# Specific Default Mode Subnetworks Support Mentalizing as Revealed Through Opposing Network Recruitment by Social and Semantic fMRI Tasks

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**Abstract:** The ability to attribute mental states to others, or "mentalizing," is posited to involve specific subnetworks within the overall default mode network (DMN), but this question needs clarification. To determine which default mode (DM) subnetworks are engaged by mentalizing processes, we assessed task-related recruitment of DM subnetworks. Spatial independent component analysis (sICA) applied to fMRI data using relatively high-order model (75 components). Healthy participants ($n = 53$, ages 17–60) performed two fMRI tasks: an interactive game involving mentalizing (Domino), a semantic memory task (SORT), and a resting state fMRI scan. sICA of the two tasks split the DMN into 10 subnetworks located in three core regions: medial prefrontal cortex (mPFC; five subnetworks), posterior cingulate/precuneus (PCC/PrC; three subnetworks), and bilateral temporoparietal junction (TPJ). Mentalizing events increased recruitment in five of 10 DM subnetworks, located in all three core DMN regions. In addition, three of these five DM subnetworks, one dmPFC subnetwork, one PCC/PrC subnetwork, and the right TPJ subnetwork, showed reduced recruitment by semantic memory task events. The opposing modulation by the two tasks suggests that these three DM subnetworks are specifically engaged in mentalizing. Our findings, therefore, suggest the unique involvement of mentalizing processes in only three of 10 DM subnetworks, and support the importance of the dmPFC, PCC/PrC, and right TPJ in mentalizing as described in prior studies. *Hum Brain Mapp 36:3047–3063, 2015.* © **2015 Wiley Periodicals, Inc.**

Key words: default mode network; mentalizing; semantic memory; spatial ICA; functional connectivity; fMRI; theory of mind

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## INTRODUCTION

A network of brain regions that has consistently been shown to be more active in human participants when not engaged in a specific task is commonly called the default mode network (DMN) [Raichle et al., 2001; Shulman et al., 1997]. The DMN comprises a distributed network that includes medial prefrontal cortex (mPFC), posterior cingulate cortex (PCC) and precuneus (PrC), and lateral temporoparietal junction (TPJ) regions. Additional regions are also sometimes reported as part of the DMN, including lateral temporal cortex and temporal pole, and medial temporal lobe, including the hippocampal formation [Buckner et al., 2008; Mars et al., 2012a].

The DMN has also been described as the "task-negative" network (TNN) [Fox et al., 2005]. This term however, has come under criticism in recent years due to the implication that the DMN is not engaged in active cognitive processes [Spreng, 2012]. A number of recent studies have in fact shown that tasks involving social cognition [Jack et al., 2013; Schilbach et al., 2008], interactive game-playing involving mentalizing (i.e., theory of mind) [Assaf et al., 2009b], empathy [Adams et al., 2010; Reniers et al., 2012], goal-directed mental simulations [Gerlach et al., 2011], and declarative (episodic and semantic) memory [Ino et al., 2011; Sestieri et al., 2011; Vannini et al., 2011; Wirth et al., 2011], none of which are truly "task-negative," activate regions overlapping the DMN. Studies of brain networks involved in social cognition, and specifically in mentalizing, have been given particular emphasis in recent years due in part to the putative involvement of these networks in a number of neuropsychiatric conditions [Brune and Brune-Cohrs, 2006; Hoertnagl and Hofer, 2014]. The significant social cognition/DMN spatial overlap in healthy individuals might be due to the great importance of social cognition in human interaction, and the related theory that social cognition (e.g., thinking about oneself and/or others) is the default mode (DM) of thought in human beings [Schilbach et al., 2008]. However, exactly which subregions of the DMN are involved in mentalizing remains an important goal of ongoing investigation [Li et al., 2014; Mars et al., 2012a].

Conversely, functional imaging tasks requiring attention to external stimuli and executive function often result in reduced blood oxygenation-level dependent (BOLD) signal in the DMN/TNN, while activity in the so-called "task-positive networks" (TPNs) is increased [Fox et al., 2005]. The TPN has been described as consisting of two core networks [Menon, 2011; Seeley et al., 2007]. The salience network, comprises the anterior insula and dorsal anterior cingulate [Elton and Gao, 2014; Seeley et al., 2007; White et al., 2010], while the central executive network comprises fronto-parietal regions, including bilateral dorsolateral prefrontal cortex (DLPFC) and lateral posterior parietal regions [Menon, 2011; Seeley et al., 2007; Vincent et al., 2008]. The three networks, default-mode, salience and central executive, constitute what has been called the "triple network model" [Menon, 2011].

One recent study demonstrated opposing modulation (or, as it was called in that study, "reciprocal inhibition") of BOLD signal in the DMN and TPNs using two highly similar fMRI tasks, with one emphasizing social interaction, and the other, physical properties of inanimate objects [Jack et al., 2013]. The two task approach arguably better revealed DM brain regions involved in social cognition than a single social task approach, because the non-social, physical task provided a second line of corroborating evidence. Specifically, using standard general linear modeling (GLM)-based fMRI data analysis, the study found that brain regions with increased BOLD signal during the social task, and with decreased BOLD signal during the physical task, overlapped the DMN.

Recent studies suggest that the DMN consists of several subnetworks with diverse and specialized roles, including subnetworks specific for self-referential or social cognitive processing [Menon, 2011; Spreng et al., 2009], or differentiating between the self and others [van Veluw and Chance, 2014]. Our primary goal in this study was to determine precisely which DM subnetworks directly support mentalizing processes. Similar to the aforementioned study [Jack et al., 2013], we used two fMRI tasks that we hypothesized would have opposing task-related recruitment of DM subnetworks. In our study, however, we examined event-related recruitment of DM subnetworks using spatial independent component analysis (sICA), rather than event-related BOLD signal changes using GLM. Spatial ICA not only extracts the DMN in its entirety (even if GLM analysis of the same task data does not) but can also split the DMN into discrete spatially distributed subnetworks, known as intrinsic connectivity networks (ICNs), which are brain regions characterized by a high degree of within-network functional connectivity (i.e., voxel time course correlation) (for more on ICNs, see [Laird et al., 2011; Rashid et al., 2014; Seeley et al., 2007; Shirer et al., 2012; Wang et al., 2013]). Using temporal regression, or "sorting," of ICN time courses (TCs) then allows identification of subnetworks (ICNs) within the DMN that are significantly recruited by task events. Conversely, GLM can only reveal brain regions that are specifically activated by the task, and while such regions might include the DMN, it does not allow determination of which discrete DM subnetworks are engaged by the task.

To determine which DM subnetworks uniquely support mentalizing, we incorporated both fMRI tasks into a single group sICA, using an approach similar to previous work [Cetin et al., 2014]. This allowed us to extract DM subnetworks common to both tasks, and then assess recruitment of these identical DM subnetworks by specific events in each task. We also used a relatively high model order ICA, in which we expected the DMN to be split into its separate subnetworks within the medial prefrontal, posterior cingulate and precuneus, and left and right lateral TPJ.

The tasks we used were: (1) a social interactive game task, Domino, that was previously shown to result in increased BOLD signal in DM-related brain regions that

were posited to support mentalizing [Assaf et al., 2009b]; and (2) a semantic object retrieval task (SORT) that involves reading, language, and verbal working memory, as well as semantic memory retrieval [Assaf et al., 2006; Kraut et al., 2007]. The SORT, unlike the physical task used in the previously described study [Jack et al., 2013], probes semantic associative processing, and according to recent studies might involve the DMN [Binder et al., 2009; Shapira-Lichter et al., 2013; Wirth et al., 2011], but does not invoke social cognition or mentalizing. Therefore, in our study, the SORT analysis served as a second line of corroborating evidence as to which DMN subnetworks are uniquely involved in social cognition and, more specifically, mentalizing processes. Additionally, the temporal poles are posited to be involved in both mentalizing and semantic memory retrieval processes [Frith and Frith, 2003; Olson et al., 2007], allowing us to further examine the relationship between these processes in bilateral temporal poles. All participants also performed a resting state (passive) fMRI session that was incorporated into a separate sICA. This separate resting state group sICA allowed us to directly and unambiguously assess the degree of spatial coincidence of resting state DMN subnetworks with the DMN subnetworks obtained for the two-task group sICA.

We hypothesized that the socially-interactive Domino task will result in increased recruitment of specific DM subnetworks that support mentalizing processes. Additionally, we hypothesized that the language-based semantic memory retrieval task, SORT, will result in decreased recruitment of these same DM subnetworks, thus providing further evidence that these specific DM subnetworks uniquely support mentalizing processes. We further posited that the DM subnetworks supporting mentalizing would show significant spatial correlation (i.e., spatial "overlap") with specific DM subnetworks derived from the separate resting state sICA.

