Neurobiological models of emotion regulation: a meta-analysis of neuroimaging studies of acceptance as an emotion regulation strategy

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Abstract

Emotional acceptance is an important emotion regulation strategy promoted by most psychotherapy approaches. We adopted the Activation Likelihood Estimation technique to obtain a quantitative summary of previous fMRI (functional Magnetic Resonance Imaging) studies of acceptance and test different hypotheses on its mechanisms of action. The main meta-analysis included 13 experiments contrasting acceptance to control conditions, yielding a total of 422 subjects and 170 foci of brain activity. Additionally, subgroups of studies with different control conditions (react naturally or focus on emotions) were identified and analysed separately. Our results showed executive areas to be affected by acceptance only in the subgroup of studies in which acceptance was compared to natural reactions. In contrast, a cluster of decreased brain activity located in the posterior cingulate cortex (PCC)/precuneus was associated with acceptance regardless of the control condition. These findings suggest that high-level executive cortical processes are not a distinctive feature of acceptance, whereas functional deactivations in the PCC/precuneus constitute its specific neural substrate. The neuroimaging of emotional acceptance calls into question a key tenet of current neurobiological models of emotion regulation consisting in the necessary involvement of high-level executive processes to actively modify emotional states, suggesting a complementary role for limbic portions of the default system.

Key words: acceptance; emotion regulation; meta-analysis; ALE; Default Mode Network; mindfulness; posterior cingulate

Introduction

Recognition of the value of emotional acceptance for emotional well-being has philosophical and religious roots that date back thousands of years (Graver, 2008). In the context of the scientific investigation, acceptance has been conceptualized as a regulation strategy based on an open and welcoming attitude towards emotions, thoughts or events (Williams and Lynn, 2010). It consists of a mental stance characterized by openness and a non-judgemental attitude towards on-going emotional experiences (Grecucci *et al.*, 2015; Goldin *et al.*, 2019), without trying to control, change, suppress or avoid them. Acceptance also refers to a sense of curiosity about emotions. This entails a perspective that does not see emotions and thoughts as threatening, but rather as mental phenomena that are temporary, transient, interesting or at least neutral, sources of information about one's current mental state, and not to be feared,

changed or expunged. Early mentions of theoretical issues relevant to acceptance emerged from the thought suppression literature, which argued for the paradoxical pathogenetic effects of attempts at mental contents control (Wegner *et al.*, 1987; Wenzlaff and Wegner, 2000). More recently, the revival within clinical psychology of ancient Buddhist traditions of mindfulness meditation—a set of techniques that raise awareness by paying attention in a non-judgmental way to mental activity (Kabat-Zinn, 2013)—has led to a growing interest in the adaptive value of non-judgemental attitudes towards emotions as a means to achieving positive mental health effects. This line of inquiry has produced evidence that emotional acceptance may be effective in diminishing emotional reactivity and physiological arousal in response to aversive emotions (Campbell-Sills *et al.*, 2006; Hofmann *et al.*, 2009; Wolgast *et al.*, 2011; Grecucci *et al.*, 2015). Moreover, self-reported acceptance may positively influence perceived daily stress (Catalino *et al.*, 2017) and is associated with better mental health outcomes (Aldao *et al.*, 2010; Berking and Wupperman, 2012). Based on the findings on its effect on coping with negative emotions and stress, acceptance may be considered as an emotion regulation strategy (Hofmann and Asmundson, 2008; Wolgast *et al.*, 2013).

The relevance of emotional acceptance to mental health is also widely recognized in clinical practice. It occupied a position of primary importance in early humanistic–experiential therapy approaches (Perls *et al.*, 1951; Rogers, 1959; Berne, 1961). More recently, acceptance-based techniques have been proposed as a specific therapeutic factor in mindfulness-based interventions (where they play a prominent role, Kabat-Zinn, 2013), dialectical behaviour therapy (Linehan, 1993), acceptance and commitment therapy (Hayes *et al.*, 1999; Grecucci *et al.*, 2018), schema therapy (Dadomo *et al.*, 2016, 2018), short-term dynamic therapies (Frederickson, 2013; Grecucci *et al.*, 2020) and emotion-focused therapy (Greenberg, 2011; Grecucci *et al.*, 2020). Acceptance-based treatments have been shown to be effective in the treatment of several forms of psychopathology (Segal *et al.*, 2002; Hayes *et al.*, 2006; Bowen *et al.*, 2011; Feliu Soler *et al.*, 2018; Grecucci *et al.*, 2018). More generally, in most psychotherapy approaches, patients are encouraged to freely observe and explore their own mental activity. Hence, acceptance may be considered a non-specific, common outcome across different psychotherapy approaches (Martin, 1997; Sambin and Messina, 2017).

