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Review

REVIEW

The inter-relationships of the neural basis of rumination and inhibitory control: neuroimaging-based meta-analyses

Xiaoqi Song[1], Jixin Long[1], Chanyu Wang[1], Ruibin Zhang[1,2,*] and Tatia M.C. Lee[3,4,5,*]

[1]Cognitive control and Brain Healthy Laboratory, Department of Psychology, School of Public health, Southern Medical University, Guangzhou, 510515, China
[2]Department of Psychiatry, Zhujiang Hospital, Southern Medical University, Guangzhou, 510285, China
[3]State Key Laboratory of Brain and Cognitive Sciences, The University of Hong Kong, Hong Kong, 999077, SAR China
[4]Laboratory of Neuropsychology and Human Neuroscience, The University of Hong Kong, Hong Kong, 999077, SAR China
[5]Center for Brain Science and Brain-Inspired Intelligence, Guangdong-Hong Kong-Macao Greater Bay Area, 510799

*Correspondence: Tatia M.C.Lee, tmclee@hku.hk, RuibinZhang, ruibinzhang@foxmail.com

Abstract

Rumination, as a clinical manifestation and pathogenic factor of depression, has long been the focus of psychological research regarding its causes and ameliorating approaches. Behavioral studies have shown that rumination is related to inhibitory control deficits, which provides ideas for reducing it. However, the neural relationship between them has not been clearly discussed. In this study, we first used multi-level kernel density analysis to conduct two meta-analyses of published functional magnetic resonance imaging studies: one was rumination comprising 17 studies with 180 foci, and the other was inhibitory control comprising 205 studies with 3791 foci. Conjunction analysis was then performed to explore the common brain regions and further decode them through Neurosynth to confirm the cognitive specificity. Results showed that rumination was mainly related to the default mode network (DMN), while inhibitory control was associated with the frontoparietal network (FPN). In addition, the common activation areas were mainly concentrated in the bilateral precuneus, right superior frontal gyrus, bilateral median cingulate, paracingulate gyri, and the left triangular part of inferior frontal gyrus (IFG). Decoding results also revealed they were involved in inhibition, memory retrieval, and self-related processes. Our findings support that rumination is associated with inhibitory control and can be explained neurologically by an antagonistic relationship between the DMN and FPN. In sum, inhibitory control may be related

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to rumination via inhibiting task-unrelated attention and controlling self-related processing. This research will help us understand and predict rumination from the perspective of inhibitory control and reduce rumination through behavioral training of inhibitory control or the application of neuromodulation techniques to common activation regions.

Key words: Rumination; Inhibitory control; Meta-analysis; fMRI

Introduction

Rumination, a stable and habitual negative response mode, refers to the process in which individuals constantly and compulsively focus on past events or negative emotions (Nolen-Hoeksema *et al.*, 2008). Such a maladaptive and self-focused thinking mode does not increase self-understanding but exacerbates negative moods (Lyubomirsky and Nolen-Hoeksema, 1995). Studies have shown that rumination may lead to a variety of negative effects, including impairing the ability to solve problems (Watkins and Moulds, 2005; O'Mahen *et al.*, 2015) and increasing self-injurious and suicidal ideation (Rogers and Joiner, 2017). Importantly, extensive evidence shows that rumination is a typical risk factor and clinical symptom of depression (Lyubomirsky *et al.*, 1999; Nolen-Hoeksema, 2000). Understanding rumination and its underlying mechanisms is of great significance to explore methods of regulating rumination and might have the potential to help reduce the risk of depression.

Behavioral evidence signifies that rumination is related to inhibitory control deficits

Inhibitory control is one of three core subcomponents of executive function (EF) (Miyake *et al.*, 2000), representing an ability to stop or cancel a thought or behavior, including inhibiting automatic or dominant responses (Williams *et al.*, 1999; Macleod, 2007). Besides inhibitory control, EF includes another two subcomponents (Friedman *et al.*, 2008): one is shifting, which involves switching back and forth between multiple tasks, operations, or mental states. The other is updating, which involves updating and monitoring working memory representation. Three subcomponents of EF are interrelated and cooperative, playing an essential role in flexible processing of goal-related information and suppression of task-irrelevant information (Miyake *et al.*, 2000). Existing studies have linked impaired EF to a variety of disorders, such as major depressive disorder (Watkins and Brown, 2002) and attention deficit hyperactivity disorder (Barkley and Murphy, 2010).

Previous studies have suggested that the occurrence and continuation of rumination may be due to defects in EF (Koster *et al.*, 2011; Van Vugt and Maarten, 2018). However, compared with the other two subcomponents of EF, more evidence was reflected in the relationship between inhibitory control and rumination. For example, Ballesio *et al.* (2019) used the task-switching paradigm to evaluate inhibition and shifting at the same time, finding that higher rumination scores were associated with impaired inhibitory but not switching capacities. Moreover, using the emotional Stroop task measuring inhibitory control and the affective version of the two-back task for assessing updating, Zareian *et al.* (2021) reported that inhibition difficulties can predict brooding and reflection (two components of rumination), while updating cannot. In recent years, a comprehensive meta-analysis of 34 studies including 3066 participants put forward that research on the relationship between rumination and two other subcomponents of EF (i.e., shifting and updating) have not yet yielded consistent results, while there is an obvious negative correlation between rumination and inhibitory control (Yang *et al.*, 2016).

Additionally, Anderson and colleagues proposed the concept of memory suppression (Anderson and Green, 2001), which refers to the suppression and stopping of retrieval of inappropriate memories even when an individual is confronted with reminders. In this and subsequent studies (Anderson *et al.*, 2004; Levy and Anderson, 2008), they showed that memory suppression was achieved through executive control, especially inhibitory control, instead of through inhibition of overt motor responses. Furthermore, a recent study has shown that inhibitory control is the basis of memory suppression and the two have similar neural correlates (Liu *et al.*, 2020). Therefore, deficient inhibitory control may compromise an individual's ability to suppress memory retrieval, which subsequently leads to repetitive negative thinking (Catarino *et al.*, 2015). This is in line with Linville (1996), who proposed that the underlying mechanism of rumination is deficits in inhibitory control, which increases the likelihood of repetitive inner thoughts, making it hard to prevent ruminative thinking from entering working memory. However, the neural mechanism underlying the association between rumination and inhibitory control still needs to be further confirmed.