## METHODS

### Participants

Fifty-three healthy, (40 right-handed, 13 left-handed, as assessed by the Edinburgh Handedness Inventory [Oldfield, 1971]), native English speakers (24 males and 29 females) were recruited from the Greater Hartford (CT) area, to participate in a study that used both the Domino and SORT tasks. Participants were between the ages of 17 and 60 (mean age 35.1, SD = 13.6) and had no current or past history of Axis I diagnosis, as assessed by the structured clinical interview for DSM-IV axis I disorders (SCID) [First et al., 2002] and no major physical illness, current or past history of neurological disease or substance abuse, or history of head trauma causing loss of consciousness. Full-scale IQ was estimated using the WAIS information and block design subsets (score range: 85–138, mean = 115.1,

SD = 11.6). All participants provided written informed consent, as approved by Institutional Review Board of Hartford Hospital, after the study had been fully explained to them. This study fully complied with the Code of Ethics of the World Medical Association (Declaration of Helsinki). The study was carried out at the Olin Neuropsychiatry Research Center of the Hartford Hospital Institute of Living, and participants were paid for their participation.

### fMRI Tasks

The social interactive game playing task, Domino, has been shown in several studies to activate regions of the DMN during the phase of the game known as "Response to Outcome," where the participant is shown the outcome of the most recent game play. During this phase, the opponent asks the participant to either expose their chip (show event) or not (no-show event). Activation in the DMN during this phase of the game is posited to occur due to mentalizing processes (e.g., trying to infer the opponent's strategy) as well as future planning (e.g., what chip to play next) and is measured by the show>no-show contrast [Assaf et al., 2010, 2009b]. In the Domino task, participants are told they are playing against either a computer, which executes automated, random moves during game play, or an actual human opponent making strategic decisions during game play. Therefore, Domino also allows the comparison of a participant's mentalizing processes during human opponent games with that of computer opponent games, the latter games serving as a control.

The SORT was developed to investigate semantic memory recall [Kraut et al., 2003, 2007]. A modified version of the SORT was used in recent studies [Assaf et al., 2009a; Jamadar et al., 2013] and involves reading word pairs and making a decision as to whether the word pair results in semantic retrieval of a third, "fused" word (retrieval versus no-retrieval event). The SORT not only activates brain regions involved in semantic memory recall, which include bilateral inferior frontal gyrus (including Broca's area), left DLPFC, left middle temporal gyrus, bilateral angular gyrus, and PCC [Assaf et al., 2006; Binder et al., 2009], but also activates salience-related regions, including dorsal anterior cingulate cortex (dACC), pre-SMA [Assaf et al., 2006] and anterior insula [Menon and Uddin, 2010], and language-related regions, specifically those involved in reading or visual word recognition, including the supramarginal gyrus [Stoeckel et al., 2009]. Full descriptions of both the Domino task and SORT, with task diagrams (Figures S1 and S2, respectively) are provided in the Supporting Information.

### Imaging Parameters

BOLD fMRI data were collected with a T2*-weighted echo planar imaging (EPI) sequence (TR/TE = 1860/27

msec, Flip angle = 70°, Field of view = 22 cm with a 64 × 64 acquisition matrix) using a Siemens Allegra 3 Tesla scanner (Siemens, Malvern, Pennsylvania) at Institute of Living, Hartford, Connecticut. Thirty-six contiguous axial functional slices of 3-mm thickness with 1-mm gap were acquired, yielding 3.4 × 3.4 × 4.0 mm voxels.

For the Domino task, 330 images were acquired during each of the four 10 min sessions. For the SORT, 426 images were acquired in a single 13 min session. For a given participant, Domino and SORT fMRI sessions were typically, but not always, acquired on the same day. For all five sessions, six "dummy" images were acquired at the beginning of each session to allow global image intensity to reach equilibrium and were excluded from data analysis. We also acquired resting state fMRI data in which 210 images were acquired, but at a TR of 1500 msec versus 1860 msec used with Domino and SORT. Only 10 of the $n = 53$ subjects had a resting state fMRI session that was performed on a different date than the Domino task and SORT (Domino task and SORT were performed on the same date for all subjects). The difference in date of the resting state scan for these 10 subjects ranged from 385 days before, and 109 days after, the Domino/SORT scan (mean ± standard deviation [SD]: 139 ± 175 days). Although the number of Domino versus SORT sessions are different (4 vs. 1), and the task sessions are of different length (10 vs. 13 min) a prior study has shown in such cases that group ICA back-reconstructed maps are a good representation of individual subject effects for each task [Cetin et al., 2014].

## Data Analysis: Preprocessing

Functional MRI datasets were preprocessed using SPM5 (www.fil.ion.ucl.ac.uk/spm/software/spm5/) running under MATLAB v7.7.0 (Natick, MA). Each individual's dataset was realigned to the first "non-dummy" T2* image using the INRIAlign toolbox (https://www-sop.inria.fr/epidaure/Collaborations/IRMf/INRIAlign.html, A. Roche, EPIDAURE Group) to compensate for any subject head movement. Movement parameters for each subject were then screened for excess head movement (> 4 mm) and six motion covariates ($x, y, z$, roll, pitch, yaw, obtained from the realignment) were included in all regression analyses, including the temporal sorting procedure described below. Next, realigned images were slice-timing corrected (36 slices) using the middle slice as the reference. The resulting images were then spatially normalized to the Montreal Neurological Institute (MNI) standard template [Friston et al., 1995], resampled to 3 × 3 × 3 mm voxels and spatially smoothed with a 9 mm isotropic (FWHM) Gaussian kernel. A high-pass filter with a cutoff of 128 sec was applied to correct for EPI signal low-frequency drift.

## Design Matrix

For both the Domino task and SORT, a general linear model (GLM) design matrix was constructed in SPM5 (Wellcome Department of Cognitive Neurology, London,

UK). For Domino, the event regressors "show match," "show non-match," "no-show match," and "no-show non-match" events from the "Response to Outcome" interval were included in the design matrix. The "Response to Outcome" event regressors were further divided according to opponent type, that is, computer (automated game) opponent for two sessions and a human opponent (interactive game) for two sessions. For SORT, the two event regressors, retrieval (R) and non-retrieval (NR) events, were also included in the design matrix in the fifth session. Regressors were modeled as boxcar functions convolved with the SPM5 canonical hemodynamic response function.

## Group Independent Component Analysis

We performed group sICA using the GIFT toolbox (http://icatb.sourceforge.net, version 2.0a). To facilitate direct comparison across our two tasks, we included both the Domino task and SORT from all 53 subjects within the same group sICA, as described in a recent study [Cetin et al., 2014]. In this method, each subject had five fMRI "sessions" where four of the sessions were the Domino task (two each for computer and human opponent), and the fifth session was the SORT. The SPM GLM design matrix for each subject included all five sessions. Resting state was excluded from this group sICA due to its different TR (1500 msec versus 1860 msec). A separate group sICA of resting state data for the 53 study participants is described in the Supporting Information.

Group sICA identifies independent component networks (ICs), that is, temporally coherent networks, through estimation of maximally independent spatial sources from the linearly-mixed fMRI signals. Each independent component has an associated TC and a spatial map (SM), both of which are calibrated by conversion to $z$-scores (i.e., high $z$-scores in the component TC represent large signal changes relative to the mean, and high $z$-scores in the SM indicate a stronger fit of a voxel's TC to the group averaged component TC, and thus higher "connectivity" with other voxels that comprise the component SM).

