Inhibition and rumination in remitted major depressive disorder

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Abstract

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Background: Rumination in response to dysphoric mood heightens the risk of major depressive disorder. Investigating the underlying cognitive mechanism of rumination can lead to a better understanding of the etiology, and development of effective treatment and prevention. Inhibition is important in controlling cognition and behavior. Previous studies have indicated that rumination and inhibition are related in major depressive disorder. This study investigates if reduced effectiveness in inhibiting prepotent responses and elevated rumination can be conceived as etiological factors in major depressive disorder.

Method: The data were collected as a part of the project “Cognitive control and serotonergic genes in emotion regulation and depressive rumination". The principal investigator of this project is Martin Aker, and the advisor is Nils Inge Landrø. The author participated in the collection of the data. Participants were 20 formerly depressed and 19 never-depressed females aged 19-63 years old. Prepotent response inhibition was assessed by the Emotional stop-signal task, and rumination was assessed by the Ruminative responses scale.

Results: Formerly depressed participants had a statistically significant longer stop-signal reaction time and a statistically significant higher rumination score compared to never-depressed participants. Across the whole sample there was a statistically significant positive correlation between stop-signal reaction times and rumination scores.

Conclusion: The present study demonstrates that remitted major depressive disorder is characterized by less effective prepotent response inhibition and elevated rumination, and that less effective prepotent response inhibition is related to elevated rumination. The reciprocal process between inhibition and rumination is discussed and considered a possible etiological mechanism in major depressive disorder.

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Table of contents

Introduction

Major depressive disorder (MDD) is one of the most prevalent mental disorders, affecting about 350 million people at any given time, and is among the leading causes of disability worldwide (World Health Organization, 2012). An estimated 14-18 % of the population will suffer from one or more major depressive episodes during their lifetime (Norwegian Institute of Public Health, 2009).

The hallmark of MDD is depressed mood but cognitive symptoms are also common, for example diminished ability to think or concentrate (American Psychiatric Association, 2000). Depressed individuals tend to have negative cognitions, and cognitive therapy targets these to alleviate the symptoms of MDD (Beck, 1967). According to the cognitive theory of depression negative self-evaluations, expectancies, and memories are organized into dysfunctional schemas. When the patient experiences something negative the cognitive schemas activate negative thoughts, which leads to negative mood. In cognitive therapy the therapist and patient seek to counter negative thoughts and change dysfunctional schemas. The focus of cognitive therapy is to change the *content* of thoughts. According to Nolen-Hoeksema's (2004) response styles theory people vary in how they respond to dysphoric mood. In the context of dysphoria a ruminative response style will exacerbate and prolong negative mood, increasing the likelihood that dysphoria becomes chronic and evolve into MDD. Metacognitive therapy for MDD seeks to reduce the amount of rumination (Wells, 2009). The focus of metacognitive therapy is to change this *process* of thoughts.

Even though many approaches in treating MDD have been developed (e.g. psychotherapy and antidepressants), efficacy of these treatments is still unsatisfactory (Cuijpers, van Straaten, Bohlmeijer, Hollon, & Anderson, 2010; Turner, Matthews, Linardatos, Tell, & Rosenthal, 2008). Even when treated with first line psychotropic medication and/or psychotherapeutic interventions relapse rate is approximately 50 % after two years (Vittengl,Clark, Dunn, & Jarrett, 2007). The cognitive theory of depression and the response styles theory have provided useful insight into etiological and maintaining factors in MDD. However, exactly what cognitive mechanism underlying for example rumination is largely unknown. Better knowledge of this mechanism is needed to develop more effective treatments.

Theoretical and empirical background

Rumination

The concept of rumination has been examined in great detail by Nolen-Hoeksema and colleagues (Nolen-Hoeksema, 1991; Nolen-Hoeksema, Wisco, & Lyubomirsky, 2008). In the response styles theory rumination is defined as a thought process that is characterized by a repetitive and passive focus on symptoms of distress, and the possible consequences of these symptoms (Nolen-Hoeksema, 1991). Examples of ruminative thoughts are: "I feel so sad and tired", "Why do I feel like this?", and "I probably won't be able to go to work if continue to feel depressed". People who are engaged in ruminative thinking tend to isolate themselves from other people to think these thoughts, and the result is often increased negative mood, which entails even more rumination (Nolen-Hoeksema, 1991).

To experimentally test the relationship between rumination and negative mood Nolen-Hoeksema and colleagues developed the rumination induction paradigm (Nolen-Hoeksema et al., 2008). In this paradigm rumination is induced by asking participants to focus on self, while another group is instructed to distract themselves. In the self-focus condition participants are asked to ruminate (focus on the meanings, causes, and consequences of their current feelings) for eight minutes. This self-focus is in itself considered neutral, and is not expected to induce negative mood in nondysphoric individuals. On the other hand, dysphoric individuals have more negative mood and cognitions, and the request to self-focus is expected to make them even more dysphoric. Distraction involves participants to focus on images not related to self, and this is expected to have no effect on the nondysphorics's mood, but temporarily relieve mood in dysphoric participants. These expectations have been supported by numerous studies (see Nolen-Hoeksema et al., 2008); induction of rumination increases dysphoric mood in dysphoric participants but not in nondysphoric participants, while distraction has no effect on the mood of nondysphoric participants but decreases dysphoric mood in dysphoric participants. Similar effects are found in clinically depressed participants. Thus, rumination in dysphoric individuals clearly has a negative effect on mood (Nolen-Hoeksema et al., 2008).

Effects of rumination

Using the rumination induction paradigm, Lyubomirsky, Caldwell, and Nolen-Hoeksema (1998) experimentally instructed participants to distract from self and their problems or to ruminate on the meanings, causes, and consequences of their current mood. Measuring recall

from autobiographical memory revealed that participants with dysphoric mood induced to ruminate recalled more negative memories than those induced to distraction. They also recalled more negative memories than nondysphoric participants induced to ruminate. Dysphoric participants who are induced to ruminate have also demonstrated increase in spontaneous talk about conflict with families or financial woes, they are more negative and self-critical, they have reduced self-confidence and optimism, and they have low expectations for future positive events. Clinically depressed people also suffer from the same effects, but these tend to disappear when participants use distraction (Nolen-Hoeksema et al., 2008). Rumination also influences personal support recieved from the social network. For example bereaved adults who are ruminating are more likely to seek social support after their loss, but actually experience more social friction and less emotional support. Social support is thought to decrease when family and friends become frustrated about the ruminators need to talk about their loss and its meaning for many months following their loss (Nolen-Hoeksema & Davis, 1999).

Problem solving is also interfered by rumination (Lyubomirsky, Tucker, Caldwell, & Berg, 1999). When participants who rated their own problems as unsolvable were induced to ruminate, the likelihood to implement solutions to the problems decreased. Focus on personal problems, a negative tone, self-criticism, self-blame, reduced self-confidence, reduced optimism, and reduced control lead to impaired problem solving. Negative content in rumination was also related to less motivation to solve one's problems.

Nolen-Hoeksema and Morrow (1991) developed the Ruminative responses scale (RRS) to measure rumination. The RRS predicts depressive symptoms after controlling for initial depressive symptoms and stress (Luminet, 2004). Most studies examining the relationship between rumination and MDD employ the RRS. In a retrospective study women surviving breast cancer were asked to recall the situation and their immediate emotional response to the finding of a lump in their breast (Lyubomirsky, Kasri, Chang, & Chung, 2006). Women rating themselves as high ruminators were found to delay their contact with healthcare professionals by 39 days compared to women who rated themselves as low ruminators, and the delay was partially moderated by the women's emotional response at the time when they discovered the lump. Similar results are found in clinically depressed individuals. When induced to ruminate individuals with MDD show deterioration in mood and problem solving, while mentally healthy individuals do not (Donaldson & Lam, 2004).