Neuroimaging studies address the association between rumination and inhibitory control

Neuroimaging techniques such as functional magnetic resonance imaging (fMRI) (Deyoe *et al.*, 1994) can help identify brain areas where neural activity changes throughout task processing; thus, we can interpret behavior from the perspective of the brain. Several fMRI studies exploring the association between rumination and inhibitory control have been reported. For example, Vanderhasselt *et al.* (2011) used an emotional go/no-go task to clarify that while inhibiting dominant responses to negative information, individuals with high ruminative tendency showed higher activation than healthy

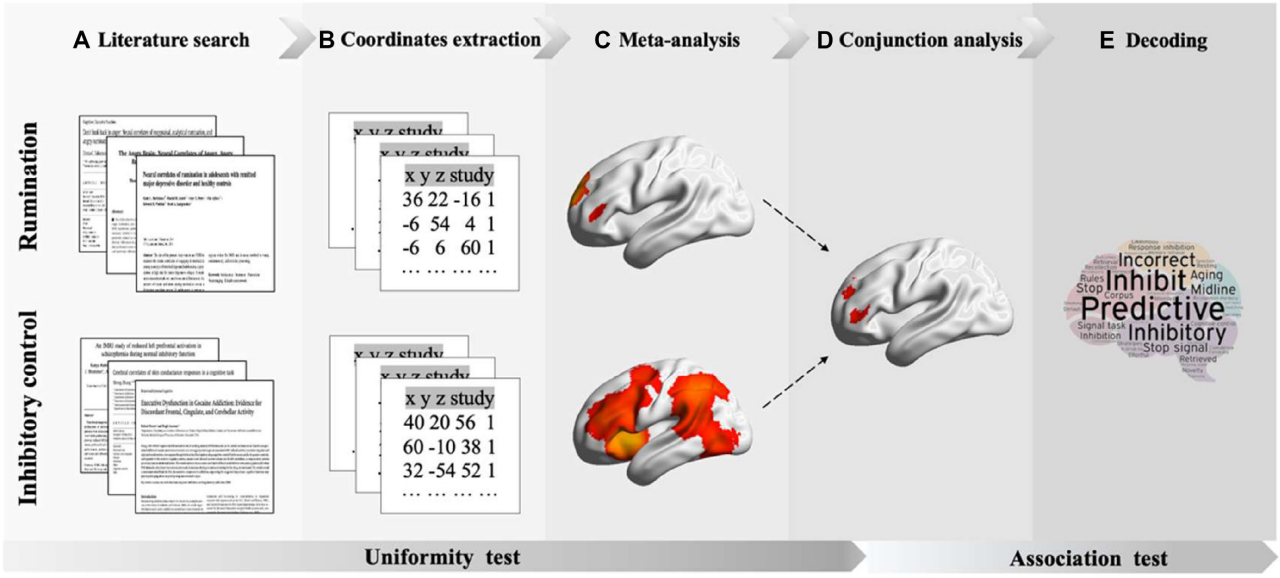

Figure 1: Overview of research pipeline used in the current study. Uniformity test—inferential process from cognitive process to brain activation region. Association test—inferential process from brain activation region to cognitive process.

control participants in the dorsolateral prefrontal cortex (dlPFC), which means the dlPFC may be the critical region for ruminating individuals to execute inhibitory control. A study of 39 women suffering from post-traumatic stress disorder found that during an emotional Stroop task—a task tapping inhibitory control—individuals with rumination displayed significant activation of the right orbital frontal cortex when suppressing or disposing of negative stimuli (Buchholz *et al.*, 2016). In the first two examples, emotional stimuli were added to the inhibitory control task. However, studies have shown that emotional stimuli interfere with cognitive inhibition (Rebetez *et al.*, 2015) and response inhibition (Shafritz *et al.*, 2006). In other words, inclusion of emotional stimuli may prevent us from clearly separating emotional processing from inhibitory control in the results. Therefore, to specifically explore the relationship between rumination and inhibitory control, tasks involving emotional stimuli should be further excluded to avoid confound in the regions activated by emotional processing. In addition, Berman *et al.* (2011) reported that depressed participants showed great activation in the left inferior frontal gyrus (IFG) (a key region in suppressing irrelevant information) compared with healthy participants, and they proposed that rumination, as a characteristic of depression, might be due to a deficit in the ability to expel negative information from short-term memory.

All these studies focused on exploring the relationship between rumination and inhibitory control. However, the intrinsic neural association between two remains unknown. In meta-analyses including rumination-related fMRI studies, Zhou *et al.* (2019) found that rumination mainly activated the anterior cingulate/paracingulate gyrus, precuneus and orbital part of the IFG. Interestingly, Zhang *et al.* (2017) conducted a meta-analysis of response inhibition (considered to be part of inhibitory control). It was found that during the response inhibition task, part of the frontoparietal network (FPN), including the dlPFC, presupplementary motor area, and temporal parietal junction, as well as the IFG and precuneus, showed consistent activation. The previously mentioned meta-analyses give hints that rumination and inhibitory control may partly share the neural regions, e.g., the IFG and precuneus, but the neural association between the two processes and the mechanisms behind them needs to be further confirmed by new studies.

Thus, the aim of this study is to explore the relationship between rumination and inhibitory control from the level of neural mechanisms. First, we used MKDA, a coordinated meta-analytic technology identifying brain regions that are consistently activated in multiple studies (Wager *et al.*, 2007), to identify the neural activation patterns of rumination and inhibitory control (Fig. 1a–c). Second, we conducted a conjunction analysis to further identify the common engaged network between rumination and inhibitory control (Fig. 1d). Finally, we decoded the obtained common activation area through Neurosynth, a database recording the cognitive processes involved in certain brain regions based on published literature to identify their corresponding specific cognitive processes (Fig. 1e). Following these analyses, it will help to clarify the key role that inhibitory control may play in the occurrence of rumination.

