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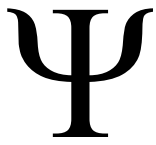

A Longitudinal Follow-up Study of Cognitive Flexibility and Rumination in First Episode Major Depression

HOVEDOPPGAVE

profesjonsstudiet i psykologi

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Forord

Datagrunnlaget for oppgaven er innhentet i forbindelse med forskningsprosjektet «Longitudinal studies of MDD and cognitive functioning and emotional processing: predictors for relapse?». Prosjektet ledes av Professor Åsa Hammar ved Bergen Mood and Cognitive Function Group, ved institutt for biologisk og medisinsk psykologi, Det Psykologiske Fakultet, Universitetet i Bergen. Datagrunnlaget for kognitiv fleksibilitet og ruminering har ikke tidligere blitt gjennomgått. Bidraget fra denne hovedoppgaven er: (1) en grundig litteraturgjennomgang av de to hovedtemaene for oppgaven, (2) utvikling av hypoteser og gjennomføring av analyser av nevropsykologisk testing som ikke tidligere er blitt analysert og (3) en diskusjon om funnenes betydning.

Denne oppgaven er skrevet som en artikkel tilpasset tidsskriftet «Frontiers in Psychology». Retningslinjene til tidsskriftet avviker fra APA 7 på noen område. Se lenker for tidsskriftet sine utfyllende retningslinjer og krav til referering.

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Abstract

Major depression disorder (MDD) is a leading cause of disability worldwide, with high rates of relapse and recurrence. Cognitive deficits are common in the disease; however, the nature of these deficits is unclear. Studies of persisting impairment in cognitive flexibility have found divergent results. Cognitive inflexibility is associated with poorer functional outcomes and could hinder effective treatment and be related to symptoms. Rumination has been linked to cognitive flexibility and is considered an important risk factor for depression. The present study investigated cognitive flexibility and rumination in a one-year follow-up study of patients diagnosed with first episode MDD. Thirty patients and 30 healthy controls were included in the study. Cognitive flexibility was measured using the Wisconsin Card Sorting Test and rumination was measured using the Ruminative Responses Scale and the Rumination-Reflection Questionnaire. Impairments in cognitive flexibility were evident in the acute phase of depression, but not in remission. The results showed a relationship between the severity of depressive symptoms, rumination and partially with cognitive flexibility. Patients that did not show remission following the acute phase were more impaired than remitted patients on some measurements. The patient group had significantly higher levels of rumination, and depressive rumination was found to predict relapse. These findings could have clinical implications for treating MDD and preventing relapse and indicate that rumination should be a target for interventions both before, during and after an episode of MDD.

Keywords: major depression disorder, cognitive impairment, executive functions, cognitive flexibility, rumination, relapse, recurrence

Sammendrag

Alvorlig depressiv lidelse er en av de største årsakene til funksjonssvikt i verden og har svært høye tilbakefallsrater. Kognitive svekkelser er utbredt i lidelsen, men hvordan disse svekkelsene oppstår og arter seg er ennå uavklart. Studier på kognitiv fleksibilitet i deprimerte utvalg har funnet varierende resultater, samtidig har flere studier dokumentert at nedsatt kognitiv fleksibilitet påvirker individets funksjonsnivå, kan hindre utbytte av behandling og være relatert til symptomer. Ruminering har blitt knyttet til kognitiv fleksibilitet og har vist seg å være en viktig risikofaktor for depresjon. Denne studien undersøkte kognitiv fleksibilitet og ruminering hos førstegangsdeprimerte i akutt fase og etter ett år. Tretti pasienter og 30 friske kontrolldeltakere deltok i studien. Kognitiv fleksibilitet ble målt ved Wisconsin Card Sorting Test, og ruminering ble målt ved Ruminative Responses Scale og Rumination-Reflection Questionnaire. Resultatene viste en sammenheng mellom alvorlighetsgraden av depressive symptomer og ruminering, og en delvis sammenheng med kognitiv fleksibilitet. Det var klare svekkelser i kognitiv fleksibilitet i den akutte fasen, men ikke ved tilfriskning. Pasienter som hadde erfart tilbakefall hadde større svekkelser enn de som var i remisjon, på noen mål. Pasientgruppen hadde høyere nivå av ruminering, og depressiv ruminering predikerte tilbakefall. Resultatene kan ha klinisk betydning for behandling av depresjon, og ruminering burde adresseres både før, under og etter behandling av alvorlig depressiv lidelse.

Nøkkelord: alvorlig depressiv lidelse, kognitive svekkelser, eksekutive funksjoner, kognitiv fleksibilitet, ruminering, tilbakefall

Introduction

Major depression disorder (MDD) is considered one of the world's leading causes of disability with more than 264 million people afflicted (James et al., 2018). It is primarily regarded as an affective disorder, characterized by dysphoric mood, rumination, and a loss of interest. In addition, a reduced ability to think or concentrate and difficulties with decision making are also diagnostic criteria, making cognitive difficulties a central feature of MDD (WHO, 2018)

Research on cognitive deficits in MDD in the last decades has found substantial evidence for multiple cognitive abilities to be influenced by the disorder (Hammar and Årdal, 2009). Impairments in memory, inhibition, attention, processing speed and executive functions (EFs) have all been identified in meta-analyses including several hundred studies (Lee et al., 2012; Bora et al., 2013; Rock et al., 2014; Snyder, 2013; Ahern and Semkovska, 2017; Semkovska et al., 2019). A large meta-analysis, including 252 studies and 11882 subjects, has found that in general, cognitive deficits experienced in MDD persists into remission, although findings regarding specific cognitive domains are inconsistent and sometimes divergent (Semkovska et al., 2019). Moreover, some impairments seem to be associated with more severe depression symptoms (Snyder, 2013). The current evidence suggests that cognitive deficits in MDD are overlooked and are not effectively treated by common treatment (Keefe et al., 2014). Also, cognitive deficits are related to functional outcomes, affecting areas such as job performance and social functioning (Jaeger et al., 2006; Kennedy et al., 2007; Ahern and Semkovska, 2017). Causal relationships are not yet firmly established; thus, this area of research warrants more attention (Hammar and Årdal, 2009).

Questions remain regarding which cognitive deficits persist after symptom reduction. Impairments in executive functioning have been shown to both diminish (Biringer et al., 2005) and persist following remission (Paëlecke-Habermann et al., 2005). Cognitive flexibility is considered a central EF, sometimes referred to as set-shifting or shifting

(Ionescu, 2012). It is defined as the ability to adjust cognitive sets or behavior to novel environmental demands, rules, or priorities in an adaptive manner (Steinke and Kopp, 2020). In other words, the ability to withdraw from an activity with certain demands, and to create and implement a new response set to a new task with other demands (Dajani and Uddin, 2015). The Wisconsin Card Sorting Test (WCST) is considered the gold standard for assessing cognitive flexibility (Steinke and Kopp, 2020). In this test, a deck of cards with differing characteristics of color, shape and number of elements are to be matched in line with a specific characteristic. The chosen characteristic is changed after ten uninterrupted correct matches (Grant and Berg, 1948). The test has seven outcome variables in total, such as perseverative errors and responses, and the number of categories completed (Miles et al., 2021).