The unquestionable clinical relevance of acceptance, however, is in contrast with the poor empirical investigation of this emotion regulation strategy in the clinical and affective neurosciences, at least when compared to other strategies (such as reappraisal). A reason of this relative neglect can be attributed to the fact that acceptance was not originally considered by influential models of emotion regulation (such as Gross's process model, Gross, 1998). In this respect, the concept of acceptance breaks with the established tradition in affective neuroscience that identifies emotion regulation with cognitive control, as this latter is recruited 'to actively modify an emotional state in terms of quality, strength, length, or frequency of emotion' (Gross, 2015). Within the affective neurosciences, evidence for this view of emotion regulation has been sought in neuroimaging studies of reappraisal, in which participants were exposed to negative emotional stimuli and were instructed to modify (the opposite of acceptance) their emotional reactions (Ochsner *et al.*, 2002). In these studies, findings of increased activation of cortical areas associated with working memory and executive function—such as the dorsolateral prefrontal cortex, the dorsal anterior cingulate and the ventrolateral prefrontal cortex—together with decreased activity in subcortical areas (the amygdala) have been marshalled in support of a dual-process model that describes emotion regulation as the result of interactions between prefrontal cognitive control systems accounting for 'top-down' modulation and subcortical systems that support 'bottom-up' emotional reactivity (Ochsner and Gross, 2005; Ochsner *et al.*, 2012; Messina *et al.*, 2015). Even if some acceptance instructions included attentional components, which would account for the involvement of controlled processes (see Table 1), they always precluded any deliberate attempt to modify emotional states. Therefore, the resulting response comes much closer to a 'let it be' non-interference attitude towards emotions, thoughts and bodily reactions associated with emotions, which consequently differs substantially from emotional control. In the following, we will refer to emotion regulation strategies based on changing affect aroused by stimuli as the 'traditional' strategies to distinguish them from acceptance-based strategies.

Due to the relevance of top-down control in traditional emotion regulation models, a first question of this study regarded the involvement of executive areas in acceptance-based regulation. Neuroimaging studies of acceptance have provided mixed evidence in this respect. In some studies, prefrontal activations of the dorsal attention network have been reported in acceptance, consistently with recruitment of cognitive control as in traditional emotion regulation strategies (Lebois *et al.*, 2015; Goldin *et al.*, 2019). In other studies, even if prefrontal activations were reported, they were less than in traditional strategies and/or located more medially (Murakami *et al.*, 2015; Smoski *et al.*, 2015; Ellard *et al.*, 2017). Finally, yet other studies reported that acceptance of emotions occurred in the absence of detectable increases in prefrontal cortical areas associated with top-down control (Kross *et al.*, 2009; Westbrook *et al.*, 2013; Kober *et al.*, 2019; Dixon *et al.*, 2020).

Besides executive areas associated with cognitive control, the neuroimaging literature has drawn attention to the possible involvement of the Default Mode Network (DMN) (Ellard *et al.*, 2017), a set of areas usually deactivated during attention-demanding tasks (Raichle, 2015) associated with mind-wandering (Mason *et al.*, 2007; Fox *et al.*, 2015; Mittner *et al.*, 2016). Since mind-wandering has been considered as the opposite of mindfulness (Mrazek *et al.*, 2012), it has been suggested that the 'interruption' of ruminative processing that characterizes mindfulness-based emotion regulation strategies may modulate the DMN activity (Ellard *et al.*, 2017). This suggestion is consistent with findings of hyper-activation of the DMN in depression (Sheline *et al.*, 2009; Messina *et al.*, 2016a), anxiety (Zhao *et al.*, 2007) and more in general in conditions of emotional dysregulation (Whitfield-Gabrieli and Ford, 2012; Buckner *et al.*, 2019). A further reason to investigate the involvement of the DMN is its relationship with semantic association areas (Binder *et al.*, 2009). In the context of emotion regulation, the DMN and the surrounding association cortex have been hypothesized to be involved in regulation by modulating semantic processing of emotional stimuli (Viviani, 2013; Messina *et al.*, 2016b, 2020).

In summary, the strategy of acceptance to regulate emotions calls into question a key tenet of current neurobiological models of emotion regulation, consisting in the involvement of top-down control associated with recruitment of cortical areas associated with working memory and executive processes. Available studies have produced mixed evidence concerning the involvement of substrates of the executive system. An alternative hypothesis consists of the modulation of the activity of the DMN. To shed light on this issue, we adopted a meta-analytic approach, which allowed us to combine data across neuroimaging studies with a similar experimental design.

