Functional Connectivity Mapping of Regions Associated with Self- and Other-Processing

Ryan J. Murray,[1,2]* Martin Debbané,[1,3,4] Peter T. Fox,[5,6] Danilo Bzdok,[7,8] and Simon B. Eickhoff[6,7]

[1]Developmental Clinical Psychology Research Unit, Faculty of Psychology and Educational Sciences, University of Geneva, Geneva, Switzerland
[2]Swiss Center for Affective Sciences, University of Geneva, Geneva, Switzerland
[3]Office Médico-Pédagogique, Department of Psychiatry, Geneva Faculty of Medicine, University of Geneva, Geneva, Switzerland
[4]Research Department of Clinical, Educational and Health Psychology, University College London, UK
[5]Research Imaging Institute, University of Texas Health Science Center at San Antonio, San Antonio, Texas
[6]South Texas Veterans Health Care System, San Antonio, Texas
[7]Institute of Neuroscience and Medicine [INM-1], Research Center Jülich, Jülich, Germany
[8]Institute for Clinical Neuroscience and Medical Psychology, Heinrich-Heine University Düsseldorf, Düsseldorf, Germany

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Abstract: Neuroscience literature increasingly suggests a conceptual self composed of interacting neural regions, rather than independent local activations, yet such claims have yet to be investigated. We, thus, combined task-dependent meta-analytic connectivity modeling (MACM) with task-independent resting-state (RS) connectivity analysis to delineate the neural network of the self, across both states. Given psychological evidence implicating the self's interdependence on social information, we also delineated the neural network underlying conceptual other-processing. To elucidate the relation between the self-/other-networks and their function, we mined the MACM metadata to generate a cognitive–behavioral profile for an empirically identified region specific to conceptual self, the pregenual anterior cingulate (pACC), and conceptual other, posterior cingulate/precuneus (PCC/PC). Mining of 7,200 published, task-dependent, neuroimaging studies, using healthy human subjects, yielded 193 studies activating the self-related seed and were conjoined with RS connectivity analysis to delineate a differentiated self-network composed of the pACC (seed) and anterior insula, relative to other functional connectivity. Additionally, 106 studies activating the other-related seed were conjoined with RS connectivity analysis to delineate a differentiated other-network of PCC/PC (seed) and angular gyrus/temporoparietal junction, relative to self-functional connectivity. The self-network seed related to emotional conflict resolution and motivational processing, whereas the other-network seed related

to socially oriented processing and contextual information integration. Notably, our findings revealed shared RS connectivity between ensuing self-/other-networks within the ventromedial prefrontal cortex and medial orbitofrontal cortex, suggesting self-updating via integration of self-relevant social information. We, therefore, present initial neurobiological evidence corroborating the increasing claims of an intricate self-network, the architecture of which may promote social value processing. *Hum Brain Mapp 00:000–000, 2014.* © 2014 Wiley Periodicals, Inc.

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INTRODUCTION

To navigate adaptively through their social environment, human beings rely on a complex psychological construct, the conceptual self. The conceptual self is thought to originate from socially engineered mental schema of motives, emotions, actions, and outcomes of both oneself and others [Conway et al., 2004; Demorest, 1995; Neisser, 1988; Tomkins, 1978] and may be essential in organizing the individual when planning for, performing in, and adapting to familiar and novel social situations [Conway et al., 2004; Hixon and Swann, 1993]. Neuroscientists have used the theoretical and psychological literatures to describe the conceptual self as an implicit organization of information made conscious via abstract mental representations of personal traits, emotions, beliefs, values, and attitudes [Martinelli et al., 2012; Morin and Hamper, 2012; Morin and Michaud, 2007]. Accordingly, the conceptual self would engender aspects of both semantic [Haslam et al., 2011], affective [Demorest and Alexander, 1992], and social [Cooley, 1902; Hixon and Swann, 1993] processing giving rise to a conscious coherent distinction of one's personal values, beliefs, and traits.

As it stands today, the theoretical and psychological literatures have actively pursued the delineation of a conceptual self [e.g., Conway et al., 2004; Kanagawa et al., 2001; Neisser, 1991; Neisser and Jopling, 1997] particularly its various components, such as self-concept [Markus and Kunda, 1986; Markus and Wurf, 1987], personal scripts [e.g., Demorest, 1995, Neisser, 1988; Tomkins, 1978], and interpersonal social representations [Cooley, 1902; Mead and Morris, 1967], and although the usage of the term "conceptual self," as a psychological construct, remains relatively sparse in the social neuroscience community [e.g., Martinelli et al., 2012; Morin and Hamper, 2012; Morin and Michaud, 2007], this psychological phenomenon has been explored implicitly in at least 17 neuroimaging studies [see van der Meer et al., 2010 for an exhaustive list] and two meta-analyses [Murray et al., 2012; van der Meer et al., 2010]. Importantly, these studies have delineated neural regions specific to processing of conceptual self and conceptual other (i.e., mental representation of close, familiar, and unfamiliar others) within the pregenual anterior cingulate (pACC) [cf. Martinelli et al.,

2012; Murray et al., 2012; van der Meer et al., 2010] and posterior cingulate/precuneus (PCC/PC) [Murray et al., 2012], respectively. Thus, the current meta-analytic literature suggests conceptual self-specific and other-specific neural regions in the pACC and PC/PCC, respectively.

Here, self-specificity refers to processes that "implicitly specify the self by implementing a functional self-/non-self-distinction in perception, action, cognition, and emotion" [Christoff et al., 2011; p. 104]. By extension, therefore, other-specificity would refer to processes that implicitly specify an individual, other than the self, by implementing a functional other-/self-distinction across perception, action, cognition, and emotion. It is important to highlight that specificity does not signify that these regions are limited to this one specific function only. That is, specificity does not imply exclusivity, wherein pACC and PCC/PC would define conceptual self and conceptual other exclusively [cf. Legrand and Ruby, 2009]. Nor does it signify "noncontingency," where the absence of pACC or PCC/PC would result in an absence of conceptual self- or conceptual other-processing, respectively [Legrand and Ruby, 2009]. Still, earlier theoretical reviews have critiqued the investigation of self-specificity, arguing for probable confounds of familiarity processing [cf. Gillihan and Farah, 2005] and task/stimulus effects [cf. Legrand and Ruby, 2009] in self- and other-processing. Controlling for both these variables meta-analytically, however, Qin and North-off [2011] demonstrated self-specificity to remain linked to pACC activation and other-specificity to PCC/PC activation. Thus, the current best estimate of pACC and PCC/PC argues that they serve as important neural hubs facilitating self-specific and other-specific processing, differentiated from generalized functions such as familiarity processing.

Furthermore, conceptual self-processing proves differentiated from semantic autobiographical memory retrieval per se, in that the former integrates general personal semantic knowledge with persistent social cues to organize a self-representation inclusive of personality traits, values, beliefs, goals, and attitudes [Conway et al., 2004; Morin and Hamper, 2012]. Neurobiological support for these distinctions comes from recent lesion data demonstrating semantic autobiographical memory [Philippi et al., in press] and self-referential processing [Philippi et al., 2012a] to depend on healthy ventromedial prefrontal activity,

whereas personality trait updating was dependent on healthy pACC activity [Philippi et al., 2012b]. This would suggest dissociated cortical regions separately subserving semantic episodic autobiographical memory retrieval and self-concept and script updating. This does not imply that the two processes are independent, however, as conceptual self- and other-processing appear nonetheless reliant on semantic autobiographical memories [D'Argembeau et al., 2008]. Therefore, delineating the cognitive–behavioral functions of these two neural regions remains vital to the debate on the constituents of a cohesive and accurate sense of self and other, and while an investigation into the cortical/subcortical plasticity of compensatory regions unaffected by trauma in light of a lesioned pACC lies beyond the purview of this study, these aforementioned findings underscore nonetheless the significance of exploring the functional connectivity of the neural hubs of conceptual self- and other-processing.

Beyond the debate of specificity lies the necessity of delineating the conceptual self, as a psychological construct, from the more frequently employed terms in the neuroimaging literature. This includes principally the "experiential self" [Northoff et al., 2006] and the "minimal self" [Gallagher, 2000; Northoff, 2013]. Specifically, conceptual self-processing relies on executive functions that are arguably more cognitively demanding than the self-referential processing identified in these latter two constructs. For instance, the "experiential self" reflects appraisals of oneself in relation to its environment [Northoff et al., 2006], while "minimal self" refers to "the self as implicitly, tacitly, and immediately experienced in consciousness" [Gallagher, 2000; Northoff, 2013]. The conceptual self, conversely, iteratively instantiates coherent and operable psychological representations of both self and others [Conway et al., 2004], which requires continuous updating and correction of personal scripts and self-concepts given current and prior available social cues and feedback [Grant et al., 2002; Satne, 2014]. Thus, while both semantic autobiographical memory and self-referencing are necessary for conceptual self-processing, neither is sufficient to instantiate a coherent and current psychological representation of one's self or other.

Finally, the conceptual self, unlike the experiential and minimal self, may be integrally embedded in social cognitive processing and decision making [Conway et al., 2004; Cooley, 1902; Mead and Morris, 1967]. For instance, primate data demonstrate the pACC to facilitate the representation of value [Rolls, in press; Vogt, 2014], which is defined as having self-relevant reward and/or punishment potential. Critically, value has been attributed to social information and feedback [Behrens et al., 2008; Ruff and Fehr, 2014], and neural regions considered to scale value representations, such as the pACC [Vogt, 2014], are argued to process the reward/punishment value of social information [Rolls, in press]. The pACC, therefore, may use social information gained from others to infer value on specific interpersonal behaviors and outcomes.