Studies of persisting impairment in cognitive flexibility have found divergent results (Biringer et al., 2005; Nakano et al., 2008; Huang, 2009; Reppermund et al., 2009; Bhardwaj et al., 2010; Li et al., 2009, Halvorsen et al., 2012; Lee et al., 2012; Snyder, 2013; Trivedi and Greer, 2014). In the most recent meta-analysis, Semkovska et al. (2019) found small persisting impairments in cognitive flexibility measured by the numbers of perseverations and number of categories completed in the WCST. However, no deficits were found for a total measure from the pooled WCST results. Overall, impairments in EFs were generally smaller than in other cognitive domains, and primarily observed on timed tasks. The authors therefore suggest that the impairments in EFs are mediated by processing speed and attentional deficits. An older meta-analysis including studies using the Intra-Extra Dimensional Set Shift-task to measure cognitive flexibility, found significant differences between healthy controls and subjects with MDD in remission (Rock et al., 2014). A review of 11 studies on remitted MDD patients found persistent impairment in attention, memory and EF when compared to healthy controls (Hasselbalch et al., 2011). One study found shifting measured by the Trail Making Test which also takes processing speed into consideration, to be the only cognitive domain to

be impaired in both the first episode and in remission (Liu et al., 2021), Thus, there seems to be indication of persisting impairments in cognitive flexibility.

The nature of persisting cognitive deficits following MDD is important to establish as they have been shown to hinder the recovery process (Jaeger et al., 2006; Kennedy et al., 2007; Ahern and Semkovska, 2017). The inconsistency in these findings relates to the ongoing trait, state, or scar debate regarding cognitive deficits in depression (Allott et al., 2016). Trait effects refer to the influence an individual's characteristics could have on symptoms, predating the onset of a disorder, thus implying some traits could be considered risk factors for specific disorders. This is opposed to state effects, which are symptoms and impairments that are assumed to exist only during a current episode. Scar effects refers to the reduction in functioning due to previous illness, affecting not only the severity of future episodes but also the probability of complete remission after episodes. This could also be related to burden effects, meaning the cumulative load of the illness influencing a person's functioning across the lifespan (Peters et al., 2017). In sum, there is a lack of consensus upon the etiology and development of cognition in depression. Identifying whether cognitive deficits should be considered trait, state or scar effects, or a combination, could influence both clinical treatment and public health initiatives (Ahern and Semkovska, 2017; Allot et al., 2016). Longitudinal studies of patients with first episode could inform these questions.

MDD is typically considered an episodic disease, however recurrence rates range from 50% within two years after the first episode (Vittengl et al., 2007), and up to 90% after three episodes or more (Burcusa and Iacono, 2007). Richards (2011) defines a relapse as meeting full syndrome criteria after being in partial or full remission for a short period. Recurrence is defined as a new episode of depression happening in a period of recovery, meaning having been symptom free for more than eight weeks. Cognitive functioning and relapse could have reciprocal effects. Cognitive deficits have been shown to worsen with repeated episodes and

appears to be an important factor influencing the risk of relapse (Snyder, 2013; Ahern and Semkovska, 2017; Semkovska et al., 2019). This could be indicative of scar effects of MDD.

Most of the research on MDD has focused on populations with recurrent depression (Hammar and Årdal, 2009). Thus, an investigation of the cognitive functioning in patients experiencing a first episode (FE) of MDD could be essential to further investigate the course of cognitive deficits from the onset of the disease and how these relate to symptoms. To our knowledge, only two meta-analyses on FE MDD populations including a measurement of cognitive flexibility have been conducted. Both studies found significantly poorer results in a range of cognitive areas compared to healthy controls (Lee et al., 2012; Ahern and Semkovska, 2017), indicating that cognitive deficits are apparent already from the first episode. In one of the meta-analyses including 13 studies, small to medium deficits were observed in multiple cognitive domains in FE MDD samples. Seven of the studies measured cognitive flexibility, and the analysis found significant deficits, although with small effects (Lee et al., 2012). The most recent meta-analysis of FE MDD pooled results from different neuropsychological tests measuring cognitive flexibility. They found small impairments in FE MDD in three of the pooled measurements; shifting between categories, total number of errors, and trials needed for completion. For a composite score and time needed for completion, the effects were moderate, and the largest impairment was found in the number of correct responses (Ahern and Semkovska, 2017). In sum, there seems to be indication of various impairments of executive functioning present in FE MDD. However, it is still unclear whether impairments in cognitive flexibility persist into remission, and if they influence the risk of relapse, thus warranting further research. This could have clinical implications for whether cognitive flexibility should be targeted early in the treatment process.

Some factors, such as the number of previous episodes, residual symptoms, and symptom severity, are established predictors of future relapses (Buckman et al., 2018). Cognitive deficits are hypothesized as potentially hindering functional recovery and deficits

could be deemed a risk factor for incomplete remission and future relapse (Zuckerman et al., 2018). Cognitive flexibility is suggested to be particularly important for cognitive restructuring, which is assumed central for the treatment of MDD (Lee et al., 2012). Studies examining cognitive deficits as predictors for relapse in a longitudinal design have found differing results. Also, few researchers have researched this in a FE population, as many focuses solely on elderly participants (Simons et al., 2009). Some studies have found cognitive deficits to be larger for patients experiencing their first episode late in life (Bora et al., 2013). A large meta-analysis found that higher levels of cognitive functioning lowered the risk for future depression, and that this relationship was caused by the impact of a depressive state at the time of measurement, rather than pre-existing deficits functioning as a risk factor (Scult et al., 2017). A systematic review found poor executive functioning to be a predictor of poor response to treatment with SSRI, and this effect was even clearer for elderly patients (Groves et al., 2018). One study found a relationship between impaired ability in the EF of inhibition/switching and the risk for experiencing a relapse one year following FE MDD (Schmid and Hammar, 2013). In addition, impaired divided attention has also been found to predict the risk of relapse for both depressed and bipolar patients (Majer et al., 2004). Another study showed a link between the tendency to perseverate and relapse in geriatric MDD patients (Alexopoulos et al., 2000), indicating that the perseveration measurements from the WCST might be a potential predictor for relapse. Contrary to this, a study using the Stroop color word test to measure executive functioning found no significant predictors for neither relapse, nor recurrence, and no significant relationship between the outcomes of the neuropsychological testing and duration of remission, residual depressive symptoms, or previous episodes (Wekking et al., 2012).

In sum, the findings above highlight the importance of evaluating cognitive deficits to predict long-term outcomes in patients with MDD. It is still unclear which impairments in cognitive flexibility persist into remission and their potential to predict relapse. As far as we

know, studies investigating FE MDD patients, cognitive flexibility, and the risk of relapse by comparing relapsed and remitted populations are scarce. Interactions between cognitive functions and symptoms could potentially explain this relationship, however.

Several studies have investigated the relationship between cognitive processes and rumination (Davis and Nolen-Hoeksema, 2000; Whitmer and Gotlib, 2013; Owens and Derakshan, 2013; Chen et al., 2016; Yang et al., 2017; Liu et al., 2017; Zetsche et al., 2018; Vălenaș and Szentágotai-Tătar, 2017). Rumination involves continuous, repetitive, and passive thoughts concerning causes and consequences, and could be paralleled to being stuck in a mental set (Nolen-Hoeksema, 1991; Davis and Nolen-Hoeksema, 2000). It intervenes with problem solving mechanisms by affecting attention and interpretation and is considered to be a hallmark feature of depression. It has been reported to correlate with levels of depressive symptoms over time, as well as risk of relapse (Nolen-Hoeksema, 2000).