Table 1. Overview of acceptance studies included in the meta-analysis

Studies	N	Design	Stimuli	Acceptance instruction	Control condition instruction	N foci A > C	N foci C > A
1. Kross et al. (2009)	24 healthy (15 F)	Blocks within subjects	Negative autobiographical memories (cue phrases)	'... to recognize that the feelings they experienced during recollection were passing mental events that were psychologically distant from the self and did not control them.'	'... to focus on the specific feelings that naturally flowed through their mind as they thought about their recalled experiences.' (CFE)	0	3
2. Lutz et al. (2014)	46 healthy (15 F)	Between-group design	Negative pictures	'Try to consciously be aware of yourself, of what happens to you at this moment. Do this while expecting the picture and while looking at it. Do not judge; remain conscious and attentive to your present state. You may focus on thoughts, on emotions or on bodily sensations.'	'... to expect and perceive the emotional stimuli.' (CNR)	3	2
3. Smoski et al. (2015a)	19 healthy (12 F)	Event-related within subjects	Sad pictures	'To accept, your task is to notice what you are thinking and feeling, and to allow those thoughts and feelings to be there. So rather than try to push the feeling or thought away or try to feel differently, you just acknowledge it, perhaps saying, "That's just how it is right now," "This feeling will come and go," or "I can accept this thought." Note that acceptance doesn't mean that you have to like the feeling, or that you are resigning yourself to the feeling. It is reminding yourself that it's ok to feel what you feel without having to change it'	'... not to regulate their emotion response.' (CNR)	8	–
4. Smoski et al. (2015b)	18 Remitted MDD (14 F)					5	–
5. Murakami et al. (2015)	21 healthy (11 F)	Event-related within subjects	Negative IAPS	'... to observe objectively and describe their subjective feelings or thoughts in their minds, and physiological changes in bodies, not with voice but just mentally, and to not suppress the emotions that are evoked by viewing the negative pictures.'	'Simply look at the neutral or negative pictures and respond naturally.' (CNR)	22	–
6. Lebois et al. (2015)	30 healthy (15 F)	Blocks within subjects	One-sentence stressful scenarios	'... to remain aware of their current physical location while thinking about the scenarios. They were further asked to notice the kinds of reactions that they normally have during immersion, but rather than "living" the event, they were instructed to simply observe their thoughts and reactions to it in the present moment. Participants were asked to perceive their thoughts about the stimuli as transitory mental states, not as parts of the scenarios, but as their psychological responses to them.'	'Become completely absorbed in the experience of the scenarios, as if they were happening in the moment. They were to mentally time travel and experience the sensory details, physical sensations, feelings, emotions, and bodily states associated with engaging in the scenario vividly.' (CFE)	14	18

Table 1. (Continued)

Studies	N	Design	Stimuli	Acceptance instruction	Control condition instruction	N foci A > C	N foci C > A
7. Westbrook et al. (2013)	47 smokers (31 F)	Event-related within subjects	Craving stimuli	'… to actively focus on their responses to the picture, including thoughts, feelings, memories and bodily sensations, while maintaining a nonjudgmental attitude toward those responses'	'… simply to relax and view the picture as naturally as possible' (CNR)	0	1
8. Ellard et al. (2017)	21 GAD (21 F)	Blocks within subjects	Worry statements	'Observe and accept. "Observing" means instead of trying to do something about the distress you feel when you read statements about things you are worried about, try to observe your reaction in an objective way[…] "Accept" means allowing yourself to feel distress, knowing that this distress will peak and fade, and that it is ok to have this initial reaction.'	'… just let yourself respond in whatever way you might naturally respond when you think about these topics. Don't try and stop yourself from worrying, just let yourself worry as you might usually do.' (CFE)	2	10
9. Kober et al. (2019a)	17 healthy (5 F)	Blocks within subjects	Negative IAPS	'… to attend to and accept their experience as it is. This instruction was modeled after the two-component […] (i) attention to present moment sensation, coupled with (ii) non-judgmental acceptance of the sensation as it is, allowing it to exist without trying to avoid it or react to it.'	'React naturally, whatever your response might be' (CNR)	0	3
10. Kober et al. (2019b)			Pain			0	9
11. Goldin et al. (2019)	35 healthy (15 F)	Event-related within subjects	Negative self-belief statements	'… simply observing and accepting without judgment from moment to moment (and not attempting to modify or change) any responses, including thoughts, emotions, memories, images, and physical sensations.'	'… reacting to negative self-beliefs by considering how it reflected something true about themselves' (CFE)	11	4
12. Dixon et al. (2020a)	113 SAD (61 F)	Blocks within subjects	Negative self-belief statements	'to regulate their reaction by cepting their reactions, which involved a nonjudgmental monitoring of thoughts, memories, emotions, and sensations as they appeared and dissolved, without modifying or avoiding them.'	'to react to the negatives statements by reflecting on how the NSB may describe something true about themselves and to let themselves feel the sting of the statement' (CFE)	2	9
13. Dixon et al. (2020b)	35 healthy (22 F)					0	6

N foci A > C = Number of foci for acceptance versus control condition.
N foci C > A = Number of foci for control condition versus acceptance.
IAPS = International Affective Pictures System.
GAD = Generalized Anxiety Disorder.
F = female.

In the present study, the coordinates-based Activation Like-lihood Estimation (ALE) method (Laird *et al.*, 2005) was used to obtain an objective, systematic and quantitative summary of previous neuroimaging studies of emotion regulation which have considered acceptance as emotion regulation strategy.