We chose a relatively high model order ICA (75 components) because previous studies have shown that high versus low-order ICA models result in components that better correspond to known anatomical and functional segmentations [Abou-Elseoud et al., 2010; Allen et al., 2011; Kiviniemi et al., 2009; Smith et al., 2009; Ystad et al., 2010]. A first-stage subject-specific principal components analysis (PCA) was performed, retaining 100 principal components (PCs). A second-stage group data reduction, using the expectation-maximization algorithm included in GIFT, retained a final set of 75 PCs. Next, we ran the Infomax ICA algorithm [Bell and Sejnowski, 1995], repeating it 15 times in ICASSO, implemented in GIFT, to generate a stable set of 75 final components. Finally, subject ($n = 53$) and session ($n = 5$) specific SMs and TCs were then estimated using the GICA3 back-reconstruction method based on PCA compression and
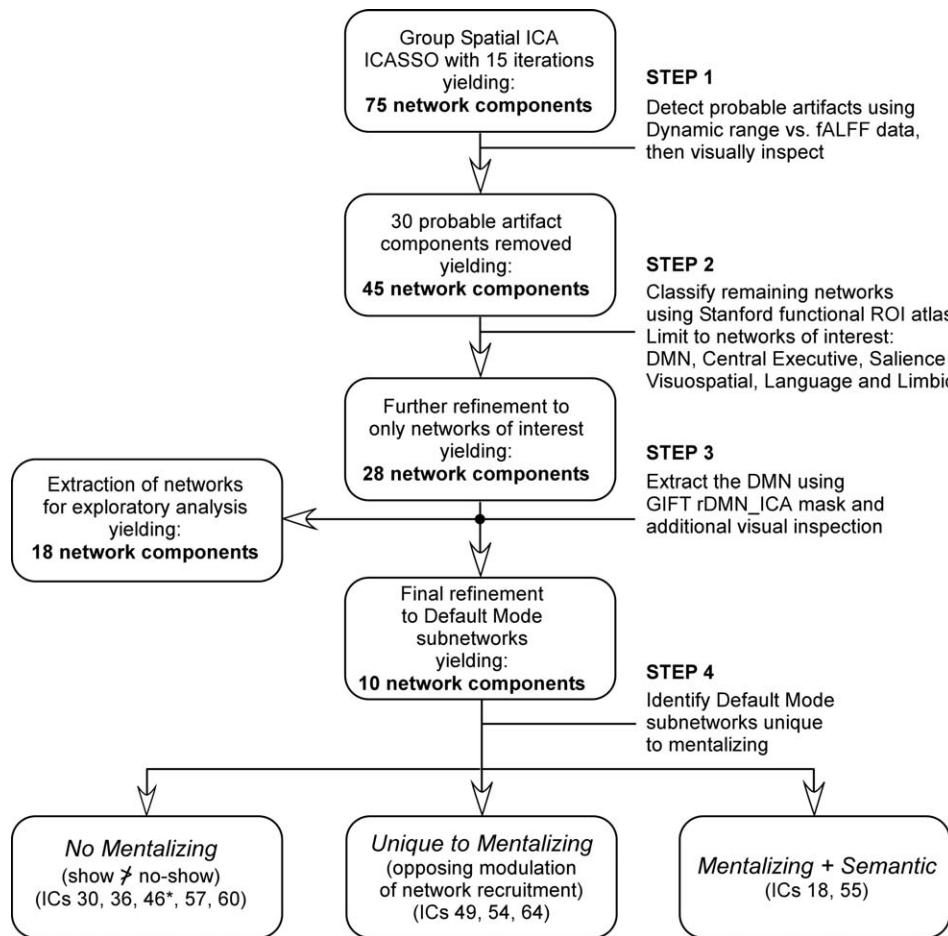
**Figure 1.**

Diagram showing the three steps performed to reduce the original 75 sICA network components to the final 10 DMN components and 18 exploratory network components. The final step (Step 4) in the diagram depicts how the 10 DMN components were classified into subnetworks that either (1) do not support mentalizing, (2) are subnetworks unique to mentalizing, or (3) are subnetworks that support both mentalizing and semantic memory recall. (IC 46, denoted with an asterisk, is classified here as not supporting mentalizing, but was however trend-level significant for mentalizing).

projection [Allen et al., 2011; Calhoun et al., 2001; Erhardt et al., 2011], yielding 53 subjects × 5 sessions × 75 components = 19,875 component SMs. As with the group-average SMs and TCs, individual subject and session SMs and TCs were also converted to $z$-scores. The $z$-scores in the subject and session level SMs indicate the goodness of fit of a given subject's voxel BOLD TC to the group averaged component TC. Thus, $z$-score conversion permits group-level analyses that test the connectivity strength, or signal synchronization, of each voxel in the subject and session level component SM to the group-level component SM.

## Component Selection from SM

Figure 1 presents a diagram showing the four steps taken in our study to extract DM subnetworks from the 75 compo-

nent networks, including a final classification step, according to our hypotheses, into DM subnetworks that are, (1) unique to mentalizing, (2) do not support mentalizing, or (3) support both mentalizing and semantic memory retrieval. From the 75 SMs calculated from group ICA, we identified a subset of 45 components that were considered BOLD-related brain networks rather than physiological artifacts (e.g., head movement, CSF pulsations, cardiac and respiratory-related signals). The full list of 45 ICNs are provided in Table S1 in the Supporting Information. To assist in distinguishing ICNs from artifacts (Step 1 in Fig. 1), we used a previously described method that uses two metrics from spectral analysis of components [Allen et al., 2011; Robinson et al., 2009; Zou et al., 2008]. Derivation of these two metrics is implemented in the component viewer utility included with the GIFT toolbox (v2.0a). In this method, the frequency spectrum of each component TC is computed, and the dynamic

**TABLE I. The 28 ICNs derived from high-order ICA arranged by classification**

| IC | Peak voxel (MNI) | Classification | Anatomical region |
|---|---|---|---|
| 18 | 0, −42, 27 | Default mode | PCC; Precuneus |
| 30 | 0, 24, −15 | Default mode | Subgenual anterior cingulate cortex |
| 36 | 0, −54, 15 | Default mode | PCC; Precuneus |
| 46 | 0, 39, 12 | Default mode | dmPFC/ACC |
| 49 | 57, −51, 18 | Default mode | R temporoparietal junction |
| 54 | 0, −60, 45 | Default mode | Precuneus |
| 55 | −51, −60, 24 | Default mode | L temporoparietal junction |
| 57 | 0, 57, 0 | Default mode | vmPFC |
| 60 | 0, 66, 15 | Default mode | mPFC |
| 64 | 0, 54, 39 | Default Mode | dmPFC |
| 24 | −36, 9, −24 | Memory/affective | Left temporal pole |
| 39 | 36, 12, −27 | Memory/affective | Right temporal pole |
| 51 | −54, 18, 24 | Executive | Bilat inferior frontal cortex |
| 53 | 45, −63, 51 | Executive | R superior parietal |
| 59 | −39, 57, 15 | Executive | L DLPFC; Parietal |
| 71 | 33, 60, 6 | Executive | Bilat frontal poles |
| 66 | −51, −66, 3 | Language | Bilat posterior temporal |
| 67 | 60, −27, −6 | Language | R superior temporal |
| 42 | 24, −18, −18 | Limbic | Hippocampus |
| 26 | −27, 0, 60 | Salience | SMA; pre-SMA |
| 43 | 63, −27, 30 | Salience | Bilat inferior parietal lobe |
| 56 | 0, 12, 42 | Salience | dACC |
| 62 | 0, 24, 45 | Salience | Dorsomedial superior frontal lobe |
| 72 | −45, 18, −6 | Salience | Bilat anterior insula; OFC |
| 14 | −24, −69, 54 | Visuospatial | L superior parietal |
| 34 | 0, −69, 60 | Visuospatial | Precuneus; Superior parietal |
| 37 | 27, −66, 51 | Visuospatial | R superior parietal |
| 40 | 21, −60, 66 | Visuospatial | Bilat superior parietal |

Abbreviations: (R) right; (L) left, (Bilat) bilateral; (PCC) posterior cingulate cortex; (dmPFC) dorsomedial prefrontal cortex; (vmPFC) ventromedial prefrontal cortex; (DLPFC); dorsolateral prefrontal cortex; (OFC) Orbitofrontal cortex; (SMA) supplementary motor area; (dACC) dorsal anterior cingulate cortex.

range (DR) and ratio of low-to-high frequency content, or fractional amplitude of low-frequency fluctuation (fALFF), are calculated from the spectral analysis. As previously demonstrated, components that are physiological artifacts often, but not always, exhibit both low DR [Allen et al., 2011; Robinson et al., 2009] and low fALFF [Allen et al., 2011; Zou et al., 2008]. The final determination of which components to omit was based on visual observation by the authors of the mean component SMs. A final visual selection was necessary because a small number of components that are clearly not artifacts will, on occasion, have low fALFF and/or DR values, and, conversely, some small number of components that are clearly artifacts (e.g., are located primarily in CSF or white matter) will have paradoxically high fALFF and/or DR values [Allen et al., 2011]. A plot of the DR versus fALFF for all 75 components is provided in the Supporting Information (Figure S3).