Ruminators have shown a greater number of perseverative errors on the WCST than non-ruminators (Davis and Nolen-Hoeksema, 2000), as well as being characterized by a general deficit in the ability to switch among materials held in working memory (Chen et al., 2016). This indicates that ruminators have difficulties maintaining adaptive and flexible behavior. A meta-analysis found a relationship between repetitive negative thinking and problems with discarding irrelevant input from working memory (Zetsche et al., 2018). Furthermore, another large meta-analysis found relationships between rumination and shifting, and rumination and inhibition (Vălenaș and Szentágotai-Tătar, 2017). In line with this, some research indicates that rumination might be mediated by a deficit in working memory and EFs, such as a deficit in inhibition of negative thoughts (Koster et al., 2011; Whitmer and Gotlib, 2013; Joormann and D'Avanzato, 2010).

Rumination seems to be elevated across multiple psychological disorders (McEvoy et al., 2013), and rumination has been found to predict psychopathology from adolescence (Hilt et al., 2014). Different measurements have been developed to capture different types of

rumination. The Rumination-Reflection Questionnaire (RRQ) has a subscale that measures neurotic rumination which correlates with the personality trait of neuroticism (Trapnell and Campbell, 1999). This trait is commonly assumed to be related to psychopathology, especially depression and anxiety (Jeronimus et al., 2016). Another widely used measurement is The Ruminative Responses Scale (RSS), which measures rumination in response to negative mood states (Treynor et al., 2003).

Rumination has been found to correlate with, and be a main causal factor for, risk of relapse in depression (Nolen-Hoeksema, 2000; Spasojević and Alloy, 2001). Michalak et al. (2011) investigated possible predictors of relapse in a sample that had received mindfulness-based cognitive therapy, which specifically targets ruminative thinking. The results showed that post-treatment rumination scores predicted relapse in a one-year follow-up. This remained the case, even after controlling for residual symptoms and previous episodes, which are other known predictors of relapse in depression.

To sum up, rumination is associated with cognitive deficits in EFs, and could influence the risk of relapse in MDD patients. The relationship between cognitive flexibility and rumination in FE MDD is not well established, although theories and research indicate that both elements play an important role in the development, maintenance, and recurrence of depression. To the best of our knowledge, studies on the relationship between rumination, cognitive flexibility and FE MDD are lacking. Assuming that rumination and cognitive inflexibility are connected, and both are present following FE MDD, this could have implications for the understanding of the development of depression, as well as prevention work, early interventions, and treatment for depression.

The main aim of this study was to examine cognitive flexibility and rumination in individuals experiencing a FE MDD and following one year later. By using a study design including patients experiencing FE MDD compared to healthy control participants, in the acute phase and after one year, we mainly tap into the trait and state effects in the acute phase,

minimizing major prospective and cumulative effects, i.e., scar and burden. The longitudinal design could contribute to the understanding of the etiology of depression and risk factors for relapse and recurrence.

This study investigated the following six hypotheses:

First, we predict that the participants with FE MDD will have a lower score on cognitive flexibility measured by the WCST compared to the control group, both in the acute phase and at the one-year follow up.

Second, we predict that the patient group will have a higher score on neurotic rumination at the one-year follow-up compared to the control group.

Third, we predict that measures of rumination will correlate with cognitive flexibility, indicating that there is a relationship between high rumination and low cognitive flexibility.

Our fourth hypothesis concerns the difference in cognitive flexibility between the subjects who relapsed or had a continued depression since the acute phase and those who are in remission one-year follow-up. We predict that the depression group has lower scores than the remission group in the acute phase and shows a smaller improvement in cognitive flexibility than the remission group at the one-year follow-up. Also, we predict that the remission group does not reach the levels of the control group on measures of cognitive flexibility.

Fifth, we predict that the depression group has a higher level of depressive symptoms and depressive rumination compared to the remission group, and a higher level of neurotic rumination compared to the remission group and the control group at the one-year follow-up. Sixth, we predict that low cognitive flexibility in the acute phase and high rumination scores increase the likelihood of experiencing relapse.

Materials and Methods

Participants and Procedure

The present study was designed as a longitudinal case-control follow-up study with assessments during the acute phase of MDD (T1) and after one year (T2). The study is ongoing, with prospective studies planned to examine different cognitive deficits measured at five and ten-year follow-ups.

Thirty participants were recruited to the patient group at T1, in cooperation with physicians and psychologists in primary healthcare and the student health service at the University of Bergen. Suitable participants who gave their consent were later contacted by the coordinator of the study. Inclusion criteria were seeking treatment for and a diagnosis of FE MDD, assessed by a trained clinical psychologist using the MINI - International Psychiatric Structural Interview (Leiknes et al., 1999). The participants were also assessed with the Montgomery Åsberg Depression rating scale, where the participants needed to attain a minimum score of 20 to be included, which indicates a moderate to severe depression (Montgomery and Asberg, 1979). Of the included participants, 23.3% received no treatment, 13.3% received medical treatment, 30% psychological treatment, and 33.3% received both psychological and medical treatment, of which the majority treated with antidepressants. All participants were outpatients. Exclusion criteria were previous diagnosis or treatment of depression, severe somatic disorders, substance or alcohol abuse, psychosis, having received electro convulsive therapy, or known brain damage.

A healthy control group was recruited at T1, matching 30 individuals to the included participants on age, gender, and years of education (+/- 2 years). Recruitment of the control group happened through the University of Bergen and by using the social network of employees at the Department of Biological and Medical Psychology. Appropriate participants were assessed and interviewed to examine if they were suitable controls. Exclusion criteria for the control group were the same as for the patient group, in addition to any present or

previous mental health issues, including, but not limited to depression. The participant flow is illustrated in Figure 1.

- *Insert Figure 1 approximately here* -

A trained senior test technician administered the neuropsychological tests in the same order over a period of approximately four hours during regular work hours, at the Institute of Biological and Medical Psychology, University of Bergen, Norway. The technician was not blinded regarding group affiliation, due to the recruitment strategy. In addition to the measurements below, the participants were tested in verbal fluency, inhibition, switching, planning and problem solving at both T1 and T2. IQ was assessed at T1 with two subsets from the Norwegian Version of Wechsler Abbreviated Scale of Intelligence (WASI), vocabulary and matrix reasoning (Wechsler, 1999).

Materials

Clinical Assessment

A trained psychologist administered the structured clinical interview MINI and screened the participants on the inclusion and exclusion criteria at T1. In addition, MADRS scores were recorded to assess severity of depressive symptoms at T1 and T2. At T2, it was assessed whether the participants in the patient group had experienced a relapse or a recurrence of MDD since T1, by using the National Institute of Mental Health prospective Life Chart Methodology (Denicoff et al., 2000). The participants could then be sorted into two subgroups. The «Depression group» consisted of the participants who had experienced one or more episodes of depression since T1, thus including both subjects lacking remission from the first episode, and those experiencing a relapse. The «Remission Group» consisted of the participants who were in remission or had been symptom free for more than eight weeks following T1.

Depressive Rumination

The Norwegian version of the questionnaire "Ruminative Responses Scale" (RRS) was used to measure self-reported depressive rumination in the patient group at T2. The scale consists of 22 items with a four-point Likert scale. A total score of the scale was calculated to represent the level of depressive rumination. The internal validity was found to be very high (Cronbach's alpha = .92).

Neurotic Rumination

The Rumination-Reflection Questionnaire (RRQ) measures both Rumination and Reflection, of which the Rumination subscale correlates with the personality trait of Neuroticism, and the Reflection subscale correlates with the trait of Openness to Experience (Trapnell and Campbell, 1999). The correlation between the two subscales has been shown to be minimal (r = .22). For our analyses, we have applied the Rumination subscale consisting of twelve of the total 24 items, measured by a five-point Likert scale. The raw scores were summed for a total subscale score, and Cronbach's alpha for the subscale was very high (r = .93). The self-report questionnaire was administered to both the patient group and the control group at T2.