Methods

Literature search and selection criteria

Rumination

A systematic search was conducted on electronic databases PubMed and Web of Science using the terms

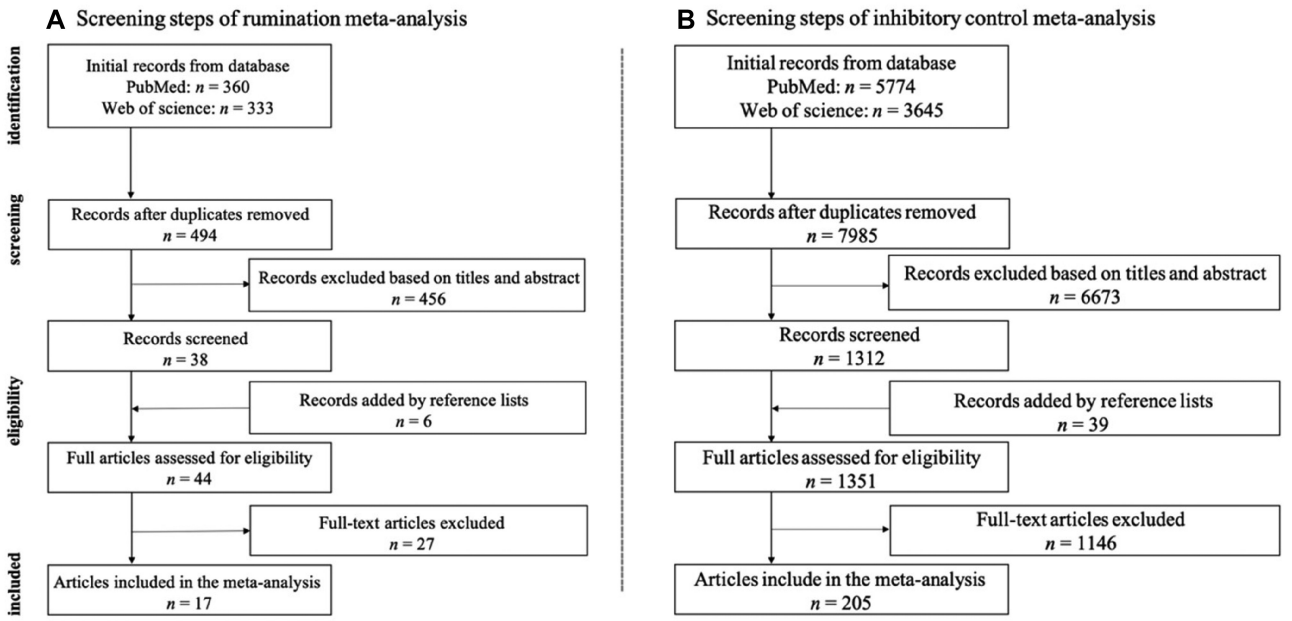

Figure 2: Flowchart of the study selection process following PRISMA. (A) Illustration of screening steps of rumination meta-analysis and (B) illustration of screening steps of inhibitory control meta-analysis.

("rumination" OR "ruminative" OR "brooding") AND ("fMRI" OR "functional MRI" OR "functional magnetic resonance imaging" OR neuroimaging" OR "functional imaging" OR "functional magnetic imaging"). A total of 693 articles were yielded through these keywords up to April 2020, including 360 from PubMed and 333 from Web of Science. All the articles obtained had to be screened. In addition, we analyzed and reported in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Moher *et al.*, 2015).

The inclusion and exclusion criteria used for screening are shown in the Supplementary Data. We also searched the references from the selected articles and other reviewed articles for rumination studies that were not encountered in the PubMed and Web of Science search results and obtained another six studies in this way. After screening, 17 studies were included in the final rumination meta-analysis. The detailed literature detection and selection steps are shown in Fig. 2a. Afterward, we extracted the following information from each piece of included literature: (i) author; (ii) year of publication; (iii) sample size; (iv) mean age of participants; (v) type of contrast (i.e., rumination vs. distraction, rumination vs. control); (vi) peak coordinates; and (vii) type of coordinate space (i.e., MNI or Talairach).

Inhibitory control

A systematic search was conducted on PubMed and Web of Science using the terms "fMRI" AND ("response inhibition" OR "interference resolution" OR "action withholding" OR "action cancellation" OR "inhibitory control" OR "stop signal" OR "stopping" OR "go no-go" OR "action restraint" OR "countermanding"). This resulted in 9419 articles published before April, 2020, including 5774 from PubMed and 3645 from Web of Science.

The inclusion and exclusion criteria used for screening are shown in the Supplementary Data. Like the rumination meta-analysis, 39 additional studies were obtained by manually searching the reference list of retrieved studies and related review articles. We finally included 205 studies for inhibitory control meta-analysis according to the inclusion and exclusion criteria. The detailed literature detection and selection steps are shown in Fig. 2b. Finally, we extracted the following information from each piece of included literature: (i) author; (ii) year of publication; (iii) sample size; (iv) mean age of participants; (v) experimental paradigms (e.g., go/no-go task, Stroop task); (vi) type of contrast; (vii) peak coordinates; and (viii) type of coordinate space (i.e., MNI or Talairach).