In the second step (Fig. 1), we further limited our ICNs of interest to networks known to be DM, central executive, salience, visuospatial, memory, or language-related, as such networks might be expected to be engaged by the SORT or Domino task based on prior studies [Assaf et al., 2006, 2009b; Jamadar et al., 2013]. To provide a framework for such a network classification, we used the Stanford functional ROI atlas (http://findlab.stanford.edu/functional_ROIs.html), consisting of 14 individual ICNs, including Anterior- and Posterior Salience, Auditory, Basal Ganglia, Dorsal- and Ventral Default Mode, Higher Visual, Language, Left- and Right Executive Control, Sensorimotor, Precuneus, Primary Visual and Visuospatial networks [Shirer et al., 2012]. We then used the spatial sorting feature within GIFT, to classify our 45 components into these 14 functional Stanford networks. From this classification, we determined the networks that were not the focus of this study, specifically the Basal Ganglia, Auditory, Higher or Primary Visual, or Sensorimotor networks, and excluded these 17 ICNs from our final analysis, leaving 28 ICNs (Table I). As our hypotheses concern only the DMN, in a third step (Fig. 1) we reduced our 28 ICNs into ten DM subnetworks, which were identified through spatial correlation using a DMN template mask provided with the GIFT toolbox (rDMN_ICA_REST_3x3x3.nii). This DMN template mask was based on resting state sICA data from 42 subjects as outlined in Franco et al. [Franco et al., 2009]. We chose this template over the two Stanford ROI DM templates (ventral and dorsal DMN masks, derived using

ICA from 15 subjects) because the GIFT template was derived specifically for the purpose of delineating the DMN, and was accomplished using the GIFT software toolbox, as used in our current study. The remaining 18 networks were included in an exploratory analysis which is presented in the Supporting Information. Lastly, the fourth and final step in Figure 1 depicts our classification of the ten DM subnetworks according to their role in mentalizing processes, per our hypotheses.

## Statistical Analysis of ICN TCs

Components derived from ICA were analyzed for task-relatedness using the "temporal sort" feature of GIFT. In temporal sorting, model TCs from the original subject-level SPM5 GLM design matrices are extracted and multiple regression of these model TCs with the back-reconstructed subject-level ICA component TCs is performed, yielding beta ($\beta$) weights for each regressor of interest, for each component and each subject. This multiple regression is essentially the same as the GLM fit performed on each voxel of the preprocessed fMRI data in an SPM analysis, but in this case the GLM fit is performed on the ICA timecourse. As described previously [Kim et al., 2009], the resulting $\beta$-weights from the regression represent the degree to which component network recruitment was modulated by the task. For a given component TC and task regressor, positive and negative $\beta$-weights indicate task-related network recruitment that is increased or decreased with respect to baseline, respectively. The $\beta$-weights from each subject's two Domino computer opponent runs, and from each subject's two Domino human opponent runs, were averaged together before statistical analysis. For each regressor and components, a group-level test was performed via a one-sample $t$-test on the $\beta$-weights to evaluate which component networks showed significant modulation of recruitment by a given task event. For the Retrieval > Non-Retrieval contrast from the SORT, paired $t$-tests were performed for each component. Lastly, the factors Opponent Type (Human > Computer) and Mentalizing (Show > No-Show) from the Domino task, were entered into a two-way (2 × 2) ANOVA for each component. The analyses for the factor Opponent Type are presented in the Supporting Information. In separate follow-up analyses, study participants' age and gender were added as covariates to the 2 × 2 ANOVA (Domino task) and paired $t$-tests (SORT).

All statistics on the $\beta$-weights for each event contrast were corrected for multiple comparisons using a false discovery rate procedure [Benjamini and Hochberg, 1995], with the number of multiple comparisons being 28, that is, the number of networks included in our study (see Table I). Statistics on the beta weights were performed using the R software package [R Core Team, 2013].

Event-related averages of back-reconstructed subject and session level ICN TCs were computed using a MATLAB routine included with GIFT (icatb_eventAverage.m). The event-related average TC for each component network is created by averaging (over all subjects and sessions) those TC segments that are associated with the same event (e.g., Domino show events). Each of these event-related TC segments begin at an event onset and include the 10 sec of TC following the event onset. The average ICN timecourse for a specific event was modified such that the first point (time zero) of the averaged TC set to an amplitude of zero to allow comparisons between different event-related average waveforms

# RESULTS

## Behavioral Findings

For the Domino task, over four sessions, study participants played an average of $12.3 \pm 0.6$ games, won an average of $2.8 \pm 1.1$ games (22.5% of all games played), and played an average of $1.7 \pm 1.2$ games that were less than 1 min in duration (13.9% of all games played; these games were not included in the analysis). We also analyzed responses from the Domino post-scan debriefing to assess participants' beliefs regarding various aspects of game-play. There were 54 questions with a Likert scale from 1 (does not apply to you at all) to 5 (applies to you very much) and a one-sample Wilcoxon signed rank test comparison (one-sided, greater than) was made with the middle score of 3. Two questions were of particular interest to this study. When asked "Q11: I did everything I could to win the game," study participants mean Likert scores were $4.58 \pm 0.84$ (human opponent; $P < 2.7 \times 10^{-10}$) and $4.56 \pm 0.87$ (computer opponent; $P < 5.6 \times 10^{-10}$). This question probed participant's engagement in the game. When asked "Q26: I took my opponent's last move into account before deciding which chip to play next," study participants mean Likert scores were $4.06 \pm 1.29$ (human opponent; $P < 6.5 \times 10^{-6}$) and $3.79 \pm 1.32$ (computer opponent; $P < 0.0004$). For Q26, the Likert scores were significantly greater for human versus computer opponent ($P < 0.008$). This question probed participant's tendency to mentalize (i.e., take opponent's thoughts during the last move into account) when playing against a human-opponent.

For the SORT, we assessed accuracy and response time of participants' responses to retrieval and non-retrieval events. In addition to assessing the accuracy from in-scanner recordings of participants' responses, we also conducted post-scan debriefing to ensure that participants correctly interpreted the word pairs presented, that is, did they understand the word pairs well enough to detect the presence or absence of a semantic association. Our findings for mean accuracy for SORT were $87.1\% \pm 10.4\%$ for the retrieval trials and $90.0\% \pm 12.8\%$ for the non-retrieval trials ($t = -1.696$, $P = 0.096$; paired $t$-test). Mean reaction times for SORT were $0.861 \pm 0.186$ sec for correct retrieval
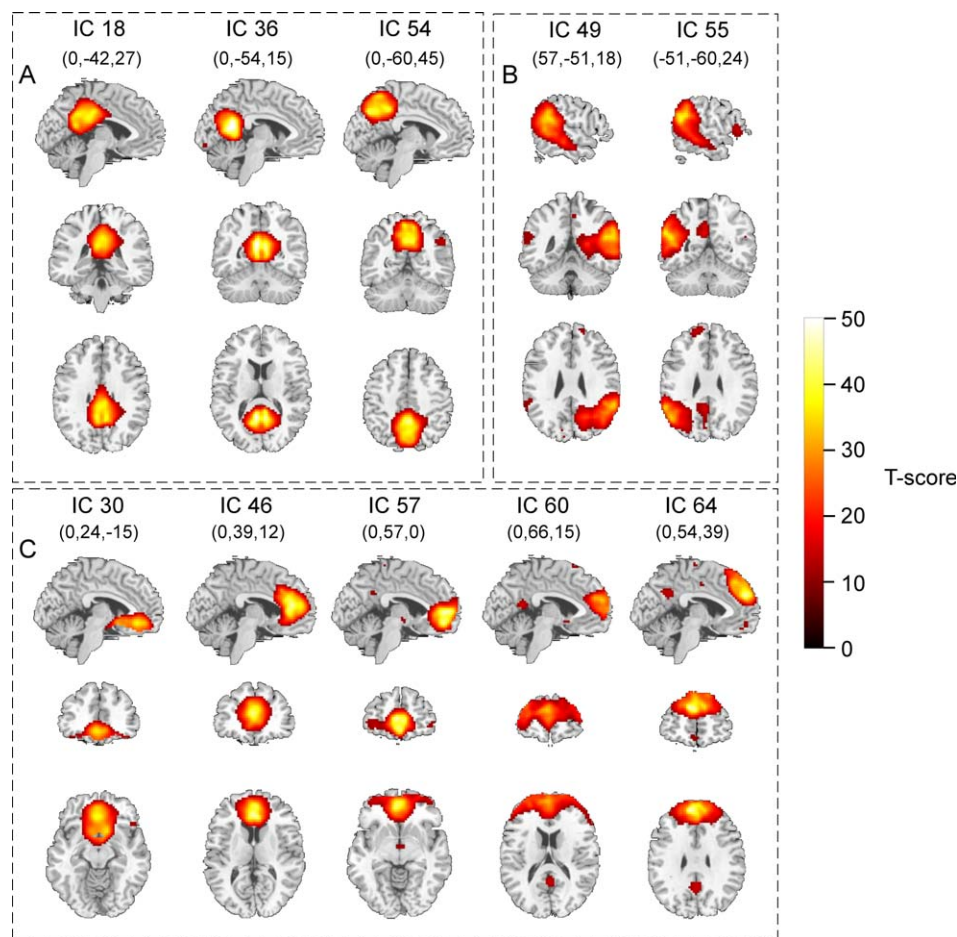
**Figure 2.**