Certainly, the aforementioned studies indicate many debilitating effects of rumination in the presence of negative mood and MDD. Induced and naturally occurring rumination in

the presence of negative mood are found to impair problem solving and thinking, worsen mood, and hamper social support. Depressive risk factors like negative cognitive styles, self-criticism, neediness, and history of past depressive episodes are also related to rumination, and rumination mediates the effect of these risk factors on future depressive episodes (Spasojevic & Alloy, 2001). Thus, rumination is considered a common proximal mechanism linking risk factors with MDD. It is clear that rumination is an important process in the development and maintenance of MDD, and more insight into the cognitive underpinnings of this process is needed.

Cognitive processes underlying rumination and major depressive disorder

Cognitive processes in MDD have traditionally been examined in the light of cognitive symptoms, impairments, or biases. One frequently mentioned impairment in depressed individuals is memory impairment (Joormann, Yoon, & Zetsche, 2007). However, memory performance in depressed individuals is actually boosted for negative memories: Negative stimuli seem more important for depressed versus nondepressed individuals, which suggests a valence-specific impairment of memory (Gotlib, Roberts, & Gilboa, 1996). Further investigation has shown that memory impairments are worse if the situation allows attention to wander off to personal concerns (Joormann, 2005). Hertel (1998) investigated this when she asked dysphoric and nondysphoric participants to remember pairs of words. After the presentation of the pairs of words participants were instructed to rate self-focused material, or rate self-irrelevant and task-irrelevant material, or just wait and do nothing in particular. The results showed that dysphoric participants had more deficits in recall of the pairs of words when they had been instructed to rate self-focused material, compared to when they were kept busy rating self-irrelevant and task-irrelevant material. However, dysphoric participants instructed to just wait also showed similar deficits in recall. Interestingly, dyshporic participants induced to self-focus and dysphoric participants asked to wait suffered the same debilitating effect on memory. This suggests that when the situation is under low control, and the mind of dyshporic individuals is permitted to wander away to self-focused material, this can interfere with cognition. On the other hand, when the situation is highly controlled mind-wandering is less likely to be activated, and cognition and memory are intact (Hertel, 1998). Rumination is indeed characterized by self-focused thoughts, and it seems that a similar interfering process was automatically activated in the dysphoric participants who were asked to wait (but not asked to self-focus). This indicates that dysphoric individuals do not seem to

have memory impairments *per se*, but rather it's the control of attention that seems to be impaired (Joorman, 2005).

Control of attention has been examined in people prone to rumination. Ruminators demonstrate problems in inhibiting negative information when it is irrelevant, they prefer negative distractors to manage negative moods, they are less likely to use positive memories to regulate mood, and they are less inclined to use positive distracting activities even when they acknowledge that it would lift their mood (Nolen-Hoeksema et al., 2008).

The dot probe task has frequently been used in studying the control of attention-impairment in depressed individuals (see Joormann et al., 2007). In this task a pair of one neutral and one emotional stimulus (e.g. faces) are presented simultaneously. The participant's attention is automatically directed to the stimuli, for example a sad face on the left and a neutral face on the right. Then the faces disappear and a dot is presented either to the left or to the right. The participant should then indicate as fast as possible to which spatial location the dot is presented. If the participant's attention was focused to the left (e.g. on the sad face) the response latency should be faster when the dot appears to the left. On the other hand, if the dot appears in the opposite location (e.g. right) the response latency should be slower. Thus, the difference in response latency is considered an effect of attention bias to either of the stimuli (sad or neutral face).

Many studies using the dot probe task reveal that depressed and dysphoric individuals respond slower when the dot is presented in the opposite spatial location of a sad face, which suggests an attention bias towards negative information (Joormann et al., 2007). Nevertheless, this bias does not affect all aspects of attention. It is only found when the faces are exposed for a longer period of time. When the dot probe task employs very short stimuli exposure it is assumed to measure activation of attention, and when stimuli are exposed longer the dot-probe task is assumed to measure inhibition of attention. When depressed individuals are shown a sad and a neutral face for a very short time (e.g. 14 ms) they perform equally well in responding to where the dot is, indicating that initial activation of attention is not directed towards the sad face. But when depressed individuals are shown a sad and a neutral face for a longer period of time (e.g. 500 or 1000 ms) they respond slower, indicating that inhibition of attention towards the sad face is less effective. These findings suggest that depressed individuals' attention is characterized by an impairment of inhibition of negative information (Joormann et al., 2007).

Inhibition

Cognitive processes collaborate and depend on other cognitive processes. For example memory is of no use without perceptual input, and perception needs to be directed by attention. Cognitive processes are controlled and coordinated by the executive functions (Miyake, Friedman, Emerson, Witzki, & Howerter, 2000). Compared to memory less is known about the processes of the executive functions. A review of the literature by Miyake et al. (2000) found accounts of the executive functions as both one unitary process and as several components. To illuminate this further they conducted a confirmatory factor analysis, which supported the earlier accounts of the executive processes as both united and diversified. The analysis indicated that the executive functions consist of three different (but related) components: "Shifting" (between tasks or mental sets), "updating" (and monitoring of working memory representations), and "inhibition" (of prepotent response).

Even though most psychologists have an understanding of what inhibition is it is not a clear cut concept, often not defined at all (MacLeod, 2007). Inhibition can be defined as "any mechanism that reduces or dampens neuronal, mental, or behavioral ability" (Clark, 1996, p. 128). MacLeod (2007) defines inhibition as "the stopping or overriding of a mental process, in whole or in part, with or without intention" (p. 5). Miayke et al. (2000) define inhibition as "one's ability to deliberately inhibit dominant, automatic, or prepotent responses when necessary" (p. 57), and Nigg (2000) defines it as "processes of intentional control or suppression of response in the service of higher order or longer term goals" (p. 238).

The race model

Similar to the aforementioned definitions Logan (1994) understands inhibition as essential for cognitive control: Something that stops active processes and makes the enabling of other processes possible. One of the more developed theories of inhibition is based on the stop signal paradigm (Logan, 1994). Logan's underlying theoretical model of the process of inhibition is captured in what he named the race model. In this model the activating process ("go") races the inhibiting process ("stop"), and whichever finishes first decides if there is action or inhibition of action. Logan developed the Stop-signal task (SST) to measure the stop-process. In a typical SST the participant sits in front of a computer and presses one of two keys as fast as possible depending on whether a X or an O appears. This keypressing becomes the prepotent response ("go"). Occasionally a tone sounds immediately following a trial and the participant should try to withhold pressing the key. The delay of the tone varies, so difficulty stopping keypress will also vary (e.g. if the delay is very long it is more difficult

to stop response). Measuring the performance of the go-process is straightforward: Record the latency between stimuli presentation (X or O) and behavioral response (keypress). On the other hand, measuring the stop-process is more difficult. The problem is registering when the stop-process is finished because successful inhibition depends on the absence of response. The SST overcomes this problem by inferring the latency indirectly by comparing the average stop-signal (tone) delay with the distribution of go-trial latencies (see Logan (1994) for detailed calculation). In this way the SST can give researchers a measure of an individual's ability to inhibit prepotent responses, named the stop-signal reaction time (SSRT). A shorter SSRT implys a more effective prepotent response inhibition, and a longer SSRT implys a less effective prepotent response inhibition.

Theoretically the stop-process is assumed to be independent of the go-process, and this has also been demonstrated empirically for example with transcranial magnetic stimulation and lesion studies (see Verbruggen & Logan, 2008). Additional evidence for the independency of the stop-process is that it has a a different developmental trajectory throughout the life span compared to the go-process. While the development of the go-process can be described as a marked u-curve (drastically improving in childhood and clearly diminishing after early adulthood; Cerella & Hale, 1994) the development of the stop-process can be described by a flatter curve. A study by Williams, Ponesse, Scachar, Logan, and Tannock (1999) demonstrated that prepotent response inhibition improved during childhood, was stable throughout adulthood, with limited slowing in older adults. Bedard et al. (2002) demonstrated similar findings.

