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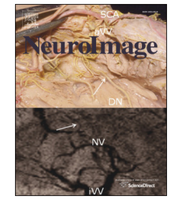

Localizing Pain Matrix and Theory of Mind networks with both verbal and non-verbal stimuli

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ABSTRACT

Functional localizer tasks allow researchers to identify brain regions in each individual's brain, using a combination of anatomical and functional constraints. In this study, we compare three social cognitive localizer tasks, designed to efficiently identify regions in the "Pain Matrix," recruited in response to a person's physical pain, and the "Theory of Mind network," recruited in response to a person's mental states (i.e. beliefs and emotions). Participants performed three tasks: first, the verbal false-belief stories task; second, a verbal task including stories describing physical pain versus emotional suffering; and third, passively viewing a non-verbal animated movie, which included segments depicting physical pain and beliefs and emotions. All three localizers were efficient in identifying replicable, stable networks in individual subjects. The consistency across tasks makes all three tasks viable localizers. Nevertheless, there were small reliable differences in the location of the regions and the pattern of activity within regions, hinting at more specific representations. The new localizers go beyond those currently available: first, they simultaneously identify two functional networks with no additional scan time, and second, the non-verbal task extends the populations in whom functional localizers can be applied. These localizers will be made publicly available.

Introduction

When people read a story or watch a movie depicting another person's experiences, remarkably reliable and robust patterns of activity are elicited in the observer's brain. For example, if the protagonist is in physical pain, observers have increased activity in "Pain Matrix" brain regions, including bilateral anterior insula and anterior middle cingulate cortex (AMCC; Botvinick et al., 2005; Bruneau et al., 2012; Singer et al., 2004); if the protagonist is befuddled by a false belief, observers have increased activity in "Theory of Mind" brain regions, including bilateral temporoparietal junction (TPJ) and medial prefrontal cortex (MPFC; C. D. Frith and Frith, 1999; Saxe and Kanwisher, 2003). These functional profiles have been observed across thousands of participants in hundreds of neuroimaging studies utilizing dozens of different tasks (for review, Lamm et al., 2011; Schurz et al., 2014), a challenge for social cognitive neuroscience remains how to relate the results of each new study to the previous ones.

The most common approach, in social cognitive neuroscience, is to compare results via meta-analyses (Costafreda, 2009; Mar, 2011; Wager et al., 2007). For example, a researcher might run a group analysis on her own data, identify the locations of maximal differences between conditions (i.e. peaks), and then compare those locations to a "library" of previously observed peaks. If the activation in her study is close to activation previously reported for many other studies examining pain empathy, she can conclude that she has activated regions involved in processing others' pain. The advantage of this approach is that it allows the researcher to compare her results to hundreds of prior studies simultaneously, with no extra cost or scan time. However, the disadvantage of this approach is that group analyses and meta-analyses lead to substantial spatial blurring, which translates to reduced sensitivity and underestimation of effect sizes (Nieto-Castañón and Fedorenko, 2012). Individual brains vary in both anatomy and function. Alignment of brains to a common space provides an approximate correspondence (Amunts et al., 2000; Crum et al., 2003; Tomaiuolo et al., 1999). That means that neighboring but functionally distinct brain regions may be aligned to the same place, and also that the functional loci in different individuals might be aligned to varying locations in the common space (Nieto-Castañón and Fedorenko, 2012; Saxe et al., 2006). Due to that blurring, important functional differences between neighboring regions may be impossible to detect.

An alternative way to link current and past results in support of theoretical progress is to identify functional regions in individual subjects. To use this strategy, the researcher would run her own experiment, and also a short, robust "localizer" task that identifies regions involved in e.g. physical pain perception in each individual subject. By running

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an individual localizer in each subject, the functional regions of interest identified are tailored to each individual's functional organization and constrained by either their anatomy or a common functional search space. In visual cognitive neuroscience, for example, almost all researchers use retinotopic mapping to identify primary visual areas (Sereno et al., 1995; Wandell et al., 2007; Warnking et al., 2002). Under some circumstances, independent localizers also allow hypotheses to be tested in a handful of "regions" instead of hundreds of thousands of voxels, thus reducing the problems of multiple comparisons and increasing the study's sensitivity.

Functional localizer tasks are already in widespread use to identify brain regions involved in a number of social cognitive processes: for example, viewing faces versus other objects, to identify regions involved in human face processing (Kanwisher et al., 1997); viewing human bodies versus other objects, to identify regions involved in human body form recognition (Downing et al., 2001); viewing biological motion versus other motion, to identify regions involved in perceiving biological motion (Grossman et al., 2000); attributing personality traits to one's self as opposed to making other judgments about the same traits, to identify regions involved in explicit self conception(Kelley et al., 2002); and reading stories about a person's mental representations versus stories about physical representations, to identify regions involved in Theory of Mind (ToM) (Dodell-Feder et al., 2011). Using these localizer tasks has allowed researchers to aggregate data across many studies (Berman et al., 2010; Dufour et al., 2013; Spunt and Adolphs, 2014) and build strong empirical and theoretical connections across different experiments (Fedorenko and Thompson-Schill, 2014; Kanwisher, 2010).

