

Mini-Review

Do Sex Differences in Rumination Explain Sex Differences in Depression?

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It is generally accepted that women tend to ruminate more than men do and these thought patterns are often associated with depressive symptoms (Nolen-Hoeksema et al., 1999). Based on these findings, we considered whether the relationship between rumination and depression is stronger in women than in men and if so, whether this might explain the higher prevalence of major depressive disorder (MDD) in women and finally, whether the association can be disrupted through a mind/body intervention. Adult men and women, most of whom were clinically depressed, participated in an intervention known as MAP Training, which combines “mental” training with silent meditation and “physical” training with aerobic exercise (Shors et al., 2014). After eight weeks of training, both men and women reported significantly fewer symptoms of depression and fewer ruminative thoughts (Alderman et al., 2016). Statistical correlations between depressive symptoms and ruminative thoughts were strong and significant ($\rho > 0.50$; $p < 0.05$) for both men and women before and after MAP Training. However, only in women did depressive symptoms relate to “reflective” ruminations, which involve analyses of past events, feelings, and behaviors. This is also the only relationship that dissipated after the intervention. In general, these analyses suggest that the strength of the relationship between depressive symptoms and rumination does not necessarily explain sex differences in depression; but because the relationship is strong, targeting rumination through intervention can reduce the incidence of MDD, which is more prevalent among women. © 2016 Wiley Periodicals, Inc.

Key words: neurogenesis; depression; stress; hippocampus; fear; rumination; learning; memory; post-traumatic stress disorder (PTSD); meditation; exercise

INTRODUCTION

Women are more likely than men to suffer with major depressive disorder (MDD) and other stress-

related mental illnesses such as anxiety disorders, post-traumatic stress disorder, eating disorders, and most phobias (Kessler, 2000). Based on these sex differences, we considered whether ruminations are more highly correlated with symptoms of depression in women than in men and if so, whether the relationship might explain, at least in part, the higher prevalence of MDD in women. In this review, we first discuss the process of rumination and its potential neuronal circuitry related to processes of learning and memory in the hippocampus. We then reanalyze a set of previously-published data assessing ruminations in women and men who were diagnosed with MDD and groups of men and women who were not clinically depressed (Alderman et al., 2016, 2015). Finally, we discuss findings, which indicate that ruminations can be reduced via intervention. The intervention, is known as MAP Training, combines

SIGNIFICANCE

It is generally accepted that women are more likely to experience depression if they ruminate; but do sex differences in rumination explain the high incidence of depression in women? In one study, ruminative thoughts and depressive symptoms were highly correlated in both sexes (Alderman et al., 2016). MAP training, an intervention that combines meditation and aerobic exercise (Shors et al., 2014), was associated with a decrease in both rumination and depressive symptoms in men and women with and without major depressive disorder (MDD). Therefore, the strength of the relationship between rumination and depression may not explain sex differences in depression, but targeting rumination could nonetheless reduce the incidence of MDD in women.

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“mental” training with meditation and “physical” training with aerobic exercise. Both men and women responded with less ruminations and fewer depressive symptoms after MAP Training. However, determining whether sex differences in rumination can explain sex differences in depression is a more difficult question to answer than may first appear.

What are Ruminations?

Ruminations are thoughts that are rehearsed over and over again, often to the exclusion of more productive thoughts. They are often autobiographical in nature, and when associated with mental states of depression and anxiety, are infused with negative content. Indeed, empirical evidence suggests that repetitive thought patterns which are negative in content are maladaptive, whereas those that are more positive and reflective are not necessarily so (Lyubomirsky et al., 2006; Segerstrom et al., 2003). That said, the content of a ruminative thought is seemingly inconsequential to its definition. The verb “ruminate” is defined by Merriam-Webster as “thinking carefully and deeply about something.” The root of the word refers to animals that chew something over and over again that already has been chewed and swallowed. This may sound unpleasant to us, but to cows, which continue to chew their cud after it has been swallowed, it is an adaptive response because it stimulates the retrieval of hidden nutrients for the animal. Perhaps its definition gets to the root of why ruminations, although useful in the short-term, can be disruptive when embedded within normal healthy thought processes. Presumably, the rehearsal of autobiographical memories has evolved to help us learn to predict what will happen in the future. When thoughts become focused on the past to the exclusion of the present, learning that could occur in the present can be disrupted, as can accurate predictions about the future.