Method

Data sources

Neuroimaging studies on acceptance were collected through advanced searches in Google Scholar (http://scholar.google.com/databases) and PubMed (https://www.ncbi.nlm.nih.gov/pubmed) of all articles that mentioned in the title the terms 'acceptance' and/or 'mindfulness' together with the terms 'fMRI' (functional Magnetic Resonance Imaging) or 'neuroimaging'. Additional studies were obtained reviewing the references of papers using the Google Scholar database. We excluded from the retrieved studies those that investigated neural effects of medi-tation or meditation trainings, that involved meditators partici-pants and that investigated acceptance and/or mindful attitude as a personality trait. We included all studies that used fMRI to investigate the neural correlates of acceptance using a typical emotion regulation design in which participants were exposed to emotional stimuli and instructed to use acceptance to reg-ulate emotional reactions compared to a control condition (see Table 1 for a review of stimuli and task instructions). As shown in Table 1, when operationalizing acceptance, researchers use dif-ferent instructions, stressing one or more components of accep-tance, such as willingness to take in emotions, being present (mindfulness), cognitive defusion, self as a context, and concen-tration on values and commitment. This variety of instructions has been previously observed also in reviews of behavioural studies (Kohl *et al.*, 2012; Wojnarowska *et al.*, 2020). Following these criteria, a total of 10 papers and more than 400 partici-pants were examined (the main features of included studies are shown in Table 1). All reported significant reductions of neg-ative emotions in the acceptance condition, compared to the control condition (with the exception of Kross *et al.*, 2009 that did not report behavioural results). Studies with two different experimental conditions (Kober *et al.*, 2019) or with different groups of participants analysed separately (Smoski *et al.*, 2015; Dixon *et al.*, 2020) were considered as separate samples (these studies are reported in Table 1 as 'a' and 'b' to mention dif-ferent conditions), yielding a total of 13 studies. From these studies, we extracted foci reported in three-dimensional (3D) coordinates (*x, y, z*) in stereotactic space that resulted signifi-cantly activated for the contrast between an acceptance regu-lation condition *vs* a control condition (increased brain activity in acceptance) and control condition *vs* acceptance regulation (decreased brain activity in acceptance). Verbatim instructions of acceptance regulation and control conditions are reported in Table 1.

Among the selected studies, we noted that two subgroups of studies differed in the control condition used in the experimen-tal design. In the first subgroup (Contrast to Natural Reaction—CNR), in the control condition, participants were instructed to naturally 'look' or 'react' to the experimental stimuli. In the second subgroup (Contrast to Focus on Emotions—CFE), more complex instructions were given to increase the focus of partic-ipants on their emotional experience. Example of these instruc-tions was 'to focus on the specific feelings' (Kross *et al.*, 2009) or 'become completely absorbed by feeling' (Lebois *et al.*, 2015). Due to possible systematic discrepancies in the patterns of brain activity across studies attributable to differences in control con-ditions used as baseline for contrast analysis, we also conducted explorative meta-analyses of CNR and CFE subgroups consid-ered separately. Among the 13 studies, 7 experiments were included in the CNR subgroup, and 6 experiments were included in the CFE subgroup.

Meta-analytic procedure

To conduct the meta-analyses, the ALE method for coordinate-based meta-analysis of neuroimaging data was used (Eickhoff *et al.*, 2009). This method is based on the evaluation of the over-lap between foci of brain activity reported in different studies and treats the reported foci not as single points, but as cen-tres for 3D Gaussian probability distributions capturing their spatial uncertainty. An algorithm is used to identify clusters of brain activity that show a convergence of activation across experiments and determine if the clusters obtained occur more frequently than in the null distribution arising from random spa-tial distribution of foci across the experiments. The procedure weights foci of brain activity reported in single studies by the number of participants, yielding a quantitative estimate of the probability of activation identifying common activations across studies (Laird *et al.*, 2005). Significance values were obtained with permutation tests. The observed values in the ALE distribu-tion are then compared to the null distribution in order to assign probability estimates to the observed data.

ALE meta-analyses were carried out using GingerALE 2.3.2 software as distributed by the BrainMap project (http://www.brainmap.org/ale/). The 'non-additive' method was used, which models each focus with a Gaussian function defined by a full width at half-maximum kernel size empirically determined by finding the maximum across each focus's Gaussian. The non-additive method allows the modelling of the spatial uncer-tainty of each focus arising from inter-subject and inter-study variability. The meta-analyses were performed in Montreal Neurological Institute (MNI) space. Coordinates reported in studies in Talairach coordinates space were transformed into MNI using the Lancaster transform, icbm2tal algorithm in Ginger ALE (Laird *et al.*, 2005). The probability maps were thresh-old at $P < 0.05$ and corrected for multiple testing using the false discovery rate approach (Genovese *et al.*, 2002). SurfIce software (https://www.nitrc.org/plugins/mwiki/index.php/surf-ice:MainPage) was used to obtain brain renderings.