Components of inhibition

The concept of inhibition is, like the executive functions, theorized to consist of different (but related) components. Nigg's (2000) taxonomy of inhibition consists of four types: Interference control, cognitive inhibition, behavioral inhibition, and oculomotor inhibition. Others have proposed inhibition as a process consisting of: Control of attention, deletion of irrelevant information in working memory (WM), and suppressing inappropriate responses (Lustig, Hasher, & Zacks, 2007). There are several other (yet similar) models of inhibition. To investigate this further Friedman and Miyake (2004) conducted a confirmatory factor analysis of three frequently proposed components of inhibition: Prepotent response inhibition, resistance to distractor interference, and resistance to proactive interference. Prepotent response inhibition is the ability to deliberately suppress dominant, automatic, or prepotent responses, and this corresponds to Nigg's behavioral and oculomotor inhibition. Resistance to

distractor interference is the ability to resist or resolve interference from information in the external environment that is irrelevant to the task at hand, and corresponds to Nigg's interference control. Resistance to proactive interference is the ability to resist memory intrusions from information that was previously relevant to the task but has since become irrelevant, and corresponds to Nigg's cognitive inhibition. Nine different tasks were used to explore inhibition, including the SST, the Antisaccade task, the Eriksen flanker task, and a task measuring negative priming. The results indicated that prepotent response inhibition and resistance to distractor interference were closely related to each other, while resistance to proactive interference was unrelated from the two. A dichotomy of inhibition was suggested: 1) response-distractor inhibition, and 2) resistance to proactive interference (Friedman & Miyake, 2004).

Inhibitory processes in rumination and major depressive disorder

When mapping vulnerability factors and the possible mechanism underlying MDD inhibitory processes seem to be more important than the other executive functions, like shifting and updating. Whitmer and Banich (2007) demonstrated this when they employed a task-switching paradigm measuring ability to shift and inhibit in undergraduate students who were high or low ruminators. The participants performed an odd-one-out search based on stimulus color, motion, and orientation, which was cued prior to stimulus display. After controlling for depressive symptoms the results suggested that executive dysfunction in high ruminators was more closely related to inhibition than to shifting. This relationship was not present when controlling for rumination. Withmer and Banich (2007) argued that rumination is not only a reaction to depressed mood, but carries its own consequences: Ineffective inhibition.

One of the first to hypothesize that impaired inhibition may be a possible mechanism underlying rumination and MDD was Linville (1996). On the basis of research on inhibition, stress, rumination, and MDD she proposed that attentional inhibition may underlie ruminative thoughts, and that inhibition may mediate the known effects of stress and depression on ruminative thoughts. The previously mentioned review by Joormann et al. (2007) confirmed that depressed individuals seem to have impaired inhibition for negative stimuli and that this is closely related to rumination.

In a series of studies Joormann and colleagues (see Joormann et al., 2007) used the negative affective priming (NAP) task to assess inhibition in dysphoric/depressed and

ruminating individuals. In the NAP task participants respond to a target adjective and ignore a distractor adjective. When the distractor from a previous trial becomes the target on the present trial response latency increases, and this is called the negative priming effect. This does not only happen when the target is identical to the previous distractor, but also if it is related to the distractor. The effect is thought to originate because inhibition of the previous distractor is still active on the present (related) target, thus delaying the response. Increased response delay indicates better inhibition of the previous distractor stimulus. The target and distractor stimuli in the NAP task are adjectives with a positive or negative valence. In the test trial the distractor and the subsequent target are related to each other, either negatively or positively (e.g. "sad" and "depressed", or "happy" and "smiling"). In the control trial the distractor and the target are not related to each other (e.g. "sad" and "happy"). Negative affective priming is assessed by comparing response delay on positive-related stimulus and negative-related stimulus, with unrelated stimulus. Using this paradigm it has been demonstrated that dysphoric participants, currently depressed participants, formerly depressed participants, and participants high in rumination all exhibit reduced inhibition of negative material that they were instructed to ignore. Hence, rumination, dysphoria, and MDD are highly related to impaired inhibition of negative material (Joormann et al., 2007). Depressed individuals also show impaired inhibition of nonverbal stimuli like sad faces (Goeleven, De Raedt, Baert, & Koster, 2006).

The impaired disengagement hypothesis

Accounting for the aforementioned studies of rumination and inhibition Koster, De Lissnyder, Derakshan, and De Raedt (2011) proposed a hypothesis of how attention, rumination, and negative affect may influence one another and cause MDD. The impaired disengagement hypothesis assumes that internal or external stressors (e.g. negative memories or interpersonal problems) that conflicts with an individual's goals, hopes, and plans for the future triggers ruminative thoughts. In searching for the causes of these stressors individuals' ruminative thoughts are often self-critical and focused on own contributions to the problem. This process is not harmful in itself, but important in adapting one's behavior to the environmental demands. Normally rumination comes to an end when an appropriate solution to the problem is reached, or if no solution is reached: When the individual initiates emotion regulation. For most individuals prolonged self-criticism is not in concordance with one's fundamental positive self-image, so cognitive dissonance is signaled after some time. Koster et al. (2011) propose that dissonance is followed by the healthy disengagement of attention from negative

thoughts and a reorientation to the problematic situation (or distraction from it). On the other hand, ruminative and self-critical thoughts do not lead to dissonance if the individual has a negative self-image and a sufficiently strong dissonance is not generated. In these individuals unhealthy rumination is prolonged and causes impaired problem-solving and negative mood. In other individuals dissonance signaling may be intact, but rumination is sustained by impaired attentional control (e.g. impaired inhibition). This is hypothesized to form a pathological mechanism, in which impaired inhibition allows prolonged rumination, subsequent impaired problem-solving, negative mood, and ultimately the development and maintenance of MDD (Koster et al., 2011).

Differentiating between types of inhibition in relation to rumination and major depressive disorder

Friedman and Miyake's (2004) distinction of the different types of inhibition calls for a more detailed assessment of exactly which types of inhibition may be related to rumination and MDD. Examining this, Zetsche, D'Avanzato, and Joormann (2011) assessed two components of inhibition: Access of irrelevant external information into working memory (interference control) and ability to remove no longer relevant information from WM. They used the Emotional flanker task to measure interference control, which consists of trials where four words are arranged in a square: One target word in green letters and three identical distractor words in red letters. Participants respond as quickly as possible to whether the target word is positive or negative. In the conflict condition the valence of the target and the distractors are conflicting, and in the neutral condition the distractor words are neutral. Slowing in response latency in the conflict condition indicates decreased interference control of irrelevant emotional material. The findings indicated that currently depressed participants had reduced interference control of negative words, but were normal on the ability to remove irrelevant information from WM. In contrast, the opposite effect was found in participants high in rumination: They exhibited impairment in removing irrelevant information from WM, but no impairment in holding irrelevant information out of WM. Zetsche et al. (2011) argue that this suggests that rumination may not be driven by problems in controlling the access of irrelevant negative thoughts to WM, but by an inability to disengage from these thoughts. High compared to low ruminators might not differ in the likelihood of initiating negative thoughts, but rather in the perseverance of rumination itself. Individuals with impaired interference control may be more easily distracted by negative irrelevant information, and this may obstruct effective problem solving and increase the risk of developing MDD when

encountering negative life events. Hence, it is necessary to differentiate between different types of inhibition when examining its relationship to rumination and MDD (Zetsche et al., 2011).

