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Executive Functions & Quality of Life in patients with Severe Mental Illness

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Abstract

In the Netherlands 216.000 patients with SMI receive mental health care. In other to improve treatment and optimize the quality of life of patients with SMI, it is essential to understand the factors that influence quality of life. This cross-sectional study aims to explore a model for executive functions influencing quality of life in patients with SMI. This study had a cross-sectional design with a cohort of patients with SMI (*N* = 54) who are admitted to long-term psychiatry units. The test battery for executive functions contained multiple subtests measuring different aspects of the overall executive functions. Subjective and objective QoL, premorbid IQ and psychopathology were measured using questionnaires. Structural Equation Modelling (SEM) was used to test the complete model. The results show that executive functions do not predict subjective QoL and that the development of interventions focussed on executive functions in patients with SMI is not recommended. Verbal intelligence significantly predicts subjective QoL and therefore might be a future target for interventions for patients with SMI. Psychopathology strongly predicted subjective and objective QoL and therefore should remain the main focus in the treatment of patients with SMI.

1 Introduction

One of the patient groups in the mental health services receiving most care consists of by patients with Severe Mental Illnesses (SMI). In the Netherlands 216.000 patients with SMI receive mental health care, but the total prevalence of SMI is estimated at 281.000 people (Delespaul & De Consensusgroep, 2013). Of all patients with SMI 31% suffers from schizophrenia and 19% from other schizophrenic disorders, 10% suffers from addiction and another 10% from (bipolar) depression in combination with psychosis (Delespaul & De Consensusgroep, 2013). Other psychiatric problems that are more common in patients with SMI compared to patients with general psychiatric disorders are drug abuse, pervasive developmental disorders and personality disorders, especially borderline (Delespaul & De Consensusgroep, 2013). Patients with SMI, who often receive years of care, form a growing financial burden on the healthcare system (Bijenhof, Folkertsma, Kommer, Slobbe, & Polder, 2012; Centraal Bureau voor de Statistiek, 2015). Therefore, there is an urgent need to lower the mental health care costs for patients with SMI. By optimizing their quality of life, patients will need less care and the mental healthcare costs will decrease.

In other to improve treatment and optimize the quality of life of patients with SMI, it is essential to understand the factors that influence quality of life. The influence of psychopathology, especially symptoms of depression and anxiety, on quality of life is most frequently researched (Ueoka et al., 2011), but the cluster of factors that is often neglected are cognitive functions, especially executive functions. This cross-sectional study aims to explore a model for executive functions influencing quality of life in patients with SMI.

Since there is no complete consensus between researchers about the definition of SMI, Delespaul and De Consensusgroep (2013) developed a definition based on analyses from different views. Delespaul and De Consensusgroep (2013) define SMI when patients suffer from a psychiatric disorder that requires treatment or care and causes severe disability in social functioning. The problems are not temporary and patients receive years of high level care while being admitted to a mental health institution. The problems of patients are interrelated and intransient.

It is well known that cognitive deficits in executive functions are an integral feature of most of the disorders, especially schizophrenia, patients with SMI suffer from (Alptekin et al., 2005;

Braff et al., 1991; Brissos, 2008; Meltzer, 1991; Saykin et al., 1994). Multiple researchers reported wide-spread impairments in many domains of neurocognitive function, including executive functions, verbal learning and memory and working memory (Alptekin et al., 2005; Braff et al., 1991; Brissos, 2008; Meltzer, 1991; Saykin et al., 1994). These deficits are increasingly considered as fundamental in schizophrenia and schizophrenic disorders (Matsui, Sumiyoshi, Arai, Higuchi, & Kurachi, 2008; Meltzer, Thompson, Lee, & Ranjan, 1996) and are found to be directly associated with functional status of patients with schizophrenia (Michael F Green, Kern, Braff, & Mintz, 2000). R. W. Heinrichs and Zakzanis (1998) reported broad cognitive impairment in schizophrenia that affected all ability domain in varying degrees. According multiple studies, the most profound deficits are observed in executive functioning (Brissos, 2008; Matsui et al., 2008; Robinson et al., 2006). Therefore, executive functions might be a possible target to improve the quality of life of patients with SMI.

Executive functions is a multidimensional and highly complex cognitive construct (Lezak, 1993) without a univocal definition (Goldstein & Naglieri, 2014). Executive processes are involved in strategic planning, sequencing and initiation of behaviour, self-monitoring and goal-directed behaviour, which is the initiation and inhibition of behaviour that is inconsistent with a specific goal (Tyson, Laws, Flowers, Mortimer, & Schulz, 2008). Planning is the ability to mentally generate a sequence of goal-directed actions and anticipate and evaluate the consequences of the actions in relation to the goal (Köstering et al., 2015). Furthermore, executive functioning includes cognitive abilities that allow for impulse control and cognitive flexibility (Goldstein & Naglieri, 2014) and it enables people to shift back and forth between different tasks or mental sets (Hofmann, Schmeichel, & Baddeley, 2012).

Executive functioning is closely related to the concept of attention and working memory, because all three are often required for the successful operation of other cognitive domains, e.g. memory. Some researchers state that executive processes guide attention as well as other processes, while other researchers use both concepts interchangeably (Tyson et al., 2008).

Neurocognitive deficits in SMI are found to predict occupational and social functioning and the level of independence in daily life (Michael Foster Green, 1996; Meltzer et al., 1996). However, the precise consequences of these deficits, especially deficits in executive function, on the life of patients with SMI remain unclear (Michael Foster Green, 1996; Matsui et al.,

2008). Quality of Life is one of the key measurements for evaluating the impact of mental disorders on the health and daily lives of patients with SMI (Matsui et al., 2008).

Quality of Life (QoL) is a multidimensional concept concerning a person's well-being (Brissos, 2008; Davis, Marra, Najafzadeh, & Liu-Ambrose, 2010). QoL represents the impact of disease and treatment across the physical, psychological, social and somatic domains of functioning and well-being (Revicki et al., 2000). The World Health Organization (1998) defines QoL as an individual's perception of their position in life in the context of their culture and values and in relation to their goals, expectations, standards and concerns. Lehman (1988) defined two major components; an objective and a subjective dimension. Objective QoL is related to external life conditions such as mobility, cognitive and functional impairments, while subjective QoL can be viewed as the satisfaction with life in multiple domains (Hansson, 2006). This division is often used in research in order to get a more complete measurement of QoL in patients with SMI (Narvaez, Twamley, McKibbin, Heaton, & Patterson, 2008).

