Consistency and functional specialization in the default mode brain network

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The notion of a "default mode of brain function" has taken on certain relevance in human neuroimaging studies and in relation to a network of lateral parietal and midline cortical regions that show prominent activity fluctuations during passive imaging states, such as rest. In this study, we perform three fMRI experiments that demonstrate consistency and specialization in the default mode network. Correlated activity fluctuations of default mode network regions are identified during (*i*) eyes-closed spontaneous rest, (*ii*) activation by moral dilemma, and (*iii*) deactivation by Stroop task performance. Across these imaging states, striking uniformity is shown in the basic anatomy of the default mode network, but with both tasks clearly and differentially modulating this activity compared with spontaneous fluctuations of the network at rest. Against rest, moral dilemma is further shown to evoke regionally specific activity increases of hypothesized functional relevance. Mapping spontaneous and task-related brain activity will help to constrain the meaning of the default mode network. These findings are discussed in relation to recent debate on the topic of default modes of brain function.

activation | deactivation | default mode | functional MRI | spontaneous activity

The notion of a "default mode of brain function" has emerged as a compelling but controversial topic in neuroimaging research (1–4). At its core, it suggests the existence of an ongoing and anatomically organized mode of neuronal activity that is preferentially engaged in the brain and that is suspended only during specific goal-directed behaviors (3). In humans, this default mode system has been linked, in part, to the spontaneous thought processes or self-oriented mental activity that define the brain's "resting state" (3, 5). To this end, the extent to which functional imaging studies of rest may help to further clarify the behavioral meaning of default mode activity, has been recently debated (1, 2, 4, 6).

The default mode network was originally identified in positron emission tomography (PET) studies and refers specifically to a set of cortical regions that show common activity decreases or deactivations when subjects perform cognitively demanding tasks (3). These regions include the posterior cingulate cortex and precuneus, the inferior parietal cortices, and dorsal and ventral areas of the medial frontal cortex (3, 7–9). The consistency of this observation, together with knowledge of the brain's basic metabolic requirements at rest, lead to the proposal that this deactivation pattern may represent an organized mode of brain function whose primary role may be to support internally oriented mental processes in humans (3, 10). Importantly, ensuing studies with functional magnetic resonance imaging (fMRI) have both confirmed and extended original findings to show that the default mode network can be readily seen as deactivations in task-related fMRI experiments (11–14), can also be identified as a pattern of resting-state functional connectivity (15–20), and may associate with specific profiles of spontaneous oscillations of electrical brain dynamics (21, 22).

Despite the robustness of the default mode network phenomenon in neuroimaging experiments, its precise meaning with respect to behavior is not well defined. From existing studies, the default mode network has been associated indirectly with the pattern of evoked activity that is observed with tasks involving self-judgments, autobiographical memory recall, moral dilemma, and prospective thinking, among others (5, 20, 23–25). In general terms, a common feature of these tasks is that they enhance subjects' attention toward themselves—a presumed behavioral correlate of resting-state imaging conditions and the spontaneous thought processes, or "mind-wandering," that accompany it (26). However, others have questioned this line of inference, arguing that the "cognitive nature at rest is at present almost entirely a matter of speculation" (ref. 2, p. 1079) and, instead, advocate the use of specific tasks to identify factors responsible for the consistency and variability within these findings.

This study sought to further constrain the meaning of default mode network function by jointly investigating its activity across three distinct fMRI contexts: task-related activation, task-related deactivation, and rest. We asked two broad but related questions: First, will the activity of default mode network regions show anatomical consistency across these distinct imaging contexts? If so, then the use of fMRI tasks to probe or "unpack" the behavioral meaning of the default mode network may prove viable, as recently proposed (2). Second, assuming some consistency exists, to what extent may tasks differentially activate default mode network regions, which have a characteristically high activity level at rest (3)? To approach this second question, we compared patterns of correlated blood oxygen level-dependent (BOLD) signal fluctuations of default mode network regions observed during a resting-state and moral dilemma experiment in the same subjects.

Results

Task Performance. Moral dilemma was chosen as the specific context to study "activation" of default mode network regions based on our own and others recent findings (25, 27, 28). Briefly, subjects ($n = 22$) responded to 24 moral dilemma and 24 memory control (non-moral dilemma) task vignettes that were presented

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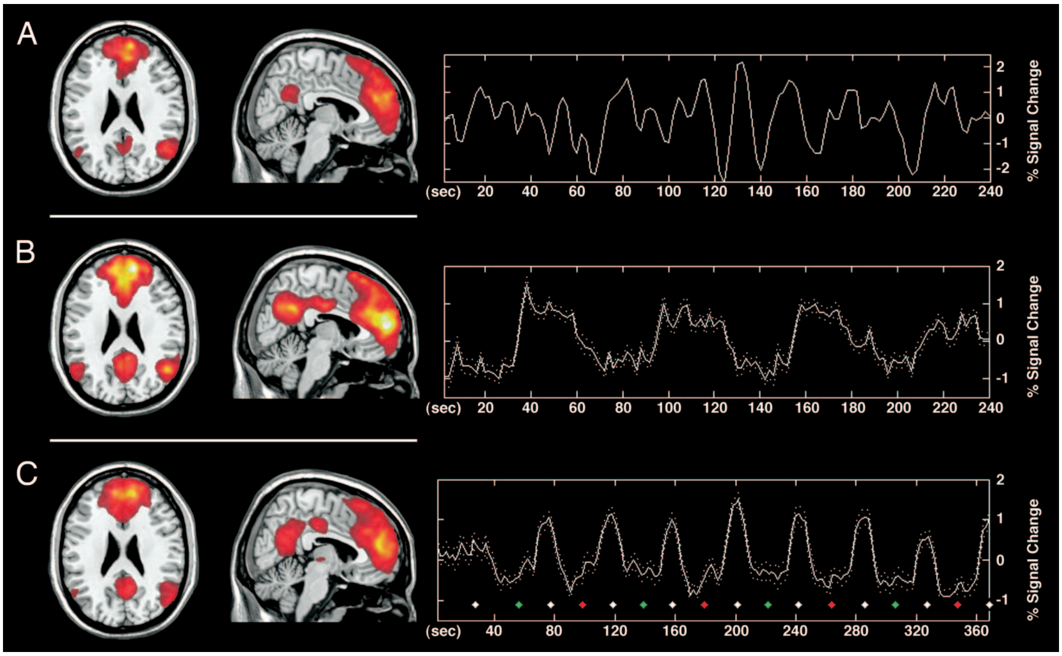

Fig. 1. Default mode network activities across the three imaging states. (*A*) Spontaneous activity in the default mode network during rest and the associated time course of a representative subject (*z* score range = 3.5 to 7). (*B*) Task-related activity of the default mode network during the moral dilemma experiment and the associated mean (solid line) and standard error (dotted line) time course estimated across all subjects (*z* score range = 3.5 to >8). (*C*) Task-related activity of the default mode network during the Stroop task experiment and the associated mean (solid line) and standard error (dotted line) time course estimated across all subjects (*z* score range = 3.5 to 7). Diamonds located below this time course correspond to the approximate middle point of each Stroop task block. White diamonds, rest-fixation periods; green diamonds, congruent trials; red diamonds, incongruent trials. Image display: left = right.

audio-visually in a block-design fMRI experiment [see full details in supporting information (SI) *Materials and Methods* and *SI Appendix*]. Performance-wise, subjects made correct responses to 95.3% of the control task vignettes (4.7% incorrect responses, including omissions). For the moral dilemma condition, the mean pattern of responses to each specific vignette is provided in *SI Appendix*.

Consistent with the hypothesized role for emotion in moral judgment (28), subjects rated the moral dilemma vignettes as significantly higher in negative emotional intensity and lower in positive emotional intensity compared with the control vignettes in a postscanning interview (Fig. S1; $P < 0.001$).

To study "deactivation" of default mode network regions, a self-paced version of the Stroop color-word interference task was used (see *SI Materials and Methods*). Briefly, subjects responded to standard congruent and incongruent Stroop color-naming trials that were interleaved with rest-fixation periods in a block-design experiment. The analysis of response error and reaction time (RT) scores confirmed subjects' attentional engagement during both of the task blocks (see results in *SI Materials and Methods*).

Identification of Default Mode Network Activity. fMRI-BOLD data were analyzed by using combined group independent component analysis (ICA) and statistical parametric mapping techniques (29). Group ICA was performed for each fMRI experiment separately, generating three sets of results that were investigated further with statistical comparisons. Full description of this analysis strategy is provided in *SI Materials and Methods*.

For each experiment, we identified a statistically significant pattern of spatially correlated BOLD signal activity [an independent component (IC)] that reproduced the major anatomical features of the default mode network ($P_{\mathrm{FDR}} < 0.05$). This was tested further and directly, using a spatial sorting analysis that estimated the spatial correlation of all IC patterns from a given set of Group ICA results with an anatomical template of the default mode network created by using a Talairach and Tournoux (30) atlas labeling system (see *SI Materials and Methods*). In each case, the default mode network pattern that we identified from each Group ICA demonstrated the highest correlation to this anatomical template with respect to other estimated ICs (Pearson's r range = 0.40 to 0.60).

Fig. 1 shows the default mode network patterns and their associated time courses that were identified in each of the fMRI experiments. For each of these observations, primary clusters of activity were located in the dorsal and polar medial frontal cortex, ventral posterior cingulate cortex, the inferior parietal and frontal cortices and lateral cerebellum. The corresponding anatomical coordinates of all regional activities and their associated statistical magnitudes and extents are provided in Table 1.

After the initial spatial identification of networks, a temporal sorting analysis was performed to determine the degree of "task-relatedness" of the moral dilemma and Stroop task default mode network patterns. For each set of ICA results, the associated time course for all ICs was correlated with an idealized reference function (task waveform) of the moral dilemma and Stroop experiments, respectively. In both cases, the identified default mode networks (Fig. 1 *B* and *C*) demonstrated the highest correlation to each corresponding task waveform of the relevant task periods.

As seen in Fig. 1*B*, the degree of task-relatedness of the default mode network activity pattern to the moral dilemma task was strong. This pattern was positively and most robustly correlated with the specific moral dilemma condition blocks (Pearson's r = 0.53) relative to other estimated ICs. Similarly, the degree of task-relatedness of the default mode network pattern to the Stroop task was also high (Fig. 1*C*). This pattern was positively and most robustly correlated with the interleaved rest-fixation periods during Stroop task performance (Pearson's r = 0.53) relative to other estimated ICs.