Cognitive Flexibility

To assess cognitive flexibility, a computerized version of the WCST was used (Heaton and Par Staff, 2008). Six different outcome variables were used in our analyses. The number of «Categories Completed» (CC), i.e., when a participant managed to correctly use a matching characteristic ten times, is an overall measure of cognitive flexibility. «Failure to Maintain Set» (FMS) is the number of five or more correct responses in a row, but less than ten, leading to not completing the category, assumed to be a measure of problems with maintaining adaptive strategies. «Perseverative Errors» (PE) is the number of errors made by a participant using the same rule for their matching as the previous matching, despite being given feedback that the characteristic used for matching is wrong. One can expect some PE

when the matching characteristic is changed, but a high number indicates an issue with set shifting. «Total Errors» (TE) is the total of all the incorrect responses and includes both «Perseverative Errors» (PE) and non-perseverative errors. «Perseverative Responses» (PR) is the number of incorrect responses that would have been correct for the previous category and is usually a response to a new or shifted category. Thus, they include some perseverative errors as well. «Trials Administered» (TA) is the total number of cards used, minus the number of the last trial (The Nutfield Foundation, 2008). Both the patient group and the control group completed the WCST at T1 and T2.

To examine the change in cognitive flexibility, change scores were computed for each of the six outcome variables. This was done by subtracting the raw score at T1 from the raw score at T2. Thus, a negative number indicates an improvement at T2, except for CC, where a positive number indicates an improvement.

Ethics and Consent

The participants received information regarding the study and gave their informed consent at their first assessment. The study was approved by the Regional Committee for Medical Research Ethics and the Norwegian Data Protection Authority. The study also complied with the ethical principles of The Declaration of Helsinki (World Medical Association, 2013).

Data Scoring and Analysis

The Statistical Package for the Social Sciences (SPSS) version 26 was used to execute the statistical analyses. We checked for potential outliers and found the scores to be within the range of possible scores and not erroneous scores, thus all values are included in the analysis. Missing data was assessed to be randomly distributed and minimal. Data collected for participants who later dropped are used in the analyses to gain greater statistical power. Preliminary analyses were conducted to examine the assumptions of normality, by visually examining the distributions presented as histograms.

Cohen's d was used to describe effect sizes, with an effect size of 0.2 considered small, 0.5 medium and 0.8 large (Cohen, 1988). Due to small sample size, Bonferroni correction for multiple comparisons was not used to reduce the chance for type-2 errors. The p-value was set to .05 for all the analysis except for the subsamples in the patient group where a p-value of .10 was adopted, due to low power.

Our analyses were conducted in four parts. First, we examined the group differences between the patient group and the control group by comparing the means and the mean ranks. The WCST outcome variables did not follow a normal distribution, thus the non-parametric Mann-Whitney U-test was used to examine the mean rank differences. All other variables followed a normal distribution and Independent samples T-test were applied for these variables.

Second, The Spearman rank-order correlation was used to assess the correlations between the rumination, MADRS and cognitive flexibility variables in the patient group, due to the non-normality of the WCST measures.

Third, we examined the group differences in the patient group with regards to whether the subjects had experienced depression between T1 and T2, by comparing the means and the mean ranks. Analysis of variance (ANOVAs) was performed for the clinical variables where the control group could be included. For the WCST measurements, the Kruskal-Wallis test was applied. We also examined the change in the scores of cognitive flexibility from T1 to T2. ANOVAs were used to compare the change scores, except for the change score of CC, which was not normally distributed.

Fourth, we examined if any of the variables that were different between the groups could predict a future relapse using logistic regression analyses. The neuropsychological variables that differed between the patient group and the control group were included in one model, except the variable of TE since it overlaps almost entirely with PE. Depressive

rumination and neurotic rumination were included in two separate models due to their high multicollinearity of 0.62 (Pallant, 2014).

Results

Demographic Data for the Patient Group and the Control Group

Independent Samples T-Tests were conducted to examine the differences between the patient group and the control group (see Table 1). The groups did not differ significantly on any of the matching criteria. The mean score of MADRS shows a large reduction in symptoms of depression from T1 to T2 for the patient group. At T1, all the participants had a score of 20 or higher. At T2, the scores range from 2 to 24. This indicates that the majority of the patient group no longer reported symptoms qualifying for a moderate to severe depression at T2.

- *Insert Table 1 approximately here* -

Differences between Groups in Cognitive Flexibility

Mann-Whitney U-tests were used to investigate group differences measured by the WCST (see Table 2). The patient group had significantly lower mean ranks for the WCST outcome variables at T1, except for FMS, showing lower cognitive flexibility in the acute phase. The effect sizes ranged from 0.27 to 0.34, indicating small to medium effect sizes, except for FMS (d = 0.06). None of the WCST conditions differed between groups at T2.

- *Insert Table 2 approximately here* -

Differences between groups in Neurotic Rumination

Independent sample T-test examined the group differences in neurotic rumination (see Table 1). There was a statistically significant difference, indicating that the patient group had

a higher score than controls on rumination as measured by the RRQ rumination subscale at T2. The calculated effect size was large (d = -1.83).

Relationship between Rumination and Cognitive Flexibility

Spearman rank-order correlations (two-tailed) were used to investigate the relationship between rumination and cognitive flexibility (see Table 3). Due to the hypothesized direction of the relationships, one-tailed correlations were calculated. RRS correlated significantly with FMS at both T1 (one-tailed, $p = .047$) and T2 (one-tailed, $p = .029$) with medium effect sizes. RRQ also correlated significantly with FMS at T2 ($p = .012$) with a medium effect size, meaning that higher levels of rumination make it harder to maintain an adaptive response. RRS-scores and RRQ-scores did not correlate significantly with any of the other measures in the WCST.

MADRS at T1 correlated negatively with CC T1 (one-tailed, $p = .043$) with a medium effect size. The correlation between MADRS T1 and CC T2 was approaching significance (one-tailed, $p = .057$), meaning a higher depression score gave fewer categories completed. This also had a medium effect size. Furthermore, MADRS at T2 correlated significantly with FMS at T2 (one tailed, $p = .021$) with a medium effect size.

- *Insert Table 3 approximately here* -

Differences between the Subgroups and the Control Group

One-way ANOVAs revealed that the subgroups did not differ regarding age, education in years or IQ, although there was a skewed gender distribution, with fewer females in remission. There were, on the other hand, significant differences in regard to the MADRS scores, indicating a more severe depression at T1, and more symptoms at T2, for the depression group. The results are presented in Table 4.

- *Insert Table 4 approximately here* -

Subgroup Differences in Cognitive Flexibility

The Kruskal-Wallis test was used to examine the differences between the groups on the WCST (see Table 5). The three groups differed significantly with medium effect sizes in the number of CC at T1 (d = 0.54) and T2 (d = 0.50). The depression group had the lowest rank at both T1 and T2. The remission group moved from a slightly lower rank than the control group at T1, to a comparable rank at T2. FMS showed no significant differences at T1 (d = 0.38) or T2 (d = 0.28), however the effect sizes were small to medium. The mean ranks showed an improvement for the remission group. There were significant differences with medium effect sizes in the number of PE (d = 0.51) and in PR (d = 0.52) at T1. There were no significant differences at T2, however the effect sizes were small to medium (d = 0.37). The mean ranks indicate approximately the same tendency to perseverate for the depression group and the remission group at T1, with the remission group approaching the rank of the control group at T2. This could indicate that the perseveration tendency was reduced from T1 to T2 for both the depression group and remission group, but more so for the remission group. No significant differences were found for the TE scores at either time; however, the effect sizes were small to medium at both T1 (d = 0.39) and T2 (d = 0.39). The mean ranks indicate that both the depression group and the remission group committed fewer errors at T2 than at T1. There were no significant differences between the groups in TA at either time, however the effect sizes were small to medium at both T1 (d = 0.32) and T2 (d = 0.37). The ranks indicate that the remission group needed the most trials at T1, although the depression group also needed more trials than the control group. At T2, the remission group had a lower rank than both control and the depression group, who were quite similar indicating a large improvement for the remission group.