Statistical analysis

Multi-level Kernel Density Analysis (MKDA)

In this study, meta-analyses were performed using the MKDA toolbox (http://wagerlab.colorado.edu) developed by Wager *et al.* (2009). First, we convolved peak effect coordinates from each experimental contrast with a spherical kernel ($r = 20$ mm) (Kang *et al.*, 2014) to get the corresponding contrast indicator map (CIM), with a value of 1 indicating a significant effect in the neighborhood and a value of 0 indicating no significant effect (for the results of convolution with an $r = 10$ mm spherical kernel, refer to Fig. S2 in the Supplementary Data). Then, a weighted average method was used to generate a summary density map in which the weight was the square root of the sample size multiplied by the adjusted weight of analysis type used for the overall inference (the weight of a random effect is 1 and the weight of a fixed

effect is 0.75). A null hypothesis followed by MKDA indicated that peak coordinates of the activation regions are randomly distributed throughout the brain (Kober and Wager, 2010). If the number of active voxels near the peak coordinates was greater than the number expected by chance, then the null hypothesis was rejected. Therefore, 5000 Monte Carlo simulations were performed, and only voxels surpassing a stringent extent-based threshold of $P < 0.001$ were considered significant. This means that the findings that were consistent across all studies in the literature would have been found by chance only 0.1% of the time (van Hoorn *et al.*, 2019). Resulting maps were subjected to a cluster-level threshold using a family-wise error rate of $P < 0.05$ (Wager *et al.*, 2007). Using these methods, we can identify brain regions that showed significant convergence in 17 rumination studies and 205 inhibitory control studies.

Conjunction analysis

Conjunction analysis can identify voxels with significant effects in all separate analyses (Hu *et al.*, 2016). The Monte Carlo overlap between the convergent clusters of rumination meta-analysis threshold $P < 0.05$) and convergent clusters of inhibitory control meta-analysis (threshold $P < 0.05$) was used (Wager *et al.*, 2009) to determine the activation regions common to rumination and inhibitory control.

Distribution of activated voxels across networks

To clarify the distribution of significant voxels in different brain function networks, for each meta-analysis and conjunction analysis result, we calculated proportions of voxels that overlapped with Yeo's seven-network parcellation [i.e., visual network, somatomotor network (SMN), dorsal attention network (DAN), ventral attention network (VAN), limbic network, FPN, and default mode network (DMN)] (Yeo *et al.*, 2011) (Fig. 4). Note that we calculated relative proportion by estimating the ratio of activated voxels of specific networks versus overall activated voxels (Zhang *et al.*, 2017).

Neurosynth decoding

Results of the meta-analysis and conjunction analysis reflect the inference from cognitive processes to corresponding activation area, qualitatively demonstrating that specific brain states generated by a cognitive process or task belong to a typical uniformity test (Henson, 2006). However, the activated brain regions may not be specific to a certain cognitive process, but rather may be activated by a series of cognitive tasks (Poldrack, 2011). Therefore, an association test is needed to associate the inference from activation area to the corresponding cognitive process (Poldrack, 2006) so as to prove the functional specificity or cognitive correlation of the brain regions. To do so, the Neurosynth Image decoder (https://www.neurosynth.org/decode/) was used to compare the coactivation statistical map obtained from conjunction analysis with the activation patterns associated with cognitive terms in the Neurosynth database to decode the related behaviors and psychological processes of the coactivation network. Decoded results from Neurosynth contained cognitive terms and anatomical terms, which were arranged in order according to correlation coefficients, representing the correlation intensities of the decoded brain regions. However, only cognitive terms represented the cognitive processes most likely to correspond to the common brain regions. Anatomical terms refer not to the cognitive processes, but to the neural structure of the brain. Therefore, we excluded anatomical terms and retained the top 50 cognitive terms with the highest correlation with common activation regions (Wakaizumi *et al.*, 2021).

Publication bias analysis

We examined the potential publication bias of the included studies. The highest *t*- or *z*-value reported in the included articles was recorded. We set the effect size as 0 for the studies that did not report a *t*-value or *z*-value in the MNI or Talairach space (Jennings and Horn, 2012). Then the *t*- or *z*-value was converted to a Pearson's *r* effect size (Cohen, 1988). We used "metafor" package in R to generate funnel plots based on the calculated effect sizes and other parameters. The points would form a symmetrical inverted funnel around the overall effect size if there is no publication bias, while the plot would be asymmetrical or skewed if publication bias exists (Jennings and Horn, 2012).

Sensitivity analysis

The imbalance between the number of eligible rumination studies and the number of eligible inhibitory control studies is an issue that needs to be taken into account when interpreting our results. To address this, two analysis strategies were adopted to test whether the imbalance had any significant effect. First, we performed an MKDA analysis (using the same parameters as in 2.2.1) with a leave-one-out strategy on the 17 rumination studies and obtained a total of 17 activation maps. Then, we calculated the number of active voxels in each map that belong to the result map of the conjunction analysis (between 17 rumination studies and 205 inhibitory control studies). The results were expressed as percentages. Second, we randomly selected 30 experiments from the 205 inhibitory control studies and performed an MKDA analysis. A previous study showed that a meta-analysis with >28 experiments would be less biased by a dominant experiment (Eickhoff *et al.*, 2016). Then, we did a conjunction analysis between the 30 randomly selected inhibitory control studies and the 17 rumination studies.

Results

Detailed characteristics of included studies

The rumination meta-analysis obtained 17 articles that met the inclusion criteria, with a total sample size of 392, of which 42.9% were men and 57.1% were women; 180