DM related ICNs derived from group sICA. (**A**) Posterior medial region ICNs including posterior cingulate cortex (PCC) and precuneus. (**B**) Temporoparietal junction (TPJ) region ICNs including left and right TPJ. (**C**) Anterior medial region ICNs including dorsomedial and ventromedial prefrontal cortex. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

trials versus $0.988 \pm 0.209$ sec for correct non-retrieval trials ($t = -7.65$, $P < 0.0001$; paired $t$-test), and $1.069 \pm 0.264$ sec for incorrect retrieval trials versus $1.094 \pm 0.264$ sec for incorrect non-retrieval trials ($t = -0.639$, $P = 0.526$; paired $t$-test). These behavioral patterns are in agreement with our previous results in healthy individuals [Assaf et al., 2009a; Jamadar et al., 2013].

### Imaging Findings

Table I lists all 28 ICNs retained from the group sICA, with MNI peak voxel location and anatomical region listed for each ICN, and arranged by Stanford network classification. We present here, however, only results for ICNs that we identified as belonging to the DMN, as the relationship of mentalizing to the DMN is the primary focus of our study. In the Supporting Information, we briefly describe results related to the salience and central executive networks to give a more comprehensive delineation of network recruitment by Domino and SORT task events (i.e., mentalizing and semantic memory). For all data presented, we performed a separate analysis where we covaried for age and gender, but found no significant effect of either age or gender on our results. Therefore, we present here all analyses without using age and gender covariates.

### DM Related ICNs

Figure 2 shows the 10 ICNs we identified as belonging to the DMN. These maps were derived from the sICA component SMs, which were first scaled to $z$-scores and then entered into a one-sample $t$-test, with the results

**TABLE II. Domino task modulation of ICA-derived Default Mode IC network recruitment, by event type**

| | Domino task | | | | | |
|---|---|---|---|---|---|---|
| | Show | | No-show | | Show > no-show | |
| IC: Region | $\beta$ M ± SE | $t$ ($q$ FDR) | $\beta$ M ± SE | $t$ ($q$ FDR) | $\Delta\beta$ M ± SE | ANOVA $F$ ($q$ FDR) |
| **18**: PCC/PrC (I) | 0.161 ± 0.023 | 4.971 (<0.001) | 0.029 ± 0.025 | 0.991 (ns) | 0.133 ± 0.034 | 15.39 (<0.001) |
| **36**: PCC/PrC (II) | 0.044 ± 0.022 | 1.417 (ns) | 0.035 ± 0.028 | 1.025 (ns) | 0.009 ± 0.035 | 0.070 (ns) |
| **54**: Precuneus | 0.127 ± 0.023 | 3.886 (<0.001) | 0.024 ± 0.024 | 0.790 (ns) | 0.104 ± 0.033 | 10.12 (0.003) |
| **49**: Right TPJ | 0.257 ± 0.025 | 6.740 (<0.001) | −0.119 ± 0.025 | −3.668 (0.001) | 0.376 ± 0.035 | 114.1 (<0.001) |
| **55**: Left TPJ | 0.208 ± 0.022 | 7.137 (<0.001) | −0.055 ± 0.025 | −1.575 (ns) | 0.263 ± 0.034 | 60.13 (<0.001) |
| **30**: Subgenual ACC | 0.028 ± 0.021 | 0.933 (ns) | 0.003 ± 0.021 | 0.138 (ns) | 0.024 ± 0.029 | 0.693 (ns) |
| **46**: dmPFC/ACC | 0.176 ± 0.022 | 7.380 (<0.001) | 0.114 ± 0.023 | 4.344 (<0.001) | 0.062 ± 0.030 | 4.177 (0.065*) |
| **57**: vmPFC | 0.183 ± 0.023 | 5.156 (<0.001) | 0.140 ± 0.028 | 4.318 (<0.001) | 0.043 ± 0.036 | 1.435 (ns) |
| **60**: mPFC | 0.072 ± 0.024 | 2.089 (0.049) | 0.062 ± 0.023 | 2.315 (0.036) | 0.010 ± 0.033 | 0.096 (ns) |
| **64**: dmPFC | 0.218 ± 0.026 | 6.288 (<0.001) | 0.084 ± 0.026 | 2.575 (0.021) | 0.134 ± 0.036 | 14.16 (<0.001) |

Abbreviations: (M) Mean; (SE) Standard error of the mean; (FDR) False Discovery Rate; (ns) not significant. ($q > 0.1$); * trend level $q < 0.1$.

statistically thresholded at $t > 11.0$ (approximately FDR $q < 1.0$ e − 10).

## DMN recruitment by task event

### Domino task

The four Domino task "Response to Outcome" regressor $\beta$-weights from the temporal regression of component TCs with the SPM-modeled TCs were entered into a two-way (2 × 2) ANOVA with the factors Opponent Type (human/computer) and Mentalizing (show/no-show). The results for the Opponent Type factor are presented and briefly discussed in the Supporting Information.

Table II summarizes the Domino task $\beta$-weight statistics for DM -related ICNs for show and no-show task events as well as show > no-show contrast (i.e., Mentalizing).

The factor of Mentalizing, as defined by the show > no-show contrast, was significant in increasing network recruitment in five of the 10 DM ICNs, including PCC/precuneus (IC 18), precuneus (IC 54), left and right TPJ (ICs 55 and 49), and dmPFC (IC 64). A trend level increase (FDR $q = 0.065$) was observed in dmPFC/ACC (IC 46).

The task events show and no-show significantly increased network recruitment in eight and four of the 10 DM ICNs, respectively. The show task event increased network recruitment in the same five ICNs as show > no-show, with the addition of dmPFC/ACC (IC 46), vmPFC (IC 57), and mPFC (IC 60). The no-show task event increased network recruitment in dmPFC/ACC (IC 46), vmPFC (IC 57), mPFC (IC 60), and dmPFC (IC 64), but decreased network recruitment in right TPJ (IC 49).

### Semantic object retrieval task

The two SORT event regressor $\beta$-weights were entered into a one-sample $t$-test to yield $\beta$-weight statistics on

retrieval and non-retrieval versus baseline, and into a paired $t$-test to yield $\beta$-weight statistics on the retrieval > non-retrieval contrast. Table III summarizes these DM-related ICN $\beta$-weight statistics for the SORT.

The retrieval and non-retrieval task events for the SORT, in contrast to Domino task events, decreased network recruitment in five and nine of the 10 ICNs comprising the DMN, respectively. Interestingly, in the DMN, the retrieval event increased network recruitment for two of the 10 ICNs, including the PCC/PrC (I) (IC 18) and Left TPJ (IC 55). Notably, the statistics on the contrast retrieval > non-retrieval show a relative increase in network recruitment in most (eight of 10) DM ICNs (see Table III). However, in IC 60 (mPFC) retrieval and non-retrieval events both showed no significant changes in network recruitment (i.e., the contrast was significant, but the individual events were not significant), and in five of these eight ICNs, retrieval events simply showed significantly less of a decrease than non-retrieval events in network recruitment.