Many of the studies showing that there is a relationship between inhibition, rumination, and MDD have applied the NAP task (see Joormann et al., 2007). However, when Friedman and Miyake (2004) examined the negative priming effect in their analysis of inhibition they argued that tasks measuring negative priming have reliability problems, and that there was no relation between negative priming and response-distractor inhibition. Friedman and Miyake (2004) concluded that great caution must be taken when using the NAP task to measure inhibition. On the other hand, the Emotional flanker task used by Zetsche et al. (2011) was found by Friedman and Miyake to reliably tap resistance to distractor interference. Research on other types of response-distractor inhibition related to rumination and MDD, such as prepotent response inhibition, is limited. This may be because response-distractor inhibition has been considered more interesting in the research of externalizing psychopathology like ADHD, and resistance to proactive interference has been proposed as more interesting in the research of internalizing psychopathology like depression and anxiety (Friedman & Miyake, 2004). However, one of the tasks used to measure response-distractor inhibition in Friedman and Miyake's study was the Antisaccade task. Using a mixed variant of this task De Lissnyder, Derakshan, De Raedt, and Koster (2011) measured participants' eye movements towards nonemotional stimuli. Nondysphoric and dysphoric participants were directed to either look at a stimulus (prosaccade) or look away from a stimulus (antisaccade). The results showed no difference on correct antisaccade latency between the dysphoric and nondyshporic participants (according to the authors probably because of the lack of emotional material in the task). Nevertheless, high ruminators versus low ruminators showed slower antisaccade latencies. This indicates that response-distractor inhibition may be impaired in high ruminators.

The SST is also used in measuring response-distractor inhibition. In a modified version of the SST, Lau, Christensen, Hawley, Gemar, and Segal (2007) used positive and negative words as stimuli to measure prepotent response inhibition in clinically depressed and nondepressed individuals. The results showed that depressed and nondepressed individuals performed equally well. Unfortunately no analysis of the possible relation between rumination on inhibition was presented in the article.

The aforementioned studies suggest that various types of inhibition need to be examined in relation to rumination and MDD. There are consistent findings using the NAP

task, but one has to have in mind the critique by Friedman and Miyake (2004) questioning negative priming effect as a reliable and valid measure of inhibition. There are fewer studies and more inconsistent findings reported on other tasks thought to tap response-distractor inhibition related to rumination and MDD.

Less effective inhibition and elevated rumination as etiological factors in major depressive disorder

Much of the research on the relationship between rumination and inhibition in MDD has examined currently depressed individuals. This has given us knowledge about rumination and inhibition in ongoing MDD. However, it is well known that ongoing MDD involves neuropsychological difficulties like impairments in the executive functions (see Landrø and Andersson, 2008). This complicates the interpretation of the significance of inhibition and rumination as etiological factors in MDD. Less effective inhibition and elevated rumination may merely be additional symptoms of depression, originating from the same etiological cause as the neuropsychological impairments and the MDD-symptoms. These symptoms can of course (and probably do over time) have their own worsening effect on depression, but the challenge in the field is to identify the main propelling mechanism that accounts for how dysphoric mood prolongs and develops into MDD. This mechanism must be evident to a certain degree before the actuation of MDD and may also underlie the maintenance of the episode. Other important aspects when examining the etiological mechanism are that women are 1.7 times more likely to suffer from MDD as compared to men (Kessler, McGonagle, Swartz, Blazer, & Nelson, 1993), woman are more likely to have a ruminating response style (Nolen-Hoeksema, Morrow, & Friedrickson, 1993), and that rumination has been found to partially account for the gender difference (Nolen-Hoeksema, Larson, & Grayson, 1999). This may indicate that the etiological mechanism can appear more clearly if researchers examine the relationship between inhibition and rumination with the sexes separated.

Separating the etiological mechanism from symptoms in MDD requires investigation of individuals the researcher assumes hold this mechanism, but who are not under the influence of the symptoms. Research on remitted MDD has resulted in the mapping of vulnerability factors, which are found to significantly increase the risk of subsequent major depressive episodes (see Ingram, Miranda, & Segal, 1998). Formerly depressed are suited participants in investigating the etiological mechanism in MDD because they have been depressed and are at risk for additional major depressive episodes (Kessler, Zhao, Blazer, &

Swartz, 1997). In other words, they are assumed to hold the etiological mechanism without the confounding influence of depressive symptoms. Demonstration of abnormal functioning in a cognitive process in formerly depressed individuals suggests an etiological factor relevant to MDD. However, what may appear as etiological factors in retrospective studies could be a result of "scarring" or residual after the major depressive episode (Rohde, Lewinsohn, & Seeley, 1990). More research on rumination's relation to different types of inhibition in formerly depressed individuals can enlighten the understanding of the etiological cognitive mechanism underlying MDD.

Hypotheses

The present study was set out to test the following hypotheses:

1. Formerly depressed participants will demonstrate less effective prepotent response inhibition compared to never-depressed participants.
2. Formerly depressed participants will demonstrate elevated rumination compared to never depressed participants.
3. Participants demonstrating elevated rumination will tend to demonstrate less effective prepotent response inhibition.

Method

The data analyzed in this study were collected by the author together with PhD candidate Martin Aker as a part of the project "Cognitive control and serotonergic genes in emotion regulation and depressive rumination" at the University of Oslo. The principal investigator of this project is PhD candidate Martin Aker and the advisor is Professor Nils Inge Landrø. The Regional committee for research ethics has approved the project, and it adheres to the Helsinki convention. All data were collected and stored according to prescribed procedures fulfilling these standards.

Participants

Females aged 19-65 years were recruited as participants. Formerly depressed participants were recruited from an outpatient clinic in Oslo, Norway. Never-depressed participants were recruited by advertisement in local newspapers and on Facebook, as well as through posters and acquaintances. Participants received oral and written information about the purpose of the study, and signed a written consent. Participants received a 250 NOK gift card.

Psychiatric evaluation

M.I.N.I. 6.0.0 (excluding the alcohol, drug, and antisocial personality disorder modules; Leiknes & Malt, 2009) was administered to check for current and former psychiatric disorders. The interview was audio taped and evaluated later if there were any diagnostic uncertainties. Alcohol Use Disorders Identification Test (AUDIT; Aasland, Amundsen, Bovim, Fauske, & Mørland, 1990) and Drug Use Disorders Identification Test (DUDIT; Kompetansesenter rus – region øst, n.d.) were administered. Beck's Depression Inventory II (BDI-II; Beck, Steer, & Brown, 1996) was administered to measure symptoms of depression. Matrix reasoning and vocabulary from Wechsler's (1999) abbreviated scale of intelligence were administered to estimate verbal and nonverbal intelligence.

Participants were excluded if they reported to have suffered from head injuries or concussion leading to unconsciousness for more than 30 minutes, or having epilepsy or other neurological disorders. Participants who met the criteria for current MDD, and current or previous psychotic disorder, manic episode, or bipolar disorder were also excluded, as well as participants reporting ADHD. Participants were excluded if they had a BDI-II score indicating

moderate or severe depression, AUDIT or DUDIT indicating abuse, or used psychotropic medication.

Emotional stop-signal task

A modified version of the Emotional stop-signal task (E-SST), by Billieux, Gay, Rochat, and Van der Linden (2010), was used. The E-SST was modified and prepared by Billieux, who added neutral and angry stimuli so the author could investigate if emotional stimuli have an effect on prepotent response inhibition. The participants completed the E-SST on a laptop computer with internal speakers. The procedure of the E-SST is presented in Figure 1. The E-SST consists of two parts: Practice and testing. First the participant completes a practice block of 40 go-trials. This establishes a prepotent response. The participant sits in front of the laptop and is instructed to keep their left finger ready on the C key and their right finger ready on the N key. The trial starts with a fixation cross (500 ms) before a male or female face (acquired from the Karolinska directed emotional faces database; Lundqvist, Flykt, & Öhman, 1998) is shown (500 ms). Then two arrows appear in the center of the screen, both pointing left or right. The participant should indicate which direction the arrows are pointing by pressing the C key if the arrows are pointing to the left, or pressing the N key if the arrows are pointing to the right. Participants are instructed to respond as fast and correct as possible. The trial is finished and repeated when the participant has responded or when the arrows have been presented for 2000 ms.