Social value representations specific to interpersonal interactions with others may in fact be instantiated by neuronal activity within the ventromedial prefrontal cortex (vMPFC) [Behrens et al., 2008] and medial orbitofrontal cortex (mOFC) [Ruff and Fehr, 2014], which demonstrate reciprocal pathways with the pACC within primate brains [Kringelbach and Rolls, 2004]. Moreover, human neuroimaging research demonstrates shared conceptual self- and other-processing in the vMPFC [Amodio and Frith, 2006; Bzdok et al., 2013a; Yaoi et al., 2009; Zhang et al., 2006]. Furthermore, functional magnetic resonance imaging (fMRI) evidence suggests a preattentive resting brain system internalizing prior social experiences for the purposes of conceptual self-updating and correction [Bzdok et al., 2013b; Schilbach et al., 2008]. The conceptual other may, therefore, constitute an essential component within the conceptual self's qualitative constitution and neural architecture, and delineating the functional connectivity of both seed regions would be crucial to understanding the holistic functioning of our mental representation of ourselves and others.

In this article, therefore, we investigated the task-dependent and task-independent functional connectivity of cortical regions consistently correlated with conceptual self-specific and other-specific processing. Consequently, we used a seed from a study that had a narrower focus than that of earlier meta-analyses, which have subsumed conceptual self-processing under a larger rubric, entitled "self," inclusive of the physical self, personal agency, and first-person perspective taking [e.g., Qin and Northoff, 2011]. Specifically, quantitative meta-analytic evidence indicates the pACC (Area 24/32) reliably yields differential blood oxygen level-dependent (BOLD) activity during conceptual self-specific processing [Martinelli et al., 2012; Murray et al., 2012; van der Meer et al., 2010]. Inversely, conceptual other-specific processing has been shown meta-analytically to yield neural activation within the PCC/PC border (Area 7a) relative to conceptual self-processing [Murray et al., 2012]. Thus, we chose the pACC and PCC/PC, respectively, as conceptual self- and conceptual other-seeds.

Here, we attempted to investigate the underlying functional connectivity of these regions as well as their functional profiles, recruiting the neuroimaging literature to provide greater clarity on the underlying processes and functional circuitry of two cortical regions consistently implicated in self- and other-processing. We, thus, retrieved our conceptual self- and other-seeds from a recent meta-analysis by Murray et al. [2012], who analyzed published neuroimaging literature reporting both conceptual self versus other and conceptual other- versus self-contrasts, within Western populations. We first performed task-dependent meta-analytical connectivity modeling (MACM) and task-independent resting-state (RS) connectivity analysis for each seed, allowing us to observe functional connectivity networks of putative conceptual self- and other-seeds during each brain state. Next, we investigated functional connectivity differentiation by comparing conceptual self- and other-seeds across both MACM and

RS, permitting functional connectivity analysis across both brains states. We also investigated overlap by conjoining conceptual self- and other-seeds. Finally, we delineated the functional profiling of the two seeds using BrainMap metadata. In a data-driven fashion, we examined the connectional and functional characteristics of the pACC and PCC/PC as conceptual self- and other-seeds.

MATERIALS AND METHODS

Seed Regions

Recent neuroimaging meta-analyses attributed conceptual self-specific processing, particularly to the pACC (Area 24/32) and conceptual other-specific processing to the PCC/PC (Area 7a/7m) [Murray et al., 2012]. These two seed regions are displayed in Figure 1. The designation of these two regions as seeds is owed to the specificity by which they are demonstrated to respond differentially to conceptual self- and conceptual other-processing. It is important to highlight that additional cortical regions have been attributed to retrieval of semantic knowledge [Garrard and Hodges, 2000; Mummery et al., 2000] and personality traits which are nonspecific to self or other [Skipper et al., 2011]. However, only pACC activation has been reliably shown to differentially respond to conceptual self-processing, with respect to conceptual other-processing (i.e., self-specific) [Martinelli et al., 2012; Murray et al., 2012], while PCC/PC activation has been shown to differentially respond to conceptual other-processing, relative to conceptual self-processing (i.e., other-specific) [Murray et al., 2012]. Accordingly, while the temporal pole is considered to be important in self- versus nonself-representations [D'Argembeau et al., 2007; Legrand and Ruby, 2009; Northoff et al., 2006; van der Meer et al., 2010], quantitative meta-analyses, integrating across all relevant studies, did not find temporal pole activations when contrasting conceptual self- against conceptual other-processing [e.g., Martinelli et al., 2012; Murray et al., 2012].

We thus conducted functional connectivity analyses and functional profiling of these two seed regions using coordinate-based meta-analytic modeling (MACM analysis). We complement this task-dependent measure of functional connectivity with task-independent time-series correlations (RS analysis) across the whole brain. For the purposes of consistency, we will refer to conceptual self and conceptual other as "self" and "other," respectively.

Task-Dependent Functional Connectivity: MACM

We delineated whole-brain coactivation maps for each seed using the BrainMap database (www.brainmap.org) [Fox and Lancaster, 2002; Laird et al., 2011]. Analyses were limited to fMRI and PET analyses using "healthy," or "normal," populations wherein whole-brain coordinate results are reported in standard stereotaxic space. Using a
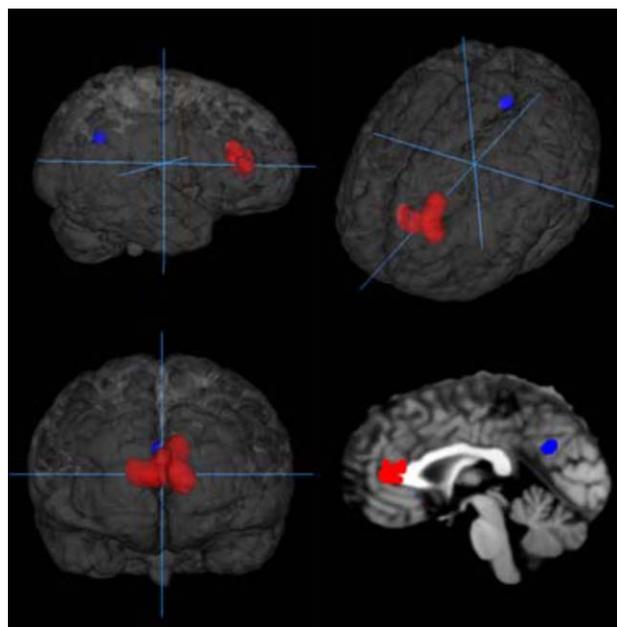

Figure 1.

Location of the seed regions. Seeds were drawn from an earlier coordinate-based neuroimaging meta-analysis on conceptual self versus conceptual other, which yielded two clusters of convergent brain activity in the pregenual anterior cingulate (red) for conceptual self > conceptual other (i.e., conceptual self) and in the posterior cingulate/precuneus (blue) for conceptual other > conceptual self [i.e., conceptual other; Murray et al., 2012]. The centers of mass of the pregenual anterior cingulate and posterior cingulate/precuneus are (x, y, z) −2, 38, 16 and 2, −61, 26, respectively. The seeds were rendered into a T1-weighted MNI single subject template using Mango (multi-image analysis graphical user interface (GUI); http://ric.uthscsa.edu/mango/). Crosshairs are positioned at (x, y, z) 0, 0, 10. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

restricted sample necessarily precludes studies including clinical interventions or populations, but also group comparisons such as age and gender. These criteria yielded roughly 7,200 eligible BrainMap studies at the time of the analysis. Our analyses remain purely data-driven, thus largely excluding a priori hypothesis, such as the relationship between tasks and brain regions. Therefore, all eligible studies were included in the analysis. Restrictions on acquisition or analysis procedures, experimental design, or stimulation procedures were not applied. The MACM process was applied independently for both self- and other-seed regions. Experiments were filtered to retain only those featuring at least one activation within the respective seeds. This yielded 193 experiments (3,197 subjects, 2,671 foci) for the self-seed and 106 experiments (1,234 subjects, 1,644 foci) for the other-seed, on which the MACM analyses were then performed individually each seed.

To reliably delineate the coactivation patterns of a specific seed, we identify the BrainMap studies reporting at

least one activation focus located within the respective seed. These ensuing studies, identified as being associated with the respective seed, subsequently underwent an activation likelihood estimation (ALE) meta-analysis, wherein all reported foci of these studies were included [Eickhoff et al., 2009; Laird et al., 2009a; Turkeltaub et al., 2002]. The principal idea behind ALE is to consider the reported foci not as single points, but rather as centers for 3D Gaussian probability distributions capturing the spatial uncertainty associated with each focus based on an empirical model of between-subject and between-template variance [Eickhoff et al., 2009]. The probabilities of all foci reported in a given experiment were then combined for each voxel, resulting in a modeled activation (MA) map [Turkeltaub et al., 2012]. Taking the union across these MA maps yielded voxelwise ALE scores describing the convergence of results at each particular location of the brain. To distinguish "true" convergence between studies from random convergence (i.e., noise), ALE scores were compared to an empirical but analytically solved null-distribution [Eickhoff et al., 2012] reflecting a random spatial association between experiments. Hereby, a random-effects inference is invoked, focusing on inference on the above-chance convergence between experiments, not clustering of foci within a particular study. Significant P values were then indicated by the proportion of equal or higher values observable under the null-distribution [Eickhoff et al., 2012]. The resulting nonparametric P values for a given meta-analysis were then thresholded at a cluster-level familywise errorrate (FEW)-corrected threshold of $P < 0.05$ (cluster-forming threshold at $P < 0.001$).