Of course, ruminations have occurred since man (and woman) could rehearse thoughts and memories. But the psychological and neuroscientific study of ruminations began in earnest with the late Dr. Nolen-Hoeksema (Nolen-Hoeksema et al., 1999, 1997, 1994). She and her colleagues demonstrated that women were more likely to internally focus attention on their depressed mood (Nolen-Hoeksema et al., 1993), and engage in more self-focused ruminative thoughts

with emotional content than men (Nolen-Hoeksema et al., 1999). Furthermore, it has been suggested that women tend to perceive social events and emotional experiences as more negative and uncontrollable than men, and they often believe they are responsible for less than ideal outcomes, both of which can exacerbate ruminative thoughts. It has been further suggested that even at a young age, girls are encouraged to express sadness and fear more readily than boys, which can set up an internal dialogue for rumination (Nolen-Hoeksema and Jackson, 2001). Within women, ruminations can change in frequency depending on menstrual stage. For example, women with increased progesterone concentrations were more likely to report intrusive recollections after viewing an emotional film (Ferree et al., 2011). Also, trauma in women, especially experiences of sexual violence, may increase rumination in part because many experiences are often not disclosed or discussed with others (Shors and Millon, 2016). It has been suggested that sex differences in sociological conditions, psychological processes, and unique life experiences contribute to a tendency for women to ruminate, and might account for the higher prevalence of rumination in women when compared to men. Perhaps more importantly, it has been suggested that the tendency to ruminate among women may account for the twofold increase in incidence of MDD in women when compared to men (Nolen-Hoeksema et al., 1999; Nolen-Hoeksema and Jackson, 2001).

The Putative Relationship between Rumination and Depression

One of the questions that continues to arise is whether ruminations actually lead to depression or whether they are simply correlated with one another. Studies on trauma provide some answers, albeit indefinite. For example, trauma and stressful life experiences can increase a person’s tendency to ruminate (Nolen-Hoeksema and Morrow, 1991; Sarin and Nolen-Hoeksema, 2010). These effects can be long lasting and can thereby lead to the emergence of stress-related mental illness. In one study, individuals who experienced acute ruminative responses about a natural disaster immediately thereafter were more likely to develop prolonged symptoms of depression than those who did not develop these thought patterns (Nolen-Hoeksema and Morrow, 1991). In another study, the degree of rumination during the grieving process predicted the likelihood of depression assessed one year later (Nolen-Hoeksema et al., 1997, 1994). These are important findings because depressive symptoms and reports of rumination are often highly correlated within individuals, rendering it difficult to dissociate the two constructs, not to mention making it nearly impossible to determine the precise nature of the relationship between rumination and depression. Overall, these data, albeit limited, suggest that stressful life experiences can increase rumination and the associated negative thought patterns may eventually produce and/or exacerbate

Abbreviations

MDD	major depressive disorder
PTSD	post-traumatic stress disorder
ERP	event related potential
MINI	Mini-International Neuropsychiatric Interview
BDI	Beck Depression Inventory
RRS	Ruminative Responses Scale
FA	focused-attention

symptoms of mental illness, especially those related to MDD. Assuming the direction of influence goes from rumination towards depression, one might even propose that reducing ruminations in otherwise healthy individuals may reduce the likelihood of future depression.

