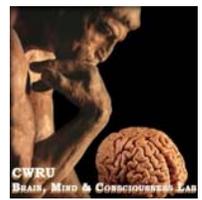


Social Brain Meta-Analysis: Regional Specialization and Relationship to Anti-Correlated Networks

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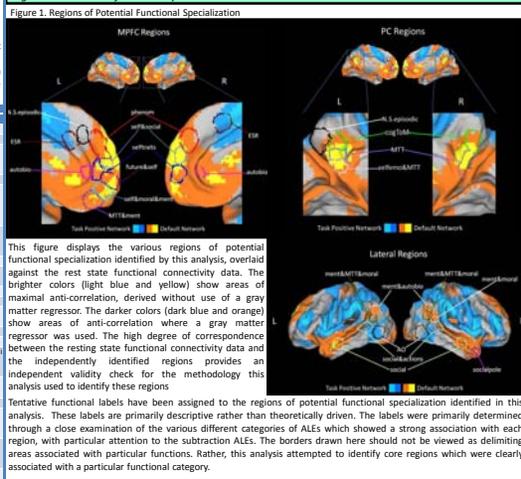
Introduction
Recently there has been a lot of research examining the function of default mode network (DMN) in human brain and its relationship to the task positive network (TPN). The DMN is a set of neural structures (including the medial prefrontal cortex (MPFC), the precuneus/medial parietal cortex (PC), and the temporal-parietal junctions (TPJ)) which has been shown to commonly deactivate in certain cognitively demanding tasks and displays an antagonistic relationship with the TPN. This analysis addresses two major theories of the DMN: the internally directed attention vs. externally directed attention theory suggests that the DMN is mainly involved in processes dealing with internally directed attention and the TPN is mainly involved in processes dealing with externally directed attention (Andrews-Hanna 2012). Proponents of this theory often assert that the central underlying function of the DMN is one of two things. Either the DMN is primarily involved in self-referential processing (i.e. introspection and self-trait judgments) (Gusnard et al. 2001), or it is primarily involved in attending to internal episodic memories/mental time travel (Buckner & Carroll 2007). Both versions of this theory hold that the TPN is primarily involved in attending to one's immediate physical environment. In contrast, the opposing domains hypothesis suggests that the DMN is mainly involved in reasoning about the social environment and the TPN is mainly responsible for reasoning about and manipulating the physical environment. This meta-analysis utilized Activation Likelihood Estimation (ALE) methodologies in an attempt to evaluate these theories of the DMN and identify any regions of potential functional specialization within the DMN.

Methods
Study Selection
Papers were primarily collected from previous meta-analyses and/or review papers on the topics of interest (i.e. social cognition, introspection, emotion, memory, action observation, and action execution). For topics where these meta-analyses were outdated, insufficient, or non-existent, various literature searches were performed using the PubMed database (www.ncbi.nlm.nih.gov/pubmed/) to supplement the data pool. The literature reviews initially yielded a total 400 papers. To be included in the analysis, the papers had to meet specific inclusion criteria. They had to:
• Be published in a peer review journal between January 1995 and January 2011
• Collect data using fMRI or PET from healthy adults and/or healthy children
• Report relevant activation data (no explicitly identified deactivations [i.e. rest > task]) in stereotaxic coordinates (data points/foci) in a standard space [Talairach or MNI]
Of the 400 papers initially found, 290 were used in the analysis, the remainder either failed to meet all the inclusion criteria or contained no data categorized into an analysis relevant category. All foci reported in MNI were converted to Talairach space using the Lancaster et al.'s (2007) conversion method.