## Event-Related Averages From ICN Timecourses

An examination of both Tables II and III reveals that three of the 10 DM ICNs (ICs 49, 54 and 64) show explicit contrasting effects between the two tasks, Domino and SORT, on modulating DM subnetwork recruitment. For these three DM ICNs, the mentalizing contrast show > no-show was significant and both retrieval and non-retrieval events showed significant negative modulation of network recruitment. To provide a visualization of these contrasting effects, we examined the event-related average TCs for each of the four events, show, no-show, retrieval, and non-retrieval. Figure 3 depicts event-related average TCs, for 10 sec following the event onset, computed from the subject and session level back-reconstructed TCs, and shows the contrasting effects of the Domino versus SORT events

**TABLE III. SORT modulation of sICA-derived Default Mode IC network recruitment, by event type**

| | SORT | | | | | |
|---|---|---|---|---|---|---|
| | Retrieval | | Non-retrieval | | Retrieval > non-retrieval | |
| IC: Region | $\beta$ M ± SE | $t$ ($q$ FDR) | $\beta$ M ± SE | $t$ ($q$ FDR) | $\Delta\beta$ M ± SE | paired $t$ ($q$ FDR) |
| **18**: PCC/PrC (I) | 0.314 ± 0.096 | 3.254 (0.004) | −0.203 ± 0.093 | −2.181 (0.041) | 0.517 ± 0.072 | 7.154 (<0.001) |
| **36**: PCC/PrC (II) | −0.055 ± 0.124 | −0.443 (ns) | −0.301 ± 0.115 | −2.615 (0.016) | 0.246 ± 0.095 | 2.577 (0.020) |
| **54**: Precuneus | −0.240 ± 0.103 | −2.328 (0.033) | −0.688 ± 0.117 | −5.873 (<0.001) | 0.448 ± 0.091 | 4.916 (<0.001) |
| **49**: Right TPJ | −0.297 ± 0.099 | −3.001 (0.007) | −0.335 ± 0.097 | −3.441 (0.002) | 0.037 ± 0.078 | 0.478 (ns) |
| **55**: Left TPJ | 0.287 ± 0.120 | 2.398 (0.030) | −0.404 ± 0.107 | −3.781 (<0.001) | 0.691 ± 0.087 | 7.975 (<0.001) |
| **30**: Subgenual ACC | −0.246 ± 0.098 | −2.523 (0.023) | −0.225 ± 0.083 | −2.694 (0.014) | −0.022 ± 0.067 | −0.325 (ns) |
| **46**: dmFPC/ACC | −0.128 ± 0.131 | −0.974 (ns) | −0.421 ± 0.115 | −3.676 (0.001) | 0.293 ± 0.093 | 3.167 (0.005) |
| **57**: vmPFC | −0.407 ± 0.087 | −4.659 (<0.001) | −0.663 ± 0.095 | −6.981 (<0.001) | 0.691 ± 0.087 | 3.200 (0.005) |
| **60**: mPFC | 0.086 ± 0.113 | 0.765 (ns) | −0.135 ± 0.086 | −1.573 (ns) | 0.221 ± 0.073 | 3.026 (0.007) |
| **64**: dmPFC | −0.429 ± 0.137 | −3.140 (0.005) | −0.657 ± 0.105 | −6.262 (<0.001) | 0.228 ± 0.085 | 2.670 (0.017) |

Abbreviations: (M) Mean; (SE) Standard error of the mean; (FDR) False Discovery Rate; (ns) not significant.

on modulation of network recruitment in precuneus (PrC) (IC 54; panel A), right TPJ (IC 49; panel B), and dmPFC (IC 64; panel C). Domino task events positively modulate these ICN TCs, whereas SORT task events negatively modulate these same ICN TCs.

In addition to the four DM subnetworks (ICs 30, 36, 57, and 60) without a significant mentalizing effect (i.e., show->no-show), we excluded an additional three ICNs, PCC/PrC (IC 18), dmPFC/ACC (IC 46), and left TPJ (IC 55) from consideration as DM subnetworks unique in supporting mentalizing processes. In the case of dmPFC/ACC (IC 46), the Domino show > no-show contrast was significant for increasing network recruitment only at the trend level, while SORT retrieval events were insignificant in modulating network recruitment, but this ICN otherwise fit the criteria for a DM subnetwork supporting mentalizing (see Fig. 4, panel A, for the event-related average TCs for IC 46). As depicted in Figure 4, panels B and C, for PCC/PrC (IC 18) and Left TPJ (IC 55), the SORT retrieval event showed positive modulation of network recruitment, therefore suggesting these two DM subnetworks were not unique to mentalizing, but also support semantic memory retrieval and/or language processing.

## Summary

To summarize, for the ten DM subnetworks, five DM subnetworks were not significant for mentalizing (ICs 30, 36, 46, 57, and 60; note, however, that IC 46 was trend-level significant for mentalizing, and also demonstrated opposing modulation of network recruitment by the two tasks), two were significant for both mentalizing and semantic memory retrieval (ICs 18 and 55), and three (ICs 49, 54, 64) were unique to mentalizing (see Fig. 1, bottom).

## DISCUSSION

Using a social interactive game task and a semantic association task, along with resting state fMRI data, all obtained from the same set of individuals, we identified a number of DM subnetworks that were engaged by the social task. This supports the claim that many subnetworks of the DMN are not truly task-negative, but rather support mentalizing processes during social interaction. We investigated task-related modulation of network recruitment in DM subnetworks using a relatively high-order sICA that combined both tasks and, as hypothesized, found an opposing modulatory effect on network recruitment within three subnetworks (ICs 49, 54, and 64) of the DMN. This effect provided additional evidence that these subnetworks were uniquely engaged in mentalizing. Finally, we also showed using a separate sICA, that resting state-derived DM subnetworks had a high degree of spatial correlation with the Domino-SORT DM subnetworks (see Supporting Information). This finding further supported our conclusion that mentalizing processes are supported by specific subnetworks in the DMN.

The findings in our study confirm prior work not only on support for mentalizing processes within the DMN [Assaf et al., 2009b; Li et al., 2014; Mars et al., 2012a] but also the involvement, although limited, of semantic memory recall within the DMN [Binder et al., 2009; Shapira-Lichter et al., 2013; Wirth et al., 2011]. Unlike prior studies on social cognition, semantic recall and the DMN, however, we demonstrated opposing task-related modulation of network recruitment in mentalizing networks using an approach in which fMRI data from two tasks collected on the same individuals was included within one (vs. separate) sICA, a method introduced only recently [Cetin et al., 2014; Demirci et al., 2009].

Importantly, we performed a relatively high-order sICA, which has been used increasingly in recent imaging studies [Allen et al., 2011] and has been shown to result in increased functional neuroanatomical precision stabilization of subsequent back reconstruction [Erhardt et al., 2011] (but at the expense of reduced repeatability [Abou-Elseoud et al., 2010]).
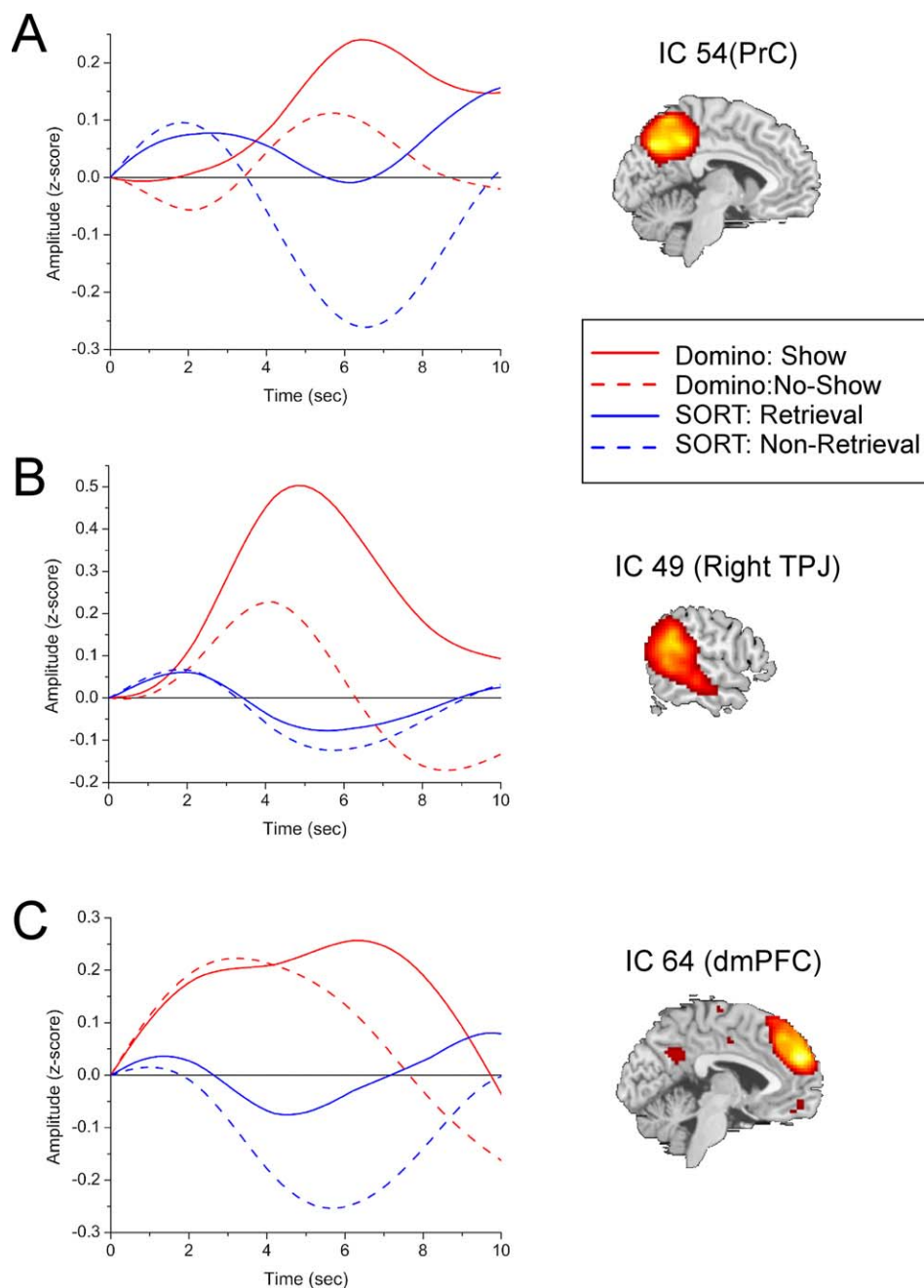
**Figure 3.**

