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*Cognitive-emotional interactions*

# Neural correlates of emotion regulation in psychopathology

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**What can psychopathology and its treatment tell us about cognitive emotional interactions? Standard approaches to interactions between emotion and cognition often adopt a variant of the idea that cognitive processes, subserved by dorsal and lateral cortical circuits, exert control and regulation of ventral, limbic brain areas associated with emotional expression and experience. However, it is becoming clear from studies on depression, post-traumatic stress disorder (PTSD) and obsessive compulsive disorder (OCD), that a binary, opponent theory of cognitive emotion interaction (CEI) and the dorsal–ventral model of neurocircuitry do not fully describe the data. We summarize recent research to suggest that networks of direct and indirect pathways exist by which cognition can regulate pathological emotion, and the inter-relationships of specific nodes within the networks need to be characterized.**

## Introduction

In the past decade, research in cognitive and affective neuroscience has begun to link neural function, cellular physiology and even molecular genetics with higher level processes that regulate emotion [1–3]. The application of this work to psychopathology has just started, providing important avenues for understanding CEI (see glossary for definition of abbreviations throughout text) *in extremis*, as well as the pathophysiology of psychiatric syndrome. There is probably no better demonstration of how thoughts and feelings bind together than psychiatric disorders, and the manner in which they do so provides an opportunity to understand normal CEI. In this article, we examine several psychiatric conditions in the context of CEI, focusing on the large-scale neural networks associated with the cognitive, volitional effort to modulate pathological emotions. We suggest that although a dorsal–ventral model of CEI, for example [4], characterizes much of the data, the multiple pathways by which an individual can change pathological emotion in psychotherapy requires a more complex psychological and neuroanatomical model.

## Pathological interactions of cognition and emotion

From the earliest theoretical formulations of Freud, psychiatric thought has set cognition and emotion if not against one another, then as opposite poles of the human psyche. In general, treatment has sought to therapeutically separate, or better integrate, emotion and cognition, when they become pathologically bound together in various syndromes. For instance, depression consists of profound sadness, and cognitively, thoughts focus on themes of guilt, worthlessness and self-doubt. Experimentally, depressed patients show a bias towards negative stimuli and away from positive stimuli, for example [5]. People with OCD experience intrusive fears that something bad will happen, or something is 'not right', unless they execute a behavioral ritual (compulsion), for example obsessions about contamination lead to hand washing [6]. Interestingly, most people with OCD recognize the irrationality of a compulsive ritual, but continue the maladaptive behavior because strong affect drives the compulsive urges. Here, the binding of affect with thought spares part of the cognition, but not enough to prevent the compulsive behavior. In PTSD, patients experience intrusive, unwanted recollections of a traumatic event, triggering extreme affects [7]. They also respond with exaggerated emotions to specific situations that, in turn, lead to the re-emergence of traumatic memories. These three common diagnostic groups provide overlapping, but distinct, examples of abnormal cognitive–emotional interaction. All three dis-

### Glossary of abbreviations

**Brain regions discussed**
**aINS** – anterior insula
**CN** – caudate nucleus
**dACC** – dorsal anterior cingulate cortex
**dlPFC** – dorsolateral prefrontal cortex
**dmPFC** – dorsomedial prefrontal cortex
**OFC** – orbitofrontal cortex
**pMFC** – posterior medial frontal cortex
**rACC** – rostral anterior cingulate cortex
**sgACC** – subgenual anterior cingulate cortex
**vlPFC** – ventrolateral prefrontal cortex
**vmPFC** – ventromedial prefrontal cortex

**Other terms**
**CBT** – cognitive behavior therapy
**CEI** – cognitive emotional interaction
**CT** – cognitive therapy
**IPT** – interpersonal therapy
**OCD** – obsessive compulsive disorder
**PTSD** – post-traumatic stress disorder
**rTMS** – repetitive transcranial magnetic stimulation

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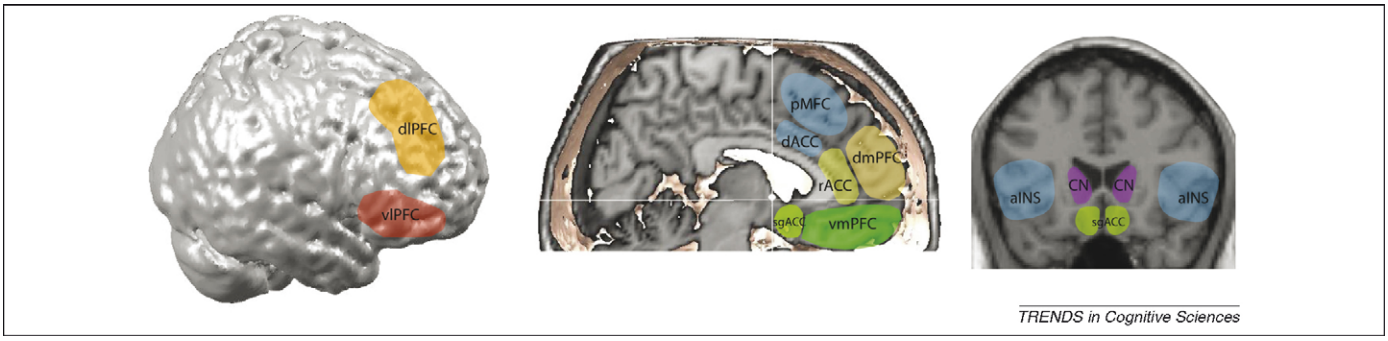