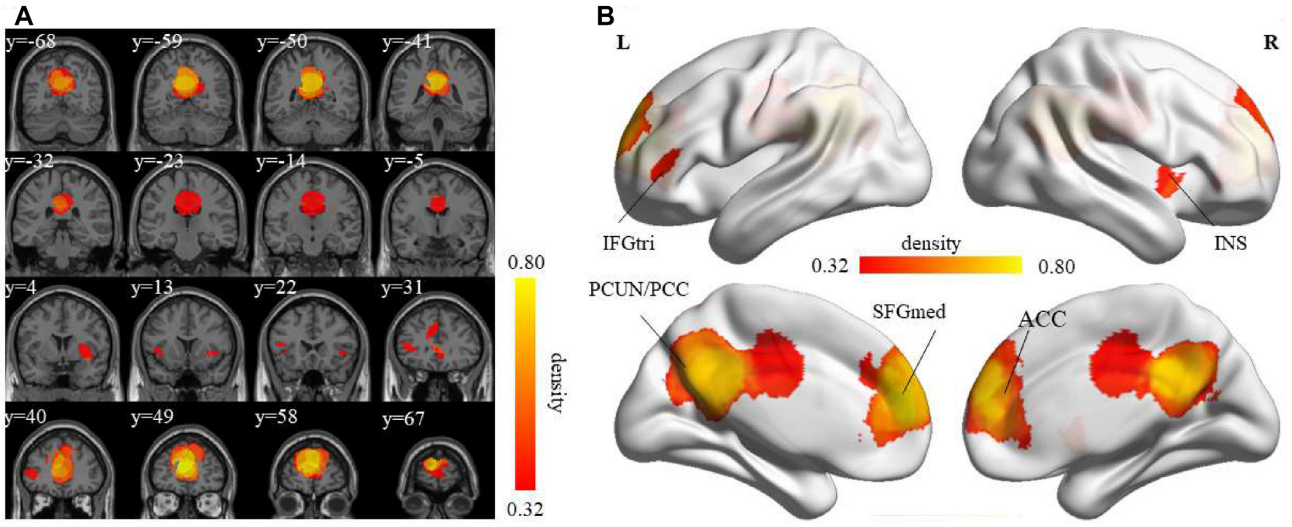

Figure 3: Results from meta-analysis of rumination. Results survived a cluster-level $P < 0.05$ family-wise error corrected for multiple comparisons and cluster-forming threshold $P < 0.001$ at voxel level. Results in transverse slices are shown on the left panel, and results projected to the surface are shown on the right panel. L/R, left/right hemisphere; IFGtri, IFG triangular part; INS, insula; PCUN, precuneus; SFGmed, medial superior frontal gyrus.

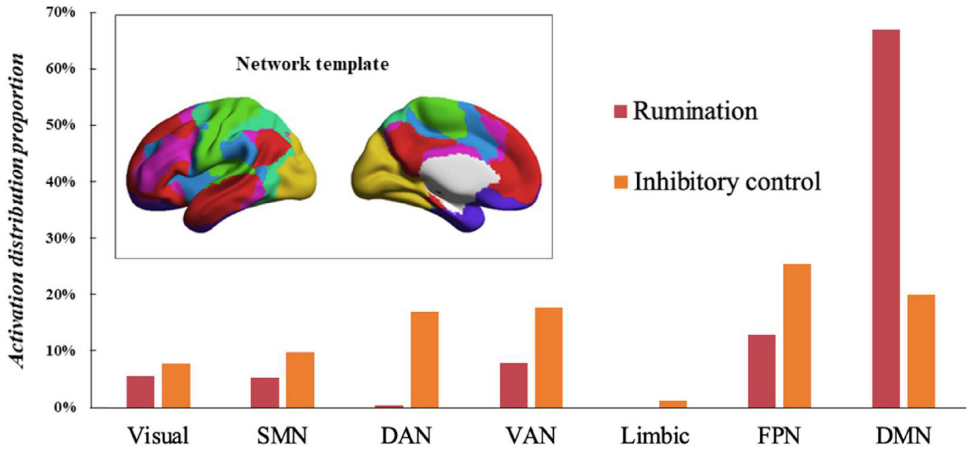

Figure 4: Relative proportions of voxels that overlapped with Yeo's seven-network parcellation. They were calculated after excluding voxels that were not classified into any of the seven networks. Visual, visual network; Limbic, limbic system.

foci were extracted, including 17 experimental contrasts (Table S1 in the Supplementary Data).

The inhibitory control meta-analysis included 205 articles that met the inclusion criteria. The sample size was 5156. The proportion of men was ~48.9% and the proportion of women was ~51.1%; 3791 foci were extracted, including 247 experimental contrasts (Table S2 in the Supplementary Data).

Main effect of rumination

An MKDA meta-analysis was performed on 180 foci from 17 studies typifying rumination. As anticipated, consistent activation was found in the bilateral insula, bilateral medial superior frontal gyrus (mSFG), left anterior cingulate cortex (ACC), left triangular part of the IFG, bilateral precuneus, and bilateral posterior cingulate cortex (PCC) (Fig. 3, Table S4 in the Supplementary Data). We further explored the distribution of rumination in different network parcellations and found that 67.5% of all voxels of rumination-related activation were distributed in the DMN, followed by 13% in the FPN, 8% in the VAN, 5.6% in the visual network, 5.4% in the SMN, and 0.5% in the DAN (Fig. 4).

Main effect of inhibitory control

MKDA meta-analysis was performed on 3791 peak coordinates from 205 inhibitory control studies. Results showed that inhibitory control activated the frontal lobe, including the bilateral middle frontal gyrus, bilateral supplementary motor area, bilateral SFG, bilateral triangular part of the IFG, and bilateral precentral gyrus, as well as the parietal lobe, including the bilateral angular gyrus, bilateral inferior parietal lobule, and bilateral precuneus (Fig. 5, Table S5 in the Supplementary Data). Notably, 25.7% of voxels were classified as part of the FPN, versus 20.2% for the DMN, 17.9% for the VAN, 17.1% for