- *Insert Table 5 approximately here* -

ANOVA analyzed the change scores in the three groups and there were no significant differences between the groups on the change scores. However, by examining the means of the change scores, the tendency is for the remission group to have a slightly larger improvement. Especially for TA, the difference in improvement is apparent, with a medium to high effect size (d = 0.67). The remission group has almost three times larger improvement than the depression group, and almost six times larger improvement than the control group. Adding to this, the effect sizes for the remaining change scores were medium, ranging from 0.39 to 0.61. Overall, the control group has a relatively small improvement from the acute phase to the one-year follow-up. The depression group has some improvement, although smaller than the improvement found for the remission group. The remission group has a substantial improvement, and the scores at T2 are approaching the mean ranks of the control group.

Subgroup Differences in Rumination

An independent-samples T-Test compared the scores on depressive rumination (RRS) between the depression group and the remission group. The results are presented in Table 4. The difference between the groups was significant (F = 2.367, p = .025, two-tailed), with the depression group having higher levels of depressive rumination at T2. The effect size was large (d = -0.93).

For neurotic rumination as measured by a subscale on the RRQ, a one-way ANOVA was performed due to the possibility to include the control group. The means are presented in Table 4. There was a statistically significant difference (F (2,50) = 25.58, p = .000), with a large effect size (d = 2.2). A planned comparison between the remission group and the depression group, showed a statistically significant difference (F (1,50) = 4.14, p = .047). The control group had a lower score on neurotic rumination compared to both patient subgroups.

Cognitive Flexibility as a Predictor of Relapse

Direct logistic regression was performed to assess if any of the measurements of cognitive flexibility in the acute phase could predict a relapse in depression by the one-year follow-up. The full model contained the independent variables CC, PE, PR, and TA, but it was not found to be statistically significant. Thus, none of the WCST outcome variables measured at T1 could predict a relapse by the one-year follow-up.

Rumination as a Predictor of Relapse

Two separate logistic regression analyses were conducted for the measurements of rumination due to their high correlation. For the RRQ, the model is approaching significance, X^2 (1, N = 28) = 3,43, p = .06, indicating that the model was not fully able to predict which patients had relapsed. For the RRS, the model was found to be statistically significant, X^2 (1, N = 28) = 5.42, p = .02, indicating that the model was able to distinguish between the subjects who reported a relapse during the last year and those that did not. The model explained between 18.2% (Cox and Snell R^2) and 24.4% (Nagelkerke R^2) of the variance in relapse status, and correctly classified 63% of cases. The odds ratio of RRS was 1.09, meaning that an increase of one point on the RRS increases the possibility of relapse with 9%.

Discussion

Overall, there was mixed support for our hypotheses. The hypothesized difference between the patient group and the control group on measures of cognitive flexibility in the acute phase was supported. The patient group had lower scores on all outcomes, except for FMS. This is in line with previous research finding that FE populations have impairments in cognitive flexibility in the acute phase of the illness (Lee et al., 2012; Ahern and Semkovska, 2017). Interestingly, these differences were not evident at the one-year follow-up. Thus, there does not seem to be a permanent impairment in cognitive flexibility in our sample, indicating that the impairments in cognitive flexibility in the acute phase are state dependent. This is supported by a meta-analysis by Ahern & Semkovska (2017) investigating FE MDD, where

shifting was found to normalize with remission. However, direct comparison is somewhat challenging as the results are pooled from studies using different measures, amongst others the WCST.

We also found support for our hypothesis that the patient group would have a higher score of neurotic rumination than the control group at the one-year follow-up. This means that despite symptom reductions in MADRS-score, neurotic rumination persists. Prior levels of neurotic rumination can only be inferred, as it was not measured in the acute phase. Thus, this should be investigated in prospective studies. Our results indicate a trait vulnerability to depression as neurotic rumination is linked to the personality trait Neuroticism. This points in the direction of neurotic rumination being a precursor of depression, that could be independent of the depressive state. This is in line with research indicating that neuroticism relates to several psychopathologies such as depression and anxiety (Jeronimus et al., 2016). One study found that Neuroticism strongly predicted unipolar depression (Zinbarg et al., 2016). Interestingly, large meta-analyses have found that neuroticism is the strongest correlation to common mental disorders, and that many disorders have similar trait profiles (Kotov et al., 2010). Our results contribute to these findings, emphasizing that neurotic rumination could be a possible marker for identifying persons at risk for developing mental health issues, and could be an important target in preventive interventions.

We hypothesized that there would be a relationship between rumination and cognitive flexibility, with higher rumination scores correlating with lower scores on cognitive flexibility. However, a clear pattern of a relationship between the RRS and the RRQ and the outcome variables on the WCST was not found, even though previous findings have indicated that ruminators perform worse on the WCST (Davis and Nolen-Hoeksema, 2000).

Our results showed positive correlations between FMS and both the RRS and the RRQ, as well as with scores on MADRS at the one-year follow-up. These correlations show that high levels of rumination and depressive symptoms are associated with an inability to

maintain a proven successful strategy. This is in line with previous research indicating an association between rumination and problems maintaining an adaptive set (Davis and Nolen-Hoeksema, 2000). The authors argue that ruminators become stuck in a mental set even when they receive feedback that their cognitive style is not adaptive.

As confirmed by the first hypothesis, the groups differed significantly on all measures of the WCST, except FMS. This finding is surprising, as the patient group consists of high ruminators relative to the control group but did not differ significantly on FMS despite the high correlation between rumination and FMS. Some argue that FMS might measure distractibility instead of cognitive flexibility, which might explain why this is the only measure on the WCST that correlated significantly with rumination. One explanation is that negative thought content could divert the participants' attention and thereby distract them from the task at hand (Figueroa and Youmans, 2013). Taking all this into account, our hypothesis suggesting a correlation between rumination and cognitive flexibility was not supported. It is evident that there could be methodological issues regarding what constructs the WCST actually measures, and that the link we discovered between FMS and rumination might have alternative explanations.

Due to the high correlation between the RRS and MADRS, it could be that the correlations found with FMS is because of the shared variance of depressive mood. Depression is known to affect attention (Keller et al., 2019), and as such distractibility. It could also be that some of the participants in the patient group lack motivation, or give random answers, which could negatively affect their scores on the WCST.

We also found that MADRS in the acute phase correlates with CC in the acute phase and is approaching significance with CC at the one-year follow-up, meaning that depressive symptoms could impact the overall ability to master the WCST. This further adds to the argument of depressive mood possibly being the strongest influence on the relationship between cognitive flexibility and rumination.