There is a growing interest for research on QoL in patients with SMI (Fujii, Wylie, & Nathan, 2004). Research has shown that these patients often have a poor QoL compared to people without mental disorders (Alptekin et al., 2005; Becker, Diamond, & Sainfort, 1993). The target for treatment of patients with SMI is more focussed on the reduction of symptoms and the optimization of the patients' QoL (Hansson et al., 1999; Mackala, Torres, Kozicky, Michalak, & Yatham, 2014) instead of complete recovery, because their disorders are complex and persistent and their prognosis for recovery is often poor. The need to understand the influence of different factors on QoL will increase as therapeutic efforts focus more on improving patients' well-being (I. B. Wilson & Cleary, 1995).

Executive Functions and Quality of Life

QoL is a very multidimensional concept and due to the objective and subjective components, there are many factors that can influence QoL. Subjective and objective QoL are found to have different predictors (Narvaez et al., 2008). External life conditions, diagnoses and psychopathology are objective factors that influence quality of life, while subjective factors more involve the satisfaction with life (Hansson et al., 1999). Personality related factors that may influence QoL are self-esteem, autonomy and self-efficacy (Hansson, 2006).

Although the literature on the predictive relationship between any cognitive function and QoL in patients with SMI is relatively lean, there are studies supporting relationships

between different cognitive functions and QoL in other populations. Brissos (2008) and Pattanayak, Sagar, and Mehta (2012) found that QoL in bipolar patients correlated significantly with worse cognitive performance, especially in executive functioning and verbal abstraction. The cognitive variables predicted up to 37% of the variance in QoL. Fujii et al. (2004) reported executive functions to be positively predictive of QoL, especially in the domains of contact with family and financial support. Lower scores on executive functions predicted a lower score on QoL measurements. Furthermore, studies with schizophrenic patients indicate the same positive relationship between cognitive functioning and QoL, especially in executive functioning (M. S. Ritsner, 2007; Tyson et al., 2008). Similarly, the results of a study conducted by Alptekin et al. (2005) showed that cognitive deficits in executive functions and deficits in working memory appear to have a direct negative impact on subjective QoL in schizophrenic patients. Overall, studies found the most evidence regarding the influence of executive functioning on QoL. Verbal intelligence or memory and working memory appear to be other central cognitive factors strongly negatively related to executive functioning (Alptekin et al., 2005; M. S. Ritsner, 2007).

The possible relationship between executive functions and QoL might be explained by the essential role of executive functioning in controlled behaviour. In order to control behaviour it is important to inhibit or override behavioural responses - bad habits or impulses - that are incompatible with a person's goal (Strack & Deutsch, 2004). Habits and impulses activate motor schemas which may lead to the expression of certain unwanted behaviour unless inhibited (Hofmann et al., 2012). Therefore, impairment of inhibition of behaviour, which is an executive function, leads to impairment of controlled behaviour (Norman & Shallice, 1986). Working memory also plays a role in controlled behaviour. Without an active representation of the goal to be attained, the behaviour is directionless and uncontrolled (Baumeister & Heatherton, 1996; Hofmann et al., 2012). Consequently, impaired executive functioning leads to many different problems on social, emotional and physical levels which are all domains of QoL. Cognitive dysfunction, including executive functioning, was found to influence community functioning in schizophrenic samples (Michael F Green, Kern, & Heaton, 2004).

It remains questionable whether the results of research in other patient populations can be generalized to a population with SMI, because most Quality of life research is focussed on schizophrenia without any comorbidity (Hansson, 2006). A population of patients with SMI

may suffer from multiple disorders and often have low cognitive abilities. Moreover, they are admitted to a mental health institute for a longer period. This influences their social network, which is found to be a determinant for a lower QoL (Kroenke et al., 2013). On top of this, patients with SMI often have a poor prognosis for treatment which increases the importance of optimizing their QoL. An understanding of the influence of executive functions on the subjective QoL in patients with SMI is essential in order to design effective clinical interventions that accomplish the highest possible QoL and potentially decrease the burden of the illnesses on the patient (Mackala et al., 2014). An increased QoL results often in a higher independence and a lower need for care, which can decrease mental health care costs. Therefore, executive functions might be a future target for treatment of patients with SMI (M. S. Ritsner, 2007).

Aims of the study

The aim of this cross-sectional study is to explore the relationship between executive functions and subjective QoL by testing a model with 4 related cognitive constructs (working memory, executive functions, verbal IQ & premorbid IQ). The model is depicted below in Figure 1. By doing this, the influence of executive functions on subjective QoL can be compared to the influence of verbal and premorbid intelligence, working memory and psychopathology. Furthermore, psychopathology and objective QoL will be included in the model in order to give a better representation of the different aspects involved in a patients' overall QoL.

The model stated below will be tested and the predictive value of the model including the independent variables working memory, executive functions, premorbid and verbal IQ and psychopathology on the dependent variables objective and subjective Quality of Life will be explored. This study will focus on the question: *What is the influence of executive functioning in predicting subjective Quality of Life?* Secondary questions are: *What is the predictive value of working memory, verbal and premorbid intelligence and psychopathology on subjective quality of life compared to executive functioning?*, *What is the predictive value of*

psychopathology on objective quality of life? and *What is the correlation between objective and subjective quality of life?*

