

## Reply to Iannetti and Mouraux: What functional MRI responses to physical pain tell us about why social rejection “hurts”

We recently reported that having participants who experienced an unwanted breakup view a photograph of their ex-partner as they thought about being rejected activated portions of the operculoinsular cortex strongly implicated in physical pain—the dorsal posterior insula (dpINS) and OP1 (the most caudal area of the parietal operculum). The same regions were also activated when participants experienced physical pain (1).

These findings were notable for two reasons. First, a wealth of data suggest that these regions, in particular dpINS, support physical pain sensation. As Craig noted recently, “the dorsal posterior insula contains the primary cortical sensory representation of temperature and pain in humans” (2). Second, a meta-analysis of more than 500 studies that we performed confirmed that physical pain reliably and specifically activates these regions.

Based on these findings, we inferred that intense social rejection and physical pain share somatosensory representations. Iannetti and Mouraux question this inference on the grounds that secondary somatosensory cortex and dpINS do not in fact support the sensory component of physical pain (3). Instead, they suggest that these regions reflect “multimodal neural processes triggered by salient sensory stimuli regardless of their sensory modality.” Thus, “observing the photograph of an ex-partner we still care about is likely to be as salient as an actual nociceptive stimulus and, hence, to trigger saliency-related multimodal responses in the secondary somatosensory and insular cortices.” This salience hypothesis is not consistent with prior research on social rejection, nor with the meta-analysis we reported in our study (1).

Salience refers to a stimulus’s capacity to “stand out” relative to the background. It is well established that negative stimuli are more salient than neutral or positive stimuli (4). Thus, if the operculoinsular regions that social rejection and physical pain coactivated in our study reflect “multimodal neural processes triggered by salient stimuli,” studies that contrast negative versus

neutral or positive stimuli should activate these regions. However, prior research on social rejection indicates that this is not the case. As Iannetti and Mouraux themselves note (5), being rejected in the Cyberball paradigm—the most frequently used task to study the neural bases of social rejection—is more salient than being accepted. However, these studies do not activate the operculoinsular regions that we observed (6).

The meta-analysis we reported in our study (1) further undermines Iannetti’s and Mouraux’s contention. This analysis included multiple studies that contrast negative versus neutral or positive stimuli—for example, studies that contrast intense negative images (e.g., pictures of bloody corpses) versus neutral images (e.g., pictures of serene landscapes)—which failed to reliably activate the operculoinsular regions that social rejection and physical pain coactivated in our experiment. Our meta-analysis also included studies that contrasted high-versus low-salience visual and auditory stimuli. These studies too failed to reliably activate these operculoinsular regions. In contrast, published studies of physical pain reliably activated these areas—a finding that is consistent with a wealth of data suggesting that these regions support physical pain sensation, and the conclusions we drew in our study (1).

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1. Kross E, Berman MG, Mischel W, Smith EE, Wager TD (2011) Social rejection shares somatosensory representations with physical pain. *Proc Natl Acad Sci USA* 108: 6270–6275.
2. Craig AD (2011) Interoceptive cortex in the posterior insula: Comment on Garcia-Larrea et al. 2010 *Brain* 133, 2528. *Brain* 134:e166.
3. Iannetti GD, Mouraux A (2011) Can the functional MRI responses to physical pain really tell us why social rejection “hurts”? *Proc Natl Acad Sci USA*, 10.1073/pnas.1105451108.
4. Rozin P, Royzman EB (2001) Negativity bias, negativity dominance, and contagion. *Pers Soc Psychol Rev* 5:296–320.
5. Iannetti GD, Mouraux A (2010) From the neuromatrix to the pain matrix (and back). *Exp Brain Res* 205:1–12.
6. Eisenberger N (2008) Understanding the moderators of physical and emotional pain: A neural systems-based approach. *Psychol Inq* 19:189–195.

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