We recently assessed ruminations in a population of depressed and otherwise healthy young adults, who were recruited from a large college student population (Alderman et al., 2016, 2015). Group data including analyses of event related potential (ERP) recordings during tasks of cognitive control were previously published and will not be discussed here. In this review, we reanalyze the psychological data according to sex differences, which have not been published. In the study, participants were recruited for their personal experience with depressive symptoms and then examined for clinical depression using the Mini-International Neuropsychiatric Interview (M.I.N.I) for DSM-IV. They then completed a series of questionnaires, including the Beck Depression Inventory (BDI-II; Beck et al., 1996) and Ruminative Responses Scale (RRS; Nolen-Hoeksema et al., 1999), among others. As expected, individuals diagnosed with MDD reported more depressive symptoms than those not diagnosed with MDD, according to scores on the BDI (Alderman et al., 2016, 2015). Moreover, participants diagnosed with MDD reported more ruminative thoughts than individuals who were not diagnosed with MDD, according to scores on the RRS. Overall, correlations between individual scores on the BDI and those on the RRS were significant for all groups (p 's < 0.05), including depressed and otherwise healthy participants (Figure 1).

Reducing Ruminations with MAP Training

MAP Training is a clinical intervention that was devised to reduce rumination and negative reflections about the past (Shors et al., 2014). The acronym MAP stands for "mental and physical training." It combines mental training through focused-attention (FA) meditation with physical training through aerobic exercise. The intervention itself was translated from neuroscientific studies (Curlik and Shors, 2013; DiFeo and Shors, 2016), which indicate that aerobic exercise increases the production of new neurons in the adult hippocampus (Nokia et al., 2016; van Praag et al., 1999), whereas effortful learning processes increase their survival (Curlik et al., 2013; Shors et al., 2014). The neurogenesis studies were conducted in laboratory animal models, and because it is not possible to measure neurogenesis in humans, we only claim here that the intervention was "inspired" by laboratory studies, not that it is possible to assess any influence on neurogenesis itself. We do nonetheless propose that the neurophysiological processes that are engaged during MAP Training are mediated, at least in part, by learning processes within the hippocampal formation combined with the well-established effects of aerobic exercise on hippocampal plasticity (Déry et al., 2013; Nokia et al., 2016; Wang and van Praag, 2012).

The hippocampal formation is necessary for acquisition and short-term (i.e. within the past year) rehearsal of these types of memories (Squire et al., 2010). Therefore, we further suggest that ruminations, because they often contain autobiographical memories, are likewise engaging the hippocampus, an idea that is supported by lesion and imaging studies in humans (Mandell et al., 2014; Squire et al., 2010).

Abbreviated Methods for MAP Training: Combining Silent Meditation and Aerobic Exercise

As noted, MAP Training combines mental training with meditation followed by physical training with aerobic exercise (Shors et al., 2014). The type of meditation used in the study is often referred to as focused-attention (FA) meditation. In traditional circles, it is most similar to Zen meditation. During the process, a participant sits cross-legged on the floor (or sits in a chair). They are instructed to place the palms of their hands one on top of the other, with the right hand on the bottom. Their eyes can be closed or left half-open and focused three feet in front of their legs. They are then instructed to begin focusing their attention on their breath, noticing as the air goes in and out. With each full exhalation, the person counts his or her breaths starting at one and continues counting until he or she reaches ten, at which point he or she begins again at one. As people lose count, typically because of interfering thoughts, they are instructed to mentally "let go" of the thought and return to counting the breath, starting again at the number one. This training process provides a context in which the person can learn to recognize the presence of interfering thoughts and can thereby train themselves to return attention to the focus stimulus, in this case the breath. The sitting component of MAP Training continues for 20 minutes, after which time the participants slowly stand up and begin to engage in 10 minutes of walking meditation. During this component of the practice, the individual focuses his or her attention on the feet while walking very slowly in a large circle with the other participants. If attention drifts off into other thoughts, the goal is to recognize the interruption in attention and once again, bring attention back to the feet as the weight of the body is shifted from one foot to the other. Immediately after the meditation component, participants engage in 30 minutes of aerobic exercise at a moderate intensity. This is achieved by running on a treadmill or cyclometer. Heart rate is maintained at 60 to 75% of maximum and is monitored at the midpoint (15-min) and the end of exercise. At this point, a single session of MAP Training is complete. Participants completed two sessions per week for 8 weeks. The Ruminative Responses Scale (RRS) and Beck Depression Inventory (BDI) were given before and after the intervention.