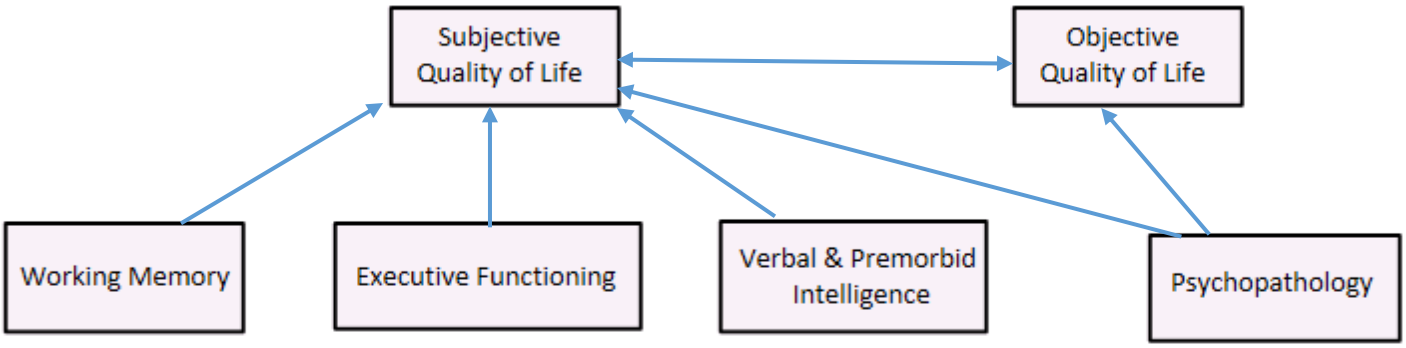

Figure 1 Model of factors influencing Quality of Life

The hypothesis is that lower or impaired executive functioning predicts a significantly lower QoL and that the contribution of executive functions in predicting QoL is comparable to the influence of working memory and verbal and premorbid intelligence. The functioning of working memory and verbal and premorbid intelligence are closely related to executive functions. Working memory and executive functions are both essential in controlled behaviour and the constructs are strongly related to each other. Intelligence is another main cognitive function that is impaired in most patients with SMI, in particular in the verbal dimension (Alptekin et al., 2005; Braff et al., 1991; Brissos, 2008; Meltzer, 1991; Saykin et al., 1994). According to Michael F Green et al. (2000), cognitive functions are directly associated with functional status, and therefore verbal intelligence should be included in the model. Premorbid intelligence is an estimation of the IQ prior the mental disorder or onset of disability (Kreutzer, DeLuca, & Caplan, 2011). Premorbid intelligence can be used to explore the influence of intelligence separate from the influence of mental disorders on intelligence. Mental disorders, especially schizophrenia, may strongly impair the intelligence.

The influence of psychopathology on subjective quality of life is expected to be smaller than the influence on objective quality of life. Priebe et al. (2011) found in this study on a schizophrenic population that subjective QoL was significantly influenced by symptoms, in particular depression and anxiety, but that the level of influence was limited. Ueoka et al. (2011) found that negative and depressive symptoms are important factors in objective measurements of QoL. This idea is supported by Browne et al. (1996). Yamauchi et al. (2008)

showed that subjective QoL was correlated with positive and negative symptoms, while objective QoL was correlated with only negative symptoms.

Objective and subjective QoL are different components from the overall QoL. The subjective satisfaction and the objective facts of patients' well-being are conceptually strongly related. On a theoretical level the components cannot be seen as completely independent. Consequently, the hypothesis is that the measurements of subjective and objective QoL are highly correlated.

It is very relevant to understand how these different factors, including executive functions, influence subjective and objective QoL. This basic understanding can help to develop interventions targeting the factors that influence QoL the most. Interventions that improve QoL through other pathways than curing symptoms can be a supplement to the regular treatment of patients with SMI. A higher QoL leads to a lower need for care and therefore a decrease in mental healthcare costs.

2 Method

Study design

This study had a cross-sectional design with a cohort of patients with SMI that participated in a larger physical activity study. Questionnaires were used to measure the subjective and objective QoL, premorbid intelligence and psychopathology. Executive functions and verbal intelligence were measured using different test batteries spread over different appointments in order to decrease the burden of the tests on the patients. Tests for QoL, executive functioning and verbal intelligence were conducted by three different pairs of researchers in order to prevent researcher bias. During the data collection the pairs of researchers were blinded for data collected by the other researchers.

Participants

All participants in this study (N = 54) were admitted to long-term psychiatry units of GGZ Centraal, location Zon & Schild in Amersfoort. The units consisted of around 10 patients receiving long-term treatment and care. The majority of the participants suffered from Schizophrenia (79.9%) and related Schizophrenic Disorders (11.3%), while other diagnoses included Depressive or Bipolar Disorders (5.6%), Pervasive Developmental Disorder or Autism (3.8%), Obsessive-Compulsive Disorder (1.9%) and Personality Disorder (1.9%).

This study was part of a large ongoing longitudinal observational study which explores the impact of a behavioural intervention on physical activity and QoL in patients with SMI. Patients were included in the current study if they were enrolled in the larger study, if there was sufficient data of them in the larger study and if their verbal IQ was measured. This limited the population to 75 patients of which 4 patients were excluded because of medical reasons, 2 patients left the mental care institution during the measurements, 11 patients refused to take part in the executive function measurements, 3 patients were excluded on recommendation of the nursing staff and 1 patient was excluded because of personal circumstances.

Patients were not excluded based on demographic variables or diagnoses which lead to a natural representation of an inpatient population with SMI. Patients were excluded if their care was not financed by the Algemene Wet Bijzondere Ziektekosten (exceptional medical

expenses act), if their understanding of the Dutch language was insufficient or if they were expected to be mentally incompetent to give their informed consent.

Procedure

Each patient unit was separately approached by the researchers and included patients were tested in context of treatment in a special reserved room in their unit or another space convenient for the patient. The nursing staff was closely involved in approaching patients for participation and scheduling appointments. All patients were informed about the purpose of the research and signed an informed consent.

The test battery for executive functions contained multiple subtests measuring different aspects of the overall executive functions. The measurement was split into two sessions of thirty to forty-five minutes in order to lower the burden of the measurement on the patient. For patients being unable to complete all subtest within two appointment due to concentration problems or other disorder related problems, a third meeting would be scheduled. Although the order of the subtest was flexible, subtests targeting the same executive function were not conducted consecutively. Premorbid intelligence was measured with a reading test in the same appointment as executive functions.

Subjective and objective QoL and psychopathology were measured in a separate appointment using questionnaires. All items of the questionnaire were asked verbally and the researched noted down all the answers. Unanswered questions due to patients being unable to understand or answer a question, were discussed with the nursing staff of that unit. The QoL measurements were conducted within maximum two months before or after the executive functions measurement.

Verbal intelligence and working memory were measured in a previous study as part of the ongoing large study on physical activity and well-being of this patient sample. Information including diagnosis, gender, age and admission duration were extracted from the patient records.

Instruments

Executive functions

There are many different tests to measure executive functions, because executive functioning is a collection of many different cognitive skills involved in controlling behaviour. A selection

of the most common used executive function instruments, which all measure different aspects of executive functions, is made to create a complete image of patients' overall executive functions.

Modified Six Elements

The Modified Six Elements is a test included in the Behavioural Assessment of Dysexecutive Syndrome (BADS). The BADS is designed to predict the presence and severity of everyday problems in executive functions (B. A. Wilson, Evans, Alderman, Burgess, & Emslie, 1997). The Modified Six Elements is one of the 7 tests included in the BADS and it measures planning, problem solving and monitoring behaviour (Norris & Tate, 2000). This test was designed to assess ability to time-manage (B. A. Wilson, Alderman, Burgess, Emslie, & Evans, 2003). The patient has 10 minutes to work independent on three different simple tasks; picture naming, simple calculations and storytelling. The patient is asked to divide the available time between the tasks while not contravening a set of rules (B. A. Wilson et al., 2003). The score is based on the number of tasks attempted and penalties are given for not following the rules or sharing time unequally between the three tasks. The minimal scaled score is 0 and the maximum scaled score is 4 (Norris & Tate, 2000).