Table 1. Default mode network regions demonstrating significant activity in the fMRI resting-state, activation (moral dilemma) and deactivation (Stroop task) experiments

Resting state						Moral dilemma						Stroop deactivation					
	Anatomy*			Statistics†			Anatomy			Statistics			Anatomy			Statistics	
Region	*x*	*y*	*z*	CS	*z*	Region	*x*	*y*	*z*	CS	*z*	Region	*x*	*y*	*z*	CS	*z*
Medial frontal gyrus	−9	56	19	3,266	6.97	Medial frontal gyrus	−9	50	17	5,242	>8	Medial frontal gyrus	−9	51	20	4,548	7.10
Inferior parietal lobe	−48	−54	25	344	6.02	Posterior cingulate gyrus	3	−51	30	1,087	6.98	Mid cingulate gyrus	−0	−18	37	131	5.88
Posterior cingulate gyrus	−3	−54	30	126	4.82	Inferior parietal lobe	−50	−57	28	604	6.98	Posterior cingulate gyrus	−6	−51	27	639	5.43
Inferior frontal gyrus	45	25	−19	71	4.75	Inferior parietal lobe	53	−57	28	383	4.90	Inferior parietal lobe	−53	−63	28	346	5.29
Cerebellum	−33	−77	−27	26	3.99	Inferior frontal gyrus	48	28	−11	70	4.31	Inferior frontal gyrus	45	26	−11	139	4.38
Inferior temporal gyrus	−56	−10	−20	27	3.80	Cerebellum	24	−74	−29	79	4.22	Inferior frontal gyrus	−39	23	−14	151	4.26
Inferior frontal gyrus	−40	31	−13	13	3.41	Inferior frontal gyrus	−45	25	−16	72	4.13	Cerebellum	−33	−77	−22	79	4.22
Parahippocampal gyrus	−37	−8	−16	7	1.68	Cerebellum	−31	−71	−30	40	4.04	Parahippocampal gyrus	−32	−5	−23	12	1.88

CS, cluster size. Consistent with some (e.g., ref. 20) but not other (e.g., ref. 16) fMRI studies of the default mode network, activity in the parahippocampal region was also observed during the resting-state and Stroop task experiments, albeit at a subthreshold level ($P < 0.05$ uncorrected).

*Activity coordinates (*x*, *y*, *z*) are given in Talairach and Tournoux Atlas (30) space. Imaging coordinates were transformed from SPM-Montreal Neurological Institute (MNI) to Talairaich space using the Brett transform implemented in GingerALE (www.brainmap.org).

†Magnitude and extent statistics correspond to a minimum threshold of $P_{FDR} < 0.05$ (range 0.05 to 0.0001).

Anatomical Comparison of Identified Networks. After the initial identification of default mode network activity patterns, our first aim was to assess the consistency of the spatial anatomy of the network across the three imaging contexts—activation, deactivation and rest. The primary intention of this analysis was to determine the extent to which the task-related activity patterns may reproduce the spontaneous anatomy of the network as characterized at rest. This was performed by calculating the percentage of common and unique voxel space in each activity map in a series of pairwise statistical comparisons (see *SI Materials and Methods*).

With reference to Fig. 2*A*, a spatial overlap of 97.3% was observed from the resting-state to dilemma task activity map, such that the dilemma map reproduced almost the entire voxel space of the default mode network represented at rest. The dilemma activity map was also 41.6% larger in additional voxel space compared with rest—an effect that was expressed predominantly in the anterior, mid, and posterior cingulate regions; right inferior parietal cortex; and dorsolateral frontal cortex.

With reference to Fig. 2*B*, a spatial overlap of 94.7% was observed from the resting-state to Stroop task activity map, such that the Stroop map also reproduced the original voxel space of the default mode network at rest. The Stroop task activity map was also found to be 48.5% larger in additional voxel space compared with rest—an effect that was expressed predominantly in the anterior, mid, and posterior cingulate cortex regions.

To extend the above approach, a group-level conjunction analysis was conducted to test the statistical consistency of default mode network regional activities across the three imaging states (see *SI Materials and Methods*). These results are presented in Fig. S2 and confirm a significant overlap in the correlated activity of major default mode network regions across all experiments (see also Table S1).

Functional Comparison of Identified Networks. Having confirmed a high degree of anatomical consistency of default mode network activity across the three experiments, our second aim was to investigate the extent to which the moral dilemma task may evoke specific changes (i.e., activity increases) in default mode network regions compared with their spontaneous activity at rest.

As a first approach, we performed a volume-of-interest (VOI) analysis that was designed to test the selectivity of changes in default mode network regions that had a common level of activity in both

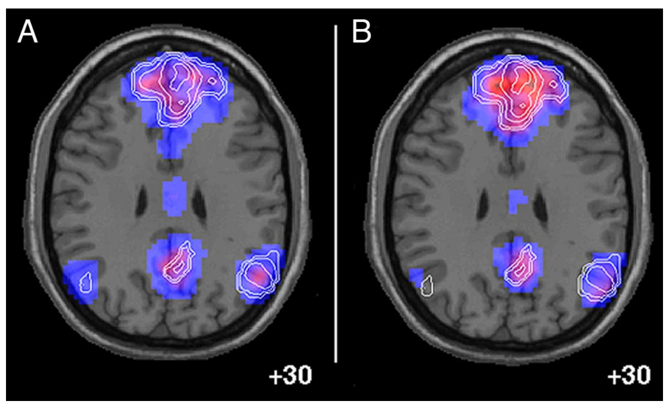

Fig. 2. Anatomical overlap of default mode network activities. (*A*) Representative axial slices showing the moral dilemma activation map (color) overlaid with the corresponding anatomy of the default mode network at rest (white contour lines). (*B*) Representative axial slices showing the Stroop task deactivation map (color) overlaid with the corresponding functional anatomy of the default mode network at rest (white contour lines). Image display: left = right.

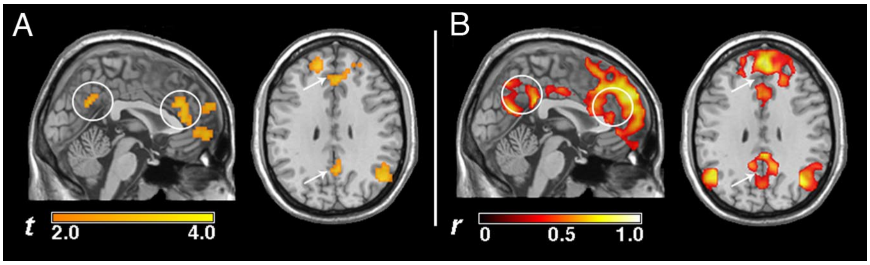

Fig. 3. Functional specialization in the default mode network. (*A*) Default mode network regions that showed relatively greater spatially correlated activity during the moral dilemma task compared with rest. (*B*) Default mode network regions whose spatially correlated activity at rest predicted their strength of correlated activity during the moral dilemma task. White circles and arrows indicate posterior and anterior cingulate cortex regions. Image display: left = right.

experimental states. VOI placements were determined by a conjunction analysis that identified regions having a consistent significant effect in both experiments ($P_{\mathrm{FDR}} < 0.05$; see *SI Materials and Methods*). Fig. S3 shows the placement of all VOIs and regions whose activity was selectively increased during the moral dilemma task compared with rest. These regions included the medial frontal cortex/rostral anterior cingulate cortex, ventral posterior cingulate cortex, and bilateral inferior parietal cortices.

As a second approach, the specificity of regional differences in default mode network activity between the resting-state and moral dilemma experiments was further tested. This was done by performing a voxelwise mean difference analysis (paired samples *t* test) of the correlated activity maps that were identified in both experiments after scaling the activity range of each image (see *SI Materials and Methods*). Relative to rest, the strength of spatial correlations among specific default mode network regions was found to be greater during moral dilemma, but not vice versa. As shown in Fig. 3*A*, regions included the superior and polar medial frontal cortex, left inferior parietal cortex, ventral posterior cingulate cortex, and rostral anterior cingulate cortex (all *P* values <0.005, uncorrected; see Table S2).

Finally, we tested the extent to which spontaneous activity of default mode network regions may predict their corresponding task-evoked activity during the moral dilemma experiment. This was examined in a pairwise cross-correlation analysis of the *z* score activity maps identified from the resting-state and moral dilemma experiments. Fig. 3*B* shows the mean pattern of cross-correlations that were estimated within all default mode network regions. The highest cross-correlations were observed primarily in neocortical areas including the dorsal medial frontal cortex ($r > 0.90$) and inferior parietal cortices ($r > 0.80$). By comparison, the lowest cross-correlations were observed in two subregions of the cingulate system, the ventral posterior cingulate cortex and rostral anterior cingulate cortex ($r < 0.10$).

Discussion

Our results show that the basic anatomy of the default mode network was remarkably consistent from its resting-state organization to associated activity patterns during two distinct functional imaging tasks. This consistency emerged not as patterns of unmodulated or spontaneous activity that persisted throughout the tasks but as clear activity fluctuations that were dependent on each task's behavioral context. The nature of these fluctuations during moral dilemma lends credibility to the idea that default mode network function is, in part, associated with self-referential mental processes in humans.

Anatomical Consistency of the Default Mode Network. The first aim of this study was to test the consistency of default mode network observations made across the distinct functional imaging contexts of task-related activation, task-related deactivation, and rest. To date, such consistency has been inferred from specific analyses of task-related deactivation of brain regions, using PET (3, 7, 9) and, to a lesser extent, from recent studies of resting-state functional connectivity (16, 31). As discussed by Raichle *et al.* (3) "whereas cortical increases in activity have been shown to be task specific and, therefore, vary in location depending on task demands, many decreases appear to be largely task independent, varying little in their location across a wide range of tasks" (p. 676). However, beyond this well studied deactivation phenomenon, the extent to which default mode network activity may be anatomically coherent in adult subjects across other imaging states has to our knowledge not been directly assessed.

Our current findings indeed confirm that a strong overlap exists in the basic functional anatomy of the default mode network when studied during rest, as a deactivation during cognitive task performance, and, additionally, as a functional activation during a moral dilemma paradigm. The consistency of this observation was highlighted by the fact that both task-related activity patterns identified here recapitulated almost entirely the resting-state organization of this network—in both cases sharing ≈95% of its resting-state voxel space (Fig. 2). This finding appears to support recent work that has emphasized the intrinsic nature of default mode network activity in functional imaging studies, having now been observed in non-human primates (31, 32) and in studies of human subjects during sleep (33). However, what our findings also suggest is that full interpretation of the consistency of default mode network activity across different imaging contexts should be extended beyond the spatial-anatomical domain.

Functional Modulation of Default Mode Network Activity. Unlike some studies that have reported enduring spontaneous or resting-like activities of the default mode network under passive or non task-related imaging states, including sleep and anesthesia (11, 20, 31, 33), the default mode network patterns that we identified in association with moral dilemma and Stroop task performance were clearly and differentially modulated by each task. For the dilemma experiment, this was observed as a positive correlation between the network's time course and the specific moral dilemma condition blocks (Fig. 1*B*), whereas, for the Stroop task, this occurred as a positive correlation with the rest-fixation periods (Fig. 1*C*). At the level of brain function, this "on–off" modulation in each time course reflects, theoretically, patterns of both stronger and weaker spatial correlations of BOLD signal activity across time between the implicated default mode network regions.

To what extent do these on–off modulations during moral dilemma represent activation and/or functional connectivity of the default mode network? Similar to conventional activation mapping approaches, this type of modulated covariance in functional imaging studies may represent brain regional activities that are truly covariant (i.e., "functionally connected") during the specific performance of a task, or those regions whose activities are more simply coactivated, but not functionally coupled, as a result of task performance (34). However, if these activity fluctuations are characterized within a clearly and consistently defined functional network, as suggested by our results, then this type of modulated covariance may be best interpreted as a pattern of task-related functional connectivity among implicated regions.