Category	Keywords	Criteria
Traitment Categories		
Mentalizing	Explicit Mentalizing Implicit Mentalizing	Subjects had to explicitly identify another's goals, intentions, and/or beliefs. Subjects completed a task which was likely to bring about thoughts about another's goals, intentions, and/or beliefs, but they were not asked to explicitly identify during the task.
Moral Judgments	Explicit Moral Judgments Implicit Moral Judgments	Subjects had to explicitly indicate whether a target individual behaved in a manner that was morally right or wrong, asked to indicate how they or another should or would respond to a morally charged situation, or they were asked to evaluate validity of a morally charged statement. Subjects were not asked to explicitly make a moral judgment, but the nature of the stimuli and/or task were likely to give rise to internal thoughts about the rightness or wrongness of an action or situation.
Self-Judgments	Self-Emotional Awareness Self-Trait Judgments	Subjects completed a task which required conscious awareness and/or evaluation of their own emotional state and/or their emotional response to a stimulus. Subjects had to evaluate their own personality traits.
Other Judgments	Other-Emotional Awareness Other-Trait Judgments	Subjects completed a task which required conscious awareness and/or evaluation of another's emotional state and/or their emotional response to a stimulus. Subjects had to evaluate another's personality traits.
General Emotion	Explicitly Emotional Implicitly Emotional	The experiments of the primary paper had to report using emotionally salient stimuli or the subjects in the initial experiment had to complete a task that explicitly deals with emotion. The categorizer judged the stimuli or task to have some affective component, but the affective component was not explicitly addressed in the paper.
Mental Time Travel	Autobiographical Recall Imagining Future Events	The participants had to recall an event that actually happened. The event that was recalled must have occurred outside the setting of the experiment. The event must also have had some social, emotional, or personal significance to the participants. The participants had to imagine an event sometime in their future. The events in question must occur outside the experiment. The events in question must also have some social, emotional, or personal significance to the participants.
Non-Social Episodic Retrieval	Retrieval Success Retrieval Failure	Correct Recognition > Correct Rejection contrasts. See Spaniol et al. (2009) Remember > Forget contrasts. See Spaniol et al. (2009)
Action Related Processes	Transitive Actions Intransitive Actions	The participants had to either physically perform an action involving the use of an object, observe another agent performing an action involving the use of an object, mentally plan how they would perform an action involving the use of an object, or imagine how they would perform an action involving the use of an object. The participants had to either physically perform an action not involving the use of an object, observe another agent performing an action not involving the use of an object, mentally plan how they would perform an action not involving the use of an object, or imagine how they would perform an action not involving the use of an object.
Emotion by Task	Self-Emotional Labeling Other Emotional Labeling Emotion Generation Emotion Modulation Passive Viewing	The participants had to identify how a stimulus makes them feel. The participants had to identify and label the emotional state of another agent presented in the stimulus. The participants had to make themselves feel the same emotions as an agent in a story. The participants had to increase or decrease their naturally occurring emotional response to a given affective stimulus. The participants were not given any task to perform in the scanner other than to attend to the stimuli presented.
Secondary Categories		These categories are combinations of components of primary categories and were not part of the categorization process.
Emotional Awareness vs. Cognitive Theory of Mind	Emotional Awareness Purely Cognitive Theory of Mind	All data classified as self-emotional awareness or other-emotional awareness was also classified as emotional awareness. All data classified as explicit mentalizing or implicit mentalizing which was not classified as explicitly or implicitly emotional, and/or explicit or implicit moral judgments was classified as purely cognitive theory of mind.
General Social	Social	All data classified as explicit or implicit mentalizing, explicit or implicit moral judgment, self-emotional awareness, self-trait judgments, other-emotional awareness, other-trait judgments, explicitly or implicitly emotional, autobiographical recall, or imagining future events which was not also classified as transitive or intransitive actions was classified as social.
Internally vs. Externally Directed Social Cognition	Internally Directed Social Cognition Externally Directed Social Cognition	All data classified as self-emotional awareness, self-trait judgment, autobiographical recall, or imagining future events was also classified as internally directed social cognition. All data classified as other-emotional awareness, other-trait judgments, explicit mentalizing, or implicit mentalizing was also classified as externally directed social cognition.

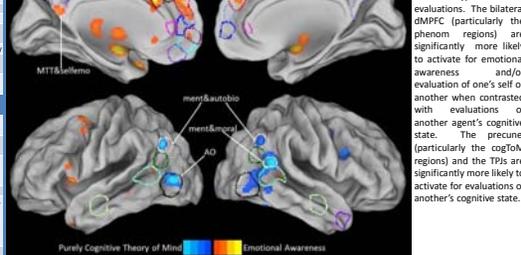
ALE Generation
Main effect ALEs and subtraction ALEs were generated using the Turkeltaub et al. (2002) methodology using GingerALE (brainmap.org).
Resting State Functional Connectivity Analysis
The resting state functional connectivity data was taken from Jack et al. (2012)
Identifying Regions of Potential Functional Specialization
To identify regions of potential functional specialization, the results from all the ALEs were systematically examined for patterns of functional involvement across categories. In order for a brain area to be identified as region of potential functional specialization it had to meet one of two initial criteria. The areas had to either (1) display a pattern of functional involvement across two or more non-overlapping categories, or (2) display a strong pattern of involvement within one or more overlapping categories consistent with previous meta-analytic findings. The areas which passed one of these criteria were examined with particular attention to functional differences as revealed by subtraction ALEs. Borders were drawn around specific regions on the basis of their functional engagement across categories. Once a region was identified, all the ALEs and subtraction ALEs which hit that region were recorded. All regions of potential functional specialization were identified independently of the resting state functional connectivity data which was used to establish the anti-correlated networks.

