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Neural substrates of rumination tendency in non-depressed individuals

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ABSTRACT

The tendency to ruminate, experienced by both healthy individuals and depressed patients, can be quantified by the Ruminative Response Scale (RRS). We hypothesized that brain activity associated with rumination tendency might not only occur at rest but also persist to some degree during a cognitive task. We correlated RRS with whole-brain fMRI data of 20 healthy subjects during rest and during a face categorization task with different levels of cognitive demands (easy or difficult conditions). Our results reveal that the more subjects tend to ruminate, the more they activate the left entorhinal region, both at rest and during the easy task condition, under low attentional demands. Conversely, lower tendency to ruminate correlates with greater activation of visual cortex during rest and activation of insula during the easy task condition. These results indicate a particular neural marker of the tendency to ruminate, corresponding to increased spontaneous activity in memory-related areas, presumably reflecting more internally driven trains of thoughts even during a concomitant task. Conversely, people who are not prone to ruminate show more externally driven activity.

1. Introduction

A trait feature of different psychiatric disorders is negative repetitive thinking (Watkins, 2008), and in particular rumination. According to the most frequent definition of this phenomenon, "ruminations are repetitive and passive thinking about symptoms of depression and the possible causes and consequences of these symptoms" (Nolen-Hoeksema, 1991). Although rumination in general can be conceptualized as a form of thinking found in different pathologies and present in everybody to some degree (Nolen-Hoeksema & Watkins, 2011; Wells, 2004), it is most often related to depressive mood (Nolen-Hoeksema, 2000) and has consistently been linked to negative affect (Thomsen, 2006). In this perspective, depressive rumination is seen as a particular response style that, instead of being oriented to problem solving, tends to enhance internal focus, pessimism, and perseverative cognitions, which may in turn exacerbate low mood (Watkins, 2008; Nolen-Hoeksema, 1991; Nolen-Hoeksema, Wisco, & Lyubomirsky, 2008; Spasojevic & Alloy, 2001). Thus, accumulating evidence points toward rumination being an important vulnerability factor in the development of depression (McLaughlin & Nolen-Hoeksema, 2011; Wiersma et al., 2011) and constituting a maladaptive mental habit (Watkins & Nolen-Hoeksema, 2014). The tendency to ruminate is commonly measured by the Ruminative Response Scale (RRS) (Davis & Nolen-Hoeksema, 2000; Nolen-Hoeksema et al., 2008; Ray et al., 2005; Spasojevic & Alloy, 2001; Thomas et al., 2011; Whitmer & Banich, 2007).

Depression is also associated with different kinds of cognitive dysfunctions (for a review, see Gotlib & Joormann, 2010). A few specific deficits have been linked with ruminations, particularly cognitive inflexibility and difficulties in disengaging attention from irrelevant information (Joormann & D'Avanzato, 2010; Koster, De Lissnyder, Derakshan, & De Raedt, 2011; Whitmer & Banich, 2007). This might be even stronger for negative material (Lissnyder, Koster, Derakshan, & De Raedt, 2010; Koster, De Lissnyder, & De

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Raedt, 2013). However, the link between rumination and allocation of attention is still unclear, because the direction of the causality is difficult to demonstrate. On the one hand, a general impairment in cognitive resources or control could explain the difficulties of the subjects to allocate their attention and thoughts away from intrusive material (Koster et al., 2011; Levens, Muhtadie, & Gotlib, 2009). On the other hand, the dominance of ruminations in the content of attention could explain the difficulties in allocating or shifting cognitive resources to other thoughts (Philippot & Brutoux, 2008). Furthermore, a state of rumination might potentially result from deficient cognitive control normally allowing the inhibition of irrelevant thoughts and/or from increased generation of intrusive material through spontaneous associations and elaborative emotional processing (Mandell, Siegle, Shutt, Feldmiller, & Thase, 2014; Piguet et al., 2010). Hence, the functional relationships of rumination tendency with attention control remain to be better understood (for a recent review, see Whitmer & Gotlib, 2013).