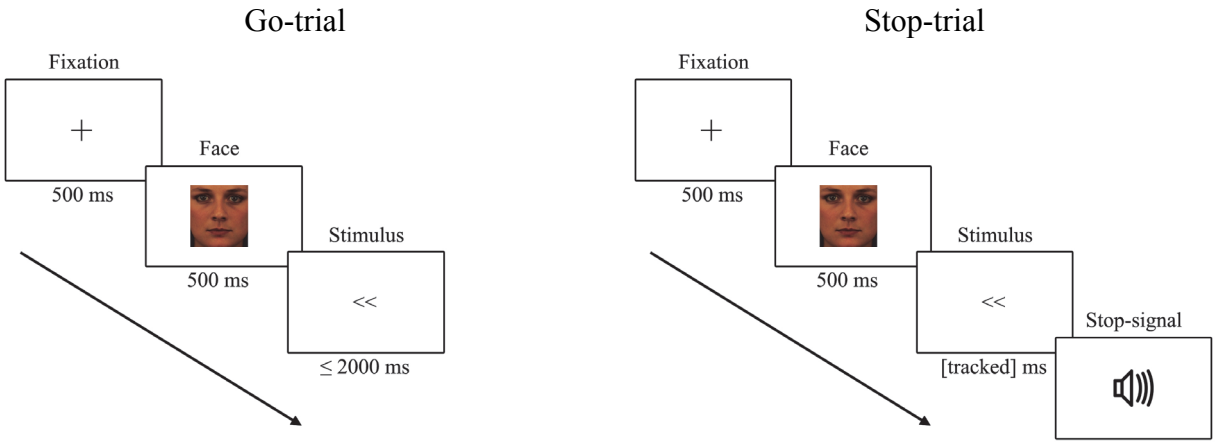

Figure 1. The Emotional stop-signal task.

The second block of practice (20 trials) also includes five stop-trials. The participant is instructed to do exactly the same as in the go-trials, but sometimes they will hear an auditory signal (the stop-signal) shortly after the arrows are presented. When they hear the auditory

signal they should not respond to the arrows, requiring the participant to inhibit the prepotent response. The stop-signal delay (SSD) between the presentation of the arrows and the stop-signal is continuously adjusted to the performance of the participant by a tracking procedure. If the participant was able to stop the delay is increased by 50 ms on the next stop-trial, making it harder to stop. If the participant was unable to stop the delay is decreased by 50 ms, making it easier to stop. Participants are encouraged to be as fast and accurate as possible, and notified that they will be able to stop in approximately 50 % of the stop-trials. During and after practice the examiner ensures that the participant has understood the task.

The data used to estimate the SSRT is recorded during the test phase when the participant completes four blocks of 40 trials (a total of 160 trials), alternating between blocks with angry faces and blocks with neutral faces (50 % male and female). The block sequence is counterbalanced between the participants. In each block there are 30 go-trials and 10 stop-trials in a random sequence. The participant's mean reaction time on the go-trials from practice and their current mean reaction time are presented after each block. This is used by the examiner to encourage the participant to respond faster if the participant is slowing down during testing (e.g. if the participant is waiting to see if the stop-signal is coming).

The E-SST provides the examiner with the data required to estimate the SSRT. The go-signal reaction times (GoRT) are recorded during successful go-trials. GoRT is a measure of the participant's psychomotor speed between onset of go stimulus and registered correct response. The SSD is recorded during the tracking procedure. There are many ways to estimate the SSRT (Logan, 1994). A commonly used method was developed by Osman, Kornblum, and Meyer (1986) and refined by Logan, Schachar, and Tannock (1997). According to this method one could expect that the participant is able to stop on approximately 50 % of the stop-trials since the SSD is continuously adjusted during the testing. That is, on 50 % of the stop-trials the stop-process will "win" and on 50 % of the stop-trials the go-process will "win". Based on this the GoRT must equal SSD plus SSRT. This method can be described by this formula:

$$\text{GoRT} = \text{SSD} + \text{SSRT} \Rightarrow \text{SSRT} = \text{GoRT} - \text{SSD}$$

The calculation is easy because the E-SST provides us with both GoRT and SSD, but it is important to remember that it is based in the assumption that the participant is actually stopping in 50 % of the trials. A more precise calculation of the SSRT can be done by taking into account the participant's actual stopping performance. To do this one must record the participant's proportion of nonsuccessful stopping on stop-trials (*n* %) and compare it to the participant's distribution of GoRT. The SSRT is estimated from the start and the finish of the

stop process. The start of the stop process is experimentally controlled by the SSD, but the finish time has to be inferred from the reaction time distribution in the observed go-trials. If responses are not stopped in *n* % of the stop trials the finish of the stop-process is on average equal to the *n*th percentile of the GoRT distribution. Hence, a more precise estimation of the SSRT involves substraction of the mean SSD from the *n*th GoRT time (Billieux et al., 2010). The estimation of the SSRT is therefore based on this formula:

SSRT = *n*th % of the GoRT distribution - mean SSD

Ruminative responses scale

The participants filled out the RRS (Nolen-Hoeksema & Morrow, 1991). Internal consistency reliability, and convergent and predictive validity of the RRS is reported to be good (Nolen-Hoeksema, 2004). The RRS was translated to Norwegian (the participants' native language) and consisted of 22 questions about one's regular responses to dysphoric mood (see the Appendix). The participants indicated how often they respond in a certain way to dysphoric mood by rating each question from 1 (*almost never*) to 4 (*almost always*). Summarizing the answers gives the full RRS score. A factor analysis has been conducted on the RRS to illuminate different types of rumination (Treynor, Gonzalez, & Nolen-Hoeksema, 2003). The analysis supported a two factor model of rumination consisting of "reflection" and "brooding". Reflection (summarizing items 7, 11, 12, 20, and 21) is thought to be a purposeful inward turning to engage in cognitive problem solving to alleviate depressive symptoms. Brooding (summarizing items 5, 10, 13, 15, and 16) is a more passive comparison of one's current situation with some unachieved goal. Reflection has been found to predict less depression over time, while brooding predicts more depression (Treynor et al., 2003). The remaining 12 items were named "depression" (summarizing items 1-4, 6, 8, 9, 14, 17-19, and 22) because they were found to be very similar to the items in BDI (Treynor et al., 2003).

Statistical analyses

Statistical analyses were performed using SPSS 20 (IBM, USA) for Windows. Hypotheses number 1 and 2 were investigated using two groups (formerly and never-depressed) in independent t-tests with SSRT and RRS score as test variables. Hypothesis number 3 was investigated using Pearson's product-moment correlation coefficient on the relationship between SSRT and RRS score.

Results

Demographic, clinical, and psychometric characteristics

The sample consisted of 39 participants who were from 19 to 63 years old (M = 38.1, SD = 12.4). Mean years of education was 16.3 (SD = 2.3). Median value for BDI-II was 3 (SD = 4.2). Median AUDIT score was 4 (SD = 2.7) and median DUDIT score was 0 (SD = 0.2). Mean scaled score on estimated verbal intelligence was 13.3 (SD = 2.0) and mean scaled score on estimated nonverbal intelligence was 12.3 (SD = 2.0).

Formerly depressed participants were on average 15.8 years older than never-depressed participants, and this was a statistically significant difference ($t(37) = 5.04$, $p < .001$). On all other demographic measures the groups were comparable (Table 1). When investigating hypothesis number 3 all participants were included in one group.

Table 1

Demographic, clinical, and psychometric characteristics of the participants

	Formerly depressed (n = 20)	Never-depressed (n = 19)
Age (M)	45.8 (10.1)	30.1 (9.3)
Years of education (M)	16.4 (2.6)	16.3 (2.1)
BDI-II (Mdn)	5 (5.0)	2 (2.5)
AUDIT (Mdn)	4 (2.6)	5 (2.9)
DUDIT (Mdn)	0 (0.2)	0 (0.2)
Verbal intelligence (M)	13.4 (1.9)	13.1 (2.2)
Nonverbal intelligence (M)	12.2 (2.5)	12.4 (1.3)

Note. Standard deviations in parenthesis. Mean verbal and nonverbal intelligence are presented in scaled scores.