**Figure 1**. Anatomy of cognitive emotional interaction regions implicated in CEI and discussed in the text, focusing on prefrontal areas. Note that vmPFC includes the medial aspect of OFC. Abbreviations: aINS, anterior insula; CN, caudate nucleus; dACC, dorsal anterior cingulate cortex; dlPFC, dorsolateral prefrontal cortex; dmPFC, dorsomedial prefrontal cortex; OFC, orbitofrontal cortex; pMFC, posterior medial frontal cortex; rACC, rostral anterior cingulate cortex; sgACC, subgenual anterior cingulate cortex; vlPFC, ventrolateral prefrontal cortex; and vmPFC, ventromedial prefrontal cortex.

orders respond to treatment with selective serotonin re-uptake inhibitors [6,8,9], suggesting shared neuroanatomical systems, and an opportunity to examine neural substrates of CEI.

## Psychiatric disorders implicate emotion-processing areas of the brain

Neuroimaging studies demonstrate that emotionally evocative tasks recruit all cortical lobes, subcortical structures and the cerebellum, although activations tend to be denser in ventral cortical [particularly vmPFC], subcortical, midbrain, brainstem and cerebellar regions [10,11] (Figure 1). Ventral and medial frontal cortex [including rACC and OFC] is particularly relevant for determining salience and generating emotional states. The anterior, dmPFC is involved in various forms of emotion regulation [12,13], whereas the vmPFC and OFC process information relevant for determining goals and evaluating outcomes [14,15]. These areas have significant projections to hypothalamic and visceromotor brainstem areas, as well as to the amygdala [16]. The amygdala, which also projects to hypothalamic and visceromotor brainstem areas, is tuned to high salience information necessary for efficient and rapid generation of emotional responses [17].

Depression, OCD and PTSD exhibit hyperactivity in the ventral (and subcortical) regions described above, with variations between diagnostic groups, as one would expect for different disorders (Table 1). Patients with depression exhibit increased activity in ventral structures, such as the sgACC and amygdala [18,19], and pharmacologic treatment is associated with normalization of activity in these regions [18]. Patients with OCD also show hyperactivity in ventral regions, such as the OFC, ACC and most consistently in the head of the CN [20]. These areas demonstrate increased activity with symptom provocation and generally decreased activity with pharmacologic treatment (e.g. [21]). In PTSD, symptom provocation studies have demonstrated hyperactivity in the amygdala and insula [22]. Although it would be misleading to suggest that there are not inconsistencies in these findings, or that only these regions show altered activity, the general pattern of results shown in Table 1 has appeared sufficiently to support the idea that aberrant affect comes, at least in part, from overactivity of these regions.

## Control of dysregulated emotions: examples from psychotherapy

Psychotherapy provides instructive examples of how cognitive, volitional intention 'regains' control over dysregulated emotions. Strategies of emotion regulation are often divided between those that utilize attentional control (e.g. selective inattention to emotional stimuli) and those that utilize cognitive change (e.g. re-appraising a negative experience in a positive light) [2,23]. A successful psychotherapy that primarily engages cognitive change and deliberate re-appraisal is CT (cognitive therapy) [24]. CT focuses on the contents of a ruminating, depressed mind – typically filled with negative thoughts about the self, a prevailing tendency to interpret events negatively and a pessimistic outlook about the future; for example, 'I'm no good; there's no use in getting up today because nobody wants me around.' CT uses a model of CEI in which the habitual patterns of thought that generate the negative emotional states are conceptualized as schemata – enduring psychological patterns of appraising the environment, and attributing importance to events and persons. CT is an active process by which the therapist guides the patient to use conscious, cognitive effort to change a schema by

**Table 1. Summary of principal neuroimaging findings in depression, OCD and PTSD**

| | Depression | | OCD | | PTSD |
|---|---|---|---|---|---|
| | Resting[a] | After drug treatment[b] | Resting[a] | After drug treatment[b] | Activated[c] |
| **Dorsal areas** | | | | | |
| dlPFC | ↓ | ↑ | | | |
| dmPFC | ↓ | ↑ | | | ↑ |
| dACC | ↓ | ↑ | ↑ | ↓ | ↓ |
| **Ventral areas** | | | | | |
| aINS | | | | | ↑ |
| vlPFC | ↑ | ↓ | | | |
| sgACC | ↑ | ↓ | | | |
| Amygd | ↑ | | | | ↑ |
| OFC | | | ↑ | ↓ | |
| **Subcortical areas** | | | | | |
| CN | | | ↑ | ↓ | |

Arrows indicate replicated findings in the literature; blank spaces represent either inconsistent findings or no findings for the region.
[a]Down arrow indicates less resting stage neural activity compared with healthy control subjects; up arrow indicates more.
[b]Change with treatment, compared with pre-treatment activity.
[c]Activity during provocative, challenge paradigms, e.g. with trauma-related stimuli, compared with healthy control subjects.