Task-related functional connectivity of the default mode network may be particularly informative if demonstrated as a spatial decoherence between spontaneous and evoked BOLD signal activity changes. This phenomenon was investigated recently in a study of the visual cortex, where spatial decoherence defined a shift in the global pattern of spontaneous correlations of this system at rest ("coherence"), into specific patterns of stronger and weaker spatial correlations in parts of this system ("decoherence") reflecting their functional specialization in response to different visual stimuli/task demands (35).

Consistent with the previous idea, we observed relative increases in the specificity and strength of spatial correlations of certain default mode network regions during the moral dilemma task compared to rest. Within this pattern of changes, some regions demonstrated especially high correlations with their spontaneous activity at rest, whereas others demonstrated almost no linear correlation at all (Fig. 3*B*). This result also appears to further inform functional specialization in the default mode network, distinguishing regions whose activity was common to the resting-state and moral dilemma experiments and those whose activity may have been more specific to the task condition.

Functional Specialization in the Default Mode Network. If the moral dilemma task does evoke functional specialization in the default mode network, which specific processes may this represent? In work by Greene and colleagues (27, 28) on the functional correlates of moral dilemma, these authors emphasized a specific role for emotion in the act of moral judgment and linked this to corresponding activations of anterior and posterior cingulate cortex regions. Notably, this activation was greatest in the context of personal versus impersonal moral dilemmas, relative to nondilemma conditions, and particularly when personal moral judgments were most difficult to make. We added to these findings by showing that equivalent activation of default mode network regions could be obtained during moral dilemma as well as a passive task condition where subjects received feedback about prior moral judgments (25). It was suggested that self-reference and emotion were relevant factors in sustaining/evoking activity of default mode network regions (see also ref. 5).

Existing imaging studies have highlighted, in particular, the rostral anterior cingulate cortex as one brain region that shows a prominent activation-deactivation duality depending on the relative emotional versus cognitive demands of imaging tasks (5, 36, 37). In the former case, activation of this region has been associated mostly with withdrawal related emotions, such as fear, sadness, and guilt (38), that may be augmented if experienced in an autobiographical context (39).

Ventral posterior cingulate cortex also demonstrates sensitivity to different forms of emotional stimulation in imaging studies, but is also responsive to nonemotive stimuli (24, 40). On the basis of such findings, it has been argued that emotional-related activity in this region might represent a general role in monitoring for the self-relevance of previously coded sensory events, and where emotional content itself is assigned and stored in subregions of the anterior cingulate cortex (40). This proposal is appealing, because it may potentially explain the known links between posterior cingulate function, spatial orientation and episodic memory, two important but distinct domains of self-referential processing (24, 40).

Unlike cingulate regions, activity in the dorsal medial frontal and inferior parietal cortices was highly correlated during the resting-state and moral dilemma experiments, suggesting some commonality of function. Based on a recent meta-analysis of studies of self-referential imaging tasks, dorsal medial frontal cortex activity was discussed with reference to higher cognitive aspects of self-referential processing, such as reappraisal and evaluation of self-relevant stimuli (24). Such activity appears to generalize to a variety of imaging contexts, across different sensory domains, and irrespective of emotion.

The idea that emotional versus cognitive aspects of self-referential processing may be dissociated among default mode network regions has some empirical basis (5, 24, 25, 27, 28, 39–41) and offers a straightforward account of the current findings. Further work exploring differences between internally and externally evoked self-referential activity in the context of resting and task-related fMRI may be useful for expanding such accounts.

Cognitive Demand and Default Mode Network Activity. Considered in the development of our moral dilemma paradigm was the strict need to control the amount of cognitive effort that was demanded from subjects when performing the task in-scanner. Put simply, the task was designed to be maximally emotionally provocative and minimally cognitively demanding. The influence of cognitive demand in deactivating the default mode network is well known and may be appreciated even during the moral dilemma task itself, where the control condition, which involved simple memory recalls, may have also to some extent deactivated the network (Fig. 1*B*). However, more salient by comparison, was the pattern of deactivation that emerged during the performance of the Stroop task (Fig. 1*C*).

Task-induced deactivations of the default mode network have been typically reported from imaging contrasts of resting-state or low demand task conditions compared with periods of cognitively demanding task performance (e.g., refs. 11 and 12). In the case of a rest minus task comparison, the appearance of default mode network regions generally signifies their greater activity during rest (or less apparent activity during tasks) and hence are labeled as "deactivated."

At first glance, our current results appear to indicate a biphasic response of this network to task performance, with both a true anticorrelated response (signal decrease) coinciding with the task blocks and a subsequent increase in signal after each of the performance blocks during rest (Fig. 1*C*). Thus, if one assumes a baseline as the initial pretask resting-state period (first 32 s), these observations appear to suggest that there was activation of the default mode network during the nontask rest-fixation periods. However, if one considers this initial pretask resting period as nonbaseline, then the observed fluctuations may be more suggestive of a classic deactivation effect. This may be the most accurate interpretation, because "first scan effects" have been identified from data-driven analyses of functional imaging data and as a presumed correlate of pretask arousal or anxiety (42).

Other Considerations. Although ICA methods have shown good utility in separating potential noise sources in task and resting-state fMRI studies, including aliased physiological signals associated with the cardiac (vascular pulsation) and respiratory (chest movement) cycles (15, 29, 43), we cannot entirely rule out the influence of these signals in this study without direct physiological monitoring. We were also unable to quantify the influence of slow variations in subjects' breathing rate and volume (reflected as small variations in arterial CO_2) on the extracted BOLD signal measurements (44). Nevertheless, the consistency among the default mode network activity patterns reported here does reduce the concern about such artifacts, given that their influence may be expected to vary distinctly across the three imaging conditions.

Conclusions

We report a high degree of anatomical consistency between direct assessments of default mode network brain activity under fMRI activation, deactivation, and resting-state conditions. The moral dilemma paradigm, in particular, was illustrative in showing that a full expression of this network's activity could be obtained in a controlled experimental context that de-emphasized the influence of rest. The nature of this activity supports the idea that default mode network regions are, in part, functionally devoted to self-referential processes in humans.

Although much remains to be known about the physiological basis of spontaneous BOLD signal fluctuations (45), understanding their relationship with the common task-evoked activity patterns reported in fMRI studies appears to be of prime importance. Our findings add constructively to recent debate on the topic of "default modes of brain function" (2, 4) and suggest that these systems can be approached with the standard tools of imaging neuroscience, but with equal focus given to a role for spontaneous brain activity in shaping their functional organization.

Materials and Methods

Twenty-two healthy subjects (12 female; 10 male; mean age ± SD = 26.0 ± 3.5 years) were assessed with fMRI during (*i*) eyes-closed spontaneous rest; (*ii*) the performance of a novel moral dilemma paradigm; and (*iii*) the performance of a self-paced version of the Stroop task. Correlated spontaneous and task-related activity among default mode network regions was identified by using group independent component analysis (ICA), followed by specific further tests of the anatomical and functional consistency/specificity of these correlated BOLD signal activity maps within subjects.

For full description of this study's materials and methods, see *SI Materials and Methods* and *SI Appendix*.

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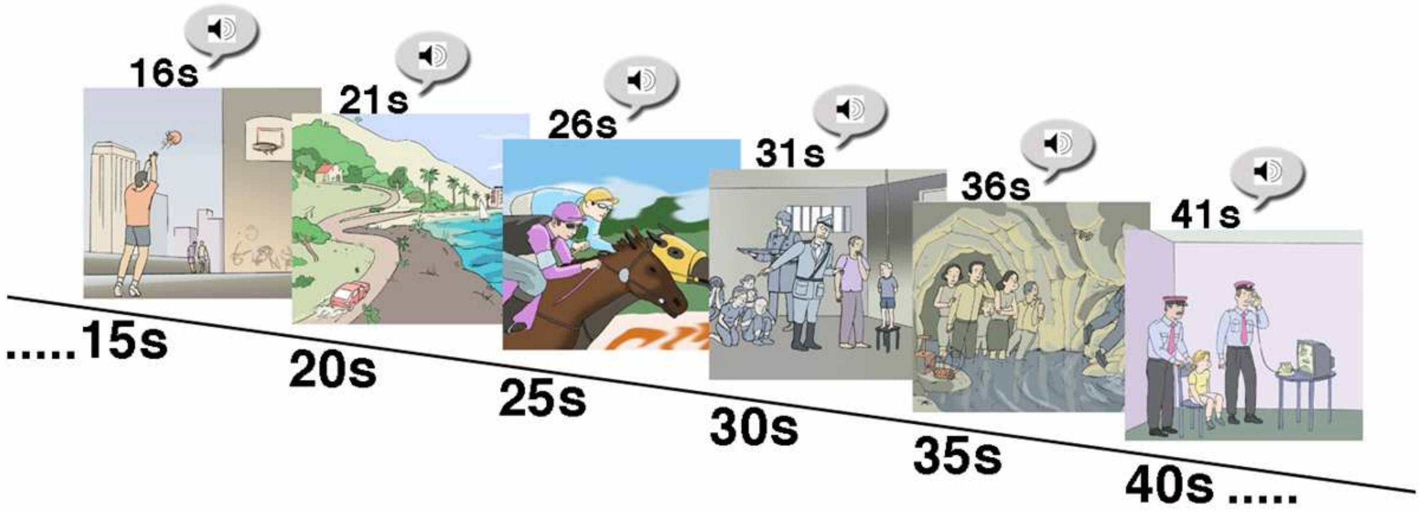


Task schematic illustrating the design of the moral dilemma paradigm used in this study. Four alternating 30 s blocks of memory control (C) and moral dilemma (D) task vignettes were presented in a CDCDCDCD design. Each block consisted of the presentation of six stimulus vignettes that subjects had been familiarized with prior to the experiment. For each stimulus interval (5 s), subjects viewed an artist-sketched cartoon of a control or dilemma scenario that was followed 1 s later by a short audio prompt for ‘yes’ or ‘no’ response to each vignette. All responses were made within this four second stimulus window with an overall response rate of 99.44 %.

MORAL DILEMMA TASK VIGNETTES
Control Task Vignettes

1. Mr. Jones is practicing his three-point throw on the basketball court behind his house. He hasn't managed to score a basket during the whole morning, despite all the practice. He concentrates hard and throws the ball one more time. This time his aim is more accurate, the ball curves through the air and falls cleanly into the basket. Mr. Jones has managed to score a basket for the first time.

Voice Prompt: Will he score?

2. This morning Mr. Jones is walking along the main shopping street in the city center. He has stopped in front of a furniture shop. In the shop window there is a chair, which would fit perfectly in his living room. The chair is expensive and Mr. Jones hadn't planned to spend so much money. Eventually, after thinking for a while, he decides to look for a cheaper piece of furniture. He doesn't buy the chair.

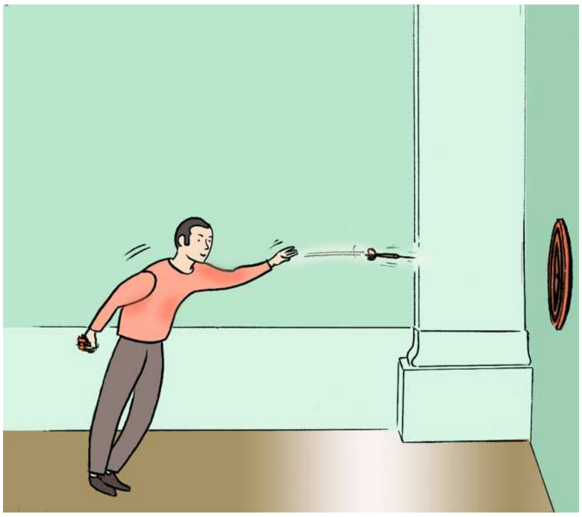
Voice Prompt: Will he buy the chair?