Event-related average ICA-derived TC from three subnetworks of the DMN showing opposing BOLD signal for Domino task and SORT events. TC amplitudes are reported as z-scores. The four event-related average TCs in each region are depicted by task and event-type (Show and No-Show for Domino, and Retrieval and Non-Retrieval for SORT). On the far right of each panel are brain images showing the corresponding DM-related ICNs. (Abbreviations: PrC, Precuneus; R TPJ, right temporoparietal junction; dmPFC, dorsomedial prefrontal cortex; ACC, anterior cingulate cortex; vmPFC, ventromedial prefrontal cortex). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]
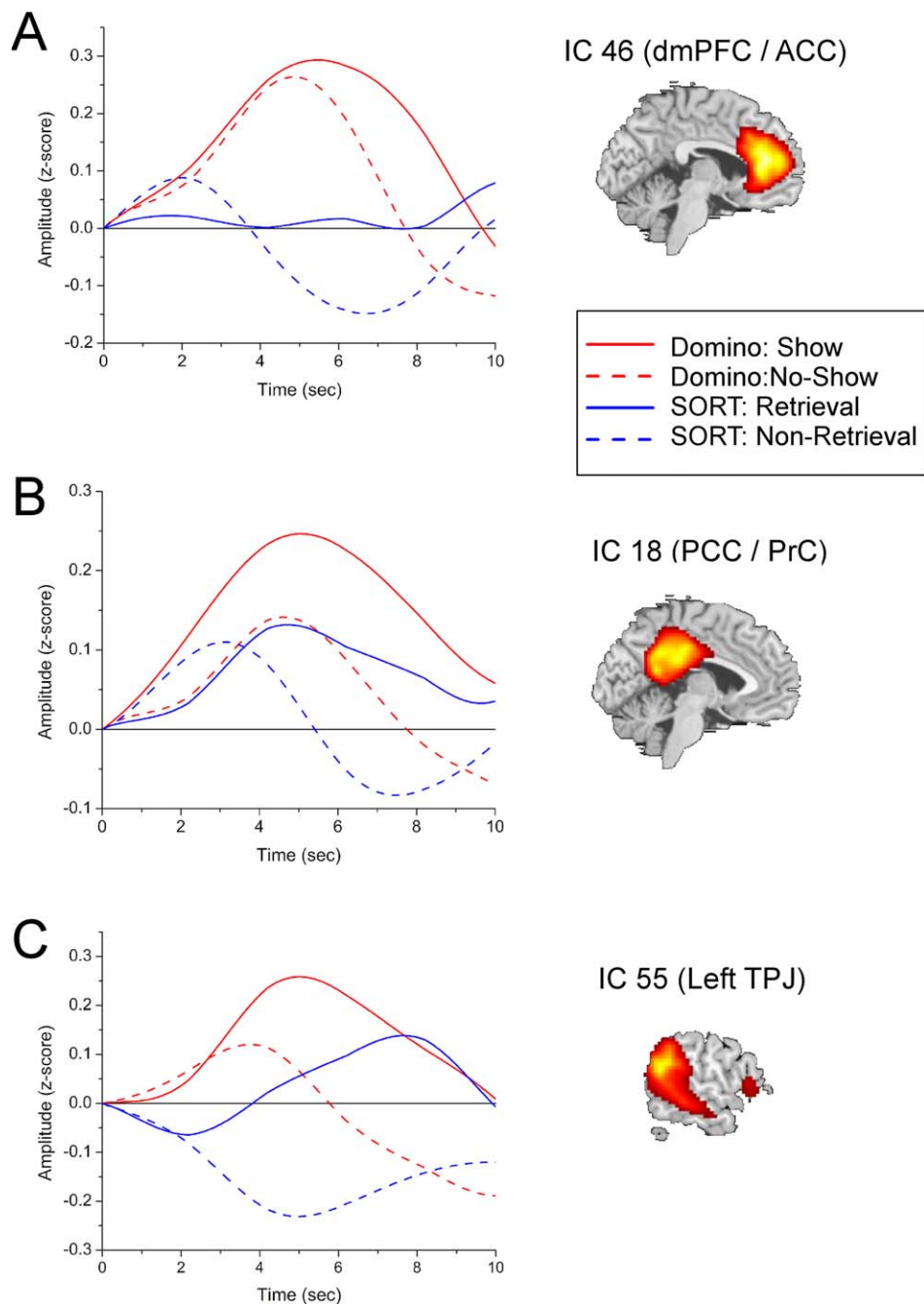
**Figure 4.**

Event-related average ICA-derived TC from three subnetworks of the DMN that were excluded as being unique to mentalizing. (**A**) The DM subnetwork in which mentalizing was significant only at the trend level (FDR $q = 0.065$) but otherwise exhibiting opposing modulation of network recruitment by the two tasks. (**B**, **C**) Two DM subnetworks exhibiting mentalizing (i.e., Domino show > no-show), but where SORT Retrieval events were also significant for increasing network recruitment. (Abbreviations: DM, default mode; FDR, false discovery rate). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Consistent with previous studies [Allen et al., 2011], high-order sICA notably split the DMN into a number of smaller regions, including five separate ICNs in the anterior medial region (Fig. 1, panel C) and three ICNs in the posterior medial region (Fig. 1, panel A) as well as separate ICNs for the left and right TPJ. This contrasts with earlier studies of resting state fMRI using low-order sICA (<= 30 components) where the DMN (excluding the temporal poles) was typically encompassed by only two to three ICNs [Assaf et al., 2010; Calhoun et al., 2008], or in some cases, by only a single ICN [Franco et al., 2009; Meindl et al., 2010; Patel et al., 2013].

In general agreement with our hypotheses, the Domino "Response to Outcome" factor of Mentalizing, as defined by the show>no-show event contrast, significantly increased network recruitment in a majority of the ICNs we identified as belonging to the DMN. These findings are in good agreement with previous GLM-based imaging studies using the Domino task [Assaf et al., 2013, 2009b]. The increased BOLD signal in the show vs. no-show events in the DMN was posited to be due to processes related to mentalizing (e.g., trying to deduce the opponent's strategy) [Assaf et al., 2009b] as the former events required the scanned participant to understand how the opponent might use the new information about his/her play (i.e., playing fair or bluffing) to adjust his/her strategy.

Due to splitting of the DMN into smaller component networks, we found that network recruitment was modulated by Domino mentalizing events (i.e., the event contrast show > no-show) in only five of 10 subnetworks we identified as DMN-related, demonstrating a differentiation of DMN regions based on the cognitive processes in which they are involved. We discuss here, for each of the three core DMN regions, which subnetworks support mentalizing in general, and more specifically, those DM subnetworks that, as suggested by the opposing modulation of network recruitment by the Domino task and SORT, uniquely support mentalizing.

### Anterior Medial Region

One DM subnetwork in the dmPFC (IC 64) was significant for the Mentalizing factor while a second dmPFC subnetwork (IC 46) was trend level significant (FDR $q = 0.065$). In both of these DM subnetworks, SORT retrieval and non-retrieval events showed opposing modulation of network recruitment, suggesting these subnetworks uniquely support mentalizing. This is consistent with the significant role of the dmPFC region in mentalizing found in prior studies [Amodio and Frith, 2006; Frith and Frith, 2006; Mars et al., 2012a; Sallet et al., 2013; Saxe and Powell, 2006; Spreng et al., 2009; van Veluw and Chance, 2014].