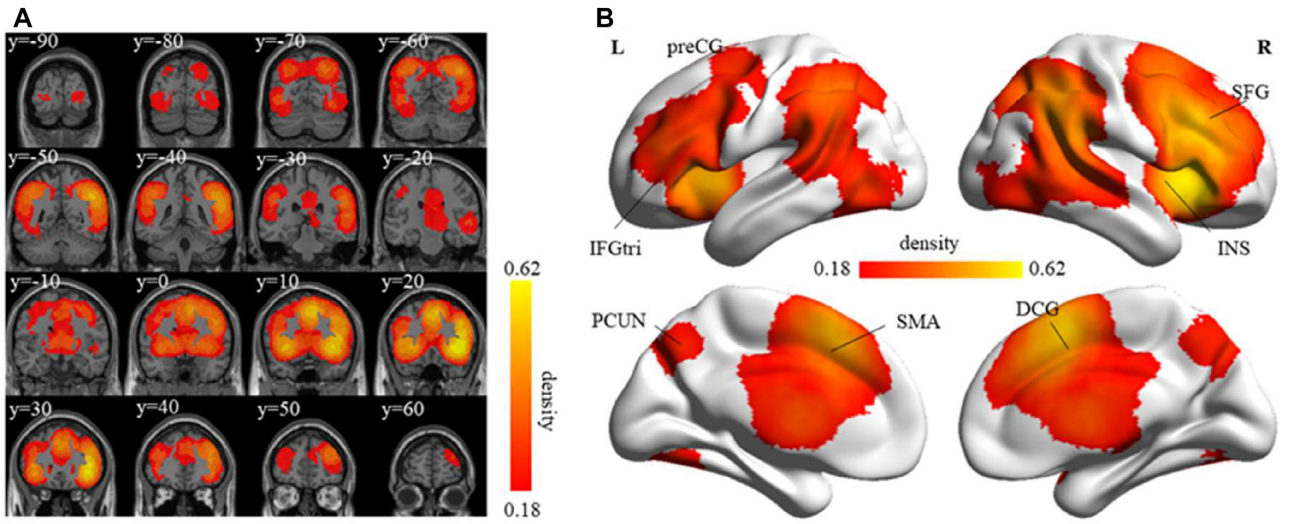

Figure 5: Results from meta-analysis of inhibitory control. Results survived a cluster-level $P < 0.05$ family-wise error corrected for multiple comparisons and cluster-forming threshold $P < 0.001$ at voxel level. Results in transverse slices are shown on the left panel, and results projected to the surface are shown on the right panel. L/R, left/right hemisphere; preCG, precentral gyrus; IFGtri, IFG triangular part; INS, insula; PCUN, precuneus.

the DAN, 10% for the SMN, 7.8% for the visual network, and 1.3% for the limbic network (Fig. 4).

Common activation regions and related cognitive processes

Results showed that the areas where rumination and inhibitory control were coactivated were mainly focused in the bilateral precuneus, right SFG, bilateral median cingulate and paracingulate gyri (DCG), and left triangular part of the IFG (see Fig. 6a). By overlapping these clusters with the seven-network parcellation, we found that the common activation areas were primarily distributed in the FPN (33.4%) and DMN (33%), while the remaining voxels were distributed in the VAN (17.2%), SMN (13.9%), visual network (1.8%), and DAN (0.7%).

To further identify the cognitive correlation of common activation regions, we decoded the brain regions acquired from the conjunction analysis. Among the top 50 cognitive terms most relevant to common activation regions (Table S3 in the Supplementary Data), words such as “inhibit,” “inhibitory,” “incorrect,” “stop signal,” and “response inhibition” all reflected the characteristics or processes of inhibitory control. Additionally, words such as “recognition memory,” “retrieved,” “memory retrieval,” and “recollection” referred to the features of rumination, that is, recalling negative past events or emotions, which is closely related to the retrieval of autobiographical memory or episodic memory (Fig. 6b and c).

Furthermore, to better understand the individual contribution of each region to cognitive correlation, we decoded the precuneus, SFG, DCG, and triangular part of IFG, and extracted the top 10 cognitive terms with the highest correlation (Fig. S1 in the Supplementary Data). Results showed that DCG mainly reflected inhibitory control, the precuneus mainly reflected rumination-related processes such as memory retrieval, and the SFG and triangular part of the IFG reflected comprehensive processes, including semantic, task, and strategy processes.

Publication bias estimation

Results are shown in Fig. S7 in the Supplementary Data. Both the funnel plots of rumination and inhibitory control meta-analysis were asymmetrical, indicating that there was a possibility of publication bias.

The imbalance of literature quantity did not significantly affect critical areas

We found relatively consistent spatial distributions, indicating that any deviation caused by a single study was not particularly large. Additionally, to provide a more intuitive representation of the consistency among the 17 rumination studies, we added up and averaged the 17 leave-one-out activation maps to obtain a mean map (Fig. S5a in the Supplementary Data). We found that the key regions shown in this figure were consistent with areas in the rumination meta-analysis (with all 17 studies). We also calculated statistics on the regions from the 17 leave-one-out meta-analysis results (Table S6 in the Supplementary Data). Additionally, results of the conjunction analysis between the 30 randomly selected inhibitory control studies and 17 rumination studies were shown in Fig. S6 in the Supplementary Data. Our sensitivity analysis results indicate that the unbalanced literature did not significantly affect the critical areas.

Discussions

In this study, we used coordinate-based MKDA analyses to determine consistent neural activation areas of rumination and inhibitory control. After that, conjunction