3. Mr. Jones is going away for the weekend. He is driving his car and comes to a fork in the road. The right turn leads to a seaside town, with a superb beach. The left turn leads to a mountain town, with beautiful views. After thinking for a moment, he decides to take the right way and spend a couple of days by the sea.

Voice Prompt: Will he go to the beach?

4. Mrs. Jones is jogging as she does every morning. After running for an hour she reaches home. She enters the building feeling quite tired and wonders whether to take the elevator or to continue her exercise and climb the stairs to the 5th floor where she lives. After thinking for a few seconds, she decides to continue her exercise for a little longer and to climb the stairs.

Voice Prompt: Will she take the elevator?



5. Mr. Jones is practicing his dart throwing, trying to improve his technique and hit the center of the board. He has not hit the center of the dartboard once during the whole morning, despite practicing non-stop. He concentrates hard and throws the dart once again. The dart flies through the air and hits the dartboard, unfortunately, far from the center.

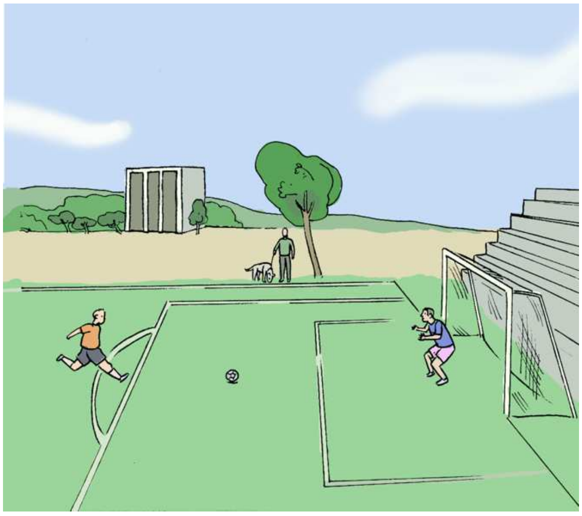
Voice Prompt: Will he score a bull's-eye?

6. Mr. Jones is practicing one of his favorite sports, horse racing. He is riding a very fast thoroughbred mare, dressed with a yellow hood. Mr. Jones's mare is fighting for the first position from the beginning of the race. In the last stretch she goes nose-to-nose with the brown horse. Finally, after a long sprint, the yellow mare wins the race, beating the brown horse by more than two lengths.

Voice Prompt: Will the yellow horse win?

7. Mr. Jones is out in the main shopping street downtown. He enters a clothes store where he tries on several garments. After thinking for a long while he makes up his mind and selects the red t-shirt.

Voice Prompt: Will he buy the blue t-shirt?



8. Mr. Jones is playing soccer with his friends as he does every Wednesday. During the middle of the game the referee awards a penalty shot in favor of Mr. Jones's team. Mr. Jones is going to shoot the ball against one of the best goalkeepers in the league. He prepares and kicks the ball but the goalkeeper predicts his shot and saves it.

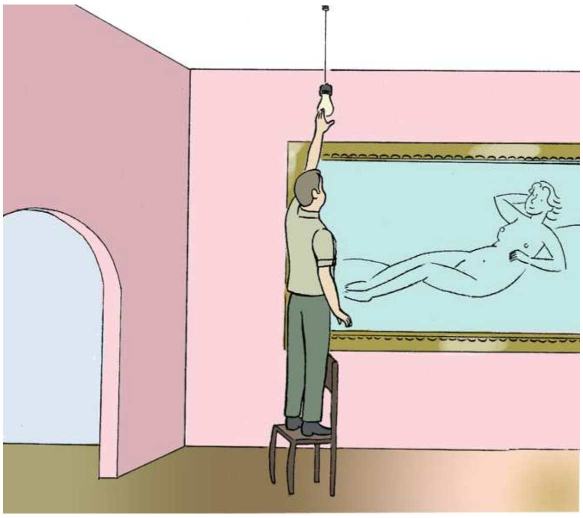
Voice Prompt: Will he score the penalty?

9. Mr. Jones has gone running as he does almost every morning. When he has almost made it to the corner of the street, he encounters a woman taking her dog for a walk. Mr. Jones loves dogs and cannot avoid stopping there to give it a pat.

Voice Prompt: Will he pat the dog?

10. Mr. Jones is on vacation for a few days visiting different towns in the mountains. He is an avid photographer. One day he is walking around the church plaza of a village and feels suddenly inspired to take a picture of this peaceful scene. After trying to focus-in on the perfect shot, he abandons the idea and decides not to take the picture.

Voice Prompt: Will he take the picture?

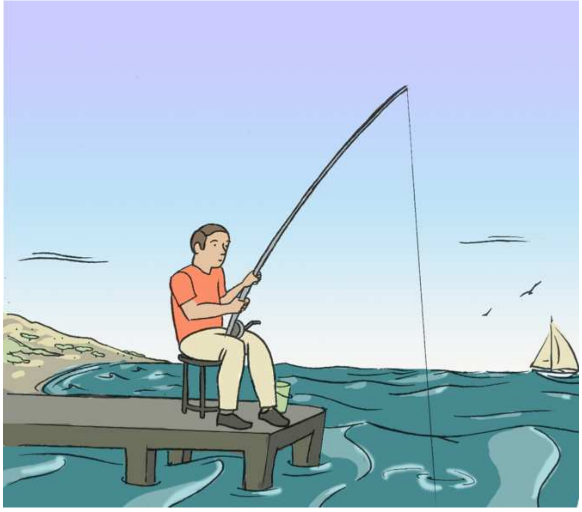


11. Mr. Jones has seen that one of the light bulbs in his living room has blown. He grabs a chair to help him reach the bulb, which is proving quite difficult to steady. He tiptoes and stretches his arm and finally he is able to steady it. This takes several minutes, but finally he replaces the bulb for a new one.

Voice Prompt: Will he replace the bulb?

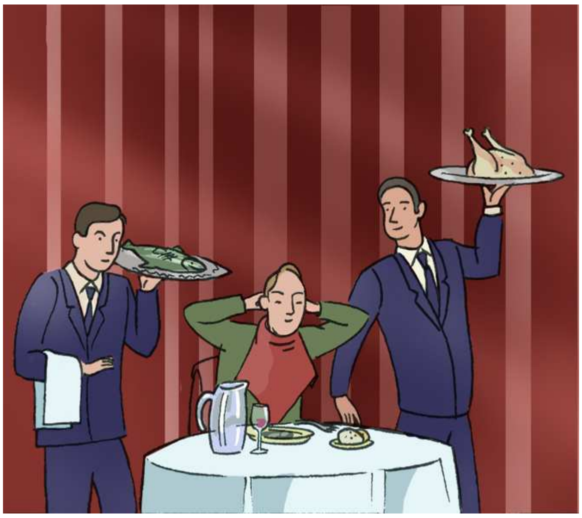
12. Mr. Jones has gone for a drink in the centre of the city. He sits down in a very popular cafe, where they make incredible milk shakes. Although he feels like tasting them, he will stick to his routine and order a white coffee as he usually does each afternoon. Without having a coffee after lunch he cannot manage to continue working.

Voice Prompt: Will he order a coffee?



13. Mr. Jones is taking a break for a few days in a small town by the coast. One day he decides to spend the day fishing, which is one of his favorite hobbies. Although he arrives at the crack of dawn and spends almost the whole day there, he returns home without a single fish.

Voice Prompt: **Will he catch anything?**



14. Mr. Jones has gone to a famous restaurant in the city, where he is a good friend of the owner. He has been invited to choose whatever meals he wants. He can’t decide whether to choose a meat dish, his favorite meal, or to choose fish. Finally, he orders the fish because it is the specialty of the place.

Voice Prompt: Will he choose meat?

15. Mr. Jones has a work meeting and needs to leave home. The weather is overcast and it looks as though it is going to rain. Mr. Jones sticks his hand out of the window to check. He decides that the chances of rain are small and leaves the house. However, after a few minutes and before he reaches the meeting point, it begins to rain heavily.

Voice Prompt: Will it rain?

16. Mr. and Mrs. Jones need to buy some new electrical appliances for their kitchen. They go to a nearby store where some discounts are on offer, particularly for fridges and washing machines. Despite the good offers, they decide just to buy the washing machine, as the both items together are too expensive for them.

Voice Prompt: Will they buy the washing machine?

17. Mr. and Mrs. Jones decide to go out for the night. They are in the middle of the city where there is plenty to do. They agree on two options; going to the theatre or watching a movie, but they can't decide. After a few minutes of thinking, they finally choose the theatre because the show has only a few days left.

Voice Prompt: Will they go to the cinema?

18. Mr. Jones is going to hang a painting on his living room wall. It is a painting of his first beloved dog, a little terrier that used to play with him when he was a boy. Mr. Jones is not much of a handy man and has to make a huge effort to avoid bending the nail. He concentrates hard and finally is able to hang it perfectly.

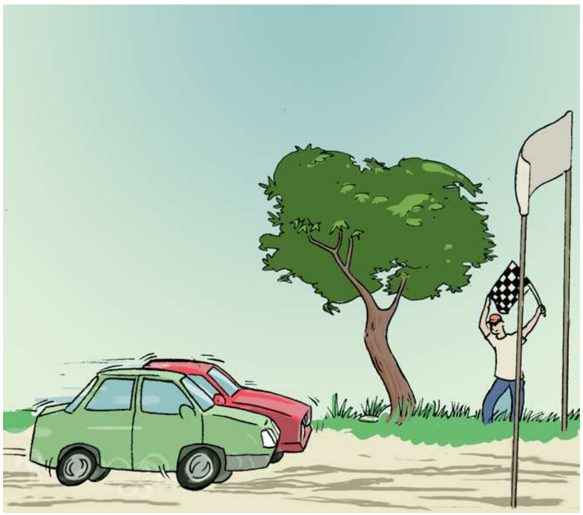
Voice Prompt: Will he hang the picture ok?

19. Mr. Jones is walking down the street thinking peacefully to himself. Suddenly he passes a boy that looks familiar, but he doesn't recognize his face immediately. He turns to look the boy one more time, and realizes that it is an old neighbor. They both stop to say hello.

Voice Prompt: Will they meet each other?

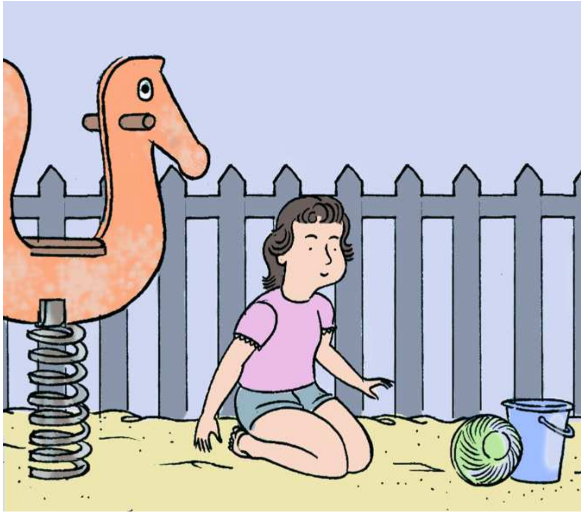
20. Mr. Jones has not been cycling for a very long time. On this day, he is riding up a steep slope that leads to a little town. Despite all his determination and effort, his legs begin to weaken and he has to get of the bike and walk.