To contrast the task-dependent functional connectivity of the different seed regions, we first calculated the voxelwise differences in ALE scores between the two MACM analyses. The experiments contributing to either analysis were then pooled and randomly divided into two groups of the same size as the sets of contrasted experiments [Eickhoff and Grefkes, 2011; Eickhoff et al., 2012; Friebel et al., 2011]. Voxelwise ALE scores for these two randomly assembled groups were then subtracted from each other and recorded. Repeating this process 10,000 times yielded an empirical null-distribution of ALE-score differences between the two conditions [Eickhoff et al., 2012]. The observed difference in ALE scores was then tested against the null-distribution, resulting in a P value for the difference at each voxel according to the proportion of equal or greater random differences. Based on this permutation (label exchange) procedure, the map of true differences was then thresholded at a posterior probability of $P > 0.95$ for a true difference between the two samples (cluster extend threshold: $k_E \geq 25$ voxels, [Rottschy et al., 2012]). A supplementary MACM analysis of task-dependent neuroimaging data was conducted using the NeuroSynth database (http://neurosynth.org; Yarkoni et al., 2011) for both self and other seeds. These results are provided in the Supporting Information (Figures S1 and S2).

Task-Independent Functional Connectivity: RS Correlations

RS fMRI images of 153 healthy volunteers (mean age 41.1 ± 18.0 [SD] years; 92 male) from the NKI/Rockland sample were obtained through the 1,000 functional connectomes project (www.nitrc.org/projects/fcon_1000/). During the RS scans, subjects were instructed to keep their eyes closed and to think about nothing in particular but not to fall asleep (which was confirmed by post-scan debriefing). All subjects gave written informed consent to the study protocol, which had been approved by the local ethics committee. For each subject, 260 RS echo planar imaging (EPI) images were acquired on a Siemens TimTrio 3T scanner using BOLD contrast (gradient-echo EPI pulse sequence, repetition time (TR) = 2.5 s, echo time (TE) = 30 ms, flip angle = 80°, in plane resolution = 3.0 × 3.0 mm^2, 38 axial slices [3.0 mm thickness] covering the entire brain). The first four scans were excluded from further processing analysis using statistical parametric mapping, software version 8 (SPM8) to allow for magnet saturation. The remaining EPI images were first corrected for movement artifacts by affine registration using a two pass procedure in which the images were first aligned to the initial volumes and subsequently to the mean after the first pass. The obtained mean EPI of each subject was then spatially normalized to the montreal neurological institute (MNI) single subject template using the "unified segmentation" approach [Ashburner and Friston, 2005]. The ensuing deformation was applied to the individual EPI volumes. To improve signal-to-noise ratio and compensate for residual anatomical variations, images were smoothed by a 5-mm FWHM Gaussian.

The time-series data of each voxel were processed as follows [Jakobs et al., 2012; Weissenbacher et al., 2009]. To reduce spurious correlations, variance that could be explained by the following nuisance variables, was removed: (i) The six motion parameters derived from the image realignment, (ii) the first derivative of the realignment parameters, (iii) mean gray matter, white matter, and cerebral spinal fluid (CSF) signal per time-point as obtained by averaging across voxels attributed to the respective tissue class in the SPM8 segmentation, and (iv) coherent signal changes across the whole brain as reflected by the first five components of a principal component analysis (PCA) decomposition of the whole-brain time-series [Behzadi et al., 2007; Reetz et al., 2012]. All nuisance variables entered the model as first and all but the PCA components also as second-order terms as previously described by Behzadi et al. [2007] and shown by Chai et al. [2012] to increase specificity and sensitivity of the analyses. Data were then band pass filtered preserving frequencies between 0.01 and 0.08 Hz, since meaningful RS correlations will predominantly be found in these frequencies given that the BOLD-response acts as a low-pass filter.

We used the same seed regions as for the MACM analysis, that is, the clusters obtained by Murray et al. [2012] for

self- and other-specific processing. Time-courses were extracted for all voxels within the particular cluster and expressed as their first eigenvariate. Linear (Pearson) correlation coefficients between the time series of the seed regions and all other gray matter voxels in the brain were computed to quantify RS functional connectivity [Reetz et al., 2012; Zu Eulenburg et al., 2012]. These voxelwise correlation coefficients were then transformed into Fisher's Z-scores and tested for consistency in a flexible factorial model across subjects ($P < 0.05$ cluster-level FEW-corrected, cluster-forming threshold at voxel-level $P < 0.001$). Thus, the same threshold for our task-dependent MACM analysis was, thus, used for our task-independent RS connectivity analysis.

Conjunction Analyses

To delineate areas functionally connected to the core regions for self and for other across both task-dependent (MACM) and task-independent (RS) states, we conducted a conjunction analysis using the strict minimum statistic [Nichols et al., 2005]. More specifically, we compared the intersection of the thresholded (cluster level FWE-corrected) maps of MACM and RS connectivity (hereafter called MACM∩RS) for self and other, individually [cf. Jakobs et al., 2012; Reetz et al., 2012]. Additionally, we wished to examine shared functional connectivity between self and other during task-dependent and task-independent states. Therefore, we conducted two separate conjunction analyses between self and other (hereafter, self∩other) for both MACM and RS, respectively, [MACM (self∩other) and RS (self∩other)].

Finally, we delineated areas of differential functional connectivity with both seeds in and across MACM and RS. To identify regions where functional connectivity was specifically stronger to the self-seed and other-seed, respectively, we thus conducted three separate sets of contrast analyses: (i) MACM only; (ii) RS only; and (iii) MACM∩RS analyses. In the first set of analyses, we contrasted the task-dependent MACM functional connectivity maps of self against those of other (i.e., MACM [self > other] and MACM [self < other]). In the second set of analyses, we contrasted the RS connectivity maps of self and other (i.e., RS [self > other] and RS [self < other]). Finally, in the third set of analyses, we contrasted the ensuing MACM∩RS functional connectivity intersection, as described above, of self against that of other (i.e., MACM∩RS [self > other] and MACM∩RS [self < other]). This third set of analyses would demonstrate regions showing a significantly stronger task-dependent and task-independent connectivity with the self- and other-seeds, respectively.

Labeling of resultant connectivity targets was triangulated using stereotaxic and anatomical localizations provided by the Atlas of the Human Brain (3rd Edition) [Mai et al., 2008], the cingulate flat map [Vogt, 2014], and the SPM anatomy toolbox (http://www.fz-juelich.de/inm/ inm-1/DE/Forschung/_docs/SPMAnatomy Toolbox/ SPMAnatomyToolbox_node.html, [Eickhoff et al., 2005, 2006, 2007]).

Functional Characterization

The cognitive–behavioral attribution, or functional characterization, of the seeds was based on the BrainMap meta-data that describe the classes of mental processes isolated by the archived experiments' statistical contrasts. Behavioral domains comprise the main categories of cognition, action, perception, emotion, and interoception, as well as their related subcategories. Paradigm classes categorize the specific task used [Fox et al., 2005].

Behavioral domains and paradigm class labels represent quality checked taxonomies developed via hierarchically structured keywords and categories by the BrainMap authors, and thus, do not reflect the individual studies' categorical nomenclatures [Fox et al., 2005]. These cognitive ontologies have been devised by psychologists and neuroscientists, proficient in their field, during annual meetings. As it stands today, there is no universal consensus on functional profiling taxonomies, and the extant domains and classes used at present may engender a degree of bias. This limitation notwithstanding, these categories are continuously refined and nonetheless represent the most consistent and widely applied ontology currently in existence.

To arrive at such classification of the seeds' functional properties, both forward and reverse inference algorithms were used. Whereas forward inference reflects the probability of observing activity in a brain region given knowledge of the psychological process, reverse inference represents the probability of a psychological process being present given knowledge of activation in a particular brain region. In the forward inference approach, the functional profiles of the self-/other-seeds were determined by identifying taxonomic labels for which the probability of finding activation in the respective cluster was significantly higher than the overall chance (across the entire database) of finding activation in that particular cluster. Significance was established using a binomial test [$P < 0.001$; Eickhoff et al., 2011; Laird et al., 2009]. That is, we tested whether the conditional probability of activation given a particular label [$P(\text{Activation} | \text{Task})$] was higher than the baseline probability of activating the region in question per se [$P(\text{Activation})$]. In the reverse inference approach, a cluster's functional profile was determined by identifying the most likely behavioral domains and paradigm classes given activation in a particular cluster. This likelihood $P(\text{Task} | \text{Activation})$ can be derived from $P(\text{Activation} | \text{Task})$ as well as $P(\text{Task})$ and $P(\text{Activation})$ using Bayes rule. In this context, the base rate denotes the probability of finding a (random) activation from BrainMap in that cluster. Significance was then assessed by a χ^2 test ($P < 0.001$). In sum, forward inference assessed the

probability of activation given a term, whereas reverse inference assessed the probability of a term given activation. It is important to appreciate that this approach aims at relating defined psychological tasks to the examined brain regions instead of claiming "a unique role" of a brain region for this task [Poldrack, 2006; Yarkoni et al., 2011]. Put differently, an association of task X to brain region Y does not necessarily imply that activity in region Y is limited to task X. A supplementary functional characterization analysis of task-dependent neuroimaging data was conducted using the NeuroSynth database (http://neurosynth.org; Yarkoni et al., 2011) for both self and other seeds. The results of this analysis are provided in the Supporting Information (Tables S1 and S2).