All participants recruited for the study ($n = 52$) participated in MAP Training (for full Methods, see Alderman et al., 2016). Twenty-two participants (17 females)

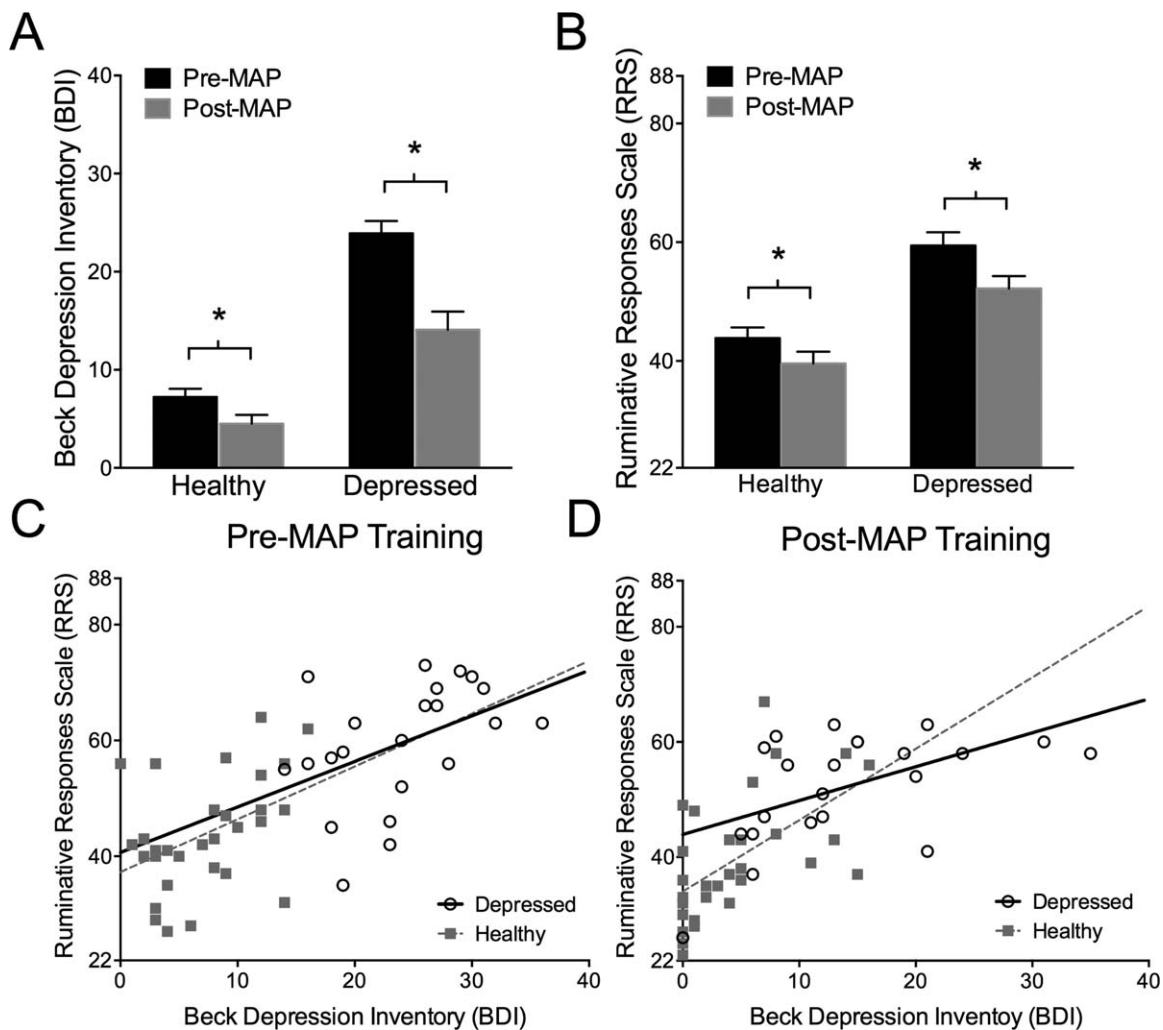


Fig. 1. Groups of individuals with MDD and otherwise healthy men and women participated in 8 weeks of MAP Training, a clinical intervention that combines meditation and aerobic exercise. MAP Training was associated with a decrease in A) severity of depression as measured with the BDI, and B) ruminative thoughts as measured with the RRS. Scores on the BDI and RRS correlated with one another C) before and D) after MAP Training, despite the overall decrease in both.

displayed BDI symptoms higher than 20, indicative of moderate to severe depression. The experimental design did not include a placebo control group, and therefore we were not able to determine whether changes in ruminative or depressive symptoms were primarily driven by meditation or exercise, and whether either treatment alone would have yielded the differences observed after the combined training. However, we were able to report that eight weeks of MAP Training (two sessions a week) was associated with a decrease in symptoms of depression as determined by responses to the BDI (Fig. 1A; Alderman et al., 2016). Moreover, eight weeks of MAP Training was related to a significant decrease in rumination in participants with MDD and otherwise healthy controls (Fig. 1B).

Sex Differences in Rumination and Depression Before the Intervention

For this review, we focus on sex differences in rumination as reported on the RRS and its relationship to depressive symptoms as reported on the BDI. Again, these sex difference data were not previously analyzed or published. Because we recruited participants who were experiencing symptoms of depression, more women than men volunteered to participate and four times more women than men completed the study. These statistics, although generally consistent with the epidemiology of depression, were likely inflated further because women may have been more attracted to the intervention than men were. It is noted that we also conducted Shapiro-Wilk tests for normality to determine skewness of the data. Within both