Voice Prompt: Will he ride up the slope?



21. Mr. Jones has taken up amateur rally car driving and he is competing against one of his friends in a race. Mr. Jones is driving a red car while his friend drives a green one. They are almost at the finishing post, when Mr. Jones accelerates and overtakes the green car, maintaining first position until the end.

Voice Prompt: Will the red car win?

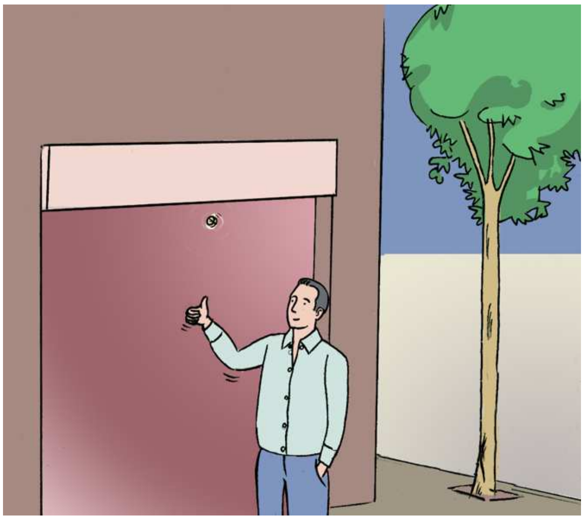


22. Mr. and Mrs. Jones have taken their daughter to the park. The girl is playing in the sand, but would like to get on the red wooden horse. She hesitates for a second, but then leaves her bucket and spade and hops on rocking horse.

Voice Prompt: Will she play with the bucket?

23. Mr. Jones and his son are playing baseball at a friend's property, which is an old mansion estate. Mr. Jones pitches the ball and his son is to take a swing. The boy has never played baseball before and is not sure about his abilities. In the end, he strikes the ball perfectly, which flies up into the sky.

Voice Prompt: Will he hit the ball?



24. After a hard working day, Mr. Jones is not sure whether to go home and to relax or to go and visit an old friend that has not seen for a long time. He feels like catching up with his friend but he is also quite tired. Because he can't make up his mind he decides to flip a coin. If it lands on heads, he will go home, but if it lands on tails, he will visit his friend. He flips the coin and it lands on tails, so finally he visits his friend.

Voice Prompt: Will it land on heads?

Moral Dilemma Task Vignettes

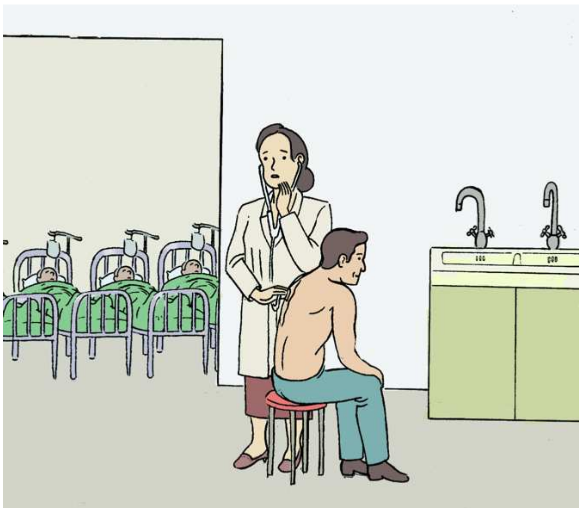
1. Mr. Jones and his only son are held in a concentration camp. His son tries to escape but he is caught. The guard watching them tells Mr. Jones that his son is going to be hanged and that it will be him (Mr. Jones) who has to push the chair. If he does not do it, not only will his son die but also five more people held in the concentration camp.
Voice prompt: Would you push the chair?
Responses: Yes (31.8%); No (68.2%)

2. Mr. Jones and his group are trapped in a cave by the sea. As they are trying to get out, the first man, who is obese, gets stuck in the escape hole and cannot move. Meanwhile, the tide is coming in and water is flooding the cave. Mr. Jones finds some dynamite. If he uses it to make the hole larger, the obese man will die, but if he does not, the man will survive but the rest of the group will die.
Voice prompt: Would you use the dynamite?
Response: Yes (68.2%); No (31.8%)

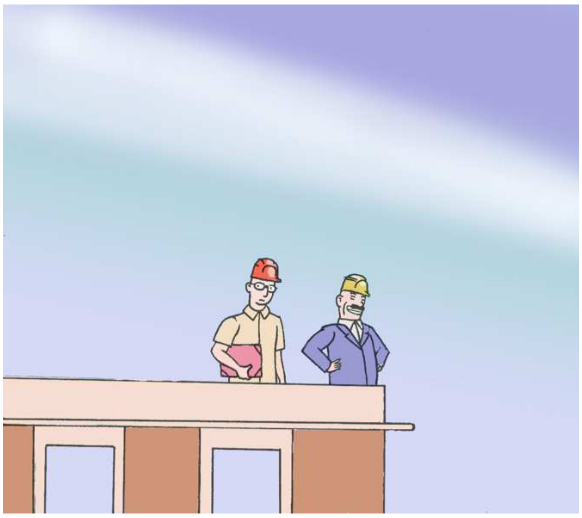
3. Mr. Jones is negotiating with a terrorist who is about to set off a bomb in the city. The terrorist refuses to tell them where the bomb is. Mr. Jones has the terrorist's teenage daughter in his custody and thinks about a possible solution. He can contact the terrorist over a video link and in front of the camera break the girl's arm and continue hurting her until he reveals the bomb's location. If he does not, the girl will be fine but many people will die.
Voice prompt: Would you torture his daughter?
Response: Yes (63.6%); No (36.4%)

4. Mr. Jones has a childhood friend. This friend explains to Mr. Jones that he has committed a crime and asks him to promise that he will never tell anybody. One day Mr. Jones discovers that an innocent man has been accused of the crime, and asks his friend to confess. His friend refuses to do so and reminds Mr. Jones of his promise. If Mr. Jones says nothing to the police, the innocent man will be imprisoned, but if he speaks, he will break his promise and his friend will go to jail.
Voice prompt: Would you inform on your best friend?
Response: Yes (59.1%); No (40.9%)

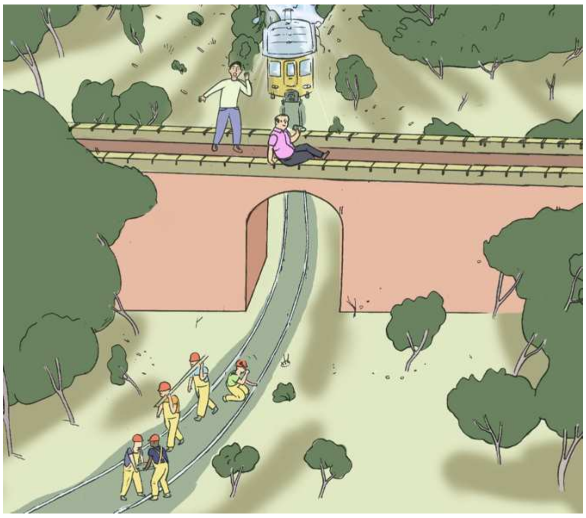
5. Mr. Jones and his wife despise each other to the point that he brought some poison to kill her. He has not decided yet whether to use it. One day, by accident, Mr. Jones's wife has put the poison in her coffee thinking it was milk. He is the only one who has the antidote. If he gives her the antidote, she will know that he has brought the poison and will report him to the police. If he does not, she will die.
Voice prompt: Would you give her the antidote?
Response: Yes (72.7%); No (27.3%)



6. Dr. Jones has five patients, each of whom is close to dying from organ failures. She also has another patient who is mostly healthy. The only way that she can save the five others is to transplant this man's organs into their bodies but against his will. If she does this, the healthy man will die, but the other five patients will live.
Voice prompt: Would you transplant the man's organs?
Response: Yes (13.6%); No: (86.4%)



7. Mr. Jones is a young architect who is visiting one of his construction sites with his boss. His boss is a despicable man who makes everyone miserable, including Mr. Jones. If Mr. Jones pushes him off the building he will die and Mr. Jones will be interviewed by the police, but if he does not his boss will continue ruining other people's lives.
Voice prompt: Would you push him off the building?
Response: Yes (9.1%); No (90.9%)



8. Mr. Jones sees a trolley car that is moving at high speed towards five workmen on the rail track. Mr. Jones is standing on a footbridge above the tracks. Next to him there is a very large and tall man. If Mr. Jones pushes the man off the bridge, he will die but his body will stop the trolley and the workmen will be saved. If he does not, all the workmen will die.
Voice prompt: Would you push the man off the bridge?
Response: Yes (13.6%); No (81.8%); Omission (4.5%)

9. Mr. Jones lives with his family in a very poor area. His crops have been very scarce and he cannot feed his three children, two boys and a girl that may not survive the winter. In his small town there is a man involved the businesses of sexual exploitation. This man proposes to Mr. Jones that if he hands over his daughter for some days he will receive enough money to feed his family for the winter. If Mr. Jones accepts his proposal, his daughter will be sexually exploited. If he does not, his three children will die.
Voice prompt: Would you hand over your daughter?
Response: Yes: (18.2%); No (77.3%)

10. Mr. Jones is fishing by the sea. He sees a group of tourists sailing for a nearby island. Soon after their departure, Mr. Jones hears over the radio that there is a violent storm approaching that will hit the tourists' boat. The only way he can warn them is by stealing a nearby speedboat. The boat belongs to a spiteful old man from the town. If Mr. Jones does not steal the boat, the storm will catch the tourists and their boat could sink. If he steals it, the boat owner will bring charges against him.
Voice prompt: Would you steal the speedboat? Response: Yes (86.4%); No (13.6%).