Results

Meta-analysis of all acceptance studies

The analysis of the contrast between acceptance *vs* all control conditions included the data collected from 13 experiments, for a total of 422 subjects, yielding 61 foci of brain activations. No significant clusters of increased brain activity emerged from this analysis.

The analysis of the contrast between the control conditions *vs* acceptance included the data collected from 10 experiments (3 experiments did not analyse this contrast; see Table 1 for information concerning reported foci of brain activity), for a total of 364 subjects, yielding a total of 109 foci of significant brain activity. A significant cluster of decreased brain activity in the acceptance condition relative to control emerged from this analysis. This cluster was located in the posterior cingulate cor-tex/precuneus (PCC), insula and limbic subcortical areas such

Table 2. Foci of significant brain activity in control conditions compared to acceptance condition

| Cluster	Areas (Brodmann's areas)	MNI coordinates			ALE score	Z	P	Cluster size (mm³)
		Y	Y	Z				
1	Culmen (BA 30)	−4	−54	6	0.013	3.99	<0.001	20 344
	Posterior cingulate (BA 31)	−6	−56	26	0.012	3.83	<0.001	
	Thalamus	−10	−32	6	0.010	3.47	<0.001	
	Thalamus	−18	−34	14	0.010	3.38	<0.001	
	Lingual gyrus (BA 27)	0	−34	2	0.010	3.36	<0.001	
	Posterior cingulate (BA 29)	6	−52	12	0.009	3.15	<0.001	
	Parahippocampal gyrus (BA 30)	−12	−44	−2	0.009	3.14	<0.001	
	Parahippocampal gyrus (BA 30)	14	−38	4	0.009	3.11	<0.001	
	Thalamus	24	−34	2	0.009	3.09	<0.001	
	Cuneus (BA 18)	−12	−72	18	0.009	3.08	0.001	
	Posterior cingulate (BA 30)	10	−54	18	0.009	3.07	0.001	
	Posterior insula (BA 13)	−38	−14	12	0.008	3.06	0.001	
	Lingual gyrus (BA 17)	−8	−70	6	0.008	3.03	0.001	
	Thalamus	−24	−22	10	0.008	2.97	0.002	
	Culmen (BA 27)	2	−46	0	0.008	2.88	0.002	

BA, Brodmann's areas.
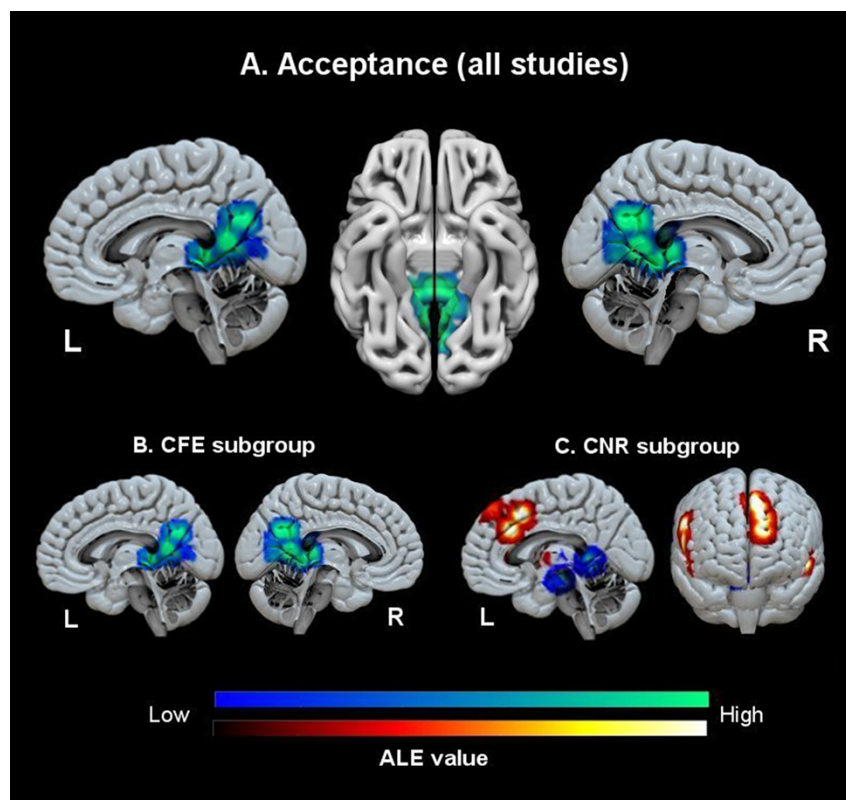
Fig. 1. Decreased (cold colours) and increased (warm colours) brain activity associated with all acceptance studies (A), CFE studies (B) and CNR studies (C).

as the thalamus and the parahippocampal gyrus (see Table 2; Figure 1).