Stroop Colour Word Interference Test

The Stroop Colour Word Interference Test is a highly reliable and stable assessment of response inhibition (Jensen & Rohwer, 1966) in which the patient is asked to deliberate inhibit an automatic, dominant or routine response. The test contains three condition and primary test condition (*color-word naming*) consists of a reading card with colour-words (red, blue, yellow, green) printed in incongruent coloured inks, for example the word red printed in yellow. The patient needs to name the ink colour that the words were printed in while ignoring the word itself (Davis et al., 2010). The two control conditions consisted of *word reading* and *color naming*. The score for the Stroop Color Word Interference Test is calculated using the time difference between the primary test conditions and the control conditions, which represents response inhibition. Smaller differences indicate a better selective attention and conflict resolution (Davis et al., 2010) and therefore a better executive functioning. The scaled cumulative percentage is converted into a score ranging from 1-19. A higher score represents better executive functioning.

Trail Making Test

The Trail Making Test (TMT) is a found to be an index for executive functions (Arbuthnott & Frank, 2000) and measures primarily set shifting. Set shifting is an individual's ability to go back and forth between multiple metal sets or tasks. The TMT contains of part A and part B. Part B measures the set shifting ability and B-A corrects for visuoperceptual and working memory demand (Sanchez-Cubillo et al., 2009). In both parts the basic task is to connect series of stimuli (numbers and letters) in a specified order as fast as possible (Reynolds, 2002). In part A the patient is asked to draw a line between either letters or numbers in ascending order or circles. In part B the patient needs to switch between letters and numbers; 1 needs to be connected to A, A to 2, 2 to B, etc. (Davis et al., 2010). In all trials the researcher will correct the patient when an error in order occurs. The amount of corrections and the time that is needed to complete the task are used to calculate a score for each trial (Davis et al., 2010). If a patient does not finish the task within the maximum time allowed for the trial, the number of missing connection will be incorporated in the scoring. The difference between part A and B is the executive function score. A smaller difference indicates higher cognitive flexibility in set shifting and therefore a higher executive functioning. Reliability of TMT range from moderate to excellent (Spreen & Strauss, 1998). The scaled cumulative percentage is converted into a score ranging from 1-19. A higher score represents better executive functioning.

Corsi Block Tapping Test

The Corsi Block Tapping Test assesses the visuospatial short-term memory and is widely used in clinical practice and experimental research (Kessels, Van Zandvoort, Postma, Kappelle, & De Haan, 2000). This test is especially suitable for patients who are difficult to test, because of the easy instructions. The material needed for the Corsi Block Tapping Test is a black board with 9 black cubes mounted to it on fixed positions. After the examiner taps a sequence of blocks, the patient has to repeat the correct sequential order by tapping the same blocks. The visuospatial short-term memory is measured by increasing the length of the sequences (Kessels et al., 2000). The test has to conditions: the forward and backward condition. In the forward condition the patients repeats the sequences in the same order as the examiner showed them, while in the backwards condition the sequences need to be repeated backwards (Kessels, van den Berg, Ruis, & Brands, 2008). The test is discontinued when a

patient makes mistakes in both sequences from the same length. A total score is calculated for each condition using the length of the longest correct repeated sequence and the total amount of correct repeated sequences. According Kessels et al. (2008) there are no significant differences between the scores on both conditions. Therefore an average is calculated and used to calculate a scaled score (range 1-19). A higher score represents better executive functioning.

Tower Test

The Tower Test is a reliable measurement of planning ability, which is a prototypical executive function (Köstering et al., 2015). Besides planning ability, problem solving skills are required for the Tower Test. The Tower Test is significantly correlated to other measurements of executive functions (Anderson, Anderson, & Lajoie, 1996). The version used is the Delis-Kaplan Executive Function System (D-KEFS) Tower Test. This version has a bigger score range compared to the Tower of London, Tower of Hanoi and Tower of Toronto. The test requires participants to build a series of nine towers that become progressively more difficult. The patient is asked to rearrange a set of disks placed on rods from a starting state to a pre-determined goal state within a limited number of moves (Yochim, Baldo, Kane, & Delis, 2009). There are a few rules ('move one disk at the time' and 'do not place a larger disk on a smaller disk') and violations of these rules is corrected by the examiner. The Tower Test is discontinued when two series in a row the patient is unable to achieve the goal state within the given time. The total score is measured using the total number of Tower problems completed, number of moves used, time spent completing the Tower problems and time spent planning the first move (Yochim et al., 2009). The total score is converted into a scaled score ranging 1-19.

Verbal Digit Span Test

The Digit Span Test (DST) is part of the Wechsler batteries and is the most common used instrument in the measurement of immediate verbal recall (D. Wechsler, 1987), which is often impaired in schizophrenic patients (Conklin, Curtis, Katsanis, & Iacono, 2000). The DST contains two sections; 'Digits forward' and 'Digits Backward'. Both sections involve different mental activities (Alptekin et al., 2005). In the 'Digit Forward' section patients repeat the numbers told by the researcher in sets increasing in length which measures mainly attention. In the 'Digit Backward' section patients are asked to repeat the sets backwards which

measures mainly working memory by requiring internal manipulation of verbal information in the absence of external cues (Conklin et al., 2000). The DST is ended when the patient recalls both sets of the same length incorrectly. The total number of correct repeated sets of digits and the length of the last correct repeated set are used to calculate the scaled scores on the subscales and the total score (range 1-19). A smaller difference between the forward and backward condition correlates with a better executive component of working memory (Kessels et al., 2008). Higher scores correlate with better executive functions.

Quality of Life

Two different instruments to measure QoL are used in this study; WHOQOL-BREF and EQ-5D. The WHOQOL-BREF is a subjective evaluation of a patient's QoL, while the EQ-5D is believed to give a more objective measurement of a patient's well-being. QoL is concerned with both the subjective evaluation of oneself as well as the social and objective status of well-being (Orley, Saxena, & Herrman, 1998).

WHOQOL-BREF

The WHOQOL-BREF is developed by the World Health Organisation (WHO) to assess the perceived QoL (The WHOQOL Group, 1998), because most QoL instruments were focussed on an objective measurement of the QoL (Orley et al., 1998). The WHO defined 24 different aspects of life, structured in four broader domains, that are considered as having a significant impact on the perceived QoL (Orley et al., 1998). The complete questionnaires has 100 items, which is relatively long for clinical usage. Therefore the WHOQOL-BREF is developed which contains 26 items. The items are categorized in four domains: physical, psychological, social relationship and environment (Alptekin et al., 2005). The physical domain contains questions regarding daily activities, pain and discomfort, sleep and energy and the psychological domain regarding self-esteem, physical appearance, personal beliefs and positive and negative feelings. The social domain includes items about personal relationships, sexual activity and social support. The environmental domain explores different aspects including physical security, financial status, availability and use of health and social care and participation in opportunities for recreation and transport (Alptekin et al., 2005). The WHOQOL-BREF is used in this study for reasons of brevity.