healthy and MDD groups, BDI scores and RRS scores before MAP Training were normally distributed. BDI scores were also normally distributed in women. However, BDI scores before MAP Training in men were not normally distributed. Thus, we transformed the raw data to standardized z-scores before performing Spearman correlations between sex groups.

With these caveats in mind, we addressed whether the relationship between rumination and depression is stronger among women than men. Spearman's correlations between scores on the RRS and the BDI were significant for both men ($\rho = 0.55$, $p < 0.05$) and women ($\rho = 0.70$, $p < 0.01$). For clarity, we also depict the raw scores for the BDI and RRS according to sex differences and with an estimated linear correlation. As shown in Figure 2A, the relationship between scores on the BDI and RRS was strong and more or less parallel in men and women before MAP Training. After the intervention, both sexes reported fewer ruminations and depressive symptoms with some individuals even reporting no depressive symptoms (BDI = 0; Figure 2B). In order to determine whether the correlations between total ruminative thoughts (RRS) and depressive symptoms (BDI) were significantly different between men and women, we performed Fisher r-to-z transformations. The relationship between overall RRS and BDI scores was not significantly different in women ($\rho = 0.70$, $n = 37$) and men ($\rho = 0.55$, $n = 15$) prior to MAP Training, ($p > 0.05$), nor was the correlation between RRS and BDI significantly different in women ($\rho = 0.68$, $n = 37$) and men ($\rho = 0.62$, $n = 15$) after MAP Training, ($p > 0.05$). Because the response to these two measures were collected at the same time, we cannot determine whether individuals who ruminate more are more likely to experience symptoms of depression or vice versa. Nonetheless, the relatively strong and significant relationship between the BDI and RRS remained for both men and women, even after MAP Training.