Emotional stop-signal task

Average proportion of correct stopping was 55 % in both formerly and never-depressed participants. In the analysis of the E-SST, data from two participants having a SSRT of ± 2.5 standard deviations were excluded (one in the neutral condition and one in the angry condition). There was no statistically significant difference in SSRT in the neutral versus angry condition in formerly depressed participants ($t(18) = 7.28$, $p = .56$) or never-depressed participants ($t(17) = 4.02$, $p = .64$). Because of this further analyses were performed using the averaged mean SSRT. The analysis revealed a statistically significant difference between the groups (Figure 2): Formerly depressed participants demonstrated 44 ms longer mean SSRT compared to never-depressed participants ($t(37) = 3.32$, $p < .01$). The magnitude of the mean difference was large (Cohen's $d = 1.09$). When age was used as a covariate in analysis of covariance the difference was not statistically significant ($F(1, 37) = 1.286$, $p = .26$).

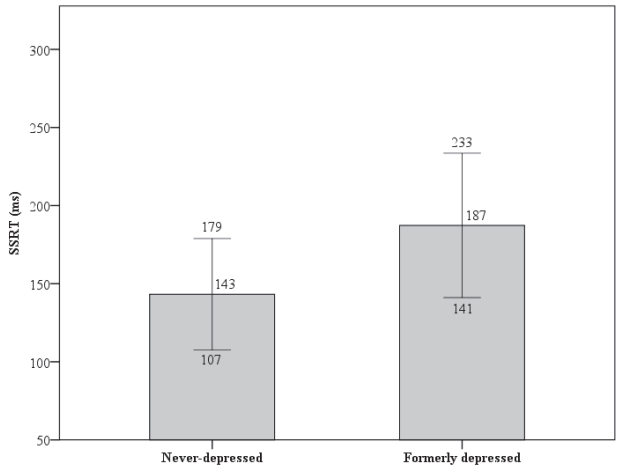

Figure 2. Formerly depressed participants demonstrated longer SSRT (in milliseconds) compared to never-depressed participants. Error bars indicate ± 1 standard deviation from the mean.

Ruminative responses scale

There was a statistically significant difference in RRS scores (Table 2): Formerly depressed participants had higher scores compared to never-depressed participants on the RRS ($t(37) = 4.24$, $p < .001$), depression-RRS ($t(37) = 4.98$, $p < .001$) and brooding-RRS ($t(37) = 2.74$, $p < .01$). The magnitudes of the mean differences in RRS scores were large (Cohen's d ranging from 0.90 to 1.63). There was no statistically significant difference in reflection-RRS ($t(37) = 1.87$, $p = .07$), but the result may be indicating a trend.

Table 2

Ruminative responses scale (RRS) scores, t-test comparisons, and Cohen's d

	Formerly depressed (n = 20)	Never-depressed (n = 19)		
	M (*SD*)	*M* (*SD*)	*t*	*d*
RRS	50.6 (11.7)	36.6 (8.3)	4.24**	1.38
depression-RRS	28.0 (7.0)	18.8 (4.0)	4.98**	1.63
brooding-RRS	11.0 (3.2)	8.3 (2.6)	2.74*	0.90
reflection-RRS	11.6 (4.1)	9.4 (3.2)	1.87	0.61

Note. * $p < .01$, ** $p < .001$

There was a significant moderate positive correlation between SSRT and RRS ($r(37) = .35$, $p = .03$) (Figure 3), and depression-RRS ($r(37) = .37$, $p = .01$). There was no significant correlation between SSRT and brooding- ($r(37) = .23$, $p = .16$) or reflection-RRS ($r(37) = .17$, $p = .29$).

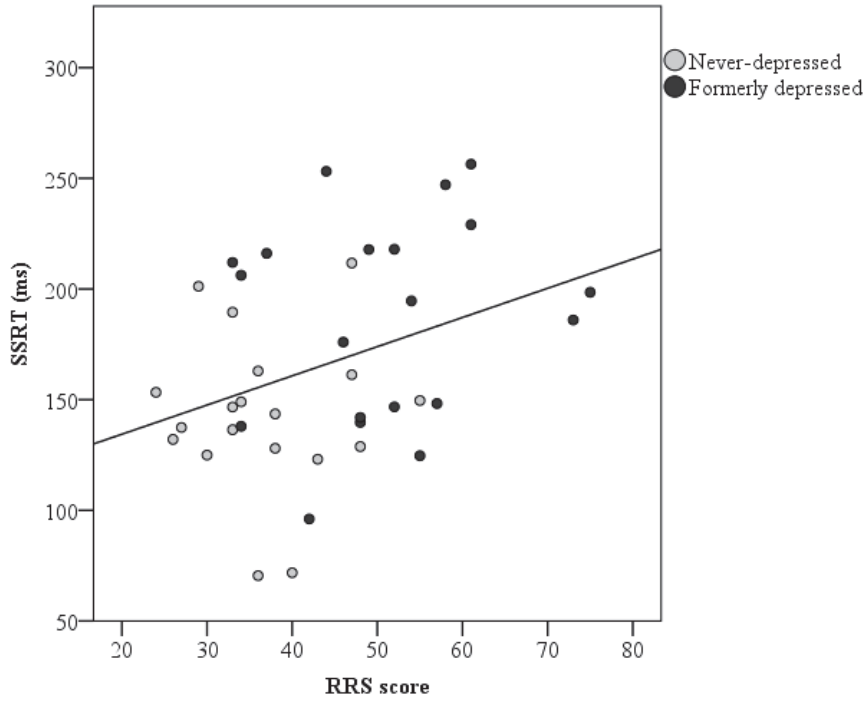

Figure 3. Scatter plot of stop-signal reaction times (SSRT) in milliseconds and Ruminative responses scale (RRS) scores (N = 39).

Discussion

The result indicates that formerly depressed participants have less effective prepotent response inhibition compared to never-depressed participants, but that this effect disappears when controlling for age. Formerly depressed participants ruminate more compared to never-depressed participants. Across the whole sample, participants who ruminate more tend to have less effective prepotent response inhibition.

Effect of major depressive disorder on prepotent response inhibition

Lau et al. (2007) demonstrated no reduced effectiveness in inhibiting prepotent responses in currently depressed. The current results indicate the opposite. There may be several reasons for this. Lau et al. (2007) used emotionally salient and neutral words, and nonwords (which resembled the words) instead of arrows as go-stimuli in the SST, and participants indicated if the stimulus was a word or a nonword. The results showed that mean SSRT was 109 ms longer than in the current study. This could indicate that the word-SST is a more complex task than the E-SST. Additionally, Lau et al.'s (2007) calculation of the SSRT was based on a less precise formula using mean go-reaction time, instead of the go-reaction time on the *n*th percentile of the go-reaction time distribution. Taken together the word-SST and the E-SST could be measuring processes that are somewhat different.