RESULTS

Below, we provide the results of our MACM and RS connectivity analyses for both conceptual self-and conceptual other-seeds.

Task-Dependent Functional Connectivity: MACM Only

For the conceptual self- (i.e., self) condition, using the pACC as the seed region, MACM-only analyses of task-dependent brain states revealed convergent activations at above-chance levels, indicative of significant coactivations, bilaterally in the anterior insula (Area 13/47), and laterally in the left striatum, right thalamus, and right amygdala (Fig. 2A and Table I). When contrasted against the conceptual other seed, however, we observed differential task-dependent coactivations within the left anterior insula only, the striatum not surviving the voxel extent threshold of 20 voxels (Fig. 2A and Table I).

For conceptual other (i.e., other), using the PCC/PC as the seed region, MACM-only analyses yielded significant coactivations bilaterally in the angular gyrus/temporoparietal junction (AG/TPJ; Area 39) and laterally within the left mOFC (Area 11), and left superior frontal gyrus (Area 9). When contrasted against self, MACM-only analyses for other revealed significant differential coactivations bilaterally within the AG/TPJ, left mOFC, and left vMPFC (Area 10; Fig. 2B and Table I).

Task-Independent Functional Connectivity: RS Correlations Only

Analysis of RS functional connectivity for the pACC (self-seed) yielded a distributed network, comprising the pACC cortex, bilaterally in the thalamus, parietal–occipital junction (Area 7/19), and laterally in the left ventromedial prefrontal/medial orbitofrontal cortex (Area 10/11), left posterior insula (Area 13), left striatum, right lateral superior frontal gyrus (Area 9), and right calcarine gyrus (Area 30; Fig. 3A and Table II). When contrasted against the other-seed (i.e., self > other), RS functional connectivity
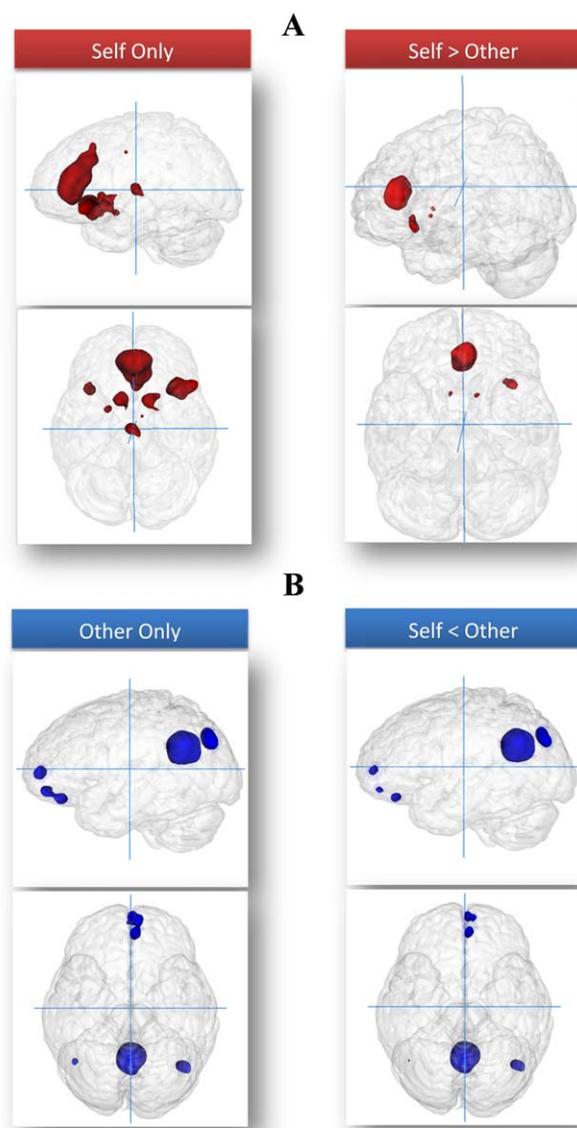
Figure 2.

MACM only significant coactivations of conceptual self- and other-seeds. Figure presents significant coactivations of (**A**) the conceptual self-(i.e., self) seed (pregenual anterior cingulate) as a main effect and when contrasted against the conceptual other-(i.e., other) seed (posterior cingulate cortex/precuneus) and (**B**) the conceptual other-seed as a main effect and when contrasted against the conceptual self-seed. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

analyses of the self-seed yielded differential correlations bilaterally within the thalamus and parietal–occipital junction, and laterally in the left middle frontal gyrus (Area 9), left vMPFC/mOFC (Area 10/11), left posterior insula (Area 13), left striatum, right calcarine gyrus (Area 30), and right superior frontal gyrus (Area 9; Fig. 3A and Table II)

TABLE I. Meta-analytic connectivity modeling (MACM) only correlations with pregenual anterior cingulate (self-seed) and posterior cingulate/precuneus (other-seed)

Region	Area	Hem	Size (voxels)	x	y	z
MACM (self)						
Pregenual anterior cingulate	24/32	L	1,978	−2	36	12
Anterior insula	13/47	L	389	−36	14	−10
		R	102	38	16	0
Striatum		L	127	−12	8	−4
Thalamus		R	106	4	−18	8
Amygdala		R	26	20	0	−14
MACM (self > other)						
Pregenual anterior cingulate	24	L	719	−2	34	2
Anterior insula	13/47	L	60	−36	14	−8
MACM (other)						
Posterior cingulate/precuneus	7a		11,562	0	−58	28
Medial orbitofrontal cortex	11	L	1,259	−2	40	−16
Angular gyrus/medial temporoparietal junction	39	L	1,187	−46	−68	32
		R	252	50	−62	24
Superior frontal gyrus	9	L	801	−2	60	6
MACM (self < other)						
Posterior cingulate cortex/precuneus	7a	R	1,328	0	−58	28
Medial orbitofrontal cortex	11	L	132	−2	40	−16
Angular gyrus/temporoparietal junction	39	L	127	−46	−68	32
		R	26	50	−62	24
Ventromedial prefrontal cortex	10	L	85	−4	58	6

Cluster labels are within ±5 mm. Voxel size = 1 mm^3. Resultant clusters with less than 20 voxels were not reported, although these clusters may appear in the figures provided. < and > denote difference analyses.
MACM, task-dependent meta-analytic connectivity modeling.

Analysis of RS functional connectivity for the PCC/PC (other-seed) also yielded distributed brain regions, bilaterally in the AG/TPJ (Area 39), middle temporal gyrus (Area 21), and cerebellum and laterally in the left hippocampus, right parahippocampal gyrus, right mOFC (Area 11), and right thalamus (Fig. 3B and Table II). Relative to self-seed RS functional connectivity (i.e., self < other), we observed differential other seed RS functional connectivity bilaterally in the AG/TPJ, fusiform gyrus (Area 36), middle temporal gyrus (Area 21) and cerebellum, and laterally in the right mOFC, right superior frontal gyrus (Area 8), right hippocampus, and right paracentral lobule (Fig. 3B and Table II).

Conjunction Between MACM and RS (MACM∩RS)

The conjunction of task-dependent MACM and task-independent RS (i.e., MACM∩RS) results for the pACC (self-seed) yielded shared functional connectivity in both left and right hemispheres. Bilaterally, MACM∩RS yielded overlapping functional connectivity in the anterior insula (Area 13). Laterally, MACM∩RS yielded activation in the left striatum and right thalamus (Fig. 4A and Table III). When contrasted against other, however, only left anterior insula coactivation for self was observed (Fig. 4A and Table III)

For the PCC/PC (other condition), MACM∩RS revealed activations in the left hemisphere. Specifically, MACM∩RS yielded activations within the left mOFC, left AG/TPJ, and left vMPFC (Fig. 4B and Table III). When contrasted against self, however, bilateral AG/TPJ differential coactivation for other was observed (Fig. 4B and Table III).

Conjunction Between Self and Other (self∩other)

Next, we addressed the convergent functional connectivity of self and other, as observed in separate MACM and RS connectivity analyses. Conjunction analyses for MACM (self∩other) revealed no shared significant coactivations between self- and other-seeds. However, conjunction analyses for RS (self∩other) did reveal shared connectivity within the anterior cortical midline structures, bilaterally in the vMPFC/mOFC (Area 10/11) bordering into the anterior cingulate cortex (Fig. 3C and Table IV).

