

## Editorial

# Meta-analytic evidence for the role of the anterior cingulate cortex in social pain

Since at least the 1930s, when the American physician James Papez highlighted the importance of the cingulate gyrus for emotional processes (Papez, 1937), researchers have been interested in the functions of this region. One issue that has been challenging to disentangle, though, is how specific psychological processes map onto the various subdivisions of the anterior cingulate cortex (ACC). Whereas early lesion studies focused on the role of the dorsal ACC (dACC) in pain experience (Foltz and White, 1962) and affective processes (Tow and Whitty, 1953), later studies from cognitive neuroscientists in the late 1990s and early 2000s focused on the role of the dACC in cognitive processes such as conflict monitoring and error detection, processes that signal the need for cognitive control (Botvinick *et al.*, 2004). Indeed, an influential review at that time suggested that the dACC was primarily involved in cognitive processes whereas the ventral ACC (vACC) was primarily involved in affective processes (Bush *et al.*, 2000). This synthesis was later overturned by a comprehensive meta-analysis showing that cognitive, affective and painful tasks all activate the dACC (Shackman *et al.*, 2011) as well as a review showing that the dACC is involved in emotional appraisal and expression, whereas the vACC is involved in emotional regulation (Etkin *et al.*, 2011). Hence, the specific role of the dACC and vACC in cognitive and emotional processing has been debated, with major pendulum shifts across decades (reviewed in Eisenberger, *in press*).

This debate about the mapping of specific ACC subregions to specific psychological processes has pervaded the study of social pain as well. Some studies have shown that experiences of rejection, exclusion or loss activate the dACC and that self-reports of social distress correlate with dACC activity (Eisenberger *et al.*, 2003; reviewed in Eisenberger, 2012). However, some researchers have suggested that the dACC response to social pain may be an artifact of the paradigm often used to induce social pain and that instead, the vACC should be sensitive to social pain (Somerville *et al.*, 2006). Specifically, in line with the dorsal-cognitive/ventral-affective account of ACC function (Bush *et al.*, 2000), it has been suggested that dACC responses to the Cyberball social exclusion task, which involves social inclusion followed by social exclusion, may be reflective of an expectancy violation, rather than social distress (Somerville *et al.*, 2006). In a formal test of this hypothesis, Somerville and colleagues found that the dACC was sensitive to expectancy violation, whereas the vACC was sensitive to social acceptance. More recent studies, however, have shown that even after controlling for expectancy violation with carefully matched control conditions, the dACC was still responsive to social rejection (Kawamoto *et al.*, 2012; Cooper *et al.*, 2014), suggesting that dACC activity to social rejection cannot simply be attributed to expectancy violation. Meanwhile other researchers have shown that the vACC, rather than the dACC, activates to social exclusion (Masten *et al.*,

2009; Bolling *et al.*, 2011; others reviewed in Eisenberger, 2012) raising the question of whether dACC activity is even a reliable response to social rejection.

This confusion in the literature sets the stage for the important contribution made by Rotge and colleagues in this issue of SCAN (Rotge *et al.*, *this issue*). Rotge and colleagues investigated which subregions of the ACC were most reliably activated in response to social pain by conducting a meta-analysis of the social pain literature. Across 46 studies of social pain (including studies of rejection, exclusion and loss), which included a total of 940 healthy subjects, Rotge and colleagues found evidence that social pain activates the dACC (which they label as the anterior midcingulate cortex; aMCC), the pregenual ACC (pgACC) and the vACC (which they label as the subgenual ACC; sgACC). Moreover, self-reports of social distress correlated with neural activity across all three subregions of the ACC. Rotge and colleagues also investigated whether activity in these ACC subregions could be differentiated based on the type of paradigm used or the composition of the subject population. Several interesting findings emerged from these analyses.