Results
Regions of Potential Functional Specialization: Examination of main effect and subtraction ALEs allowed us to identify 32 discrete regions involves distinct social functions. This included 24 bilateral regions which displayed similar functional specialization in both hemispheres, and 8 regions which were functionally distinct and unilateral.



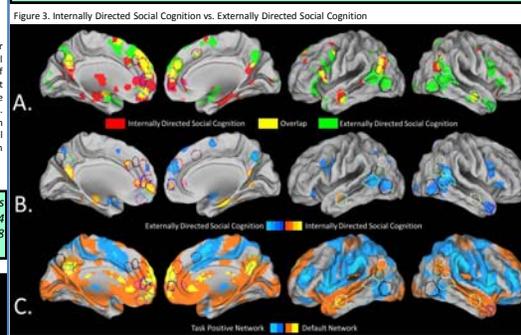
This figure displays the various regions of potential functional specialization identified by this analysis, overlaid against the rest state functional connectivity data. The brighter colors (light blue and yellow) show areas of maximal anti-correlation, derived without use of a gray matter regressor. The darker colors (dark blue and orange) show areas of anti-correlation where a gray matter regressor was used. The high degree of correspondence between the resting state functional connectivity data and the independently identified regions provides an independent validity check for the methodology this analysis used to identify these regions.
Tentative functional labels have been assigned to the regions of potential functional specialization identified in this analysis. These labels are primarily descriptive rather than theoretically driven. The labels were primarily determined through a close examination of the various different categories of ALEs which showed a strong association with each region, with particular attention to the subtraction ALEs. The borders drawn here should not be viewed as delineating areas associated with particular functions. Rather, this analysis attempted to identify core regions which were clearly associated with a particular functional category.

Emotional Social Evaluations vs. Cognitive Social Evaluations: Different regions were identified as preferentially involved in attributing cognitive states, attributing emotional states, and being in an emotional state.

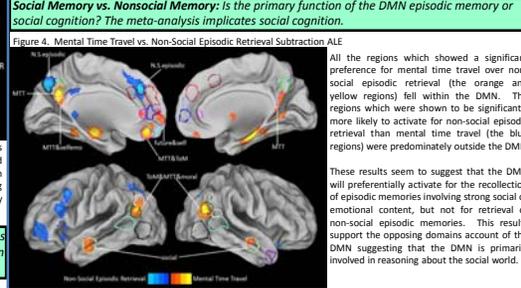


The dMPFC's preference for emotional social evaluations is also supported by the self emotional awareness vs. self trait judgments subtraction ALE (which showed self emotional awareness > self trait judgments in the right dMPFC phenom region) and the other emotional awareness vs. other trait judgments subtraction ALE (which showed other emotional awareness > other trait judgments in the right and left dMPFC phenom regions).
The emotion by task analysis showed that the dMPFC is not significantly likely to activate for passive viewing of emotional stimuli but was significantly likely to activate for Emotional Labeling tasks (self emotional labeling + other emotional labeling). This suggests that the dMPFC's preference for emotional social evaluations is not driven by the physiological experience of affective states; rather it is likely driven by a cognitive process dealing with evaluation of affective or phenomenological states.
The results from emotional awareness subtraction ALEs, the emotion by task analysis, and functional trends in the phenom regions of the dMPFC across the various social categories, suggest that this region may be highly involved in, if not specialized for, the cognitive representations of emotional or phenomenological states.

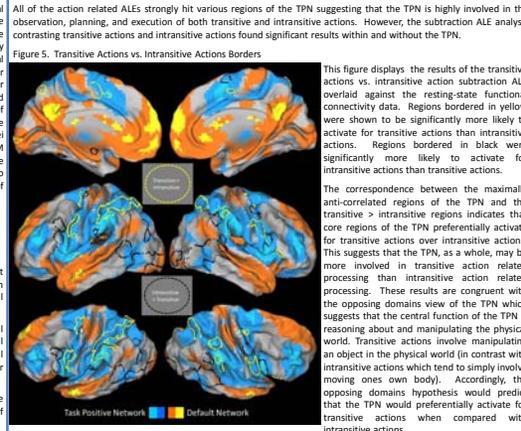
Internally Directed Attention vs. Externally Directed Attention: We identified a dorsal-ventral distinction, present bilaterally in both medial parietal and medial prefrontal cortices, between regions preferentially involved in external (other-related) and internal (mnemonic or self-related) social cognition.



Social Memory vs. Nonsocial Memory: Is the primary function of the DMN episodic memory or social cognition? The meta-analysis implicates social cognition.