The neural substrates of rumination remain largely unresolved. Recent studies point to an involvement of heightened emotional reactivity, but also weaker cognitive control. An early study (Ray et al., 2005) examined how brain activation during cognitive reappraisal of emotional pictures varied with trait rumination tendency, and found that the latter correlated with higher amygdala response when increasing negative affect, and lower medial prefrontal activity when decreasing negative affect. Another study (Johnson, Nolen-Hoeksema, Mitchell, & Levin, 2009) reported that higher trait rumination in depressed individuals correlated with greater difficulties in deactivating the posterior cingulate cortex (PCC), a region associated with self-focused processes, when engaged in an external (non-self-referential) task. They also reported lower activation of anterior cingulate cortex (ACC). Cooney, Joormann, Eugene, Dennis, and Gotlib (2010), using a rumination induction task, found that depressed patients showed increased activation in amygdala, rostral anterior cingulate cortex/medial prefrontal cortex (PFC), dorsolateral PFC, and parahippocampal cortex, during rumination relative to an abstract distraction task. Another study, using the recall of autobiographical negative memories and subsequent focus on elicited emotions as a proxy for rumination, found that the latter correlated with activity in subgenual ACC (sgACC) and medial PFC (Kross, Davidson, Weber, & Ochsner, 2009). More recently, Freton et al. (2013) showed that lower brooding scores measured by the RRS (emphasizing the maladaptive component of self-reflection) correlated with increased activation of the posterior midline structures during analytical compared to experiential self-focus, which may account for impaired cognitive control on self-focus in high brooders. Finally, in depressed patients, using a factor structure derived from multiple questionnaires and a paradigm alternating cognitive and emotional tasks in depressed patients, Mandell et al. (2014) showed that trait rumination correlated not only with amygdala but also hippocampus activity. Other regions in PCC, MPFC, dorsolateral PFC, and anterior insula also exhibited differential patterns as a function of ruminations traits. Taken together, these studies suggest that self-referential and memory-related activity, in addition to emotional factors, may be associated with the presence and content of ruminative thinking, but they do not elucidate a possible role for attentional control abilities in promoting the appearance or persistence of rumination activity.

A few other recent fMRI studies investigated the link between depressive rumination and brain activity in the so-called default mode network (DMN), which is typically associated with self-reflective processes and observed in resting state conditions, but deactivated during attention demanding tasks. Hyperconnectivity between components of the DMN in PCC and sgACC was found at rest for patients with Major Depressive Disorder (MDD), correlating with RRS scores, and more specifically the brooding subscore (Berman, Peltier, et al., 2011). Another study comparing DMN and task-positive networks in MDD showed that ruminations were associated with increased DMN dominance at rest (Hamilton et al., 2011). Finally, by computing whole-brain correlation between RRS and resting state activity, Kühn, Vanderhasselt, De Raedt, and Gallinat (2012) found a negative relation with right inferior frontal gyrus, right ACC, and sgACC. They also found increased functional connectivity of the left striatum with left inferior frontal gyrus in healthy individuals experiencing more unwanted thoughts (Kühn, Vanderhasselt, De Raedt, & Gallinat, 2013). This is consistent with higher rumination scores (as assessed by the RRS) being associated at rest with lower connectivity between sgACC and the middle and inferior frontal gyri in adolescents with a first-episode depression (Connolly et al., 2013). Again, increased activity and/or connectivity within areas of the DMN involved in emotional and self-referential processing might contribute to ruminations tendency, in addition to decreased activity in cognitive control regions. Altogether, this literature points to a link between rumination and cortical midline structure (Nejad, Fossati, & Lemogne, 2013), with an imbalance between the recruitment of externally directed attention/executive control networks (in fronto-parietal cortices) and internally directed self-referential/memory networks (in midline and limbic brain systems), particularly during rest (Marchetti, Koster, Sonuga-Barke, & De Raedt, 2012). However the relationships between the attention state, the cognitive control abilities and the activity in other brain structures remain unclear in the context of rumination.

To clarify the neural substrates of rumination tendencies in the absence of depressive illness, the current study used fMRI in the same group of healthy participants, both during a demanding cognitive task with different degrees of attentional load, and during a resting state condition with no external demands. First, we specifically tested the hypothesis that lower attentional shifting abilities in high ruminators may release ruminative processes and thus lead to higher activation of self-related regions during lower cognitive load. Second, we hypothesized that a direct comparison between the resting and cognitive states, hence two separate datasets from the same population, should allow us to determine whether the neural activation pattern associated with rumination tendency seen at rest would resemble the pattern seen in the low demanding condition of the cognitive task. Specifically, we expected not only that brain areas reflecting attention control should show reduced engagement in people with higher rumination tendencies, but also that this should in turn promote a release of activity in brain areas involved in the generation of ruminative thoughts.

2. Methods

2.1. Participants

Twenty healthy subjects (10 women and 10 men) participated in this study, recruited through local advertisement, and filled informed consent. Participants reported having no neurologic or psychiatric medical history and taking no medication. Mean age was 24.9 (std 5.457, ranging from 18 to 37). The Ethical Committee for Psychiatry and Rehabilitation of the University Hospital of Geneva approved this study.

2.2. Questionnaires

Participants filled the 22-items of the Ruminative Response Scale (RRS) (Nolen-Hoeksema & Morrow, 1991) on the day of the MRI session. This questionnaire assesses the tendency of individuals to ruminate when they feel depressed. This trait measure has been widely used in clinical studies (e.g. Vanderhasselt & De Raedt, 2012) as well as neuroimaging studies (see Section 1). Participants also filled the Beck Depression Inventory-II (BDI, Beck, Steer, & Brown, 1996) and the Beck Anxiety Inventory (BAI, Beck, Epstein, Brown, & Steer, 1988).

2.3. Behavioral task

As an active cognitive condition, we used a task switching paradigm (Piguet et al., 2013) with emotional faces. On each trial, participants first saw a cue for 150 ms, either the word “emotion” or “color” or “gender”, instructing them to judge