However, there are significant practical and theoretical obstacles to using localizer tasks in social cognitive neuroscience. First, the use of functional localizers is expensive, in both time and money. The cost of localizers can easily compound, too, as important scientific questions in social cognitive neuroscience often concern the relative or interacting roles of multiple regions or networks. Second, there are no established "localizer" tasks for some key cognitive functions. For example, Pain Matrix brain regions can be identified by having participants experience painful shocks in the scanner, but these experiments require special expertise and materials, and current protocols are impractically long. In addition, localizing Pain Matrix through felt pain may not target part of the Pain Matrix that are specifically sensitive to observed or perceived pain (Morrison and Downing, 2007), which might be of specific interest for social cognitive neuroscientists studying empathy, for example. Third, many existing localizer tasks require participants to follow complicated instructions or read sophisticated verbal texts. These tasks therefore cannot be used to identify relevant networks in lower-functioning participants or pre-verbal children. Finally, localizer tasks are a relatively blunt tool, identifying large regions involved in many aspects of a task. For example, "face localizer" tasks identify many different brain regions associated with face processing. Consistently localizing the set of brain regions allows for follow-up experiments, which could help to clarify which regions are involved in processes such as recognizing face identity versus facial expressions.

The central goal of the current study is to introduce two novel functional localizers for social cognitive neuroscience. Both of these localizer tasks are designed to circumvent some of the challenges described above. In one task, participants read short stories about characters experiencing physical pain or emotional suffering (the E/P stories task). Participants were explicitly instructed to rate the pain or suffering that the character was experiencing. In the second task, participants watched a short non-verbal animated cartoon (that was made for broad entertainment by Pixar Studios and not designed for an experiment). During the movie, characters experience physical pain and consider other characters' thoughts (the movie task). Participants passively viewed the movie, so any activity was elicited spontaneously by the events depicted.

The localizer tasks were designed to be short – each novel localizer task defined both ToM and Pain Matrix brain regions in less than 10 minutes of scanner time – and they were required to be robust and reliable; that is, activity in response to physical pain versus mental states should be observed in the same regions within individuals and should be identifiable in the vast majority of participants. Each task allows the user to identify two distinct functional networks simultaneously: regions involved in processing of perceived pain and bodily states (e.g. insula, middle cingulate, secondary sensory regions) and regions involved in ToM (e.g. bilateral temporoparietal junction, posterior cingulate, and medial prefrontal cortex). In addition, the movie task has other advantages: it is extremely short, non-verbal, and requires no instructions, and thus could in principle be used with younger, lower-functioning, or non-native English-speaking participants.

As a benchmark, we compared both tasks to the most commonly used localizer task for identifying ToM regions, the false-belief task (Dodell-Feder et al., 2011). Because the false-belief task has been used in many prior studies, it is important to validate any new localizer task against this benchmark (Spunt and Adolphs, 2014). Directly comparing the three tasks also allows us to test the similarity and stability of responses to ToM tasks across verbal versus non-verbal stimuli, across three different explicit tasks, and across a range of emotional contents.

Methods

Participants

Twenty right-handed adults (12 females, mean age 25.3, range 18–39) participated in the study for payment. All participants were fluent English speakers, with no neurological or psychiatric conditions, and had normal or corrected to normal vision. All participants gave written informed consent in accordance with the requirement of MIT's Committee on the Use of Humans as Experimental Subjects.

False-belief task (FB)

The publicly available false-belief (FB) localizer (Dodell-Feder et al., 2011) includes twenty stories, all of which describe an outdated representation. The false representation is either mentally held by a person (belief condition – 10 stories) or physically present on an object, such as a photo or map (photo condition – 10 stories). The stories were presented in two functional runs with 5 belief and 5 photo stories per run. Each story was presented for 10 seconds, followed by a true/false question about the either the true state of the world or the false representation (4 seconds). Stimuli were separated by 12 seconds inter-stimulus intervals, resulting in a total task runtime of 9 minutes, 4 seconds. The contrast of interest in the task is the belief condition relative to the photo condition (belief > photo).

Emotional/physical pain stories task (E/P)

In the emotional/physical pain stories task (E/P), participants read short verbal narratives describing people experiencing events that were either physically painful (P condition – 10 stories) or emotionally painful (E condition – 10 stories). The stimuli were pulled from a larger set of 24 E and 24 P stories (Bruneau et al., 2012) and represent the 10 E and 10 P stories that were rated to involve the most "emotional pain" and "physical suffering," respectively, by an independent group of online participants. The stories were presented in two functional runs with 5 E and 5 P stories per run. Each story was presented for 12 seconds, followed by 4 seconds in which participants rated how much pain or suffering the protagonist experienced, from (1) "None" to (4) "A lot." Stimuli were separated by 12 seconds inter-stimulus intervals, resulting in a total task runtime of 9 minutes, 44 seconds. The contrasts of interest in the task are E > P (ToM network contrast) and P > E (Extended Pain Matrix contrast).

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