The use of words as stimuli versus faces may also explain the opposite result because of complex cognitive mechanisms related to MDD. It has been demonstrated that the effect of emotional faces are important in MDD (e.g. in the dot-probe task; see Joormann et al., 2007). Depressed and formerly depressed individuals are often characterized by impaired interpersonal functioning, and because faces are thought to be richer in interpersonal information than detached words cognitive impairments in formerly depressed individuals may be elicited more readily by facial stimuli (Joormann & Gotlib, 2007). A face could be a more ecological valid stimulus. The effect of emotional faces on cognitive control in MDD was recently investigated in a study by De Lissnyder et al. (2012). Using a task measuring internal cognitive control they found a general impairment in switching between internally held representations related to MDD, but no additional impairment in the presence of negative emotional faces. This missing valence effect is in accord with the current results. Nevertheless, many previously mentioned studies have demonstrated the opposite. Verbruggen and De Houwer (2007) also showed that the valence of pictures had little or no

effect on prepotent response inhibition, but that high-arousing emotional pictures irrespective of valence caused less effective inhibition. Verbruggen and De Houwer (2007) argue that this is because emotional stimuli in general interrupts ongoing cognitively controlled activities because they attract attention away from these ongoing activities. Thus, the lack of results by Lau et al. (2007) may be because the emotionally salient words weren't sufficiently arousing, and that this explains why less effective inhibition wasn't elicited in the depressed participants. The current result shows that the valence (neutral versus angry) had no effect on inhibition, yet formerly depressed participants demonstrated less effective inhibition. Taking into account the aforementioned studies this could indicate that both neutral and angry faces were equally arousing for both formerly and never-depressed participants, but that inhibition was more hampered in formerly depressed participants. Alternatively that formerly depressed participants had less effective inhibition because they were more aroused by the faces. A study investigating arousal in response to the Karolinska directed emotional faces picture database showed that angry faces cause more self-reported arousal than neutral faces, but also cause less arousal compared to other sets of faces (Adolph & Alpers, 2010). It is uncertain to what degree the formerly depressed participants were aroused by the current stimuli, and if this caused less effective inhibition. The importance of emotional, interpersonal, and arousing stimuli in prepotent response inhibition warrants further investigation. Studies should use both high and low-arousing stimuli like faces or interpersonal material, while measuring arousal in the participants.

The etiological mechanism of MDD in men can be somewhat different compared to women (e.g. men are ruminating less and have a lower prevalence of MDD). The lack of differentiation between male and female participants in Lau et al.'s (2007) study may have attenuated the effect on prepotent response inhibition. Alternatively, the absence of effect could also result because less effective inhibition isn't evident in currently depressed, but only appears *after* a major depressive episode. However, this seems unlikely because 84 % of the currently depressed in Lau et al.'s (2007) study had recurrent MDD and should already have developed a less effective inhibition (a "scar"). Lau et al.'s (2007) results and the current results could only coincide if the effectiveness of inhibition is normal during the major depressive episode and deteriorates in remission. This interpretation is very unlikely because many other previously mentioned studies have demonstrated less effective inhibition in ongoing MDD, and because neuropsychological difficulties in MDD generally improve in remission (e.g. Biringer et al., 2005). Another aspect of Lau et al.'s (2007) study is that almost 50 % of the currently depressed participants used antidepressants (users of antidepressants

weren't excluded). This may have concealed less effective inhibition in the currently depressed because antidepressants affects the brain and initiates antidepressive cognitive processes (e.g. influences emotional processing in currently depressed; see Harmer, Goodwin, & Cowen, 2009). It is paramount to control for confounding variables such as for example psychotropic medication and ongoing depression when investigating the possible etiological mechanism underlying MDD.

To conclude that the difference in prepotent response inhibition was because the participants had been depressed or not one has to control for confounding variables. Control is achieved when the groups are demographically comparable, the procedures of data collection were identical, participants were screened for illnesses affecting the brain, et cetera. However, there was a difference in age between the formerly depressed and never-depressed participants. It was indicated when age was controlled for that the age difference could confound the conclusion that less effective inhibition was an effect of MDD. This could be the case if for example the development of the stop-process resembles the development of the go-process (peaking in early adulthood and then declining, Cerella & Hale, 1994). If this is true one cannot conclude that the difference in inhibition was caused by MDD. It could be that older individuals have less effective inhibition in general, and that the formerly depressed participants demonstrated less effective inhibition because they were older, and not because of MDD. The developmental trajectory of prepotent response inhibition has been investigated in two studies with large samples that were similar in demographically terms as to the current study. Williams et al. (1999) demonstrated that performance in inhibiting prepotent responses was completely stable during adulthood. On a selective SST (considered more complex than the original SST) improvement of prepotent response inhibition was found in young adults, remained stable during adulthood, with the first signs of decline in seniors (Bedard et al., 2002). Hence, age related decline is only evident for individuals not included in this study. It may therefore be unwise to control for age. The current study does not provide *empirical* control for age, but the studies by Williams et al. (1999) and Bedard et al. (2002) may provide *theoretical* control. Taken together it is assumed that the effect of MDD on prepotent response inhibition disappeared when age was controlled for because the formerly depressed participants were incidentally older, and not because of a true effect of age on inhibition. If one accepts this assumption the reduced effectiveness in inhibition in formerly depressed participants can be attributed to the fact that they have been depressed. However, this conclusion must be taken with caution as the possible effect of age on inhibition has not been disproven in the current study.

The bulk of the literature on inhibition and MDD indicates that currently and formerly depressed individuals have less effective resistance to proactive interference and resistance to distractor interference. This is the first study using a stop-signal paradigm with facial stimuli demonstrating that formerly depressed individuals also have reduced effictiveness in inhibiting prepotent responses.

Effect of major depressive disorder on rumination

A key question regarding the relationship between MDD and rumination is whether rumination can be conceived as a stable trait predisposing the person for MDD, or if elevated rumination is a state characteristic or consequence of MDD. Rumination is related to undesirable personality characteristics such as dependent and clingy personal style, aggressive tendency, and desire for revenge (Nolen-Hoeksema et al., 2008). The responses styles theory posits that rumination is a stable disposition (Nolen-Hoeksema, 1991), which tends to make the individual act in a consistent manner (engage ruminative thoughts) in specific circumstances (dysphoric mood). If rumination is to be considered a trait it must be present before depressive symptoms develops, and may be considered a possible etiological factor in MDD. However, elevated rumination in formerly depressed individuals can also reflect a residual consequence of the disorder itself (Rohde et al., 1990).

Depressive patients under psychotropic treatment have showed moderate test-retest stability in rumination over one year (Just & Alloy, 1997). Bagby, Rector, Machiochi, and McBride (2004) have distinguished between absolute stability and relative stability when investigating if rumination can be conceived as a trait. If mean rumination for a group is stable over time there's absolute stability. If the individual difference in rumination over time is stable there's relative (test-retest) stability. Bagby et al.'s (2004) study and review of the literature shows only weak support for absolute stability in rumination: Rumination is stable in currently depressed, but decreases when they recover. Relative stability is higher regardless of changes in depressed mood and symptom severity. Bagby et al. (2004) found that so called self-focused rumination (somewhat overlapping with reflection) is more stable over time, compared to symptom-focused rumination (somewhat overlapping with brooding). They argue that this is because symptom-focused rumination is more directly linked to the presence of depressed mood/symptoms, which wax and wane in accordance with symptom levels, and that symptom-focused rumination requires the individual to have experienced at least some symptoms of depression to ruminate on. Their conclusion is that elevated rumination seems to

be present both during and following episodes. If rumination was to be conceived as only a state characteristic, elevated rumination should only be apparent during depressive episodes.

Vanderhasselt and De Raedt (2012) have recently demonstrated that rumination can be conceived as a stable trait when they used a well-designed longitudinal study to examine the causal relationship between rumination and dysphoric mood in never-depressed individuals. Their results indicated that rumination is a stable underlying mechanism mediating dysphoric mood and negative thoughts. This is in accord with the current results: Formerly depressed participants are ruminating more (and they had higher levels of depressive rumination and brooding). In the light of the aforementioned literature the current result confirms that rumination is an important factor in the etiology of MDD.

The relationship between prepotent response inhibition and rumination

Previously mentioned literature and the current result shows that individuals who have less effective inhibition are ruminating more. The impaired disengagement hypothesis (Koster et al., 2011) predicts that less effective inhibition may lead to prolonged rumination. The current result lends support to this hypothesis. However, it was unexpected that the relationship was absent regarding brooding. This may be explained by the small sample size, and that the brooding measure provides low variance in the data because it's based on only five items. As expected, reflection was not related to prepotent response inhibition, which is in accord with the literature that posits reflection is a more adaptive way of rumination. Howbeit, one cannot dismiss that a larger sample size could also reveal a reflection-inhibition relationship. A larger sample size is probably needed to clarify the importance of the differentiation between reflection and brooding.