Explorative subgroup analyses

CNR subgroup. Seven experiments reported results of the contrast acceptance *vs* natural reactions, yielding a total of 164 subjects, and 38 foci of brain activations. Four clusters of increased brain activity were found for acceptance relative to control. These clusters were located bilaterally in the inferior frontal gyrus, extending to the anterior insula and the putamen on the left side and to the frontal pole and the medial prefrontal cortex/anterior cingulate cortex (see Table 3).

Four experiments reported results of the contrast natural reaction *vs.* acceptance, yielding a total of 106 subjects, and 15 foci of brain activations. Significant clusters of decreased brain activity in acceptance relative to natural reaction were located in the posterior cingulate cortex/precuneus (PCC), right hippocampus and right superior temporal gyrus (see Table 3).

CFE subgroup. With regard to the analysis of the contrast acceptance *vs* focus on emotions (increased brain activity for

Table 3. Significant clusters of brain activity in CNR and CFE subgroups

Cluster	Areas (Brodmann's areas)	MNI coordinates			ALE score	Z	P	Cluster size (mm³)
		Y	Y	Z				
Acceptance *vs* CNR								
1	Anterior insula (BA 13)	−36	26	−4	0.012	4.40	<0.001	16 792
	Inferior frontal gyrus (BA 47)	−52	16	−6	0.009	3.64	<0.001	
	Anterior insula (BA 13)	−32	16	12	0.009	3.64	<0.001	
	Putamen	−15	3	6	0.002	1.97	0.024	
2	Inferior frontal gyrus (BA 45)	54	24	6	0.009	3.84	<0.001	10 520
	Inferior frontal gyrus (BA 45)	58	24	14	0.009	3.64	<0.001	
	Inferior frontal gyrus (BA 9)	60	18	30	0.008	3.56	<0.001	
	Inferior frontal gyrus (BA 47)	50	30	−6	0.008	3.53	<0.001	
3	Superior frontal gyrus (BA 8)	−10	52	46	0.009	3.86	<0.001	8800
	Superior frontal gyrus (BA 8)	−6	46	52	0.009	3.64	<0.001	
	Superior frontal gyrus (BA 8)	−14	58	36	0.008	3.61	<0.001	
	Superior frontal gyrus (BA 9)	−14	66	24	0.008	3.53	<0.001	
4	Medial frontal gyrus (BA 32)	10	16	42	0.009	4.01	<0.001	8544
	Medial frontal gyrus (BA 6)	6	18	44	0.009	3.97	<0.001	
	Anterior cingulate gyrus (BA 32)	4	28	30	0.008	3.56	<0.001	
CNR *vs* acceptance								
1	Lingual gyrus (BA 27)	−5	−36	5	0.009	1.68	0.046	15 872
2	Hippocampus	22	−14	−12	0.009	4.26	<0.001	12 824
	Hippocampus	12	−18	−14	0.008	3.86	<0.001	
3	Superior temporal gyrus (BA 48)	51	−24	18	0.008	3.75	<0.001	10 776
	Superior temporal gyrus (BA 48)	70	−33	24	0.007	3.34	<0.001	
CFE *vs* acceptance								
1	Precuneus (BA 30)	−4	−54	6	0.013	4.07	<0.001	19 928
	Precuneus (BA 23)	−6	−56	26	0.012	3.93	<0.001	
	Lingual gyrus (BA 27)	0	−34	2	0.009	3.39	<0.001	
	Thalamus	−18	−34	14	0.009	3.39	<0.001	
	Thalamus	−10	−34	4	0.009	3.30	<0.001	
	Posterior cingulate gyrus (BA 30)	6	−52	12	0.009	3.21	<0.001	
	Parahippocampal gyrus (BA 27)	−12	−44	−2	0.009	3.21	<0.001	
	Lingual gyrus (BA 18)	18	−54	2	0.009	3.19	<0.001	
	Parahippocampal gyrus (BA 27)	14	−38	4	0.009	3.18	<0.001	
	Thalamus	24	−34	2	0.009	3.16	<0.001	
	Cuneus (BA 18)	−12	−72	18	0.009	3.15	<0.001	
	Posterior cingulate gyrus (BA 30)	10	−54	18	0.009	3.14	<0.001	
	Lingual gyrus (BA 17)	−8	−70	6	0.008	3.10	<0.001	
	Thalamus	−24	−20	10	0.008	3.01	0.001	

acceptance), 6 experiments reported significant results and were included in the analysis, yielding a total of 258 subjects, and 23 foci of brain activations. No significant clusters emerged from this analysis.

In the contrast focus on emotions *vs* acceptance, 6 experiments reported significant results, yielding a total of 258 subjects, and 94 foci of brain activations. One significant clusters of decreased brain activity in acceptance relative to focus on emotion was located in the posterior cingulate cortex/precuneus (PCC), thalamus and parahippocampal gyrus.