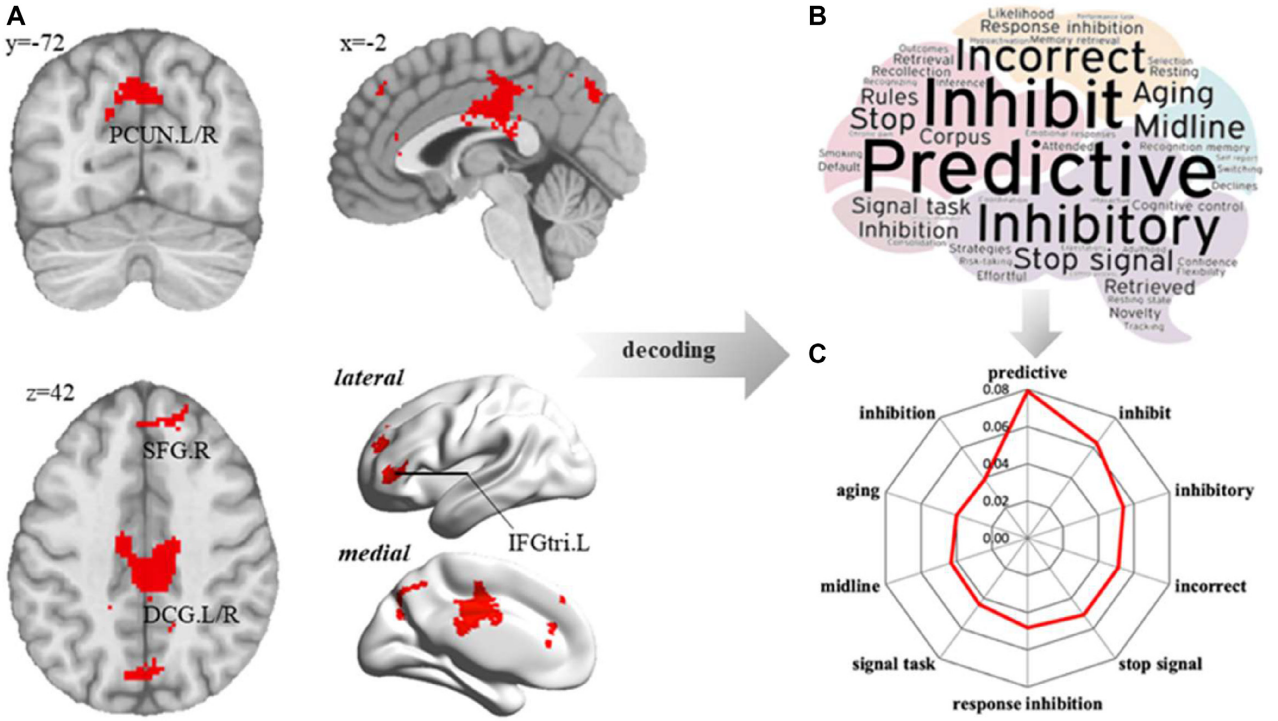

Figure 6: Results of conjunction analysis and Neurosynth decoding. (A) Common activation regions between rumination and inhibitory control. L/R, left/right hemisphere; PCUN, precuneus; IFGtri, IFG triangular part. (B) The top 50 cognitive terms were presented in a word cloud in which text size corresponded to the strength of association between the terms and common activation regions (anatomical terms were removed). (C) The polar chart showed correlation coefficients of the top 10 cognitive terms, which revealed the specificity of cognitive function decoded from meta-analysis.

analysis was performed to identify the common engaged network between these areas. Our meta-analytic findings on rumination revealed a broad DMN, including the mSFG, precuneus, and PCC, while the inhibitory control meta-analysis showed significant activation in the FPN, including the middle frontal gyrus, triangular part of the IFG and supplementary motor area. Moreover, the results of the conjunction analysis and decoding suggest that rumination and inhibitory control are spread over shared brain regions, including the precuneus, SFG, DCG, and the triangular part of the IFG, which can help to understand and predict the occurrence of rumination from the perspective of inhibitory control.

Rumination involves negative emotions, memory retrieval and self-referential processing

The involvement of the bilateral insula, bilateral mSFG, left ACC, left triangular part of IFG, bilateral precuneus, and bilateral PCC were reported in our rumination meta-analysis results. The medial prefrontal cortex (mPFC), which encompasses the mSFG, is considered the main neural basis of self-referential processing (De Pisapia *et al.*, 2019). In particular, the ventromedial PFC is always active during autobiographical recalling and thinking about self-related events (Bonnici and Maguire, 2018). The activation of ventromedial PFC, in addition, is directly related to the occurrence of negative emotion (Etkin *et al.*, 2011). Other brain areas in our meta-analysis are also related to self-processing. For instance, an fMRI study demonstrated that the PCC was significantly activated when engaging in self-referential processing (Kelley *et al.*, 2002). Further subdividing the types of self-referential processing, Lian *et al.* (2010) found that both explicit and implicit self-processing activated the PCC and precuneus. Therefore, both the PCC and precuneus are associated with processing self-related information (Buckner *et al.*, 2008; Freton *et al.*, 2014), and the precuneus is involved in episodic memory retrieval (Cavanna and Trimble, 2006). To a certain extent, these findings explain the phenomenon that ruminating individuals recall self-related events and emotions, and carry out excessive self-processing.

Generally, the ACC is involved in negative emotion and cognitive control (Tolomeo *et al.*, 2016). Furthermore, when the ACC is over-activated, it will affect attentional shifting (Wu *et al.*, 2017), and people are more likely to be attached to their thoughts and behaviors, which is in line with the characteristics of rumination (Koster *et al.*, 2011). Additionally, neuroimaging studies have found that the insula may be closely related to negative emotion (Stein *et al.*, 2007). In short, these brain regions reflect processes related to self-referential processing, episodic memory retrieval, and negative emotions, which represent the core processes of rumination.

An antagonistic relationship between the DMN and FPN reveals the possible effect of inhibitory control on rumination

Our study found that 67.5% of rumination-activated voxels were distributed in the DMN and 25.7% of inhibitory control voxels were distributed in the FPN. This is consistent with previous studies' findings that DMN was the principal neural substrate of rumination (Zhou *et al.*, 2019) and the FPN was the most involved network in inhibitory control (Zhang *et al.*, 2017). Importantly, the common activation regions between rumination and inhibitory control are mainly distributed in the DMN (33%) and FPN (33.4%), which operate in a competitive and antagonistic relationship during tasks requiring externally directed attention (Gao and Lin, 2012; Xin and Lei, 2015). The DMN participates in the adjustment of the internal guidance process, which is strongly linked to self-related processing (Raichle *et al.*, 2001). The FPN allows individuals to focus attention on goal-directed information and block goal-irrelevant information through top-down control (Camilleri *et al.*, 2018). Low activation or deactivation of the DMN therefore helps individuals suppress irrelevant ideas and focus on a task (Xin and Lei, 2015).

Similarly, Brzezicka (2013) found that in patients with depression, the DMN showed aberrantly high activity, while the activity of the FPN circuit was decreased significantly. He pointed out that deficits in the FPN may be the key mechanism causing problems with flexible cognitive and EF, and therefore may be the core reason for typical depressive symptoms such as rumination. Therefore, the antagonistic relationship between the DMN and FPN support an understanding of the relationship between rumination and inhibitory control. Deficits in inhibition control affect the ability to control the content of working memory, which may lead to some adverse cognitive and emotional consequences, one of which is rumination (Joormann *et al.*, 2008).