Sex Differences in the Subtypes of Rumination

As presented above, the relationship between depressive symptoms and ruminative thoughts was significant for both men and women, although somewhat stronger for women when the data were normalized (men: $\rho = 0.55$, $p < 0.05$; women: $\rho = 0.70$, $p < 0.01$). It was surprising to us that the difference was not more pronounced, given the high incidence of MDD in women and their reportedly higher ruminative thought processes. It is nonetheless possible that sex differences would emerge for specific types of ruminative thoughts (Treynor et al., 2003). Some researchers distinguish different types of thoughts gleaned from the Ruminative Responses Scale. The three subtypes are: 1) depressive, 2) brooding, and 3) reflective thoughts. Examples of "depressive" thoughts include thinking about how alone you feel or how angry you are with yourself. Brooding thoughts include asking yourself "What am I doing to deserve this?" or "Why do I always react this way?" Reflective types

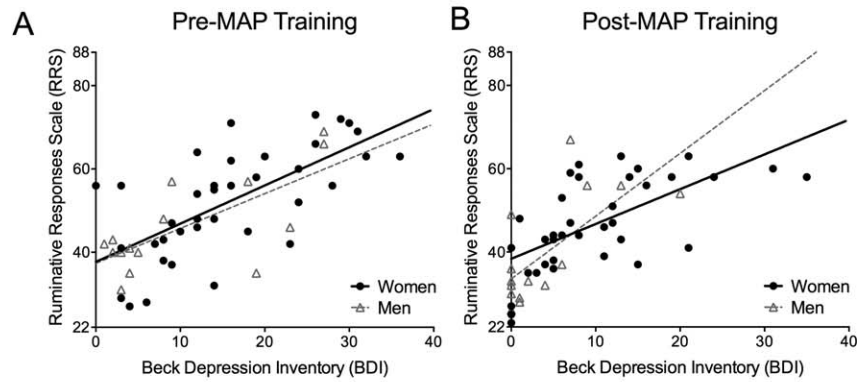
include those thoughts that might occur while you are writing down your thoughts and/or trying to analyze and reanalyze them in your mind. As such, reflective thoughts tend to include questions related to the "analysis" of previous behaviors and events, especially if the person is trying to understand why he or she feels a certain way or the situations that led to specific feelings.

We next asked whether the relationship between depression and rumination depends on the type of ruminative thoughts that arise. Therefore, in this section, we focus on subtypes of ruminative thoughts in men versus women before and after they engage in the MAP Training intervention (Figure 2). As noted, scores on the RRS and the BDI were highly correlated for both men and women before and after MAP Training (even though MAP Training was associated with a decrease in both measures). But sex differences did arise when we analyzed the data according to the three subtypes of rumination. In the first subtype, known as depressive rumination, symptoms of depression (on the BDI) were highly correlated for both men ($\rho = 0.77$, $p < 0.01$) and women ($\rho = 0.73$, $p < 0.01$) and the relationship persisted after the 8-week intervention in both sexes (men: $\rho = 0.59$, $p < 0.05$; women: $\rho = 0.74$, $p < 0.01$). The same was true for the second type of rumination, known as brooding: brooding symptoms correlated with BDI scores in men ($\rho = 0.54$, $p < 0.05$) and women before training ($\rho = 0.64$, $p < 0.01$) and they remained correlated after MAP Training, particularly among men (men: $\rho = 0.73$, $p < 0.01$; women: $\rho = 0.58$, $p < 0.01$). However, sex differences were evident for the reflective subtype of ruminations. In men, scores attributed to reflection did not relate to depression either before ($\rho = -0.13$, $p > 0.05$) or after MAP Training ($\rho = 0.24$, $p > 0.05$), whereas in women, the scores for reflective rumination did relate to depressive symptoms prior to training ($\rho = 0.38$, $p < 0.05$). Interestingly, this relationship was no longer evident after MAP Training ($\rho = 0.15$, $p > 0.05$). In summary, these data suggest that depressive and brooding types of rumination are related to symptoms of depression in both men and women. However, thoughts that were related to the analysis and reanalysis of events and feelings may be especially related to depressive symptomology in women and may be more amenable to clinical interventions.