Interestingly, the SORT retrieval event, when compared with the non-retrieval event, consistently showed either less of a decrease, or no change, in network recruitment in most DM subnetworks in all four core DMN regions, including ICs 46, 57 and 64 in the anterior medial region. Consistent with these findings, Wirth et al. used sICA in a study of semantic memory involvement in the DMN and found that a semantic decision task deactivated the DMN less than phonological and perceptual decision tasks [Wirth et al., 2011].

For the remaining three anterior medial regions subnetworks, we found that IC 30 (rostral ACC), was not significantly modulated by show or no-show events, nor by the event contrast, show>no-show, while network recruitment in IC 60 (mPFC) and IC 57 (vmPFC), although significantly increased by both show and no-show events, was not modulated by the event contrast, show>no-show. This suggests a lack of involvement in mentalizing processes in all three of these DM subnetworks.

We provide here possible explanations as to why network recruitment in these ICNs were not modulated by the mentalizing event contrast, show>no-show. The anterior medial network, IC 30, is located in subgenual ACC, a region included as part of the DMN in some studies [Amft et al., 2015; Schilbach et al., 2012], is postulated to be involved in emotional regulation and arousal [Rudebeck et al., 2014]. Thus, it might only play a role in mentalizing processes involving affective states not elicited by the Domino task. The subnetwork IC 60 (mPFC), although partially overlapping ICs 46 and 64, maps spatially more extensively onto polar and lateral frontal regions, and therefore might not be part of the medial prefrontal network related to mentalizing. The subnetwork IC 57 (vmPFC), given the strong show and no-show event-related increases in network recruitment, and strong decreases in network recruitment by SORT retrieval and non-retrieval events, indicates it is very likely a part of the DMN, but for the Domino task, appears to not be involved in mentalizing.

### Posterior Medial Region

The Domino show>no-show contrast, was significant in two of the three posterior medial region DM subnetworks (ICs 18 and 54). The SORT, however, only showed opposing modulation in one of the three (IC 54). The subnetwork IC 18, with peak voxel in the PCC, is the probable "hub" of the DMN. The increase in network recruitment by SORT retrieval events in PCC/PrC (IC 18), however, is consistent with prior studies suggesting that the DMN "hub" in the PCC is involved in semantic memory retrieval [Burianova et al., 2010; Daselaar et al., 2009].

Network recruitment in one of the posterior medial subnetworks (IC 36, PCC/PrC) was not significantly modulated by show or no-show events, nor by the event contrast, show>no-show. For SORT, only non-retrieval events showed a significant decrease in network recruitment. A possible explanation is that location and extent of

IC 36 appear very similar to the so-called "transitional component" described by Abou-Elseoud et al., which appears only at higher orders (>30 components), includes visual processing related regions (e.g., lingual gyrus, cuneus) and is, therefore, likely not a DMN-related component [Abou-Elseoud et al., 2010].

### Temporoparietal Junction

Another default-mode region notable for its involvement in processes related to mentalizing and social cognition is the right TPJ [Decety and Lamm, 2007; Mars et al., 2012a, 2013, 2012b; Saxe and Wexler, 2005; Young et al., 2010]. In particular, we observed that the right TPJ (IC 49) showed a significant increase in network recruitment for mentalizing (although not significant for the Opponent Type factor) with decreased modulation by SORT. The right TPJ has been described as functionally and structurally heterogeneous, with recent studies suggesting multiple subregions with different functions [Geng and Vossel, 2013; Mars et al., 2012b; Scholz et al., 2009]. In addition to mentalizing [Saxe and Wexler 2005; Scholz et al., 2009], the right TPJ has also been posited to be involved in attentional selection (or reorienting) [Corbetta et al., 2008; Scholz et al., 2009]. While examination of right TPJ functional heterogeneity is beyond the scope of this study, our findings support the role of the right TPJ in mentalizing processes, where Domino show events positively modulate network recruitment in the right TPJ, while Domino no-show events and SORT retrieval and non-retrieval events negatively modulate the network recruitment. Regarding the role of right TPJ in reorienting of attention, it can be argued that both Domino and SORT use "unexpected" random stimuli (task events) that should reorient attention, for example, show versus no-show events for Domino, and retrieval versus non-retrieval events for SORT are randomly presented but only Domino events positively modulate network recruitment in right TPJ.

In subnetwork IC 55 (left TPJ), SORT retrieval events resulted in increased network recruitment, indicating this subnetwork is not unique to mentalizing, but also supports semantic memory retrieval. The positive modulatory involvement of SORT retrieval events in this network recruitment is consistent with findings that this region is involved in semantic memory retrieval [Burianova et al., 2010]. Notably, the left TPJ network partially overlaps language processing brain regions (e.g., Wernicke's area) that is expected to be engaged by SORT events, and this fact might explain increased network recruitment by SORT retrieval events in this region. However, network recruitment in left TPJ was decreased by SORT non-retrieval events, which does not support this explanation.

### Summary

In summary, of the 10 ICNs we identified as subnetworks of the DMN only three (or perhaps four, if IC 46 is included) ICNs are specifically engaged in mentalizing processes. These three (or four) subnetworks, located in the dmPFC, right TPJ and precuneus, all showed opposing network recruitment by Domino and SORT task events, suggesting that they are unique to mentalizing compared with semantic memory processes. An additional two subnetworks in the left TPJ (IC 55) and in the PCC (IC 18, the DMN "hub"), appear to support not only mentalizing, but semantic memory retrieval as well. Finally, four of the DM subnetworks did not show a modulation effect by mentalizing. Our results are in good agreement with the study by Jack et al., in which the dmPFC, right TPJ, and posterior cingulate/precuneus were the three regions most strongly activated by the social>physical task contrast [Jack et al., 2013].

### Resting State DMN versus two-Task sICA: SM Correlations

Table S2 in the Supporting Information compares the 10 DM-related Domino-SORT ICNs that were best matched, as determined by spatial correlation, with the resting state DM-related ICNs. Notably, there was only a single ICN in ventromedial PFC ($IC_{RS}$ 18) for resting state that matched two separate vmPFC ICNs (ICs 57 and 60) derived from the two-task sICA. Supporting Information Figure S3 shows the degree of overlap of DM subnetworks from the two sICAs. In general, overlap between the ICN SMs for the DMN was very strong for all ICNs, with differences mainly in the spatial extent of the networks, with the Domino/SORT ICNs being in every case of greater spatial extent. The greater spatial extent in the two-task sICA was not due, however, to the greater number of fMRI sessions/timepoints, as even a single Domino session (computer opponent) had average component maps of similar spatial extent to the components based on the full complement of four sessions of Domino plus one session of SORT. Our findings, therefore, strongly suggest that the DMN subnetworks active during resting state are essentially the same as those whose network recruitment is modulated by Domino or SORT task events.

### Study Limitations

Our study limitations include the use of a different fMRI repetition time for resting state (TR = 1500 msec) versus Domino/SORT (TR = 1860 msec) which prompted us to perform a separate sICA for the resting state data. A separate resting state sICA, however, might not have been necessary, as a comparison between resting state and Domino/SORT DMN component SMs shown in Figure S3 (Supporting Information) indicates a high degree of similarity, despite the separate sICA estimations.

Another limitation was that resting state fMRI scans for 10 of the $n = 53$ subjects were acquired on a different date, where five of them were acquired more than one-half year

earlier than the Domino/SORT scans (note that for all subjects, SORT and Domino task data were acquired during the same scanning session). Several recent studies of test-retest reproducibility for time-concatenated ICA (i.e., our ICA method in this study) of resting state fMRI, however, indicate very good reproducibility when the resting state sessions are performed within one year of each other [Guo et al., 2012; Meindl et al., 2010; Zuo et al., 2010]. Therefore, we would not expect significant changes in resting state component SMs if the resting state scans had been performed on the same day as Domino/SORT scans.

## CONCLUSIONS

Our findings in this study are in very good agreement with recent work showing that brain regions involved in mentalizing are part of the DMN, and while network recruitment in the DMN is negatively modulated by many tasks, such as the SORT, it is positively modulated by tasks that involve mentalizing, such as the Domino task. Regional specialization for mentalizing is also reflected in differing modulation of network recruitment by the two tasks within certain default-mode subnetworks, with the Domino task in particular emphasizing the role of specific subregions of the dmPFC and precuneus and the right TPJ in mentalizing processes during competitive social interaction. Semantic retrieval events resulted in an increase network recruitment in the DMN hub in the PCC, as well as in left TPJ. In many other default-mode subnetworks, semantic retrieval events simply resulted in less of a decrease in network recruitment than non-retrieval events, consistent with findings in prior studies. In conclusion, our study shows that certain DM subnetworks are not task-negative, but instead uniquely engage in mentalizing during a social task.

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