When looking at the subgroups, we have partial support for our hypotheses. The depression group performed worse than the remission group and control group in the acute phase, with significant differences found between the scores of CC, PE, and PR, with medium effect sizes. At the one-year follow-up, we only found significant differences between CC with a medium-high effect size, indicating that the differences from T1 diminishes at T2. Although not significant, the depression group overall has lower ranks than the remission group at both points in time. This might be due to a relationship between symptom severity and cognitive deficits, as the depression group has significantly higher MADRS scores at T1. Despite the differences in the WCST not being significant, the tendency is in line with research finding greater neuropsychological deficits for participants experiencing more severe current depression symptoms (Snyder, 2013). There is also more recent support for this; Azzam et al. (2020) found that patients with recurrent MDD had significantly more impaired EFs than patients with FE MDD. Longitudinal studies with larger subsamples could further illuminate whether the impairments in cognitive flexibility will differ later in the course of depression between patients who have relapsed, and patients who have experienced a single episode.

Regarding the improvement from the acute phase to the one-year follow-up, the tendency was a smaller improvement for the depression group than the remission group, although none of the differences were significant. This could indicate that persistent cognitive deficits are associated with higher risk of relapse or severity of course of illness. The effect sizes are medium-to-high for the change scores. In sum, the patients who had relapsed, initially had lower scores on cognitive flexibility at T1 on some measures, and a tendency for smaller improvement the following year. Given this relationship, we suggest that impaired cognitive flexibility is associated with a more severe course of depression. Overall, our samples are too small for any firm conclusions to be drawn. The overall tendency when comparing the means and the mean ranks, is that the levels of the remission group approach,

but does not fully reach the levels of the control group. This does not support our hypothesis of the deficits to persist into remission. This adds to the research implying that the majority of deficits are state-dependent (Ahern and Semkovska, 2017).

Regarding the hypotheses concerning the differences in rumination between the depression group and the remission group, the depression group had significantly higher scores on both rumination scales at the one-year follow-up, thus confirming our hypotheses. The difference in the MADRS scores at T1 indicates that the participants in the depression group initially had a more severe first episode than the participants who did not later experience a relapse, supporting the assumption that symptom severity predicts later depression. The analysis of neurotic rumination showed that the difference was not only found between the patient and the control group, but also between the subgroups in the patient group. This indicates that both heightened neurotic and depressive rumination could lead to a more severe course of depression, which adds to the literature showing that rumination exacerbates depression and potentially predicts the onset of an episode (Nolen-Hoeksema et al., 2008).

We did not find support for our hypothesis regarding the predictive value of cognitive flexibility for relapse, and the scores on the WCST at T1 could not predict which subjects experienced a relapse in the following year. Due to the depression group having lower scores in the acute phase on all WCST outcomes except FMS, one could assume that measures of cognitive flexibility could predict future relapse, but this was not the case. This is in line with previous research on other EFs not being predictors of future relapse (Wekking, 2012). Others have found divergent results regarding the association of cognition with the future course of depression (Hasselbalch et al., 2011).

Our findings indicate that participants that are remitted at the one-year follow-up, do not have lasting impairments in cognitive flexibility. We suggest that cognitive flexibility as measured by the WCST can indicate state-related deficits but is not a suitable marker for

targeting those who have a greater risk of relapsing. Cognitive flexibility as measured by WCST does not seem to be a significant predictor or a trait-related impairment. It should however, alongside other identified cognitive deficits in the acute phase, receive attention in treatment, to reduce the negative impact on functional outcomes. The planned future follow-up studies on the same sample could reveal higher relapse rates, thus our results are not conclusive.

Our hypothesis regarding rumination and risk of relapse was supported. At the one-year follow-up, depressive rumination predicted relapse. Neurotic rumination was approaching significance, in terms of predicting relapse. This indicates that rumination can be a valuable marker for who is at risk for relapse in MDD, even after just one episode. Although neurotic rumination as a predictor for relapse was only approaching significance, the effect size is considered very high. This might be indicative of a real predictive value of neurotic rumination but should be interpreted with caution due to small sample size.

The link between rumination and depression is well documented (Nolen-Hoeksema, 2000; Michalak et al., 2011; McEvoy et al., 2013; Jeronimus et al., 2016). Rumination seems to have a negative impact on coping and functioning in several ways; it seems to prolong negative mood states, interfere with adaptive problem-solving mechanisms, act as a transdiagnostic vulnerability factor, limit the efficacy of treatment and psychological interventions, as well as exacerbate stress responses (Watkins and Roberts, 2020; Aker et al., 2014). Moreover, rumination has shown to mediate the relationship between previous episodes of depression and relapse risk (Spasojević and Alloy, 2001).

The current study found evidence for impairments in WCST being associated with the depressive state. In addition, our results indicate that rumination could be interpreted as an inherent vulnerability for MDD. Depressive rumination could be central for a worsening of the disorder, and therefore give a higher risk for recurrence and relapse (Zinbarg et al., 2016). Ideally, future studies should assess neurotic rumination before the onset of disease and in the

acute phase, to examine whether the depressive state is influenced by the level of neurotic rumination, and to further illuminate its predictive value.

Strengths and Limitations

The present study has several strengths. By longitudinally investigating a FE MDD sample, we minimize the possible scarring effect of previous episodes. Furthermore, the groups consist of almost equal representations of both genders and they do not differ in IQ. In addition, the patient group consists of outpatients and the sample is relatively young. This could be considered strengths of our study, as we potentially limit known confounding variables that have been documented to affect cognitive performance, such as age, severity, comorbidity, and hospitalization (Snyder, 2013).

However, our study is not without limitations. As mentioned, the participants in the patient group were all outpatients and were mostly university students with higher IQ than the average population. This indicates that our patient group consists of high functioning individuals, and this should be taken into consideration when generalizing the results to other populations. Some of our subjects were also receiving medical treatment which could be confounding. Our sample is also relatively young, which makes it difficult to compare results with other studies focusing primarily on older subjects (Lee et al., 2012; Ahern and Semkovska, 2017).

Our samples consisted of fewer than 30 subjects, giving us low power to detect any significant differences. In addition, the effect sizes calculated should also be interpreted with caution since they could be inflated due to small sample sizes (Button et al., 2013). Our subgroups are small and have a disproportionate gender distribution, with a majority of females having experienced depression since the acute phase. Research on gender differences in depression provide inconsistent findings, however women are more likely to seek help which in turn can influence the gender distribution in clinical samples (Parker and Brotchie,

2010). Future studies should replicate these findings including larger groups with a comparable number of men and women.

Another important consideration for the present study is the use of the WCST to measure cognitive flexibility. First, non-parametric analyses were used due to the non-normality of the WCST outcome scores, which are stricter and thus give us less power (Pallant, 2014). Second, the WCST is a complex test which involves several cognitive processes. It produces a large number of outcome variables which is problematic when it comes to interpreting how the different outcomes relate to the assessment of cognitive flexibility. The scoring methods of the task also differ and have evolved, and there is evident confusion especially concerning the scoring of the perseveration measures PE and PR, which is a possible source of error. The internal validity of WCST should be examined further due to high task impurity (Miles et al., 2021).

Some point to the fact that the WCST was designed to detect severe neuropsychological frontal lobe deficits, and that it is not sensitive enough to measure specific cognitive control functions (Snyder et al., 2015). Also, this type of cognitive tests performed in staged laboratory settings have been critiqued for not being transferable to functioning in real life. The added use of self-report behavioral questionnaires to measure cognitive flexibility could enhance the ecological and construct validity in research on cognitive flexibility (Uddin, 2021).

Furthermore, there are variations in terminology in the field. Some use cognitive flexibility interchangeably with shifting or set shifting, while others use different operationalizations and neuropsychological tests. This taps into the disagreements regarding whether cognitive flexibility itself should be considered a separate cognitive ability or if it should be considered a property of various cognitive processes (Ionescu, 2012). When WCST is pooled together with other measurements, for instance when compiling a total score of executive functioning, other elements such as processing speed and working memory could

also affect the combined results. This complicates the comparison from our study with conclusions drawn from these studies.