Discussion

In the present meta-analytic study, we provided a synthesis of functional neuroimaging studies investigating the neural correlates of regulating emotions through acceptance-based strategies, in which participants were instructed to take on a non-judgemental attitude towards on-going emotional experiences, contrasted to naturally react or focus on negative emotions control conditions. Due to their relevance for neurobiological models of emotion processing and regulation, we were interested in clarifying the involvement of executive areas and of the DMN in the acceptance strategy.

When we tested the presence of increased brain activity in all studies included in the present meta-analysis (the main contrast acceptance *vs* control conditions)—despite decreased activity in limbic regions in acceptance (thalamus and hippocampus/parahippocampal gyrus) accounting for regulation efficacy (Frank *et al.*, 2014; Morawetz *et al.*, 2017)—no areas associated with executive processes resulted to be significantly activated by acceptance (or indeed any other cortical area). This result is in line with previous studies that reported the absence of increased activity in executive areas, and more generally with reports of the absence of increased brain activity in association with acceptance in the whole brain (Kross *et al.*, 2009; Westbrook *et al.*, 2013; Kober *et al.*, 2019; Dixon *et al.*, 2020). However, when we explored the involvement of substrates of executive functions in two different subgroups of studies differing in the control condition contrasted to acceptance, we found a significant increased activity in executive

areas only in the subgroup of studies characterized by the use of natural reaction as the control condition (Contrast to Natural Reactions—CNR; e.g. 'react naturally'). In contrast, no significant clusters of increased brain activity were observed in studies that used more complex instructions related to increasing the focus on emotional experience (Contrast to Focus on Emotions subgroup—CFE; e.g. 'become completely absorbed').

The involvement of executive areas is consistent with previous attempts to conceptualize acceptance as a specific variety of reappraisal (Webb et al., 2012; Wolgast et al., 2013) and with the presence of attentional element in acceptance instructions (see Table 1). However, this effect was not significant when acceptance was compared to control conditions requiring some amounts of cognitive load (CFE), even if these control conditions did not include instructions to down-regulate emotional response. The increased activity of executive areas only in the CNR subgroup may result from a difference in cognitive effort between the acceptance and the natural reaction control conditions, rather than a specific regulation effect. Indeed, the prefrontal effects of acceptance in the comparison with the natural reaction control condition in the CNR group overlapped with those reported in a meta-analysis of the effects of task difficulty across tasks (Radua et al., 2014).

Beyond the effects of acceptance in executive areas associated with top-down control, a remarkable aspect of many of these studies is given by frequent reports of decreased activity in acceptance relative to the control conditions, even in studies in the CNR subgroup (Lebois et al., 2015; Ellard et al., 2017; Dixon et al., 2020). These findings are upheld by the second result of the present study, which was the decrease of brain activity in the posterior cingulate cortex posterior cingulate cortex (PCC)/precuneus, posterior insula and limbic lobe in the acceptance compared to control conditions. There are two reasons for attributing this effect to acceptance, rather than to the control conditions. First, this finding was obtained regardless of the control condition. The PCC cluster was significant also when considering the two CNR and CFE subgroups separately, even if these groups differed in the control conditions they used. Second, previous meta-analyses of traditional emotion regulation studies (Buhle et al., 2014; Messina et al., 2015), did not report effects in this area in any of the considered contrasts, even if these meta-analyses were conducted on a larger database of studies than the present one.

However, effects in the PCC have been reported in individual studies in the emotion regulation literature. Activations of PCC have been reported in emotion regulation processes that, on the contrary of acceptance, have included aspects of emotional avoidance. For instance, PCC modulations have been reported in self-distancing from negative emotional pictures (Koenigsberg et al., 2010), in down-regulating the reaction to a negative stimulus by self-distraction (Kanske et al., 2011), in association with amount of eye movements to directing gaze so as to avoid aversive emotional stimuli (van Reekum et al., 2007) and in association with individual differences in spontaneous avoidance of emotional words (Benelli et al., 2012). PCC activity modulation has also been observed after psychotherapy (Buchheim et al., 2013). Thus, emotional avoidance and acceptance studies seem to show two sides of the same coin, possibly highlighting a neglected component of emotion regulation which has its neural correlate in the PCC. Future studies, specifically designed to test the association of PCC activity modulation with effective down-regulation of negative affect, may provide further evidence in support of this hypothesis.

With regard to the nature of the contribution of PCC to emotion regulation, the literature offers several hypotheses. A first interpretation emerges from considering brain activity as the result of activation and deactivation patterns in large-scale connected networks (Fox et al., 2015). The PCC is a key part of the DMN, associated with mind-wandering (Mason et al., 2007; Fox et al., 2015; Mittner et al., 2016) and ruminative processes (Cooney et al., 2010; Berman et al., 2011). Hence, the present findings would be consistent with the hypothesis that modulations of PCC activity during acceptance may be associated with the interruption of ruminative, self-reflective processes over emotions (especially when acceptance is compared to focus on emotion, which can be viewed as related to ruminative processes). Also, the posterior insula may contribute to this process, due to its role of bringing visceral sensation to the posterior network (Taylor et al., 2009; Cauda et al., 2011). Note, however, that ruminative processes, which may be expected to be most prevalent during the baseline or fixation phase rather than in a control condition, were not directly investigated in the studies included in the present meta-analysis.