EuroQol 5D

The EuroQol 5D (EQ-5D-5L) is a generic health status instrument (Badia et al., 2001; The EuroQol Group, 1990; Van de Willige, Wiersma, Nienhuis, & Jenner, 2005). The EQ-5D is a feasible and valid instrument to measure QoL in various diseases (Kind, Dolan, Gudex, & Williams, 1998). The questionnaire consist of three parts: a descriptive system, a visual analogue scale (EQ-VAS) for the measurement of overall self-rated health and the EQ Index. In this study only the results of the EQ Index will be used, because the descriptive system provides a health profile, which is of limited use in statistical analyses, while the EQ-VAS provides a subjective measurement of perceived health. The EQ Index can be used to measure the objective QoL in 5 different dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension contains one question with a Likert-scale ranging from 1 ('I have no problems '/'I have no…'/'I am not…') to 5 ('I am unable to …'/'I have extreme…'/'I am extremely…'). The IQ Index ranges from 0 to 1 with 0 indicating the lowest QoL possible (equivalent to death) and 1 indicating perfect health.

Verbal and premorbid Intelligence, Working memory and psychopathology

PANSS-r

The PANSS is a reliable rating scale that measures positive, negative and general psychopathology (Kay, Flszbein, & Opfer, 1987). The complete questionnaire contains 30 items. Bell, Lysaker, Beam-Goulet, Milstein, and Lindenmayer (1994) introduced five factors, in which the questions could be characterized: positive factor, negative factor, cognitive factor, emotional discomfort factor and hostility factor (Yamauchi et al., 2008). All items are scored on a 7-point-Likert scale, with 1 as lowest score ('no problems') and 7 as highest ('severe problems'). For this study a selection of all items is made, based on the PANSS-r. The PANSS-r is a remission tool, which can be used to measure remission of schizophrenic symptoms (Os et al., 2006). The PANSS-r contains 3 items from the positive factor (delusions, conceptual disorganization, and hallucinatory behaviour), 3 items from the negative factor (blunted affect, passive/apathetic social withdrawal, lack of spontaneity and flow of conversation) and 2 items from the general psychopathology factor (unusual thought content and mannerisms/posturing) (Opler, Yang, Caleo, & Alberti, 2007). The PANSS-r is used to measure psychopathology related to schizophrenia in a population were schizophrenia is most common. The shorter version of the PANSS is selected, because even simple tasks can be a burden for patients with SMI.

Verbal IQ

Verbal IQ is a subscale of the Wechsler Adult Intelligence Scale-third edition (WAIS-III) (D. Wechsler, 1997). The WAIS was established to assess cognitive ability and examines the relationship between memory and intellectual functioning (D. Wechsler, 2014). The WAIS-III is the most widely used instrument for the measurement of intelligence. The test is free of a theoretical model and is very practical and fitted for clinical use. The WAIS-III has excellent psychometric properties, especially in reliability and standardization. Verbal IQ is a measurement of classic crystalized intelligence, which contains cognitive functions like abstract reasoning, general knowledge, memory and mathematical skills. This instrument contains two main subscales: verbal IQ and Performance IQ (Donders, Tulsky, & Zhu, 2001). The verbal IQ contains the subtest Vocabulary, Similarities, Information, Comprehension, Arithmetic, Digit span and Letter-Number Sequencing (D. Wechsler, 1997). The verbal IQ score is based on the average of the subtest scores. The validated Dutch version of the WAIS is used in the current study.

Working memory Index

The Working Memory Index (WMI) is one of the four factor index scores of the WAIS-III (D. Wechsler, 1997). Verbal IQ subscale is divided in the factor index scores for Verbal Comprehension Index and WMI. The WMI is an indication of the working memory capacities (Etherton, Bianchini, Ciota, Heinly, & Greve, 2006). Working memory is conceptualized as the amount of information an individual can process at a given time. The subtests measure simple and complex attention processes and the ability to retain and manipulate information mentally (Etherton et al., 2006). Increasing the amount of information and attending to more than one task at a time are techniques to challenge the working memory. WMI consists of three subtests: Arithmetic, Digit Span, and Letter-Number Sequencing. The average of these subtests is used to calculate the WMI.

NLV

The 'Nederlandse Leestest voor Volwassenen' (NLV, Dutch Reading test for Adults) is a word reading test estimating the premorbid crystallized intelligence (Schmand, Lindeboom, & Harskamp, 1992). Crystallized intelligence is stored knowledge and skills, such as vocabulary knowledge and reading pronunciation skills (R. E. Green et al., 2008). Crystallized intelligence

is acquired (Burin, Jorge, Arizaga, & Paulsen, 2000) and relatively resistant for impairment (Lehrl, Triebig, & Fischer, 1995). Therefore crystallized knowledge - measured with the NLV - is a good indicator of the intelligence before the impairment due to the SMI, which is called premorbid intelligence. The NLV consists of 50 words which have a different pronunciation than would be expected from the orthography of the word (Gerritsen, Berg, & Deelman, 2001). The patient is asked to read all words out loud while the examiner scored the pronunciation with a 0 (incorrect) or a 1 (correct). Norms are used to determine the premorbid IQ scores (Gerritsen et al., 2001).

Data Analysis

The baseline characteristics of the participants (age, gender, duration of admission, diagnoses) are analysed in order to get a general impression of the studied sample. The subtests of the executive function battery, the total executive function score, total psychopathology, verbal intelligence, premorbid intelligence and working memory are explored, before analysing the outcome measurements of subjective and objective QoL. It is tested if all variables meet the requirements for parametric testing; normal distribution and homogeneity of variance.

Structural Equation Modelling (SEM) was used to test the complete model. SEM can answer a set of interrelated research question by modelling the relationships among multiple independent and dependent constructs simultaneously. SEM presents a more complete picture of an entire model, because first generation techniques like regression can only analyse separate relationships. Preliminary factor and reliability analyses are not required in SEM because the testing of measurement properties of the instruments is simultaneous with testing of hypotheses. SEM also generates an overall fit of the model for the data. In this way the predictive value of the whole model and of the separate factors is viewed. Regression analyses are used to explore the relationship between executive functions and subjective QoL independent of the other factors. Based on both the SEM and regression analyses conclusions are made about the predictive value of executive functions in subjective QoL.