Overall, the basis of comparison for our results differs in many aspects. Populations vary from study to study, with different diagnoses, clinical assessment, apparatus, and clinical status at the time of assessment, to name some. The meta-analyses on the topics pool together many differing studies with different operationalization of cognitive functions, and combine results from a wide array of neuropsychological tests to create overall construct categories. Methodological issues may be the cause of the discrepancy between our results and previous research.

To measure rumination in depressed samples, The RRQ is not widely used. Hence there is not a lot of literature to compare our findings from the RRQ to. In addition, measurements on both RRQ and RRS at T1 could have provided greater insight into the development of depression and the predictive value of rumination in terms of experiencing relapse.

The strength and the limitations mentioned here highlight the importance of replicating the present study. Future studies should focus on investigating cognitive flexibility and rumination in the course of MDD and include a larger sample of subjects in each subgroup.

Our findings increase the awareness of both state and trait vulnerability factors as well as relapse risk factors for MDD. Cognitive inflexibility is suggested to reduce cognitive restructuring in therapy, thus targeting cognitive deficits early in the course could facilitate better functional outcomes and potentially positively influence the recurrence rates (Lee et al., 2012). Moreover, rumination is argued to hinder the incorporation of adaptive strategies and to interfere with therapy due to several underlying mechanisms (Watkins and Roberts, 2020). Therefore, future directions for treatment should involve specific interventions for both rumination and cognitive inflexibility, and tools to monitor whether treatment is helpful in

reducing rumination and increasing cognitive flexibility. Computerized cognitive training is suggested to improve cognitive flexibility (Uddin, 2021). The same goes for targeting rumination, where computer-based training is put forward as a more advantageous treatment strategy than mere verbal interventions (Zetsche et al., 2018). In addition, mindfulness-based cognitive therapy has provided promising results in reducing ruminative thinking related to depression (Michalak et al., 2011).

Overall, cognitive deficits, and a tendency to ruminate, are well established features of MDD. The present study investigated these factors in FE MDD. A depressed state was found to be associated with lower levels of cognitive flexibility and higher levels of rumination. Impairments in cognitive flexibility did not persist into remission, although there was a tendency of less improvement for the depression group at the one-year follow-up. Our findings further add to the pool of research with divergent results, which point to the need for future studies. Rumination seems to exacerbate depression, and depressive rumination predicted relapse and recurrence of depression. This indicates that rumination could be a trait and state marker, and an important vulnerability factor for the development and recurrence of depression. The relationship between cognitive flexibility and rumination remains unclear, and there are some potential challenges with using the WCST as a measure of cognitive flexibility. Early identification of cognitive deficits and ruminating tendencies could be essential for prevention work, as well as early interventions. Better treatment for MDD will have a positive impact on an individual's functional outcome, but also on the socio-economic costs of the disease. These findings could help guide clinical decision making and warrants further research.

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Figure 1

Recruitment and participant flow

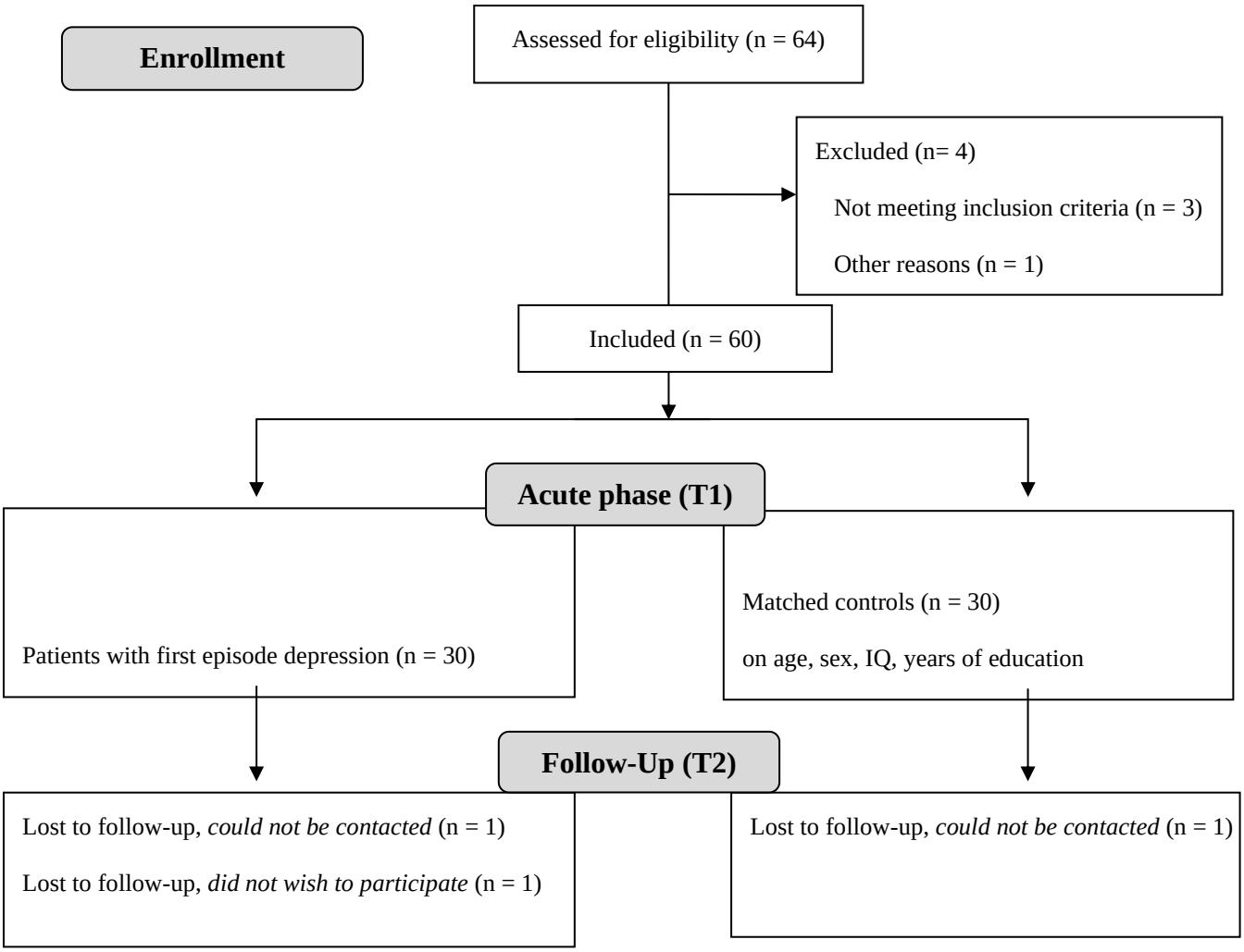

Table 1

Sociodemographic Characteristics and Clinical Assessment of Participants

	Patient Group (N = 30)		Control Group (N = 30)	
	M	*SD*	*M*	*SD*
T1				
Gender (Male/Female)	16/14	-	16/14	-
Age	25.96	5.60	25.93	5.21
Education in years	13.88	1.74	14.14	1.65
WASI IQ	117.44	7.72	121.25	8.30
MADRS	24.60	3.73	-	-
T2				
MADRS	9.96	6.01	-	-
RRS	45.15	11.95	-	-
RRQ Rumination *	44.76	8.58	30.54	6.98

WASI = Wechsler Abbreviated Scale of Intelligence. MADRS = Montgomery Åsberg Depression rating scale. RRS = Ruminative Responses Scale. RRQ = The Rumination-Reflection Questionnaire.