11. Mr. Jones goes to the hospital to visit a sick friend. There he meets a young man who explains to Mr. Jones that his father has been admitted to the hospital and only has one more week to live. He explains that his father has a substantial life insurance policy that will expire at midnight and offers Mr. Jones $12,000 to kill him. If Mr. Jones accepts the offer, he will have to kill the old man but he will receive the money. If he does not, the insurance will expire and neither of them will receive a cent.
Voice prompt: Would you kill the old man?
Response: Yes (9.1%); No (90.9%)

12. Mr. Jones is a war veteran who has lost his eyes on the battleground. Due to recent medical advances, it is now possible to perform eye transplants, but there are no willing donors. A black-market surgeon offers help to Mr. Jones, and tells him of a contact who can get the eyes for him. If Mr. Jones does not accept the proposal, he will continue to be blind. If he accepts, an innocent person will lose their eyes.
Voice prompt: Would you accept the surgery?
Response: Yes (31.8%); No (68.2%)

13. Mr. Jones's plane has crashed in the Himalayas. The only survivors are one other man, a young boy and himself. To live they must find their way to a small town on the other side of the mountain. They trek for three days in the extreme cold. The young boy falls and breaks his leg, critically reducing his chances of survival. The other man suggests to Mr. Jones to sacrifice the boy and eat his remains in order to survive. If Mr. Jones accepts the proposal they will have enough strength to make it to the small town. If he does not, the boy will eventually die and they will too.
Voice prompt: Would you kill the young boy?
Response: Yes (22.7%); No (77.3%)

14. During the Second World War in Poland Mrs. Jones and her children, a girl and a boy, are imprisoned in a concentration camp. Once they are there, a guard tells Mrs. Jones that she must choose one of her children to live. The other will die in the gas chambers. If she does not choose either of them, both will be killed.
Voice prompt: Would you choose one of your children?
Response: Yes (68.2%); No (31.8%)

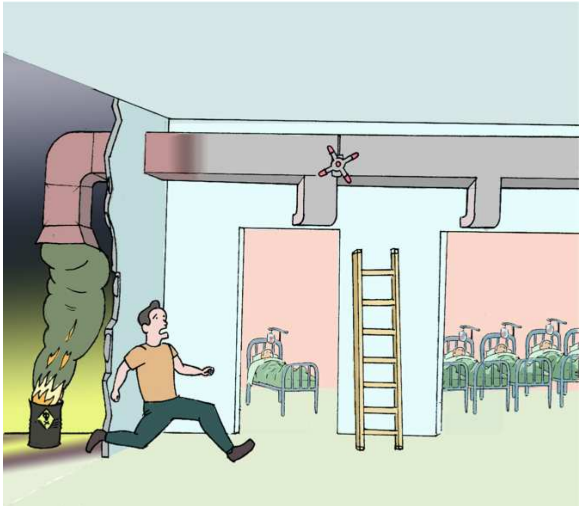
15. Mr. Jones lives in a war zone. Enemy soldiers have taken over his town and have orders to kill all remaining civilians. Mr. Jones, his six-month baby and some of his neighbours have sought refuge in the cellar of a large house. Outside, Mr. Jones hears the voices of soldiers who have come to search for civilians. His baby begins to cry loudly. He covers the baby's mouth to dull the noise. If he does not remove his hand, the baby will be suffocated to death. If he removes it, the crying will attract the attention of the soldiers who will murder them all.
Voice prompt: Would you remove your hand?
Response: Yes (63.6%); No (31.8%); Omission: (4.5%)

16. Mr. Jones is walking down the street when he finds across a wallet lying on the ground. He opens the wallet to see that it contains $900 in cash as well as the owner's driver’s license and credit cards. From the contents, Mr. Jones can see that the owner has been hit by hard times. He considers mailing the wallet back to the owner with all its contents from the address on the driver’s license, or keeping the $900 and sending back just the credit card and license.
Voice prompt: Would you keep the $900?
Response: Yes (54.5%); No (45.5%)

17. Mr. Jones is on a cruise ship when there is a fire on board and the ship must be abandoned. The lifeboats are carrying too many people. The ocean starts to get rough and the boat begins to fill with water. On board is an injured man that will probably not survive. If Mr. Jones throws this man overboard he will certainly die but the boat will stay afloat and the others may survive. If he does not do so, the boat will probably sink and all of them will die.
Voice prompt: Would you throw the injured man overboard?
Response: Yes (54.5%); No (45.5%)

18. Mr. Jones is working on a section of the rail track where two separate tracks converge. A runaway train is heading towards Mr. Jones’s position. On the tracks travelling to the left there is a group of five railway workmen. On the tracks to the right there is a single workman. If Mr. Jones does nothing, the trolley will proceed to the left and kill the group of five men. If he changes the train’s direction, the trolley will divert to the right killing only the one workman.
Voice prompt: Would you switch on the dashboard?
Response: Yes (63.6%); No (36.4%)

19. Mr. Jones is part of a group of ecologists who are living in the jungle. The entire group, which includes eight children, has been taken hostage by rebel forces. One of the rebels takes a liking to Mr. Jones and tells him that his leader plans to kill them all the following morning. The rebel is willing to help Mr. Jones and the children escape, but to guarantee his trust, he wants Mr. Jones to kill one of the fellow hostages. If he accepts to kill a hostage while being filmed, he and all the children will be set free. If he refuses to do it, all of them will die the next morning.
Voice prompt: Would you kill your fellow hostages?
Response: Yes (31.8%); No (63.6%); Omission (4.5%)



20. Mr. Jones is the night watchman in a hospital. Due to an accident in the building next door, there are deadly fumes rising up through the ventilation system. In one room of the hospital there are three patients and in another there is only one. If Mr. Jones does nothing, the fumes will go into the room of the three patients causing their death. If he turns the ventilation system's lever, the fumes will go into the single patient's room who will die.
Voice prompt: Would you turn the lever?

Response: Yes (72.7%); No (27.3%)

21. Mr. Jones is a waiter. He overhears one of his customers saying that he is about to go to jail and that in his last 48 hours of freedom he plans to infect as many people as possible with HIV. Mr. Jones knows that the man has a severe allergy to peanuts. If he puts smashed peanuts in his drink, he will die from an allergic reaction. If he does not, lots of innocent people will be infected.

Voice prompt: Would you give him the peanuts?
Response: Yes (54.5%); No (45.5%)

22. Mr. Jones is the leader of a small army consisting of warriors from two tribes, the hill tribe and the river tribe. He does not belong to either of them. One of the hill tribesmen has murdered a river tribesman. The river tribe demands revenge but the hill tribe refuses to kill one of its own warriors. If Mr. Jones does not take part in the conflict, a war will erupt and lead to the death of hundreds. If he executes the murderer by cutting of this head, the war will be avoided.
Voice prompt: Would you execute the murderer?
Response: Yes (40.9%); No (59.1%)

23. A viral epidemic is killing millions of people across the world. Dr. Jones has developed two substances in his home laboratory. He knows that one of them is a vaccine and the other is a fatal poison but he is not sure which one. He also knows that the other agent is deadly. Dr. Jones has two patients with him under his care, and the only way to identify the vaccine is to inject each one with a different substance. If Dr. Jones injects the substances, one of his patients will die but he will save millions of lives with the vaccine. If he does not, the epidemic will continue spreading, and people will die.
Voice prompt: Would you inject the substances?
Response: Yes (50.0%); No (45.5%) Omission (4.5%)

24. Mr. Jones is an ex-convict that has escaped from justice. He has been a fugitive for a long time because of a robbery he committed. He now uses a false identity but is a good man and is well integrated in society. One day, Mr. Jones discovers that a homeless man has been arrested because the police have falsely identified him as Mr. Jones. If he does not reveal his true identity, the man will be punished for the robbery. If he confesses, he will be sent to prison and loose all the time he has spent becoming a good citizen.
Voice prompt: Would you reveal your identity?
Response: Yes (59.1%); No (40.9%)

Supporting Information

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SI Materials and Methods

Participants. Twenty-two healthy subjects were included in this study (12 female; 10 male; mean age ± SD = 26.0 ± 3.5 years) from an original sample of 24. Two male subjects were excluded because of technical issues (see below). None of the retained cohort had a personal history of neurological or psychiatric illness and all subjects had normal or corrected-to-normal vision. Each subject underwent the Structured Clinical Interview for DSM-IV (SCID) non-patient version (1). The mean education level of the group was 17 ± 3 years. All subjects gave written informed consent to participate in the study, which was approved by local research and ethics committees.

Imaging Acquisition and Tasks. A 1.5-T Signa Excite system (General Electric) equipped with an eight-channel phased-array head coil and single-shot echoplanar imaging (EPI) software was used. Functional sequences consisted of gradient recalled acquisition in the steady state [time of repetition (TR), 2,000 ms; time of echo (TE), 50 ms; pulse angle, 90°] within a field of view of 24 cm, with a 64 × 64 pixel matrix and a slice thickness of 4 mm (interslice gap, 1 mm). Twenty-two interleaved slices, parallel to the anterior–posterior commissure (AC–PC) line, were acquired to cover the whole-brain for all functional sequences. The first four (additional) images in each run were discarded to allow the magnetization to reach equilibrium.

Spontaneous Resting-State. A 4-min continuous resting-state scan was acquired for each subject. Subjects were instructed to relax, to stay awake and to lie still without moving, while keeping their eyes closed at all times. This scan generated 120 whole-brain EPI volumes and was acquired as the first functional imaging sequence for each subject.

Activation (Dilemma Task). Within 1 week before the study, subjects were familiarized in detail with the 24 moral dilemma and 24 control task vignettes that are provided in full description in *SI Appendix*. This training session lasted approximately 1 h and was performed to ensure that subjects had a clear understanding of the task and to assist the recall of each control and dilemma vignette on the study day. In this session, subjects viewed artist-sketched diagrams of the dilemma and control situations, together with an examiner-read description of each event. The moral dilemmas were described as non-personal events involving an imaginary third person and in no instance was the subject asked to provide his or her own moral judgment. This training was performed in a hospital environment by a study psychiatrist.

On the day of the experiment and before commencing scanning, subjects verified that they could remember each task vignette and were then instructed how to respond during the actual scan. For the control condition, subjects were told to simply indicate the outcome of each event when voice-prompted for a "yes/no" answer, by raising either their index finger (yes) or index and middle fingers (no). For the moral dilemma condition, subjects were informed that during scanning they would be prompted for their own moral judgment to each of the dilemma vignettes, again by raising their index finger to indicate "yes" or index and middle fingers to indicate "no."

All of the voice prompts that accompanied the presentation of the control and moral dilemma vignettes were prerecorded and programmed to occur one second after the presentation of the visual stimuli. The total stimulus interval for each visual presentation was 5 s. Subjects' responses were made within a four-second window using the response commands described above, which were recorded by an examiner. The control (C) and dilemma (D) scenarios were presented as four 30-s, alternating blocks of six stimulus presentations each (CDCDCDCD), lasting 4 min in total and generating 120 whole-brain EPI volumes.

Deactivation (Stroop Task). To study functional deactivations of default mode regions, we developed a self-paced computerized version of the Stroop color-word interference task. With regards to deactivation, prior studies have used working-memory, target-detection and stimulus-response incompatibility tasks (including rest-fixation periods), to exert the level of cognitive demand that generates significant deactivation of the default network (2–6). Although these paradigms have been effective as deactivation probes, it is difficult to know the extent to which attentional lapses during performance may have influenced its characterization (7). To address this, we used a self-paced version of the Stroop task that emphasized both speed and accuracy as performance criteria, in an attempt to promote robust deactivation of the default network by keeping subjects continually engaged in task performance.

This paradigm involved three conditions: resting visual-fixation (R), congruent color-word stimulus blocks (C), and incongruent color-word stimulus blocks (I). The paradigm began with an initial resting block of 32 s, followed by four 30-s congruent and incongruent stimulus blocks, interleaved sequentially by eight 12-s blocks of resting visual-fixation (RCRIRCRIRCRIRCRIR). During congruent trials, the stimulus "XXXX" was centered on a black screen in either one of three colors: red, green, or blue. Correct responses were mapped to the following target stimuli; "RED," "GREEN," or "BLUE," located below the cue stimulus and displayed in congruent ink color. The location of the targets (left, middle, right) corresponded to specific hand-held button device responses. During incongruent trials, the same stimulus configuration was presented; however, the cue stimulus was instead one of the same three words presented in incongruent ink color. Subjects were instructed to match the color of the cue stimulus with the corresponding target word stimulus as quickly and accurately as possible, while mentally vocalizing their response (color naming). There was no interstimulus interval between consecutive stimulus presentations. Instead, new stimuli appeared at a pace determined by each subjects' rate of responding. The paradigm ran for a total duration of 6 min, generating 180 whole-brain EPI volumes.