It is important to caution that the relationships observed are based on correlations. This study provides results indicating (but not causally establishing) that less effective prepotent response inhibition leads to elevated rumination. Nevertheless, recent findings by Demeyer, De Lissnyder, Koster, and De Raedt (2012) lend support to the idea that impaired cognitive control *causes* elevated rumination and subsequent MDD. They demonstrated a significant influence of impaired cognitive control at baseline depressive symptoms in a one year follow-up prospective study, and this was fully mediated by rumination. Demeyer et al. (2012) conclude that this demonstrates the importance of cognitive control abilities underlying rumination and the etiology of MDD.

General discussion

A problem in the understanding of rumination, inhibition, and their effect on the development and maintenance of MDD is to establish causality. It could be that formerly depressed participants ruminate more because they have been depressed. Rumination could be considered a vulnerability factor if formerly depressed participants also ruminated more before they became depressed. Similarly, MDD could lead to less effective inhibition, or it could be that formerly depressed participants were characterized by this before the development of MDD. The exact mechanism underlying the relationship between rumination and inhibition still remains unknown. Rumination could lead to less effective inhibition or vica versa, or it could be that both are caused by some other factor(s). When investigating the etiological cognitive mechanism in MDD a major challenge is that it is a gradually developing illness, often with no clear cut beginning or end, with several risk factors and stressors predisposing the individual for MDD. No single factor has been proved to be an essential trigger of a major depressive episode. Many psychological, biological, and social factors are involved to a varying degree from individual to individual, and the impact and timing of different factors in MDD are probably also varying.

The impaired disengagement hypothesis (Koster et al., 2011) outlines how inhibition and rumination influences one another, and how this leads to MDD. The following is an interpretation of the current results in the perspective of the impaired disengagement hypothesis. Healthy stopping of rumination requires 1) sufficient dissonance signaling, and 2) effective inhibition. It is normal for a person to ruminate to a certain degree when dysphoric, but rumination becomes unhealthy if it doesn't lead to an improvement in the person's situation, becomes habitual, and makes the person even more dysphoric. Normally the person will disengage rumination before she develops MDD. *Engagement* of rumination is automatic in the presence of dysphoric mood, and can be viewed as the prepotent response in Logan's (1994) race model. The ruminative thought in itself can be viewed as the go-process. Several ruminative thoughts can be seen as a chain of go-processes engaged by a lasting dysphoric mood. The stop-process has to be initiated and win against the go-process for the successful disengagement of ruminative thoughts, and this requires a sufficiently effective stop-process. If the stop-process successfully disengages rumination the frequency of negative thoughts will decrease, and this will over time reduce negative mood. Less negative mood decreases the probability of activating the prepotent response to engage in rumination, which causes fewer negative thoughts, a further reduction of negative mood, and so on. In other words, if a person

who tries to stop rumination has a sufficiently effective prepotent response inhibition it is less likely that dysphoria prolongs and develops into MDD. On the other hand, an individual who is susceptible to ruminate when dysphoric could have a difficulty in inhibiting prepotent responses. Less effective prepotent response inhibition may be caused by many factors, for example gene variants, prolonged stress or trauma in early development, social learning, personality, alcohol or drug abuse, et cetera. Additionally, a state of high arousal (e.g. a stressful situation) can amplify the problem in inhibiting prepotent responses, which could lead to more unsuccessful disengagement of rumination, prolonged dysphoria and heightened risk for MDD.

Implications

Relapse in depressed individuals provides an important challenge as psychotropic medication and psychotherapy are insufficient in preventing recurrent MDD. The current finding that less effective inhibition may play a role in MDD leads to a promising prospective target in interventions. An important goal for patients in metacognitive therapy for MDD is to notice ruminative thoughts and then to disengage from them, but psychologists observe that this is difficult (Wells, 2009). This study might provide insight into the cognitive mechanism causing the difficulty of stopping rumination. Improvement of psychotherapy for MDD can involve interventions that increase the likelihood of disengaging rumination, and improve the effectiveness (or avoid the hampering) of this mechanism. Psychotropic medication, physical, and nutritional advice should improve the neurophysiological processes underlying effective prepotent response inhibition. Developmental factors causing less effective inhibition should be investigated and counteracted if possible. Public health programs or schools can teach people when it is important to disengage from rumination, and what the individual can do to increase the probability of effective disengagement. A better understanding of the inhibition-rumination mechanism may also lead to the development of a more precise diagnosis based on causal processes (and not only the symptoms), and a more precise understanding of the etiology of MDD.

Strengths and limitations

The study's major strength is that it examines formerly depressed participants, which enables the researcher to disentangle a possible etiological mechanism from symptoms. Another strength is that the study is based on the stop-signal paradigm and the response styles theory. Both have a solid theoretical and empirical foundation, and the SST and the RRS are reliable

and valid measures. Another strength is the exclusion of participants who used antidepressants, or had alcohol or drug abuse, since this can influence the cognitive processes measured or related to MDD.

The major limitations in the study are the relatively small sample size and the problem of assessing causality. Longitudinal studies, rumination induction and experimental manipulation of inhibition can help clarify this question.

Concluding remarks

Rumination is an important factor in the development of MDD, but the underlying cognitive mechanism is unknown. This study demonstrates that less effective prepotent response inhibition is related to elevated rumination, and may be an important etiological factor in MDD. A reciprocal process between inhibition and rumination may constitute the mechanism that prolongs dysphoric mood and causes MDD. Improved understanding of this mechanism is a promising perspective in future treatment and prevention.

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Appendix

The Ruminative Responses Scale

Folk tenker og gjør mange forskjellige ting når de føler seg triste, nedstemte eller deprimerte. Du vil her få en liste med mulige reaksjoner. Marker om du nesten aldri, noen ganger, ganske ofte, eller nesten alltid tenker eller gjør hver av disse tingene når du føler deg langt nede, trist eller deprimert. Vennligst marker hva du *vanligvis* gjør når du føler deg slik, ikke hva du synes du burde gjøre.

		Nesten aldri	Noen ganger	Ganske ofte	Nesten alltid
1	Tenker på hvor alene du føler deg	1	2	3	4
2	Tenker "Jeg vil ikke klare å gjøre jobben min hvis jeg ikke bryter ut av dette"	1	2	3	4
3	Tenker på dine følelser av å være sliten og å ha det vondt.	1	2	3	4
4	Tenker på hvor vanskelig det er å konsentrere seg	1	2	3	4
5	Tenker "Hva har jeg gjort som fortjener dette?"	1	2	3	4
6	Tenker på hvor passiv og umotivert du føler deg	1	2	3	4
7	Analyserer nylige hendelser for å forsøke å forstå hvorfor du er deprimert	1	2	3	4
8	Tenker på at det virker som du ikke føler noen ting lengre	1	2	3	4
9	Tenker "Hvorfor klarer jeg ikke å komme i gang med noe?"	1	2	3	4
10	Tenker "Hvorfor reagerer jeg alltid på denne måten?"	1	2	3	4
11	Går bort for deg selv og tenker over hvorfor du føler det slik	1	2	3	4
12	Skriver ned hva du tenker og analyserer det	1	2	3	4
13	Tenker på en nylig hendelse og ønsker at det gikk bedre	1	2	3	4
14	Tenker "Jeg klarer ikke å konsentrere meg hvis jeg fortsetter å føle det slik"	1	2	3	4
15	Tenker "Hvorfor har jeg problemer som andre mennesker ikke har?"	1	2	3	4
16	Tenker "Hvorfor kan ikke jeg håndtere ting bedre?"	1	2	3	4
17	Tenker på hvor trist du føler deg	1	2	3	4
18	Tenker på alle dine mangler, svakheter, feil og tabber	1	2	3	4
19	Tenker på hvordan du ikke føler deg opplagt til å gjøre noenting	1	2	3	4
20	Analyserer din personlighet for å prøve å forstå hvorfor du er deprimert	1	2	3	4
21	Går et sted alene for å tenke over følelsene dine	1	2	3	4
22	Tenker på hvor sint du er på deg selv	1	2	3	4