* Sig = .000

Table 2

Assessment of Cognitive Flexibility measured by the Wisconsin Card Sorting Test in the Patient Group and the Control Group

	Patient group (N = 30)		Control group (N = 30)		Statistics		
	Mean rank	Md	Mean rank	Md	Mann Whitney *U*	*Z*	*p*
T1							
Categories Completed	28.00	6.0	33.00	6.0	375.00	-2.31	.021
Failure to Maintain Set	31.38	0.0	29.62	0.0	423.50	-0.47	.637
Perseverative Errors	36.23	6.0	24.77	5.0	278.00	-2.58	.010
Perseverative Responses	36.32	6.0	24.68	5.0	275.50	-2.62	.009
Total Errors	35.50	12.5	25.50	10.0	300.00	-2.23	.026
Trials Administered	35.15	79.5	25.85	77.0	310.50	-2.07	.039
T2							
Categories Completed	27.96	6.0	30.00	6.0	377.00	-1.45	.146
Failure to Maintain Set	28.14	0.0	29.83	0.0	382.00	-0.50	.619
Perseverative Errors	29.79	5.0	28.24	5.0	384.00	-0.36	.718
Perseverative Responses	29.66	5.0	28.36	5.0	387.50	-0.30	.762
Total Errors	29.25	10.0	28.76	10.0	399.00	-0.11	.911
Trials Administered	28.18	77.5	29.79	77.0	383.00	-0.37	.712

Table 3

Spearman Rank Order correlations for Clinical Assessment and Cognitive Flexibility in the Patient Group

		T1							T2								
		MADRS	WCST CC	WCST FMS	WCST PE	WCST PR	WCST TE	WCST TA	MADRS	RRS	RRQ R	WCST CC	WCST FMS	WCST PE	WCST PR	WCST TE	WCST TA
T1	MADRS	1.00															
	WCST CC	-0.32	1.00														
	WCST FMS	-0.02	-0.22	1.00													
	WCST PE	-0.05	-0.66**	0.35	1.00												
	WCST PR	-0.06	-0.66**	0.36	0.99**	1.00											
	WCST TE	-0.03	-0.65**	0.25	0.88**	0.89**	1.00										
	WCST TA	-0.03	-0.65**	0.48**	0.79**	0.79**	0.90**	1.00									
T2	MADRS	0.41*	-0.13	0.01	-0.08	-0.08	-0.05	-0.06	1.00								
	RRS	0.47*	-0.20	0.33	-0.09	-0.09	0.03	0.06	0.75**	1.00							
	RRQ R	0.44*	-0.18	0.10	-0.27	-0.26	-0.09	0.06	0.40*	0.62**	1.00						
	WCST CC	-0.31	0.71**	-0.07	-0.46*	-0.46*	-0.42*	-0.41*	0.01	-0.12	-0.28	1.00					
	WCST FMS	0.08	-0.02	0.08	-0.26	-0.26	-0.17	0.03	0.39*	0.37	0.49*	-0.16	1.00				
	WCST PE	0.13	-0.45*	-0.04	0.47*	0.47*	0.54**	0.55**	-0.06	0.03	0.16	-0.46*	0.28	1.00			
	WCST PR	0.12	-0.47*	-0.03	0.49**	0.49**	0.56**	0.57**	-0.06	0.04	0.14	-0.46*	0.27	0.99**	1.00		
	WCST TE	0.15	-0.48*	0.22	0.53**	0.53**	0.52**	0.56**	-0.06	0.11	0.11	-0.45*	0.18	0.92**	0.92**	1.00	
	WCST TA	0.18	-0.51**	0.28	0.35	0.35	0.48*	0.60**	0.08	0.24	0.30	-0.45*	0.52**	0.84**	0.84**	0.85**	1.00

MADRS = Montgomery Åsberg Depression Rating Scale. RRS = Ruminative Responses Scale. RRQ R = Rumination-Reflection Questionnaire Rumination Subscale. WCST = Wisconsin Card Sorting Test. CC = Categories Completed. FMS = Failure to Maintain Set. PE = Perseverative Errors. PR = Perseverative Responses. TE = Total Errors. TA = Trials Administered.

*. Correlation is significant at the 0.05 level (2-tailed).

**. Correlation is significant at the 0.01 level (2-tailed).

Table 4

Sociodemographic Characteristics and Clinical Assessment of Subgroups

	Depression group (N = 16)		Remission group (N = 12)		Control Group (N = 30)	
	M	*SD*	*M*	*SD*	*M*	*SD*
T1						
Gender (Male/Female)	4/12	-	10/2	-	16/14	-
Age	26.50	6.24	25.25	4.09	25.93	5.21
Education in years	13.88	1.63	14.25	1.96	14.14	1.65
WASI IQ	117.94	7.63	119.08	9.65	121.25	8.30
MADRS *	26.13	4.24	23.00	2.49	-	-
T2						
MADRS *	12.13	7.00	7.42	3.53	-	-
RRS *	49.67	12.58	39.50	8.58	-	-
RRQ Rumination **	47.27	7.91	41.00	8.54	30.54	6.98

WASI = Wechsler Abbreviated Scale of Intelligence. MADRS = Montgomery Åsberg Depression rating scale. RRS = Ruminative Responses Scale. RRQ = The Rumination-Reflection Questionnaire.

* Sig ≤.050 ** Sig =.000

Table 5

Assessment of Cognitive Flexibility measured by the Wisconsin Card Sorting Test in the Subgroups and the Control Group

	Depression group (N =16)		Remission group (N = 12)		Control group (N = 30)		Statistics	
	Mean rank	*Md*	*Mean rank*	*Md*	*Mean rank*	*Md*	Kruskal-Wallis *H*	*p*
T1								
Categories Completed	26.03	6.0	29.13	6.0	31.50	6.0	5.71	.057
Failure to Maintain Set	29.25	0.0	30.25	0.0	29.33	0.0	0.05	.977
Perseverative Errors	34.19	6.0	35.42	6.0	24.63	5.0	5.39	.068
Perseverative Responses	34.13	5.5	35.54	5.0	24.62	5.0	5.44	.066
Total Errors	33.06	12.0	35.21	14.0	25.32	10.0	3.97	.138
Trials Administered	32.06	78.5	35.46	84.5	25.75	77.0	3.36	.186
T2								
Categories Completed	26.44	6.0	30.00	6.0	30.00	6.0	5.22	.074
Failure to Maintain Set	29.94	0.0	25.75	0.0	29.83	0.0	0.98	.613
Perseverative Errors	30.78	5.0	28.46	5.5	28.24	5.0	0.27	.873
Perseverative Responses	30.72	5.5	28.25	5.0	28.36	5.0	0.25	.882
Total Errors	29.44	10.0	29.00	10.5	28.76	10.0	0.02	.991
Trials Administered	29.06	78.5	27.00	77.5	29.79	77.0	0.243	.886
Change scores								
Categories Completed	32.28	0.00	29.46	0.00	27.00	0.00	5.38	.068
	Mean	*SD*	*Mean*	*SD*	*Mean*	*SD*	*F*	*p*
Failure to Maintain Set	0.00	0.82	-0.42	1.31	-0.03	1.12	0.63	.537
Perseverative Errors	-2.19	3.99	-2.33	4.30	-0.69	2.58	1.50	.232
Perseverative Responses	-2.43	4.46	-2.83	5.15	-0.69	2.90	1.75	.184
Total Errors	-4.25	9.69	-6.25	9.47	-1.48	5.67	1.76	.182
Trials Administered	-4.25	15.79	-11.50	13.79	-2.21	12.98	1.89	.161