Stroop task performance data were analyzed using two-way, within-group repeated-measures ANOVA. Subjects made more frequent error commissions during the incongruent compared with congruent task blocks (main effect of condition; $F_{1,\ 21} = 6.45$, $P = 0.02$), but with an overall low rate of error commissions (mean ± SD = 3.3% ± 2.1%). Subjects also recorded faster RT scores during the congruent compared with incongruent task blocks (main effect of task condition: $F_{1,\ 21} = 26.37$, $P < 0.0001$; congruent RT mean ± SD = 894.8 ms ± 252 ms; incongruent RT mean ± SD = 1,058.8 ms ± 351 ms), generating a mean Stroop RT interference effect = 164.2 ms ± 149.7 ms.

Both imaging tasks were programmed using Presentation software (www.neurobs.com) and presented to subjects using MRI-compatible high-resolution goggles and headphones (VisuaStim Digital System, Resonance Technology). During the Stroop task, subjects' responses were registered online using a hand-held (optical fiber) response device (Nordic NeuroLab).

Task performance data were analyzed in the Statistical Package for the Social Sciences version 11.0 (SPSS).

Image Preprocessing. Imaging data were transferred and processed on a Microsoft Windows platform running MATLAB version 7 (The MathWorks, Inc.). Image preprocessing was performed in SPM5 (www.fil.ion.ucl.ac.uk/spm), and involved motion correction, spatial normalization and smoothing using a Gaussian filter (full-width half-maximum, 8 mm). Motion correction was performed by aligning (within-subject) each time-series to the first image volume using a least-squares minimization and a six-parameter (rigid body) spatial transformation. Data were normalized to the standard SPM-EPI template and resliced to 3-mm isotropic resolution in Montreal Neurological Institute (MNI) space. We excluded data from two male subjects from the larger original sample of $n = 24$, one because of failure to complete the fMRI tasks and another because of excessive head movement during each of the three scans (z axis translation >2 mm).

Group ICA. Independent component analysis (ICA) is a data-driven statistical method that is able to decompose high-dimensionality data, such as the fMRI time-series, into discrete signal and noise covariance components (8, 9). Group ICA methods have received increasing attention in the analysis of fMRI studies for their robust and flexible modeling nature, including several recent and specific studies of the default mode network (2, 3, 10–12). In addition to providing a data-driven and multivariate characterization of fMRI studies, ICA results also provide an estimate of functional connectivity in such studies—"the temporal correlation between remote neurophysiological measurements" (13). In the case of Group ICA, "functionally connected" voxels or regions are defined spatially by their same dependency of temporal variation as a system, which is estimated in the higher-order (or complete) statistical sense (for discussion, see ref. 14).

In this study, ICA was performed using the Group spatial ICA for fMRI Toolbox (GIFT, Version 1.3b; http://icatb.sourceforge.net/) run on MATLAB 7, using methods and algorithms described in recent studies (15, 16). Briefly, for each of the three fMRI experiments, a single Group ICA was performed at the group level after subjectwise data concatenations, and back reconstruction of single-subject time courses and spatial maps from the raw data matrix (15). As detailed in recent studies, GIFT performs this procedure as three stages: (*i*) data reduction, (*ii*) application of the ICA algorithm, and (*iii*) back reconstruction.

During stage 1, principal component analysis (PCA) (with three reduction steps) was used to reduce individual subjects' data in dimensionality (for computational feasibility). The dimensionality of these data, or number of components, was estimated using the minimum description length (MDL) criterion in GIFT, which attempts to minimize mutual information between components (17). For the resting-state study, data from each subject ($n = 22$) were initially reduced from 120 to 17 dimensions, followed by a second concatenation into five groups ($n = 4, 4, 4, 4, 6$), each of which was reduced from 68 dimensions to 17. This was followed by an ultimate concatenation and reduction into one group with 17 components. An identical data reduction was estimated for the activation (moral dilemma) study. For the deactivation (Stroop) study, data from each subject ($n = 22$) were first reduced from 184 to 19 dimensions followed by a second concatenation into five groups ($n = 4, 4, 4, 4, 6$), each of which was reduced from 76 dimensions to 19. This was followed by an ultimate concatenation and reduction to one group with 19 components.

In stage 2, the estimation of independent sources was performed using the Infomax algorithm (18). During stage 3 of back reconstruction, individual subject image maps and time courses were estimated using the group solution to accurately represent the subject-to-subject variability existing in the data (15). The resulting single-subject time course amplitudes were then calibrated (scaled) by using the raw data to reflect percentage fMRI-BOLD signal strength. In this process, the estimated time course is treated as the model and is fitted to the raw data using an intercept term. This fit is then used to scale (or normalize) the component images into z score units also reflecting the deviation of the data from the mean, thus, enabling second-level (subtractive or conjunctive) random effects analyses to be performed (15, 16).

Identification of Default Mode Network Activity. To reduce observer bias in the selection of independent component patterns for further statistical analysis, we performed a spatial sorting analysis in GIFT. For each respective set of Group ICA results, independent components were spatially correlated with an anatomically defined default mode template and were ranked according to a "highest correlation" criterion (Pearson's r) with this anatomy (for a similar approach see Greicius *et al.* (12)). This template was created using the Wake Forest University Pick atlas (www.fmri.wfubmc.edu), based on the Talairach labeling system provided in the Talairach Daemon Atlas database (19). The basic anatomy of the template included the posterior cingulate cortex, and medial frontal and inferior parietal lobes. Although objective, we note that this process confirmed essentially what was evident upon a visual inspection of the data.

The degree of task-relatedness of the identified networks from the dilemma and Stroop experiments was also examined to confirm their appearance as activation or deactivation phenomena (see also ref. 12). This was performed using a temporal sorting analysis in GIFT where each component's associated time course was correlated with an idealized reference function (task waveform) of the given paradigm (e.g., as typically modeled in SPM). We used SPM5 to define regressors (boxcars) that modeled each condition of the dilemma and Stroop paradigms, respectively. To create these regressors, the timing of the task blocks was convolved with a canonical hemodynamic response function. Task-relatedness was defined according to a highest correlation criterion (Pearson's r) with the relevant task blocks for each paradigm.

Statistical Significance Testing of Networks. One-sample (within-condition) t tests in SPM5 were used to assess the statistical significance of each identified default mode network pattern. For a particular pattern, each subject's respective independent component image (z score spatial correlation map) was entered into a second-level random-effects analysis and assessed statistically using a threshold of $P_{FDR} \leq 0.05$ (whole-brain corrected) and minimum cluster size of ≥ 8 contiguous voxels.

Anatomical Comparison of Identified Networks. Consistency in the spatial distribution of the default mode pattern across the three study conditions was assessed by calculating the percentage of overlap of voxels in each activity map in a series of pairwise comparisons. Initially, each map was scaled and binarized as a global mask that represented all suprathreshold brain voxels. The total number of voxels in each map was then calculated. For each comparison, the number of voxels contained within a union of the two given masks was also estimated. With these data, it was then possible to determine the percentage of overlap of voxels, and the percentage of unique voxel space, in one network relative to the other.

The consistency of regional activity in the three default mode network patterns was also examined using a conjunction analysis in SPM5 adopting the global null approach (20). Evidence for a conjunction between the three task states was assessed statistically using a threshold of $P_{FDR} \leq 0.05$ (whole-brain corrected). The results of these analyses (Fig. S2 and Table S1) indicate those default mode network regions that showed significantly consistent activity across the three experiments.

Functional Comparison of Identified Networks. First, a volume-of-interest (VOI) approach was performed to test the selectivity of regional differences observed between the resting-state and moral dilemma experiments. VOI placements were determined by performing a conjunction analysis (conjunction null approach) that identified those regions that showed a statistically significant effect ($P_{FDR} < 0.05$) in both experimental states (20). VOIs were defined for all regional clusters that resulted as significant from this analysis, using 5 mm radial spheres (10 mm diameter), which corresponded to 20 contiguous resampled voxels. This VOI size was chosen to obtain a close measurement of the peak activity value observed within the resel (resolution element) centered on each cluster's maxima. For each subject, the first eigenvariate of all voxel values (z scores) contained within each VOI was calculated. These values represent a summary of the statistical strength of each region's activity during both experiments.

To explore for differences in the magnitude of correlated activity in default mode network regions during the resting-state and moral dilemma experiments, their associated activity maps were compared by direct comparison in a paired-samples t test. Both datasets had equivalent input (scan number) and output (number of total independent components) data dimensionality. Images were proportionally scaled to account for potential effects due to an absolute difference in the range of image values between conditions. Taking into account the high activity level of default mode network regions at rest (21, 22), we used a more lenient statistical threshold to test for relative differences between both experiments as suggested in Fig. 1 ($P < 0.01$ uncorrected). This analysis illustrates that the magnitude of activity differences between the moral dilemma and resting-states occurred within a range of $P < 0.004$ to 0.001 uncorrected (cluster range = 79–204 contiguous voxels).

To assess the extent to which spontaneous activity in default mode network regions might predict their task-related activity during moral dilemma, we calculated Pearson's correlation coefficient in a pairwise manner between all voxel values (z scores) in both activity maps. The resulting cross-correlation map was then masked to display only those default mode network regions that were statistically consistent across all experimental states (i.e., as shown in Fig. S2).