3 Results

Descriptive Statistics

In total the data from 54 completers was analysed. The sample consisted of 20 females and 34 males with an average age of 54.69 years old (see Table 1). The youngest participant was at the moment of measurement 36 and the oldest 73. In the sample 87% was diagnosed with schizophrenia. Female patients are on average 13.30 years admitted, while the mean for male patients' admission is 19.97 years. However, there are no significant differences between male and female patients.

The executive functions subtests with the lowest average scores are Tower of London (*m* = 5.70, *SD* = 3.90) and Verbal Digit Span (*m* = 6.85, *SD* = 2.69). The Stroop Color and Word test (*m* = 11.20, *SD* = 2.83) is the subscale with the highest average score. The mean total executive function, which is the sum of all the scaled scores of the subtests, is 49.79 (*SD* = 14.80). Furthermore, in the other dependent variables it is remarkable that the average score on the premorbid IQ test (*m* = 91.02, *SD* = 14.93) is 17 IQ points higher than the verbal IQ score (*m* = 74.22, *SD* = 12.54). This suggests that the IQ of patients with SMI on average decreases with 17 points compared to before the SMI occurred. The mean score on the subscale positive symptoms on the PANSS (*m* = 2.46, *SD* = 1.18) is higher than the means score on negative symptoms (*m* = 1.97, *SD* = 1.18). This suggest that the patients in this sample display more positive symptoms than negative. The mean score on WHOQOL-BREF is 97.15 (*SD* = 13.50) and the mean score on EQ-5D is 0.75 (*SD* = 0.22). Almost all variables are normally distributed, expect for the Corsi Block test (mean of forward and backward condition), negative symptoms subscale PANSS and total PANSS.

Table 1 Characteristics of the sample and descriptive information of dependent and independent variables

		Total Sample (*n* = 54)	Male (*n* = 34)	Female (*n* = 20)
Sociodemographic variables				
Age in years, mean (SD)		54.69 (9.31)	54.47 (8.56)	55.05 (10.69)
Duration of admission, mean in years (SD)		17.50 (10.92)	19.97 (10.91)	13.30 (9.83)
Diagnosis, *n* (%)	Schizophrenia	47 (87)	30 (88)	17 (85)
	Other diagnosis	7 (13)	4 (12)	3 (15)
Executive Function				
Total score executive functioning, mean (SD)		49.79 (14.80)	50.87 (14.30)	47.65 (15.99)
Stroop, scaled mean score (SD)		11.20 (2.83)	11.12 (3.03)	11.21 (2.51)
Trail Making Test, scaled mean score (SD)		7.28 (4.50)	7.35 (4.44)	7.16 (4.72)
Corsi Block test, scaled mean score (SD)		7.54 (3.00)	7.42 (2.79)	5.90 (2.25)
Verbal digit span, scaled mean score (SD)		6.85 (2.69)	8.26 (3.17)	4.50 (4.05)
Tower of London, scaled mean score (SD)		5.70 (3.90)	6.41 (3.69)	7.94 (3.40)
6 Elements, scaled mean score (SD)		8.15 (3.22)	10.31 (4.95)	9.61 (4.81)
Other dependent variables				
Verbal IQ, mean (SD)		74.22 (12.54)	77.68 (12.84)	68.35 (9.73)
Premorbide IQ, mean (SD)		91.02 (14.93)	93.65 (15.88)	86.32 (12.04)
Working memory IQ, mean (SD)		76.28 (14.04)	79.00 (14.41)	71.65 (12.36)
PANSS, mean (SD)	Positive symptoms	2.46 (1.18)	2.35 (1.01)	2.63 (1.44)
	Negative symptoms	1.97 (1.18)	2.05 (1.25)	1.83 (1.06)
	total	2.10 (0.84)	2.09 (0.77)	2.13 (0.96)
Quality of life				
WHOQOL-BREF, mean (SD)	Physical domain	26.00 (4.03)	26.26 (3.99)	25.55 (4.17)
	psychological domain	21.45 (3.90)	21.71 (3.44)	21.00 (4.17)
	social domain	11.43 (2.35)	11.12 (2.27)	11.95 (2.46)
	environmental domain	31.50 (5.35)	31.50 (5.30)	31.50 (5.59)
	total	97.15 (13.50)	97.15 (13.53)	97.15 (13.78)
EQ-5D, mean (SD)		0.75 (0.22)	0.81 (0.19)	0.65 (0.24)

No significant differences between males and females (Bonferroni correction $\alpha = 0.05/22 = 0.0023$)

Inferential Statistics

SEM on the complete model is conducted in SPSS Amos and shown in Figure 2. The relationship between the total executive function score and the WHOQOL-BREF is weak and not significant (B = -0.082, p > 0.05), which rejects the primary hypothesis. Similarly, the relationships between Working Memory index IQ and WHOQOL-BREF is weak and non-significant (p > 0.05), while the relationship between Premorbid IQ and WHOQOL-BREF is slightly stronger, but non-significant (B = -0.081, p > 0.05). This is not in line with the hypothesis which stated that both Working Memory Index and Premorbid IQ were predictors

of WHOQOL-BREF. However, the relationship between Verbal IQ and WHOQOL-BREF is strong and significant (B = -0.348, p > 0.05). In line with the hypotheses, the relationship has a positive direction and implies that higher scores on Verbal IQ predict higher scores on the WHOQOL-BREF. The influence of Verbal IQ on WHOQOL-BREF is not comparable to the contribution of executive functions, premorbid IQ and Working Memory Index, as was hypothesized.

Furthermore, the relationship between PANSS-r and WHOQOL-BREF is highly significant and very strong (B = -6.047, p < 0.01), which confirms the hypothesis. A lower score on the PANSS-r is predictive of a higher score on the WHOQOL-BREF. A significant relationship in the similar direction is found between PANSS-r scores and EQ-5D scores (B = -0.77, p < 0.05). However, this relationship is not very strong.

Besides predictive relationships, the model gives information about the correlations of related terms. The SEM results show a high correlation between Working Memory index IQ and Executive Functions total score. There is a similar high correlation between Verbal IQ and premorbid IQ. This confirms the hypotheses based on theoretical overlap between these pairs of concepts.

SEM can also generate an overall fit of the model for the data. This is expressed by the Comparative Fit Index (CFI) and the Root Mean Square Error of Approximation (RMSEA). The CFI is 0.419 and the RMSEA is 0.301, which both indicated a bad fit of the overall model.