Action Understanding and the TPN: Does the mirror neuron network support social reasoning or reasoning about how to manipulate objects? Overlap between regions involved in transitive actions and the TPN support the latter hypothesis.



Summary & Discussions

The results across all of these analyses can be used to address one underlying question, which theory, internally vs. externally directed attention or the opposing domains hypothesis, best accounts for our findings in the DMN?

- Previous work with the internally directed attention theory has suggested that the main function of the DMN is either general internally directed attention (Andrews-Hanna 2012), self-referential processing (e.g. introspection and self-trait judgments) (Gusnard et al. 2001), or episodic recall of past events (Buckner & Carroll 2007). Buckner & Carroll (2007) claimed that one of the central functions of the DMN is to recall past experiences and use them to adaptively "imagine perspectives and events beyond those that emerge from the immediate environment," (Buckner & Carroll 2007). All these versions of the internally vs. externally directed attention theory predict that the DMN should display a consistent preference for internally generated information.
- In contrast, the opposing domains hypothesis asserts that the underlying function of the default network is social cognition/reasoning about the social world. As such, it predicts social cognition, regardless of the type or attentional direction, should hit the DMN.

The results from this meta-analysis clearly support the opposing domains account of the DMN

- The comparison of internally and externally directed social cognition in Figure 3 not only shows that there is substantial overlap between internally directed and externally directed social cognition throughout the default network, but it also shows that a majority of the default network either shows no significant preference for internally or externally directed social cognition, or shows a significant preference for externally directed social cognition. Furthermore, this analysis found that regions of maximal anti-correlation in the DMN (i.e. core regions of the DMN) displayed no consistent pattern in these results. Some maximally anti-correlated regions displayed a preference for internally directed social cognition, other maximally anti-correlated regions showed a preference for externally directed social cognition, and still other maximally anti-correlated regions displayed no significant preference for either internally or externally directed social cognition. This lack of a consistent preference for internally directed social cognition in the DMN seems to run counter to the internally directed attention theory of the DMN; however, it is strongly consistent with the opposing domains account of the DMN.

- The results from the social memory vs. nonsocial memory analysis are also consistent with the internally directed attention theory of the DMN and seem to run counter to prior claims asserting that episodic recollection is a central function of the DMN (Buckner & Carroll 2007). The analysis suggests that the DMN will only activate for social memories/internal information (not for non-social memories/internal information) in two ways:

- i. The subtraction analysis contrasting mental time travel (i.e. social memories/social internal information) and non-social episodic retrieval (i.e. non-social memories/non-social internal information) showed that core regions of the DMN will preferentially activate for social memories over non-social memories (see Figure 4).
 - ii. A comparison of the main effect ALE for non-social episodic retrieval with the resting state functional connectivity data showed that non-social episodic retrieval only minor overlap with the DMN. This lack of overlap suggests that the DMN is not significantly likely to activate for non-social episodic retrieval.
- These results suggest that the DMN only activates when recalling social memories (or attending to socially valenced internal information) and will not activate when recalling non-social episodic memories (or attending to non-social internal information). While this preference for social information supports the opposing domains hypothesis, it runs counter to internally directed attention theory of the DMN which suggests that the DMN should activate for all episodic recall/internal information (regardless of social content).
 - As noted above, the internally directed social cognition vs. externally directed social cognition analysis did show that some regions of the DMN significantly preferred internally directed social cognition; however, these areas were mainly limited to ventral medial DMN structures. This ventral preference for internally directed social cognition replicates and extends prior findings made by Denny et al. (2012). Denny et al. (2012) examined self and other related judgments within the MPFC and found that MPFC seemed to be organized on a dorsal-ventral gradient of self and other judgments. They found that the MPFC, as a whole, is involved in both self and other judgments, but as one moves ventrally down the MPFC it becomes more self related and less other related (and vice versa). Our findings extend Denny et al.'s (2012) findings, in two key ways:

- i. Denny et al.'s analysis was limited to a single contrast between self judgments (which were akin to our self-trait judgment category) and other judgments (which was akin to a combination of our other trait judgment category and our mentalizing category). Our analysis found similar dorsal-ventral trends in three largely distinct contrasts. These contrasts included the self-trait vs. other trait subtraction analysis, the self-emotional awareness vs. other emotional awareness subtraction analysis, and the mentalizing vs. mental time travel subtraction analysis. Since our contrasts were not limited to self and other judgments, our findings open up the possibility that the MPFC is organized along an external-internal social cognition gradient (rather than a other-self gradient).

- ii. Denny et al.'s (2012) gradient was limited to the MPFC. This meta-analysis found similar dorsal-ventral patterns of externally and internally directed social cognition in the MPFC and bilaterally in precuneus/medial parietal cortex.

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