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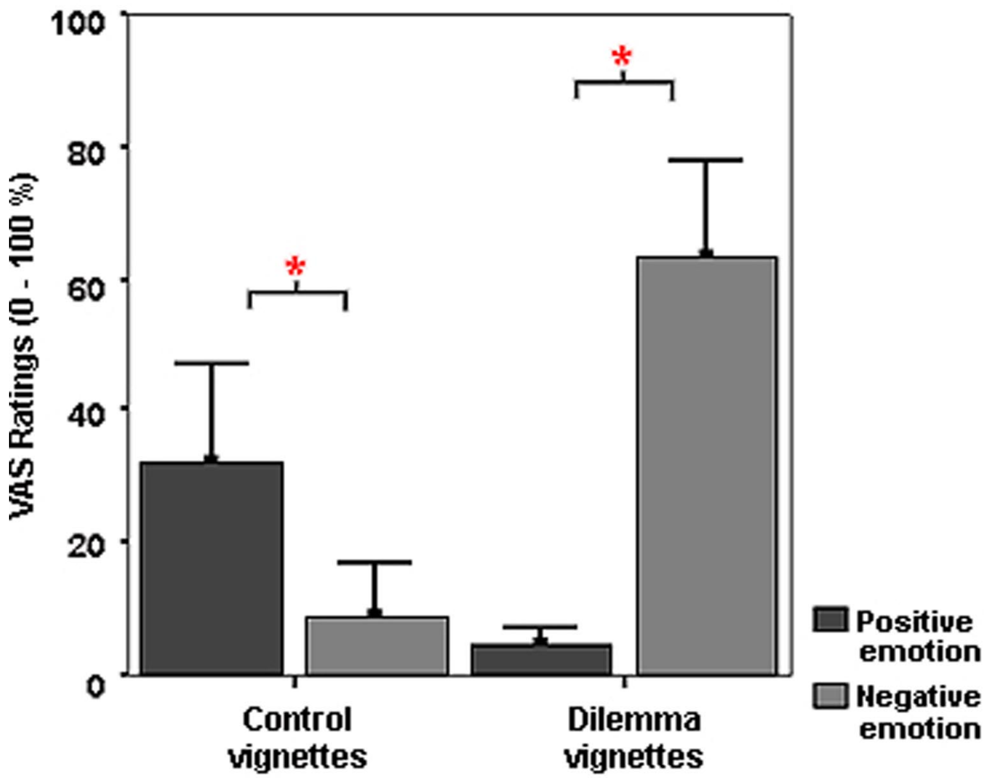

Fig. S1. Bar plot of the mean (including 95% confidence interval) visual analogue scale (VAS) ratings of the global positive and negative emotional intensity evoked by the moral dilemma and control task vignettes (0%, not at all intense; 100%, extremely intense). These scales were administered postscanning and assessed the intensity to which the moral dilemma and control task vignettes evoked negative and positive emotional feelings, e.g., ''How much did the moral dilemmas make you feel bad?'' and ''How much did the moral dilemmas make you feel good?'' Data were assessed in a two-by-two repeated-measures ANOVA, which indicated a significant interaction between task vignette type and emotional valence ($F(1, 21) = 41.1$, $P < 0.001$). Follow-up pairwise t tests showed that ratings of negative emotion were significantly greater ($P < 0.001$) in association with moral dilemma (mean = 63.4, SD = 32.3) compared with the control task (mean = 8.7, SD = 18.5), but vice versa for positive emotion ($P < 0.001$; dilemma task (mean = 4.4, SD = 5.7); control task (mean = 32.1, SD = 33.3). These differences are marked by an asterisk in the figure.

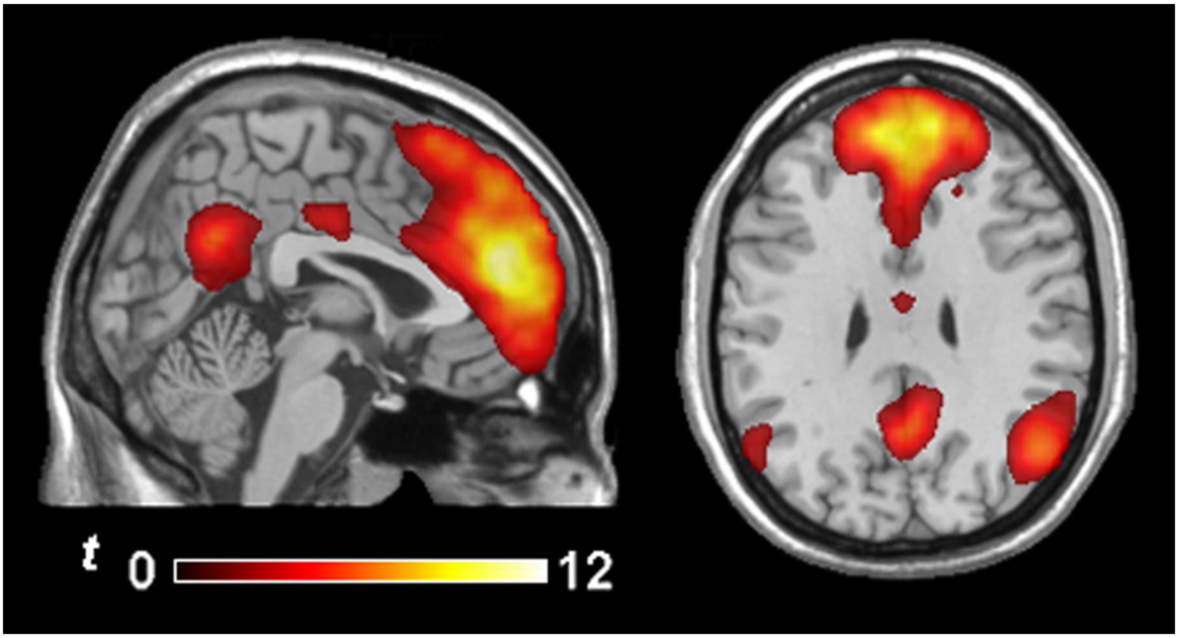

Fig. S2. Conjunction analysis results (global null approach) between the resting-state, activation and deactivation experiments ($P_{\mathrm{FDR}} < 0.05$). Image display: left = right.

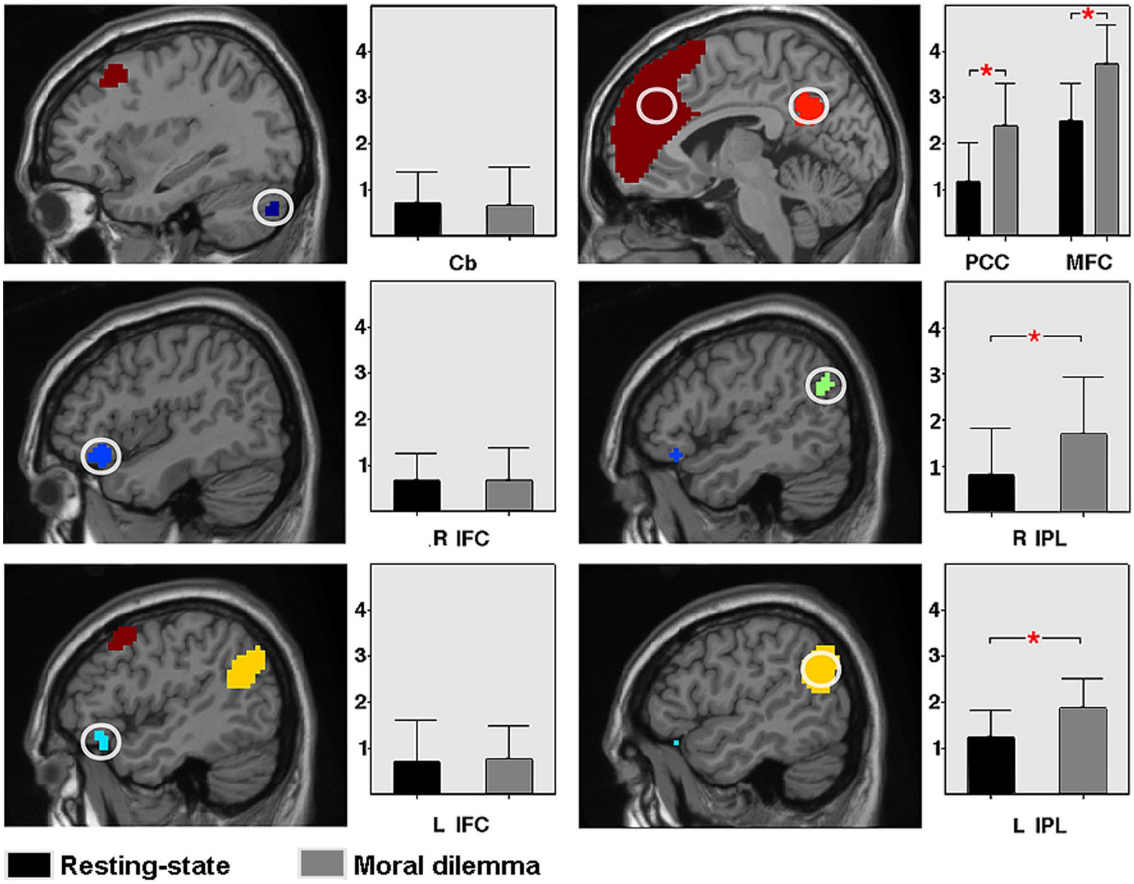

Fig. S3. Default mode network regions that showed selective increases in activity during the moral dilemma versus resting-state experiments (activity clusters). White circles highlight each of the regional clusters included in this analysis (not the VOI dimensions). Accompanying bar plots display the magnitude of the statistical effect represented in each VOI, which was summarized as the first eigenvariate of voxel values (*z* scores) contained in each VOI. Black bars correspond to the resting-state experiment and gray bars correspond to the moral dilemma experiment. Four of the seven regions demonstrated significantly increased activity during the moral dilemma experiment compared with rest (all P values <0.001). Cb, cerebellum; R IFC, right inferior frontal cortex; L IFC, left inferior frontal cortex; PCC, posterior cingulate cortex; MFC, medial frontal cortex; R IPL, right inferior parietal lobe; L IPL, left inferior parietal lobe.

Table S1. Conjunction analysis results (global null approach): Default mode network regions demonstrating significantly consistent activity across all experimental states

	Anatomy*			Statistics†	
Region	*x*	*y*	*z*	CS	*z*
Medial frontal gyrus	−9	51	20	5,326	>8
Inferior parietal lobe	−50	−54	25	744	>8
Posterior cingulate gyrus	−3	−54	30	602	>8
Inferior frontal gyrus	48	28	−14	189	>8
Inferior frontal gyrus	−44	28	−4	208	7.08
Cerebellum	−33	−77	−24	179	5.75
Mid. cingulate gyrus	−3	−12	33	162	6.83
Inferior temporal gyrus	−60	−13	−19	233	6.45
Inferior parietal lobe	50	−56	27	238	6.02
Cerebellum	21	−82	−24	151	6.00
Inferior frontal gyrus	−50	24	4	26	4.12
Inferior temporal gyrus	63	−26	−11	44	3.95

CS, cluster size.

*Activity coordinates (*x*, *y*, *z*) are given in Talairach and Tournoux Atlas space [Talairach J, Tournoux P (1988) *Co-Planar Atlas of the Human Brain* (Thieme, Stuttgart).]. Imaging coordinates were transformed from SPM-Montreal Neurological Institute (MNI) to Talairaich space, using the Brett transform implemented in GingerALE (www.brainmap.org).

†Magnitude and extent statistics correspond to a minimum threshold of $P_{FDR} < 0.05$ (range 0.001 to 0.0001).

Table S2. Increased spatially correlated activity of default mode network regions during the moral dilemma task compared with rest

Moral dilemma minus resting state

	Anatomy*			Statistics†	
Region	x	y	z	CS	z
Medial frontal gyrus	15	19	49	152	3.90
Anterior cingulate gyrus	2	29	31	204	2.87
Posterior cingulate gyrus	−2	−57	25	18	2.78
Inferior parietal lobe	−42	−66	28	78	2.76
Superior frontal gyrus	−18	25	44	79	2.82

CS, cluster size.

*Activity coordinates (x, y, z) are given in Talairach and Tournoux Atlas space [Talairach J, Tournoux P (1988) *Co-Planar Atlas of the Human Brain* (Thieme, Stuttgert).]. Imaging coordinates were transformed from SPM-Montreal Neurological Institute (MNI) to Talairaich space, using the Brett transform implemented in GingerALE (www.brainmap.org).

†Magnitude and extent statistics correspond to a minimum threshold of $P < 0.01$ uncorrected (actual P range = 0.004 to 0.001).