Functional Characterization

Finally, we assessed the behavioral domains and paradigm classes, which were associated at above-chance levels, with the self- and other-seeds, respectively. All results may be observed in Figure 5. Significant representation of the self-seed was identified in the behavioral domains of emotion, cognition, and action/inhibition, perception, and

A

B

C
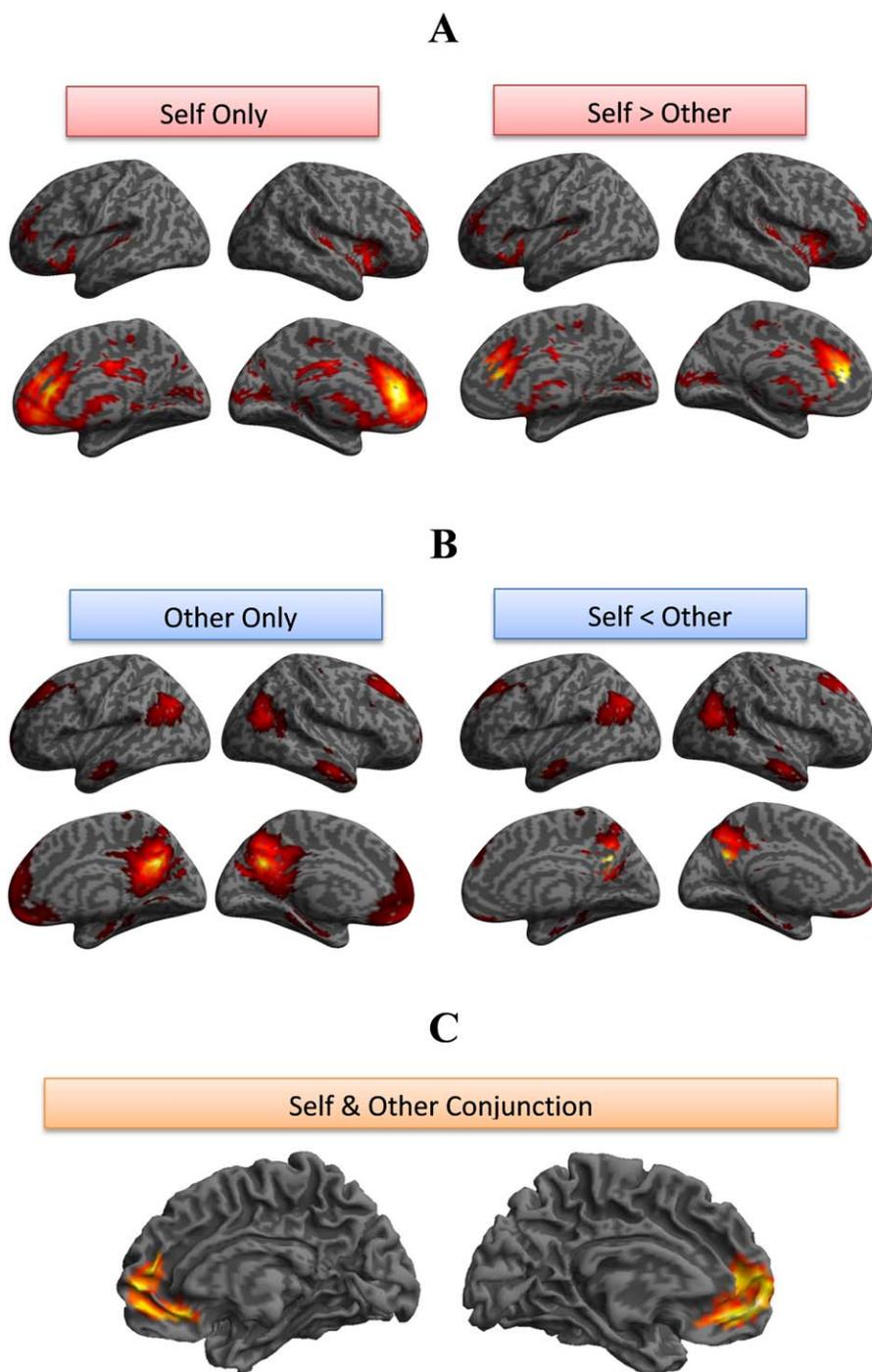
Figure 3.

Resting-state (RS) only functional connectivity of the conceptual self and other seeds. Figure represents significant RS correlations of (**A**) the conceptual self- (i.e. self) seed (pregenual anterior cingulate) as a main effect and when contrasted against the conceptual other- (i.e., other) seed (posterior cingulate cortex/ precuneus), (**B**) the conceptual other-seed as a main effect and when contrasted against the conceptual self, and of (**C**) the conjunction of both conceptual self- and other-seeds. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

TABLE II. Resting-state (RS) only correlations with pregenual anterior cingulate (self-seed) and posterior cingulate/precuneus (other-seed)

Region	Area	Hem	Size (voxels)	x	y	z
RS (self)						
Pregenual anterior cingulate	24/32		32,959	0	36	12
Calcarine gyrus	30	R	2,654	17	−69	9
Superior frontal gyrus	9	R	2,094	23	44	21
Middle frontal gyrus	9	L	1,982	−26	41	26
Thalamus		L	616	−11	−38	2
		R	324	17	−39	2
Parietal–occipital junction	7/19	L	450	−8	−81	38
		R	296	11	−72	36
Ventromedial prefrontal/medial orbitofrontal cortex	10/11	L	263	−27	44	−18
Striatum		L	144	−26	−32	20
Posterior insula	13	L	72	−41	−18	−6
RS (self > other)						
Pregenual anterior cingulate	24/32		23,524	0	36	12
Calcarine gyrus	30	R	2,445	17	−69	9
Superior frontal gyrus	9	R	1,793	23	44	21
Middle frontal gyrus	9	L	1,701	−27	41	26
Orbitofrontal gyrus	11	L	263	−27	44	−18
Thalamus		L	171	−15	−36	2
		R	105	17	−39	2
Striatum		L	118	−26	−32	20
Posterior insula	13	L	72	−41	−18	−6
RS (other)						
Medial orbitofrontal cortex	11	R	22,726	3	57	−14
Posterior cingulate/precuneus	7a/7m	R	18,584	2	−62	27
Angular gyrus/temporoparietal junction	39	R	6,933	47	−71	27
		L	6,620	−44	−69	32
Middle temporal gyrus	21	R	3,942	60	−5	−21
		L	2,783	−65	−8	−21
Hippocampus		L	1,356	−26	−15	−23
Parahippocampal gyrus		R	1,266	26	−18	−24
Cerebellum		L	761	−8	−53	−44
		L	319	−14	−84	−42
		L	181	−32	−84	−33
		R	137	15	−83	−42
Thalamus		R	62	17	−29	9
RS (self < other)						
Medial orbitofrontal cortex	11	R	11,130	2	59	−18
Superior frontal gyrus	8	R	8,317	23	27	42
Angular gyrus/temporoparietal junction	39	R	6,933	45	−71	29
		L	6,620	−44	−69	32
Posterior cingulate/precuneus	7a/7m	R	6,617	2	−62	27
	23/30	R	589	9	−54	18
Middle temporal gyrus	21	R	3,487	60	−5	−23
		L	2,694	−65	−8	−20
Parahippocampal gyrus	35	R	202	20	−11	27
		L	141	−21	−12	−27
Hippocampus		R	871	26	−15	−24
Cerebellum		L	659	−8	−53	−45
		L	315	−14	−83	−44
		L	160	−32	−84	−33
		R	137	15	−83	−42
Fusiform gyrus	36	L	415	−29	−38	−15
		R	251	29	−33	−18
Paracentral lobule	4/6	R	178	2	−32	66

Cluster labels are within ±5 mm. Voxel size = 1.5 mm^3. Resultant clusters with less than 20 voxels were not reported, although these clusters may appear in the figures provided. < and > denote difference analyses.
RS, task-independent resting-state.
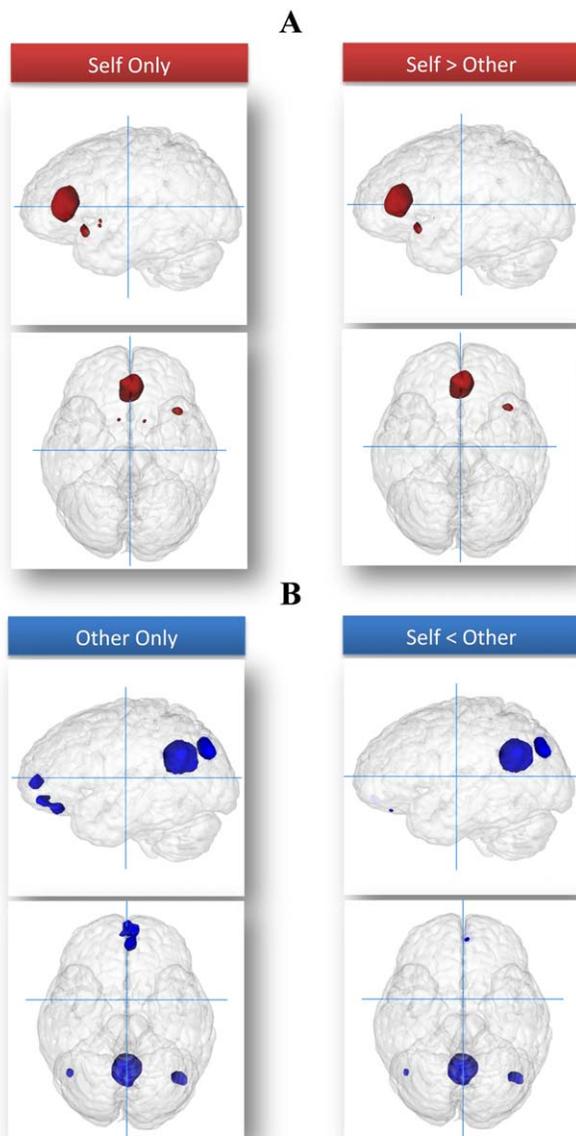
Figure 4.