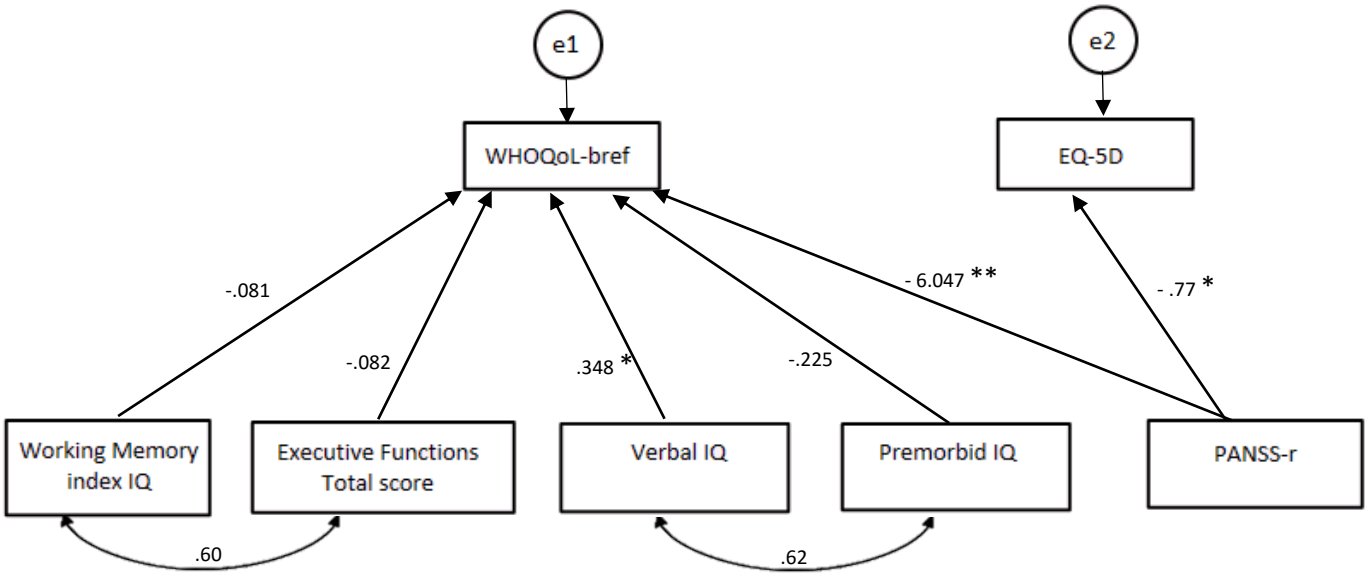

Figure 2 Structural Equation Modelling * Significant at p<0.05 ** Significant at p<0.01

Table 4: Single linear regression on the influence of Executive Functions, total score and subscales, on WHOQOL-BREF for the total sample

	WHOQOL-BREF		
	B	***SE B***	***β***
Total score Executive Functions	-0.66	0.46	-0.73
Stroop Color Word Interference Test	0.68	0.83	0.15
6 Elements	-0.70	1.48	-0.07
Trail Making Test	0.69	0.70	0.23
Corsi Block Tapping Test	-0.52	1.04	-0.10
Tower of London	1.93	0.97	0.56
Digit Span Test	-0.52	1.04	-0.10

Bonferroni correction for multiple testing: $\alpha = 0.05/7=0.007$
All variables are not significant, p>0.007

Regression analyses are conducted in SPSS in order to analyse the influence of executive functions on subjective quality of life, separate from the other factors in the model (see Table 4). A Bonferroni correction was used to correct for multiple testing. All subtest for executive functions do not significant influence the score on WHOQOL-BREF. Similar insignificant results are found for the total score of executive functions. In conclusion, the results of the regression test are in line with the results form SEM and reject the hypothesis that executive functions predict WHOQOL-BREF.

Correlation between subjective and objective QoL is analysed separately. Scores on both questionnaires are highly significant correlated ($p < 0.01$) with a Pearson's Correlation of 0.487. The direction of the correlation is positive, which means that higher scores on WHOQOL-BREF are related to higher scores on the EQ-5D. This is in line with the hypothesis.

4 Conclusion & Discussion

Executive Functions

The results show no significant relationship between executive functions and QoL in patients with SMI. This suggests that impairments in executive functions does not predict a lower QoL in patients with SMI. These findings reject the hypothesis of a predictive relationship and are not in line with previous research on QoL. Previous research on executive functions and quality of life shows a significant relationship between the two factors in other patient groups than patients with SMI. For example, Brown and Landgraf (2010) found a correlation between improvement in executive functions and improvement in QoL in patients with attention-deficit/hyperactivity disorder (ADHD), which suggests a positive relationship between executive functions and QoL. Furthermore, research by Newman et al. (2001) shows a strong relationship between neurocognitive functioning, including executive functions, and QoL 5 years after cardiac surgery . Research on epilepsy shows that executive dysfunctions is a significant predictor of lower QoL (Sherman, Slick, & Eyrl, 2006). Research in patient groups with mental health problems like schizophrenia or bipolar disorder shown the same positive relationship (Alptekin et al., 2005; Brissos, 2008; Fujii et al., 2004; M. S. Ritsner, 2007; Tyson et al., 2008). Pattanayak et al. (2012) conducted research on bipolar patients and found that a lower QoL was correlated with significantly worse executive functioning. Research conducted by Sota and Heinrichs (2004) shows that executive ability and verbal memory predict lower subjective QoL in neuroleptic-naïve schizophrenia patients. Research showing no relationship between QoL and executive functions has not been found, which might be due to publication bias. Therefore, it might be possible that other unpublished research supports the findings of this study.

Intelligence & Psychopathology

The analyses of the model show two significant relationships and one highly significant relationship. First of all, verbal intelligence significantly predicts subjective QoL. A higher verbal intelligence predicts a higher QoL. Research suggests that patients with SMI and a lower intelligence have a worse prognosis and poorer social functioning (Aylward, Walker, & Bettes, 1984). This might explain why patients with a lower verbal intelligence report a lower average QoL. The same positive relationship has also been found by Corrigan and Buican (1995). Their research shows a significant inverse relationship between verbal intelligence and subjective

QoL in patients with SMI. However, this relationship was not found in a healthy population (Watten, Syversen, & Myhrer, 1995).

Second of all, there is a significant relationship between psychopathology and subjective QoL. More psychopathology strongly predicts a poorer subjective QoL. Research on this relationship is contradictory. Awad, Voruganti, and Heslegrave (1997) reported that subjective QoL is greatly influenced by psychopathology. However, there is also research showing a limited influence of psychopathology in subjective QoL (Lehman, 1983).

