link to generic QoL scales, such as the globally used WHO-BREF or SF-36, warrants further investigations as they may be more useful in pre-stages of dementia and the general population when studying the relationships to memory and other cognitive domains in future studies.

A recent review by Jing et al (2016) concluded that, among people with dementia, aspects such as demography, physical, psychological, social, and religious can affect QoL. No unique or common factors associated to QoL from early to severe stages of dementia were found in that study. In the present study, for the full cohort, the strongest correlation was found between memory ability and depressive symptoms. There was, however, a lot of scatter around the regression lines (as shown in figures 1). We have also identified some deviating patterns for subgroups within our cohort in all correlations. In turn, this raises questions about how to promote and support QoL and affective states in the aging population and at different parts of the Alzheimer spectrum. In any case, as an important part of meeting the global challenge of an increasing elderly population with increasing prevalence of dementia, informed decisions regarding health care in the aging population are likely to benefit from a more solid knowledge base. Specifically, we encourage more studies which aim to ascertain relationships based on quality-assured measurements, together with further treatment and intervention studies.

When interpreting the findings in this study, there are two main methodological considerations. First, the NeuroMET cohort was not recruited specifically to study relationship between memory ability, depressive symptoms and wellbeing, thus, no power analysis was undertaken before, and the sample size is small. Secondly, while the NMM has undergone extensive metrological development and validation, as yet the same comprehensive way for measuring wellbeing aspects is not available. On the other hand, as emphasized above, compensating for ordinality and using measurements of depressive symptoms and wellbeing aspects separated from item difficulty rather than raw scores are steps towards improved measurement quality assurance.

Conclusion

The relations between memory ability, depressive symptoms, and wellbeing raised in this study corroborate some of the results of previous studies in the area, but critical differences remain. Some of these differences might be explained by different cohort compositions, different scales used for measurements or different measurement models. This study suggests that associations might be distinct for different stages of cognitive impairment, and different scales and measurement models might be needed depending on the stage of cognitive impairment. Notably, we found that lower memory ability was linked to lower well-being primarily in individuals with SCD, but not in those with more advanced cognitive decline. This may reflect heightened concerns about perceived cognitive decline in this group.

In this study, we have challenged previously reported associations while encouraging further studies using quality-assured measurements to improve the knowledge base of the associations between memory ability, depressive symptoms and wellbeing in the aging population. Thus, we believe that the methodology utilized in this study can provide a better understanding of the relationships between memory, depression and wellbeing thereby enabling well-informed decisions to address more effectively health- and QoL issues among the aging population.

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An unauthorized version of the German MMSE was used by the study team without permission and this has been rectified with PAR. The MMSE is a copyrighted instrument and may not be used or reproduced in whole or in part, in any form or language, or by any means without written permission of PAR ([http://www.parinc.com)] www.parinc.com).

Declaration of interest statement

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Disclosure statement: The authors have no conflicts of interest to declare.

Ethics approval: The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of the Charité University Hospital, Berlin, Germany (EA1/197/16 approval on October 13th 2016 and EA2/121/19 approval on October 10th 2019)

Consent to participate and publication: Participants gave written informed consent in the participation and publication of this study.

Data availability statement: Data with person characteristics and measures of memory ability (measured with NMM), depressive symptoms (measured with GDS) and well-being (measured with the full WHOQoL-BREF or WHOQoL-BREF domains) can be retrieved at Zenodo [10.5281/zenodo.10686131].

Code availability: Following code has been used for the Rasch analysis: GitHub - pgmj/RISEkbmRasch: R package for Rasch Measurement Theory based psychometrics, for use with the scientific publishing system Quarto. Code adjusted for the specific analysis can be retrieved through the HTML files on Zenodo.

Authors' contributions: The manuscript was designed by JM and LP. MP conducted a literature review and summary. LG provided the data for the empirical example. MP conducted the analyses. JM and LP validated the analyses. MP drafted the manuscript. MP, JM, LG, LP and AF edited and revised the manuscript. All authors read and approved the final manuscript.

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