First, the authors showed that the Cyberball task activated the dACC to a lesser extent than other experimental social pain tasks. This finding is consistent with the suggestion from other researchers (Kross *et al.*, 2011) that the social pain that follows from Cyberball is less intense than the social pain that follows from more personal forms of social rejection, such as a relationship breakup, as Cyberball involves being rejected by strangers (which is likely less impactful). Second, the authors found that children showed greater activation in the vACC to social pain than adults. This pattern has been noted before (Eisenberger, 2012), is consistent with models suggesting that the dorsal emotion-processing network develops later (Hung *et al.*, 2012), and fits with empirical evidence showing that dACC responses to threatening stimuli do not become evident until later in development (Hung *et al.*, 2012). Future work will be needed, however, to determine what this developmental difference in dACC vs vACC activation means for the processing and experience of social pain. Finally, the authors found that longer bouts of inclusion and exclusion were related to greater activity in the dACC, whereas shorter bouts were related to greater activity in the vACC. Although it is not yet clear what this pattern means, the authors offered several explanations including the possibility that longer bouts of inclusion may induce stronger expectancies that would later be violated. Another possibility is that shorter bouts of exclusion, because they are typically repeated multiple times, may be less believable to subjects (i.e. subjects may become suspicious if they see that they are excluded multiple times, especially if the exclusion occurs at regular intervals), which could lead to less dACC activity.

Through their meta-analysis, Rotge and colleagues make an important contribution to the understanding of the neural correlates of social pain by showing that multiple subregions of the ACC respond to social pain and that neural activity across these regions correlates with

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socially painful feelings. Obviously, though, this study represents a beginning and not an end to the investigation of how various subregions of the ACC contribute to social pain. The next step, of course, is to further elucidate how each of these ACC subregions contributes to the specific psychological processes that underlie social pain. Indeed, one variable that may prove critical in helping to parcel out the specific contributions of ACC subregions to social pain is psychological experience. While it is, no doubt, important to understand how the specific features of a task (timing, repetitions of trials, etc.) lead to activity in different ACC subregions, I would argue that it is even more important to understand how these specific features of a task affect psychological experience, as this is truly what is being captured by differential patterns of neural activity.

For instance, unlike some fMRI-based tasks in which subjects' responses are fairly uniform (e.g. looking at a visual stimulus, listening to tones), psychological responses to social pain are inherently complex and variable. Individuals' responses to social pain are comprised of multiple processes—including the social cognitive processing that enables one to identify that one has been socially devalued by others, the emotional response to that situation, generating social cognitive explanations for why the rejection might have occurred, and the regulation of the emotional response, among others. Each of these processes is likely to activate different neural regions and to be engaged differentially across different tasks and across different people. Thus, the Cyberball task may induce more self-protective emotion regulation strategies than other social pain tasks because of the unwanted discomfort associated with being unknowingly rejected or excluded by others, especially in the context of being watched by experimenters. Other tasks that rely on subjects' willingness to relive or re-experience a socially painful event may be less likely to engage self-protective attempts at emotion regulation and hence may allow for a greater emotional experience. Hence, these two tasks, through engaging different psychological processes, may also engage different neural regions.

Moreover, in addition to psychological differences across tasks, it is also important to consider psychological differences across people. Hence, there is no guarantee that putting a subject through, for example, the Cyberball task will actually make that subject feel rejected; some will feel hurt and rejected, others may regulate their responses, some will doubt that the situation is real, and still others will be unaffected by the actions of a stranger (even if they might be affected by the actions of a friend). Hence, with the study of social pain, it is extremely important to assess subjective experience either through self-reports or other means (behavioral responses). Gaining some traction on individual differences across studies in terms of whether subjects actually believed they were being rejected as well as subject's feelings in response to the task (which are not consistently assessed across studies) may help us to further understand the neural underpinnings of social pain. Thus, if a certain area is hypothesized to be involved, for example, in the painful experience of social rejection, we would not expect to see that region activated in a study in which subjects did not report feeling hurt or did not believe they were rejected. Simply using a social pain task is not enough to ensure that

subjects are having the intended experience. Greater attempts at assessing subjective responses are necessary to truly understand the neural underpinnings of social pain.

In sum, Rotge and colleagues provide a critical first step in understanding the accumulation of research on social pain by showing that social pain activates various regions of the ACC. Future studies will hopefully pick up where Rotge and colleagues left off by further exploring how various aspects of the psychological response to social pain map onto these distinct ACC subregions.

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