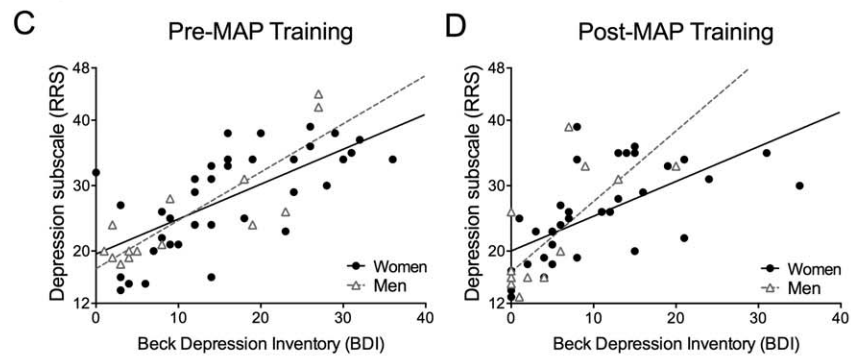
Rumination and the Hippocampal Formation

The tendency to ruminate is relatively stable and as such, it is often considered a "trait" rather than a "state". Given this view, it would seem unlikely to change via intervention. However, the process of rumination has also been considered a "habit", which can be learned and "unlearned." Because MAP Training has been shown to reduce ruminations in several populations (Shors et al., 2014; Alderman et al., 2016), we suggest that it can change. But how might this happen? We propose that these ruminative thought processes, especially those related to reflection, are akin to declarative memories that

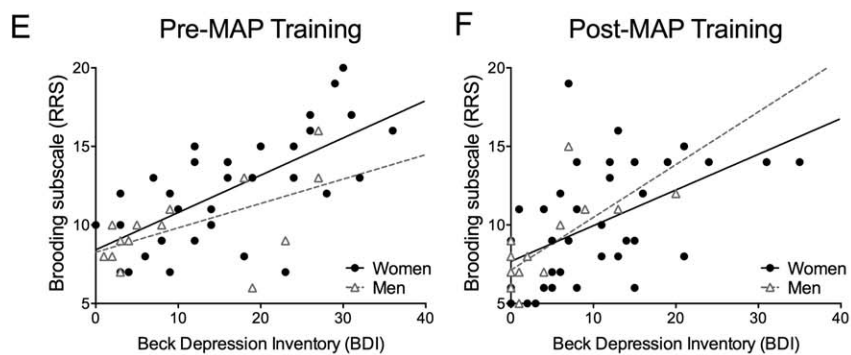
Total RRS



Depression subscale



Brooding subscale



Reflection subscale

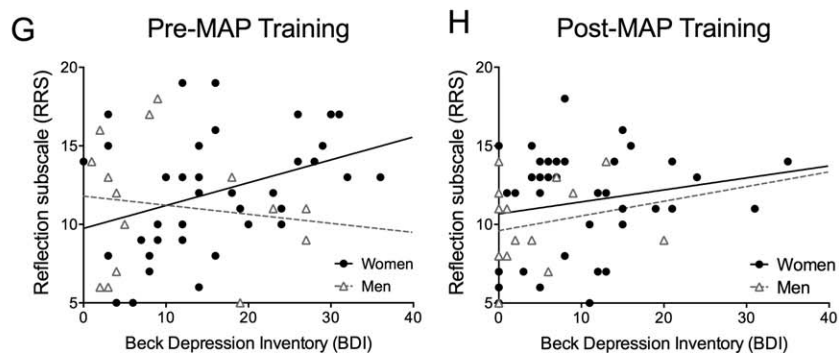


Fig. 2. The raw scores for symptoms of depression (BDI) and ruminative thoughts (RRS) are presented. Overall, scores for the RRS and the BDI in men and women related to one another A) before and B) after MAP Training. Scores on the Depression subscale related to BDI scores in men and women C) before and D) after MAP Training.