Third of all, the relationship between psychopathology and objective QoL is also significant. More severe psychopathology predicts a poorer objective QoL. However, the influence of psychopathology is stronger and greater on subjective QoL than objective QoL. There is not much research comparing the influence of psychopathology on subjective and objective QoL. The model supported by research of M. Ritsner et al. (2000) shows that general psychopathology mainly influences objective QoL and not subjective QoL, which is inconsistent with the findings in this study. However, there is extended research showing an influence of psychopathology on either subjective or objective QoL. Yamauchi et al. (2008) showed that psychopathology, especially negative symptoms, influences both objective and subjective QoL. Similar results were found by Narvaez et al. (2008); severe depressive symptoms significantly predicts a worse subjective QoL, while severe negative symptoms predict a worse objective QoL.

Overall, the results of this study imply that a patients executive function does not influence QoL while his/hers psychopathology and verbal intelligence predicts QoL. One of the implications of these findings is that psychopathology should remain the main focus in treatment, because improving symptoms also improves QoL. Another implication is that extra effort should be directed towards patients with a low verbal intelligence in order to achieve a better QoL.

Strengths & Weaknesses

It is possible that there is a relationship between executive functions and subjective QoL in patients with SMI, but that this study was unable to detect this due to certain limitations. Patients with SMI staying in long term psychiatry institutions are a very difficult research population. The tests and questionnaires can be very demanding for these patients. In total, 8 patients in the sample were excluded on advice of the nursing staff, because the executive

function test battery was too much of a burden for them due to medical reasons or mental problems. Furthermore, 11 patients refused to take part in the study. Besides this, only patients who completed the verbal intelligence measurement were approached to participate in this study. Patients with severe problems that disabled them to take part in the verbal intelligence measurement, were already excluded in an earlier stage of this study. The consequence of this is that it is possible that only the more motivated patients with less mental problems were included. The patients dropping out might be the patients that score very low on executive functions, while the patients scoring higher participated in the study. The hypothesis might be true for patients with severe deficits in executive functions, because these deficits could decrease their QoL, while the hypothesis might be rejected for the group scoring high on executive functions. A lower variety in scores may have led to insignificant results. The results of this study might not be applicable for the most severe patients with SMI.

On the other hand, the difficult population is also a strength of this study. Due to the difficulties, research on SMI patients often consists of case studies. Furthermore, patients with comorbid disorders are often excluded and research is mostly conducted in patient populations with homogeneity in type of disorder. The heterogeneity of the population used in this study is highly comparable to the variation of patients in health care institutions. Recently, research in clinical psychology is criticized for drawing their evidence based on populations that are unrepresentative of those encountered in routine clinical practice (Sturmey & Hersen, 2012). The strength of this study is the inclusion of patients with different diagnoses, but the same level of care, which lead to a better external validity. The results of this study are therefore more generalizable to all patients with severe problems in mental institutions than studies with homogeneous samples.

Another strength of this study is the use of multiple tests to measure executive functions. Executive functions consists of many different cognitive functions that are used in controlled behaviour. Multiple test can give a more complete measurement of different aspects of executive functions. However, the instruments selected might also have influenced the results. The instrument selection is based on research and the test battery contains a combination of the most common used instruments for executive functions. However, many different instruments are used in practice and research and a different selection of

instruments could have led to different results. There is little consensus on the best way to measure executive functions (Miyake & Friedman, 2012). This is in line with the lack of consensus on which functions are called executive functions (Goldstein & Naglieri, 2014; Lezak, 1993). Chan, Shum, Toulopoulou, and Chen (2008) discuss in their article that there are many different models on executive functions which all lead to different measurement instruments. This raises the question whether we can accurately measure executive function and compare results of different tests and studies with each other. More research is needed to fractionate the executive system by assessing different functions and verify their neuroanatomical correlates in order to develop a more complete and uniform measurement of executive functions (Chan et al., 2008).

Similar conceptual problems are found with QoL. Over the years, QoL became very important in evaluating the outcome of health care (Fujii et al., 2004). However, there are multiple definitions and visions on what QoL is and how to measure it (Theofilou, 2013). There are different theories and concepts published, but with limited influence on measurement techniques (Moons, Budts, & De Geest, 2006). Furthermore, QoL is defined as a collection of different factors, but which factors should be included in QoL is an ongoing discussion in the field of QoL research (Theofilou, 2013). Moons et al. (2006) proposes in their analyses of different concepts of QoL that QoL should be defined in terms of life satisfaction, because this definition successfully deals with all the conceptual problems that other definition face. However, QoL cannot be seen separately from objective factors like psychopathology, which is shown in this study. These conceptual problems surrounding QoL and executive functions complicate the interpretation of the results of this study and the comparison with other research.

Besides the conceptual problems, the selection of the subjective and objective measurements instruments for QoL measurements is another limitation of this study. The instruments selected (WHOQOL-BREF and EQ-5D) are both developed as measurements of QoL and not as specific instruments for objective or subjective QoL (EuroQoL Research Foundation, 2015; The WHOQOL Group, 1998). Moreover, there are validated specific instruments for the measurement of QoL in patients with schizophrenia, for example the Quality of Life Scale (D. W. Heinrichs, Hanlon, & Carpenter, 1984). This instrument might give a more accurate measurement for the patients that suffer from schizophrenia. However, not all patients with

SMI suffer from schizophrenia and patient that do suffer from schizophrenia in a population of patients with SMI often have other comorbid mental problems. Therefore it was decided to use instruments that are validated on a broad population, but other QoL instrument could have led to different results.

Overall, this study was able to contribute to the knowledge of QoL in patients with SMI. The results show that executive functions do not predict subjective QoL and that the development of interventions focussed on executive functions in patients with SMI is not recommended. Verbal intelligence significantly predicts subjective QoL and therefore might be a future target for interventions for patients with SMI. Psychopathology strongly predicted subjective and objective QoL and therefore should remain the main focus in the treatment of patients with SMI.

It is recommended that future research focusses not only on the factors that may influence QoL, like executive functions, but also at fundamental research into the concept and measurement of QoL. A more specific concept of QoL can lead to a more reliable measurement of QoL. However, research on the factors that influence QoL can also contribute to the development of a more specific concept of QoL, because QoL consists of a broad range of different factors. Both research on the fundamental concept of QoL and the factors that influence QoL are advised in order to develop a better understanding of QoL. Research into QoL is highly relevant in order to understand the impact of SMI on the life of patients. The biggest impact factors can be possible targets for treatment. By treating the main factors that influence QoL, we can go beyond recovering symptoms and into achieving the best possible QoL for patients with SMI.

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