MACM and RS functional connectivity for conceptual self and other seeds. Figure presents conjunction of significant MACM coactivations and RS correlations of (**A**) the conceptual self-(i.e., self) seed (pregenual anterior cingulate) as a main effect and when contrasted against the conceptual other-(i.e., other) seed (posterior cingulate cortex/precuneus) and (**B**) the conceptual other seed as a main effect and when contrasted against the conceptual self. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

interoception. Behavioral domains of perception and interoception included particular subdomains of pain and sexuality, respectively. In terms of paradigm classes, the self-seed was attributed to reward tasks, the Stroop task, and go/no-go tasks (Fig. 5A).

Concerning the other-seed, significant representation of the other-seed was identified in the behavioral domains of cognition. Cognition included subdomains social cognition, language/semantics, and explicit memory. The other-seed was further attributed to the paradigm classes of theory of mind task and face monitoring/discrimination (Fig. 5B).

DISCUSSION

We investigated functional connectivity of both conceptual self (hereafter, self) and conceptual other (hereafter, other) using task-dependent MACM and task-independent RS functional connectivity analyses. Our goal was to unveil the neural networks associated with self and other during both brain states and to identify regions showing differential and overlapping functional connectivity. Quantitative meta-analytic data showed the pACC [Martinelli et al., 2012; Murray et al., 2012; van der Meer et al., 2010] and PCC/PC [Murray et al., 2012] to be reliably involved in self-specific and other-specific reflection, which we used as self and other seed regions, respectively. Last, using BrainMap-derived hierarchical taxonomies, we further performed functional profiling of the self-seed (pACC) and other-seed (PCC/PC) to objectively identify their associated psychological processes and to better define the global functioning of these two regions, irrespective of self- or other-related processing.

Delineating a Conceptual Self-Network

When conjoining both task-dependent (MACM) and task-independent brain states (RS), we found self-seed (pACC) connectivity with the anterior insula, thalamus, and the striatum. Notably, only anterior insula functional connectivity survived the contrast against the conceptual-other seed (PCC/PC). Additionally, functional profiling illustrated the self-seed to be selectively associated with conflict detection/resolution, emotion, action/inhibition, reward, and interoception. With regards to the two former characterizations, the self-seed demonstrates a selective association with conflict detection/resolution per our observation of the Stroop paradigm class association, but also with the domain of emotion. As the pACC has been linked with emotional conflict resolution in healthy and clinical populations [Etkin et al., 2006; Rey et al., 2014; Taylor et al., 2006], wherein participants inhibit cognitive interference caused by task-irrelevant emotions [Etkin et al., 2006], our observed functional profile may, therefore, indicate the pACC to facilitate cognitive control when faced with emotionally salient information that conflicts with one's self-concept [Epp et al., 2012; Fitzgerald et al., 2011].

Additional neural regions, such as the insular cortex, may also play a role in affective information processing. Specifically, the anterior insula's functional connectivity with the pACC may also be elemental in updating

TABLE III. MACM and RS Conjunction relative to pregenual anterior cingulate (self-seed) and posterior cingulate/precuneus (other-seed)

Region	Area	Hem	Size (voxels)	x	y	z
MACM∩RS (self)						
Pregenual anterior cingulate	24/32	L	1,952	−2	36	12
Anterior insula	13	L	257	−36	14	−10
		R	97	38	16	0
Striatum		L	113	−12	8	−4
Thalamus		R	75	4	−16	8
MACM∩RS (self > other)						
Pregenual anterior cingulate	24	L	716	−2	34	2
Anterior insula	13	L	50	−36	14	−8
MACM∩RS (other)						
Posterior cingulate/precuneus	7a		1,324	0	−58	28
Medial orbitofrontal cortex	11	L	131	−2	40	−16
Angular gyrus/temporoparietal junction	39	L	127	−46	−68	32
Ventromedial prefrontal cortex	10	L	84	−2	60	6
MACM∩RS (self < other)						
Posterior cingulate/precuneus	7m	R	1,316	4	−66	18
Angular gyrus/temporoparietal junction	39	L	127	−46	−68	32
		R	26	50	−66	22

Cluster labels are within ±5 mm. Voxel size = 1 mm³. Resultant clusters with less than 20 voxels were not reported, although these clusters may appear in the figures provided. < and > denote difference analyses while ∩ denotes conjunction analysis.
MACM, task-dependent MACM; RS, task-independent RS.

affective self-representations [Mendez and Shapira, 2011; Philippi et al., 2012b], potentially through viscerosensory information feedback [Craig, 2009; Kurth et al., 2010]. Functional profiling additionally illustrates the self-seed to associate with interoceptive processing, primarily in relation to motivational states, particularly sexual desire. Elemental in orienting oneself in one's physical body [Legrand and Ruby, 2009], interoception reflects the mental organization of afferent visceral cues [Aziz et al., 1995; Pollatos and Schandry, 2004] and internal states [Farb et al., 2013] and may serve as a basic form of self-representation [Northoff and Panksepp, 2008]. The anterior insula remains an established neural hub for interoceptive processing [Craig, 2009; Kurth et al., 2010], but may be more significantly implicated in evaluating the salience of interoceptive cues [Wiech et al., 2010], as has been sug-

gested by a recent meta-analysis [Cauda et al., 2012]. The anterior insula may thus organize interoceptive information, most likely relayed by the posterior insula [Cauda et al., 2012] as well by upstream "low-road" signaling from afferent thalamic projections, which would serve as an input for external environmental stimuli [Grabenhorst and Rolls, 2011; LeDoux, 1994, 2000]. Such signals may be consolidated in the posterior insula to be organized, represented, and appraised for salience within the anterior insula [Cauda et al., 2012]. As a result, pACC–anterior insula connectivity may facilitate continuous relevant self-representations across task-dependent and task-independent brain states.

Coupled with pACC functioning, the anterior insula has been evidenced as a crucial region for self-representation within the clinical and lesion literatures. For instance,

TABLE IV. Conjunction of conceptual self (i.e., self) and other (i.e., other) seeds for MACM and RS

Region	Area	Hem	Size (voxels)	x	y	z
MACM (self∩other)						
No significant coactivations						
RS (self∩other)						
Ventromedial prefrontal cortex/medial orbitofrontal cortex	10/11	L/R	6,204	−2	60	−5

Cluster labels are within ±5 mm. ∩ denotes conjunction analysis. Voxel size = 1 mm³.
MACM, task-dependent meta-analytic connectivity modeling; RS, task-independent resting-state.
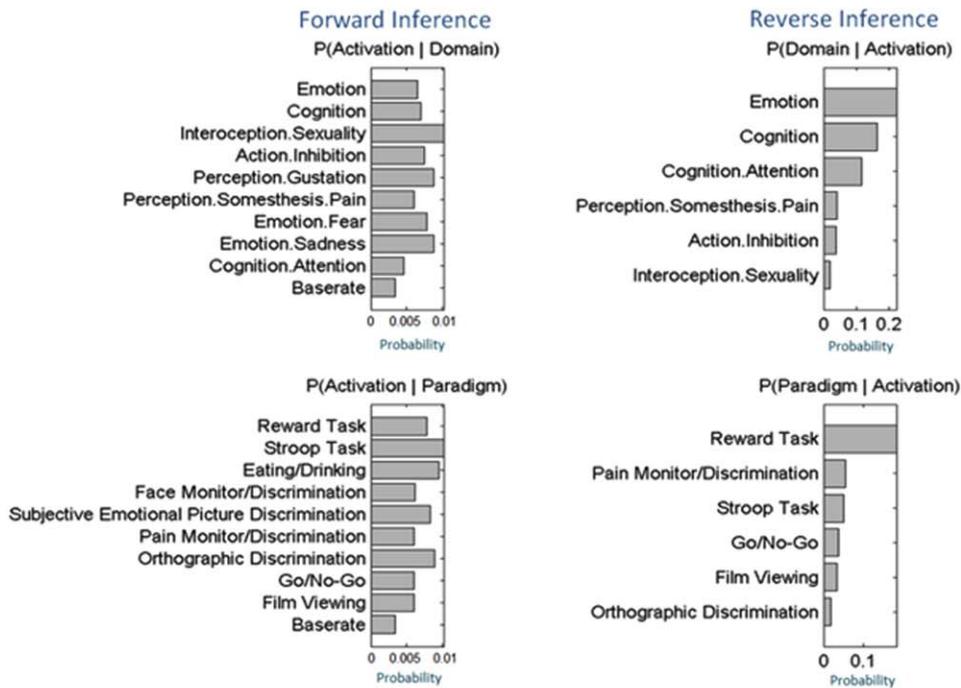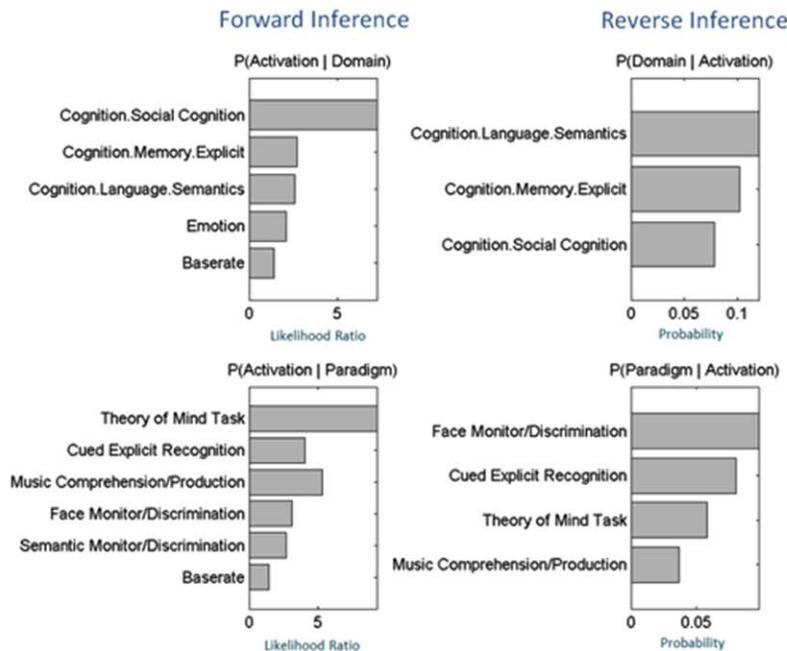
Figure 5.