Scores on the Brooding subscale related to BDI scores in men and women E) before and F) after MAP Training. G) However, scores from the Reflection subscale related to BDI scores in women before training, but not men. H) After MAP Training, reflective rumination scores were no longer related to BDI scores in women.

depend upon neuronal activity within the hippocampus. It is well known that autobiographical memories are encoded through activity in the hippocampus (Squire et al., 2010; Squire et al., 2015) and that mechanisms related to stress and learning interact in the hippocampus (Bangasser and Shors, 2007), including those related to the emotional content of autobiographical memories (Phelps, 2004). Others have reported relationships among ruminative thoughts, hippocampal activity and depression. In one study, individuals with depression expressed more activation in the right hippocampus when engaging in a digit-sorting task during experimentally-induced rumination (Cooney et al., 2010). In another study, rumination was related to the amount of hippocampal activity, when controlling for amygdala activity (Mandell et al., 2014). Because most of these are human studies, we cannot know whether increases in neuronal activity (or more accurately blood flow) are *necessary* for ruminative processes to occur. In other words, changes in activity may simply be a correlate of the ruminative process and not a necessary component. In general, studies do support the notion that interactions among emotion-related brain regions and those necessary for the rehearsal of autobiographical memories coexist (Mandell et al., 2014). That said, processes of rumination are complex interconnected thought patterns and are thus unlikely to be localized in specific brain regions but rather represent dynamic neurophysiological processes, which engage both central and peripheral nervous systems. For example, one study reported that the association between more frequent brooding ruminative thoughts and decreased heart rate variability was moderated by the *COMT* genotype, a previous marker of heightened amygdala activity and deficits in prefrontal function (Woody et al., 2014). To be clear, we are not claiming that the strong relationship between rumination and depressive symptoms discussed here are necessarily mediated by the hippocampus or any particular brain structure. What the present results highlight is a strong relationship between rumination and depression in both men and women, with some potentially subtle sex differences for reflective and analytical types of rumination.

Learning Not to Ruminate

We do not currently know the neuronal mechanisms through which the experience of MAP Training reduces rumination and depression. However, we propose that these changes occur through processes of learning. During the practice of FA meditation, a person learns to “watch” thoughts as they appear and disappear without following associations to other thoughts or emotions. Many thoughts are associated with some kind of emotional response, which become conditioned through repeated rehearsals. During FA practice, a person learns not to associate a thought with a particular emotional response or feeling, but rather to let it passively dissipate. On a very simplistic level, this process might be considered a form of extinction training. In other words, the

conditioned stimulus (which in this case may be an autobiographical memory or negative thoughts about that memory) arises in the mind of the participant, but when an emotional response (an unconditioned response) does not automatically arise, a person “learns” that the two events are not necessarily or always associated. An interruption of these learned associations with new learning may “simply” override the learned tendency to ruminate about the past, at least in the short term.

CONCLUSION

We reanalyzed published data to show that rumination and depressive symptoms are highly related to one another in both sexes (Alderman et al., 2016). Overall, these new analyses suggest that sex differences in rumination *do not necessarily explain* sex differences in depression, at least to the extent that they were highly related to one another in both sexes. Regardless of depression status, both sexes reported fewer ruminative thoughts after MAP Training. However, reflective ruminations were more associated with depressive symptoms in women than in men, and the association was disrupted after participation in the intervention. In general, the combination of meditation and aerobic exercise represents an effective means of engaging in learning processes to reduce rumination for both men and women. Because more women than men are likely to experience MDD, interventions which reduce ruminations will nonetheless be useful for decreasing the number of women with MDD.

CONFLICT OF INTEREST STATEMENT

All authors declare that they have no known or potential conflicts of interest, including financial, personal, or other relationships, which could inappropriately influence or be perceived to influence the work presented here.

ROLE OF AUTHORS

All authors had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: TJ, BA. Acquisition of data: TJ, BA, RO. Analysis and interpretation of data: EM, RO. Drafting of the manuscript: TJ, EM, HMC. Critical revision of the manuscript for important intellectual content: TJ, EM, HMC, BA. Statistical analysis: EM, RO. Obtained funding: TJ, BA. Administrative, technical, and material support: TJ, EM, HMC, RO, BA. Study supervision: TJ, BA.

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