Common brain regions and decoding results reflect the process of rumination and inhibitory control

The conjunction analysis indicated that rumination and inhibitory control involved common areas in brain, supporting the conclusions of existing behavioral studies that rumination is related to inhibitory control (Ballesio *et al.*, 2019; Zareian *et al.*, 2021). Among the brain regions revealed by results, the SFG and IFG, as part of the PFC, are closely related to attention, action planning, EF, and emotional regulation (Funahashi and Andreau, 2013; Numan, 2015). The PFC is involved in higher-order EF; the right hemisphere is particularly important for behavioral inhibition (Arnsten, 2006). In addition, the reduction of prefrontal lobe control is the core of long-term self-referential thinking (Koster *et al.*, 2011). An impaired PFC, therefore, will lead to distraction and EF deficits, causing an inability to divert attention from the self and inhibiting task-irrelevant behaviors, which may be the key to explaining the occurrence of rumination. Additionally, the precuneus, as one of the overlapping regions between rumination and inhibitory control, not only plays a role in episodic memory retrieval and self-processing, as mentioned, but also participates in response inhibition (Criaud *et al.*, 2017; Lemire-Rodger *et al.*, 2019). We also performed conjunction analyses between rumination and subcomponents of inhibitory control (i.e., cognitive inhibition and response inhibition), which again highlighted the brain regions mentioned previously (Figs S3, S4 in the Supplementary Data). In recent years, some studies have integrated emotional stimuli into the inhibitory control paradigms (Verbruggen and Houwer, 2007; Sagaspe *et al.*, 2011), and classified emotional interference as a subtype of inhibitory control. Their findings imply that inhibitory control in the presence of emotional information may be different from inhibitory control in neutral situations (Kalanthroff *et al.*, 2013). Emotional interference, however, was not included in our study in consideration of the fact that emotional processing typically activates its unique neural system such as the amygdala (Han *et al.*, 2014). Additionally, existing studies have revealed that rumination reflects the failure of cognitive control over the events that have occurred and is related to negative cognition (Ciesla and Roberts, 2007), while negative emotion is the consequence and external manifestation of rumination (Watkins and Roberts, 2020). Therefore, our discussion of the mechanism of rumination focuses on the cognitive aspects of inhibitory control (i.e., cognitive inhibition and response inhibition) rather than on emotional interference.

Cognitive processes decoded by common regions include not only the core processes of inhibitory control, but also the core processes of rumination. On one hand, this proves the functional specificity of the coactivated areas. On the other hand, these coactivated brain areas may serve as key nodes, and cognitive processes in which they are involved further link inhibitory control with the occurrence of rumination. Consequently, applying neuromodulation techniques to pivotal brain areas may improve ability of inhibitory control and reduce rumination. For example, using transcranial direct current stimulation to stimulate the left prefrontal cortex can provide beneficial changes in the inhibitory control process and reduce rumination (Vanderhasselt *et al.*, 2013). Some researchers believe that the tendency of rumination can be reduced by some methods of improving inhibition control (Roberts *et al.*, 2016), such as working-memory training programs (Jaeggi *et al.*, 2015).

Limitations

Based on previous theoretical and empirical studies, we hypothesized that inhibitory control may be involved in rumination, which was supported by our results. However, our study was not preregistered, which might lead readers to be more cautious about the conclusions. In

the future, we will preregister the followup studies in time. What is more, some limitations in the current study need to be considered. First, only 17 articles were included in the rumination meta-analysis due to the limited number of relevant fMRI studies, which was relatively unbalanced compared with inhibitory control. Although our sensitivity analysis showed that the unbalanced quantity of including studies did not significantly affect the core brain regions, future research should be updated to make it more comprehensive and persuasive. Second, coordinate-based meta-analysis methods, including MKDA, use peak coordinates from neuroimaging studies, thus ignoring some useful information in raw coordinate data. Third, the impact of sex differences is unclear (Puiu *et al.*, 2020). For example, some evidence indicated that women showed greater activation in numerous cortical areas than men during inhibition-related tasks (Garavan *et al.*, 2006), while other evidence showed the opposite (Li *et al.*, 2006). Future endeavors should highlight sex-specific neural networks. Fourth, results show a widespread brain network in inhibitory control, which could be related to the quantity of studies included in this meta-analysis. While this may have a little effect on the accuracy of our conjunction analysis, our stability analysis indicates that we can still be confident about the conclusions. In the latter, we randomly selected 30 inhibitory control studies for a meta-analysis and then conducted a conjunction analysis with the rumination meta-analysis result (17 studies). The stability analysis yielded no significant difference from the original conjunction analysis result. Future studies should attempt to include more studies or adopt other parameters to make the results more comprehensive and convincing. Fifth, our study focused on the relationship between inhibitory control and rumination, that is, difficulty in inhibiting negative cognition may be responsible for rumination. However, inhibitory control is regarded as an implicit or automatic means in emotion regulation (Braunstein *et al.*, 2017), and it is necessary to further explore the mechanism of rumination in combination with explicit emotion regulation strategies such as reappraisal (Aldao *et al.*, 2010).

Conclusions

Rumination was mainly related to the DMN, while inhibitory control was associated with the FPN. The antagonistic relationship between the FPN and DMN links control to self-related processes, providing a unique perspective to understand the relationship between rumination and inhibitory control. Additionally, conjunction analysis determined that they have common activation regions, and decoding results further suggested that inhibitory control may connect with rumination by suppressing task-irrelevant attention and dominating self-related processing. Taken together, these results provide hints for improving the treatment of rumination, whether through behavioral training of inhibitory control or the application of neuromodulation techniques to common brain regions.

Supplementary data

Supplementary data are available at *Psychoradiology* online.

Conflicts of interest statement

Dr. Tatia M.C. Lee, being an associate editor of *Psychoradiology*, was not involved in the review and the decision on the manuscript.

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