Domain and paradigm associations of the conceptual self-seed and conceptual other-seed. Inference scales represent a probabilistic measure of association between a cognitive concept and a brain activity. BrainMap metadata were used to perform functional forward (left column) and reverse (right column) inference for both conceptual self-(i.e., self) and conceptual other-(i.e., other) seeds. Conceptual self-seed refers to the pregenual anterior cingulate and the conceptual other-seed refers to the poste-rior cingulate/precuneus. Forward inference determines above-chance brain activity given the presence of a term, while reverse inference determines the above-chance probability of a term given observed brain activity. Base rate denotes the general probability of BrainMap activation in the cluster. The inference scales thus represent the likelihood of a significant term to be associated with a given seed. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

lesioned pACC and anterior insula have related to impairments in motivational behavioral responses to interoceptive feedback, such as toward one's own serious physical illness [Philippi et al., 2012b] suggestive of deficient salience detection of physical states. Furthermore, clinical neuroscience has illustrated healthy pACC neural functioning [Boes et al., 2008], structure [Etkin et al., 2006; Wagner et al., 2008], and connectivity with the anterior insula [Horn et al., 2010] to mediate conflict between negative emotionally salient information and one's conceptual self. The anterior insula's role in updating one's conceptual self-representations is also suggested in lesion data. For instance, damaged pACC, coupled with lesioned anterior insula and medial prefrontal cortex (mPFC), related to an incapacity to update one's pretrauma personality [Philippi et al., 2012a], suggesting a potential deficiency when integrating new salient information with older self-concept representations. Deficient updating of conceptual self-representations has also been exhibited in frontotemporal dementia, wherein the anterior insula, pACC, and vMPFC exhibited severe atrophy [Mendez and Shapira, 2011]. These findings indicate that pACC and anterior insula are vital in unlearning old conceptual self-representations for the sake of restructuring salient, new, and adaptive cognitive and affective representations of one's actual state. As reported above, pACC lesion data are generally accompanied by additional lesions, particularly within the anterior insula and mPFC. Future research is thus warranted to ascertain the extent to which the anterior insula coordinates with the pACC to facilitate flexible motivational responses to emotionally conflicting self-relevant stimuli. In sum, the self-seed is associated with interoceptive processing, most likely related to the representation of salient, motivational, physical states [Herbert and Pollatos, 2012], which may be facilitated by preferential connectivity with the anterior insula [Craig, 2009; Kurth et al., 2010].

Additionally, functional profiling demonstrated pACC association with reward. The pACC has been associated with value assessment [Hayden et al., 2011a, b], reward representation [Rolls, in press], and social value computations [Vogt, 2014]. For instance, lesioned pACC has related to decreased sexual desire in humans [Devinsky et al., 1995], implicating deficient value representation of canonically motivational reward. Assessment, representation and computation of reward may, in fact, rely on striatum functional connectivity, which we observed in our MACM/ RS conjunction for self only. PACC-striatum connectivity has been illustrated by primate axonal tracing [Kunishio and Haber, 1994; McFarland and Haber, 2000], and is linked with reward processing [Haber and Knutson, 2010]. In humans, the pACC and striatum have demonstrated significant neural responses to reward cuing, such as in addicted users viewing cues of their preferred substance [e.g., Wilson et al., 2013]. Within primates, the pACC has illustrated dense afferents projecting to striosome compartments within the dorsal striatum [Eblen and Graybiel,

1995], a neural circuitry with preferential access to the dopamine-containing neurons of the substantia nigra, as postulated by Amemori and Graybiel [2012]. These neurons may be accessed either directly [Fujiyama et al., 2011] or indirectly via the lateral habenula of the epithalamus [Graybiel, 2008; p. 784]. Importantly, the lateral habenula may play a crucial role in motivational decision making [Hikosaka, 2010] as well as negative reward prediction error mediation via dopamine inhibition [Amemori and Graybiel, 2012; Ji and Shepard, 2007; Matsumoto and Hikosaka, 2007; Quina et al., 2014]. Amemori and Graybiel [2012] postulate, therefore, that the pACC, in interaction with the striatum, may thus be necessary in "interrelating cognitive and emotional processing to modulate behavior by affecting evaluation of aversive outcome" [Amemori and Graybiel, 2012; p. 784]. Hence, the self-seed is selectively associated with reward and value assessment and representation, likely due to its functional connectivity with the striatum [Nakamura et al., 2012; Szamosi et al., 2013], which we observed across both MACM and RS.

Functional connectivity with the striatum may also allow for the pACC to update appropriate self-enhancing behavioral responses to present and future social cues [Rolls, in press], thus superseding obsolete behaviors which no longer carry self-relevant value [c.f. Hayden et al., 2011b]. Among the functional characterizations of this study, we witnessed significant probability of action and inhibition processing within the pACC. Translating self-relevant social value into appropriate action tendencies may indeed depend on the afferent projections of the pACC to the striatum [Grabenhorst and Rolls, 2011], but may also benefit from reciprocal communication with the striatum, the latter having also been illustrated in nonhuman literature [Middleton, 2009]. As the striatum is heavily implicated in habit learning behavior [cf. Tricomi et al., 2009; Wunderlich et al., 2012], the pACC may encode value-based decision information, signaling the relative self-relevant reward of abandoning previously learned behavior for the sake of updating and learning new self-enhancing behavior via striatum functional connectivity [Hayden et al., 2011b]. Thus, the functional connectivity between the pACC and striatum may promote adaptive social behavior through effective appraisal and updating of appropriate self-relevant action tendencies.

In sum, our findings present functional connectivity across task-dependent and task-independent brain states between the pACC, anterior insula, striatum, and thalamus, which may assist the pACC in performing emotional conflict resolution and motivation processing relevant to action tendencies and reward/value appraisals. Importantly, relative to conceptual other functional connectivity, the pACC showed differential functional connectivity with the anterior insula, suggesting viscerosensory interoceptive information processing to underlie a continuous self- versus nonself-representational distinction across both task-independent and task-dependent brain states.

Delineating a Conceptual Other-Network

We observed other-seed (PCC/PC) connectivity with the AG/TPJ, mOFC, and vMPFC across MACM and RS. Relative to the conceptual self, however, the PCC/PC yielded differential functional connectivity with only the AG/TPJ bilaterally, suggesting potential attention orientation and social cognition processes [cf. Krall et al., in press] subserving an other- versus self-distinction [Heinisch et al., 2012] across task-dependent and task-independent brain states. Furthermore, our functional profiles demonstrated the other-seed to be selectively associated with social cognition, face discrimination, and language/semantics, the former two of which suggest social orienting. Corresponding with our findings, literature demonstrates PCC/PC and mOFC volume to correlate with socially oriented behaviors, including increased curiosity in monkeys [Phillips et al., 2012], and social openness in humans [Fuentes et al., 2012]. Moreover, AG/TPJ has been demonstrated to relate to outward altruistic behavior [Morishima et al., 2012], moral cognition and theory of mind [Bzdok et al., 2012], and self–other distinction [Heinisch et al., 2012].

Socially oriented behaviors encompass other- versus self-perspective taking, an underlying requisite for social cognition, as is suggested by human neuroimaging literature. For instance, PCC/PC damage relates to diminished manipulations of allocentric (third-person) representations [Weniger et al., 2009], while transcranial magnetic stimulation of the AG/TPJ potentially alters other–self-distinction [Heinisch et al., 2012]. Furthermore, the vMPFC may play a crucial role in interpersonal processing, particularly social cognition [Bzdok et al., 2013a], the representation of social value [Ruff and Fehr, 2014], and approach/avoidance-modulating processing [Bzdok et al., 2013a]. Moreover, reduced PCC/PC functioning may relate to impaired discrimination of third- from first-person agency representations in hallucination-prone individuals [Dahoun et al., 2013]. Two very recent meta-analyses demonstrated the AG/TPJ to underlie higher order executive functioning associated with attention orientation and social cognition, particularly theory of mind [Bzdok et al., 2013b, Krall et al., in press]. Thus, social orienting during conceptual other processing may be subserved via processes related to perspective taking, social cognition, and social value representation.