A second alternative interpretation of the present findings posits that PCC would be normally activated in response to emotional stimuli and the use of acceptance strategy may modulate this activation appearing as decreased activity in the contrast with control conditions. This interpretation also accounts for the fact that in the meta-analysis, only PCC, and not the whole DMN as in mind-wandering, was found to be modulated by acceptance. However, a study specifically looking at this issue found that PCC was deactivated while appraising emotional material relative to the fixation baseline (Benelli et al., 2012).

A third interpretative approach, which is also compatible with the hypothesis of interruption of ruminative processes associated with DMN modulations, recognizes deactivation of PCC as the neural substrate of acceptance. The idea of functional deactivations related to stimulus processing is not new in the literature (Shulman et al., 2007). Research and theories are converging on the notion of brain function as computing a hierarchical predictive model of the world in which functional processing hierarchies are not confined to sensorimotor systems but terminate in heteromodal association areas where predictions are generated (Huntenburg et al., 2018). The most innovative aspect of these models is to realize that these heteromodal association areas are organized around a core constituted by the DMN (Margulies et al., 2016), which is usually deactivated by the task. Indeed, together with cortical limbic areas, heteromodal association areas are precisely those where functional deactivations are observed (Viviani et al., 2020), justifying the current interest on neural inhibition as a mechanism to select representations at the top of the sensory processing hierarchy (Hunt and Hayden, 2017). This suggests that a simple dichotomy between top-down and bottom-up processes may not adequately describe emotion regulation processes as a whole (Messina et al., 2016b).

In line with this notion, the role of cortical limbic areas, including the PCC, has been recently redefined considering their involvement in representing sensory input based on past experience, placing them at the top of the predictive hierarchy (Chanes and Barrett, 2016). Mental processes implicated in avoidance *vs* acceptance of emotional reactions may be associated with recruitment of specific hubs of the DMN, in which deactivations of PCC are functionally related to acceptance. Hence, emotion regulation may act at this level of cortical processes influencing the impact of emotional events independently of the involvement of high-level executive cortical processes, instead modulating emotion processing through the recruitment of emotional

and schematic representations (Viviani, 2013, 2014; Messina *et al.*, 2016b).

The insights gained in the present study may be useful to understand the mechanism of psychotherapy. The traditional conceptualization of emotion regulation as a form of cognitive control is only partially compatible with models of psychotherapy. Considering the neural substrates of emotional and schematic representations may help elucidate the mechanisms of cognitive restructuring of dysfunctional cognitions that characterize cognitive-behavioural therapies (Beck *et al.*, 1979), where this restructuring has been shown to be a mediator of the therapeutic outcome (Wishman, 1993; Clark, 1999). In contrast, the concept of cognitive control is not consistent with the putative mechanism of action of 'expressive' psychotherapy approaches, which encourage individuals to experience their emotions, related thoughts and bodily sensations fully to put them in contact with their own internal experiences (instead of controlling emotions). These mechanisms also appear to apply to psychodynamic therapies (Grecucci *et al.*, 2018; Messina *et al.*, 2020) and 'third-wave' behavioural therapies (Hayes *et al.*, 1999, 2004). In this context, we have argued for limiting the importance of executive functions only to specific forms of emotion regulation, emphasizing the importance of enlarging neurobiological models of emotion regulation beyond cognitive control (Messina *et al.*, 2015, 2016b). Moving the focus of emotion regulation models from executive to semantic processes may bridge the gap between clinical models of psychotherapeutic interventions and affective neuroscience. Regardless of the specific psychotherapy model, psychotherapy theories are often concerned with changes in semantic representations of the self, past experiences interpersonal situations (including the therapeutic relationship) that function as 'schemas' (Beck *et al.*, 1979) or internal working models (Bowlby, 1988) to organize and interpret the emotional significance of everyday emotional experiences.

The present study has some limitations. First, the number of studies that have investigated acceptance-based regulation strategies is relatively exiguous. Due to the scarcity of available studies, we were not able to statistically compare the interaction between acceptance and the CNR and CFE subgroups (contrast analysis is unlikely to have enough statistical power to show significant differences with less than about 15 experiments in each data set). Second, the analyses provided here using the ALE methodology were based solely on reported peak activation coordinates. Therefore, we were unable to take into account information on the whole extent of estimated effects. Third, the definition of acceptance, together with instructions provided to the participants, remains somewhat inconsistent in the literature. For example, some definitions emphasize the attention to body sensations, whereas others are more focused on emotions and thoughts. All these issues should be considered in future studies.

Conflict of interest

None declared.

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