Social orienting and adaptive interpersonal interactions equally depend on the accurate discrimination of external social cues, particularly the emotional facial expressions and cues of others. Accordingly, clinical neuroscience literature has illustrated an important role of the PCC/PC in processing emotional faces of others. For instance, deficits in emotional-face processing in humans have been linked to PCC/PC hyperactivation in autism [Aoki et al., 2014; Oblak et al., 2011] and human precuneus cortical thinning in Alzheimer's [Kumfor et al., 2014]. In fact, the precuneus may play a key role in distinguishing other-faces from self-face via "social cognition processes involving judg-

ment of self-facial resemblance to others," as was demonstrated in a recent deep brain stimulation study [Jonas et al., 2014; p. 336]. In sum, the other-seed is selectively associated with socially oriented functions of social cognition and face discrimination, likely facilitated by connectivity with the AG/TPJ, mOFC, and vMPFC, which we witness across MACM and RS.

Our other-seed was additionally associated with language/semantics, here defined as "the mental faculty associated with knowledge of meaning in language forms" (BrainMap.org). While AG/TPJ functioning and structure relate to semantic processing and encoding in both clinical [Harasty et al., 1999] and healthy populations [Visser et al., 2012], the PCC/PC may facilitate semantic discrimination via contextual integration. A single-neuron study demonstrated increased primate PCC/PC activity when social preference choice was anomalous with normally chosen standard options [Heilbronner et al., 2011], illustrating the PCC/PC to facilitate the integration of new contextual information with stored semantic schema. Thus, the other-seed is selectively associated with semantic monitoring/discrimination, which may relate to contextual integration, facilitated by connectivity with the AG/TPJ.

Furthermore, the AG/TPJ is considered to be a highly associative area consistently involved in high-level processes [Bzdok et al., 2013b], inclusive of attentional orienting and theory mind [Krall et al., in press], which would be fitting of conceptual other-functioning. Intuitively, conceptual other-processing avers to be more cognitively demanding than conceptual self-processing, as it is arguably more difficult to conceptualize beliefs and attitudes of others, whose thoughts are not accessible to us, than to conceptualize one's own personal attitudes and beliefs. Hence, relative to the self-seed, the PCC/PC demonstrates differential functional connectivity with the AG/TPJ, a region established for higher-level executive processing and social functioning such as attentional orienting and theory of mind [Krall et al., in press].

Socially oriented self-regulation bears important implications in interpersonal interactions, whereby accurate inferences of others' intentions and emotional states demand adequate integration of contextual information. This requires higher-order operations, including processing complex emotional facial expressions [Frischen et al., 2007], prioritizing allocentric over egocentric perspectives [de Vignemont, 2008; Frith and de Vignemont, 2005], and integrating contextual cues with stored semantic schemas [Harris and Fiske, 2007]. These operations are illustrated in our functional profile for our other-seed as well as our observed differential other-network. Together, we present an other-network integrating dynamic socially oriented processes relevant to contextual integration, social cognition, and face discrimination, the latter two of which may underlie a greater function of socially oriented processing. These operations may be facilitated by our observed connectivity of the other-seed with the AG/TPJ, mOFC, and vMPFC. Notably, we distinguish an other-specific

network, relative to that of the conceptual self-seed, via PCC/PC-AG/TPJ functional connectivity, signaling a potential reliance on attentional orienting and social cognitive processes to maintain effective conceptual other mental representations which remain distinct from those of self.

Self and Other Conjunction Analyses

Our findings show no overlapping task-dependent (MACM) functional connectivity of the self and other seeds. As task-dependent states represent active cognitive engagement with external stimuli, absence of shared self/ other functional connectivity in MACM would indicate independent self- and other-networks when engaged with the external environment. However, a conjunction of self- and other-RS functional connectivity networks yielded shared topographical connectivity in the vMPFC (Area 10) and mOFC (Area 11). Afferent projections to the pACC from Areas 10 to 11 are well established in primate literature [cf. Morecraft and Tanji, 2009; Rolls, in press]. In humans, recent literature demonstrates functional and structural connectivity between the pACC and Area 10 of the vMPFC [Chavez and Heatherton, 2014]. Furthermore, these authors use both diffusion tensor imaging and fMRI to link frontostriatal functional and structural connectivity between the pACC, vMPFC, and striatum directly with self-esteem maintenance. Moreover, a recent review demonstrates the importance of the pACC, striatum and vMPFC in the representation of social value and reward in decision making within humans [Ruff and Fehr, 2014]. Thus, the pACC may rely on vMPFC to perform value appraisals of self-relevant and potentially rewarding social information.

Social value representations may be facilitated by neuronal activity within both the vMPFC and mOFC [Rolls, in press], which demonstrate reciprocal pathways with the pACC within the primate brain [Kringelbach and Rolls, 2004]. Moreover, human neuroimaging research illustrates shared conceptual self- and other-processing in the vMPFC [Amodio and Frith, 2006; Bzdok et al., 2013a; Yaoi et al., 2009; Zhang et al., 2006], which may receive afferent projections from the orbitofrontal cortex [Kringelbach and Rolls, 2004]. Furthermore, RS is associated with internally focused self-referential processes [Christoff et al., 2011; Schilbach et al., 2012], subserving autonoetic consciousness (i.e., cohesion between past and present selves contributing to self-updating) [Lou et al., 2010]. Our observed vMPFC/mOFC overlap between self and other may, therefore, suggest integration of previous social experiences at the service of self-updating during rest. This is supported by the extant literature [e.g., Bechara et al., 2003; Beer et al., 2006; Northoff and Bermpohl, 2004; Philippi et al., 2012a; Rosen et al., 2010]. Conventional neuroimaging (fMRI/PET) studies in healthy populations link the vMPFC with the mental generation and representation of self-referential stimuli [Northoff and Bermpohl, 2004]. Furthermore,

lesioned vMPFC/mOFC relates to disrupted self-processing, including impaired self-appraisal [Rosen et al., 2010], self-relevance attribution [Bechara et al., 2003], self-monitoring [Beer et al., 2006], and self-referencing per se [Philippi et al., 2012a]. During rest, therefore, the vMPFC/ mOFC may sustain self-relevance attribution to particular previous social experiences and feedback from others in order to permit self-concept updating via pACC functioning.

LIMITATIONS

It is important to highlight a few limitations within the methodology employed in the present functional connectivity analysis. First, the ALE analysis does not include information on effect sizes [Decety and Lamm, 2007]. Notwithstanding, the robustness of current ALE meta-analyses is optimum given the current state of database sharing. That is, statistical meta-analyses based on original data sets are not yet possible until researchers reach a consensus on appropriate data sharing policies [Krall et al., in press; Mar, 2011]. Moreover, the ALE algorithm does not investigate power across studies, but rather the function and significant spatial convergence of findings across neuroimaging studies [Fox et al., 1998]. This thus reduces the likelihood of reporting false positives, also known as the "file drawer problem" [Rosenthal, 1979], which would result in a publication bias [Easterbrook et al., 1991; Felson, 1992; Fox et al., 1998; van der Meer et al., 2010].

Second, fMRI meta-analyses globally engender a degree of noise and variability. Unfortunately, biases in fMRI findings are not yet well characterized, in large part due to the high degrees of freedom in the analysis (e.g., templates, normalization, general linear model (GLM), and inferences). Specifying such parameters, however, remains outside the scope of our current work. Still, extracting the peak coordinates and pooling and analyzing foci for functional brain activation clusters across studies result in a non-negligible loss of spatial sensitivity and specificity particular to experimental parameters, like "scanner strength, imaging acquisition and analysis, subject sample size and individual variability, and variations in behavioral conditions" [Laird et al., 2013; p. 512]. These limitations notwithstanding, observing significantly consistent coactivations across whole-brain studies only, in spite of such variability, nonetheless reflects an underlying statistical power when measuring brain responses to task demands [Laird et al., 2013].

CONCLUSIONS

The conceptual self is crucial in maintaining goal-relevant behaviors pertinent to one's social adaptation and fitness. The updating of self, however, depends greatly on interactions with and feedback from others [Fonagy et al., 2002], implicating shared neural functioning between self

and other [Amodio and Frith, 2006]. As the relation between self- and other-neural networks remained unexplored, we investigated self- and other-functional connectivity and their interaction across task-dependent and task-independent states, using pACC and PCC/PC as self- and other-seeds, respectively [cf. Murray et al., 2012]. As a result, we associated the self-seed with emotional conflict resolution and motivational processing via interoceptive feedback (mapping), action/inhibition and reward-related processing, potentially mediated by its connectivity with the anterior insula, striatum, and thalamus. Notably, we observed self-specific functional connectivity, relative to the conceptual other seed, between the pACC and anterior insula only, suggesting potential viscerosensory processing of physical states underlying a continuous distinction of self- versus nonself-across task-dependent and task-independent brain states. Next, we associated the other-seed with socially oriented processing and contextual information integration, facilitated by its connectivity with the AG/TPJ, mOFC, and vMPFC. Critically, other-specific functional connectivity, relative to the conceptual self seed, arose between the PCC/PC and bilateral AG/TPJ only, indicating potential attention orientation and social cognitive processes giving rise to conceptual other representations, distinct from those of self, during both task-dependent and task-independent brain states. Finally, we observed self/other overlap in the vMPFC/mOFC during RS, suggesting self-updating via self-representation, self-relevance attribution, and integration of previous social experiences [cf. Bzdok et al., 2013a]. These findings help reconcile theoretical and neurobiological literatures relevant to the integration of other and self. Additionally, they open avenues for developmental connectivity research relevant to the self's emergence as well as the delineation between self and other from infancy to adulthood.

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