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Abstract

The default mode network (DMN) is the core brain system supporting internally oriented cognition. The ability to attenuate the DMN when switching to externally oriented processing is a prerequisite for effective performance and adaptive self-regulation. Right anterior insula (rAI), a core hub of the salience network (SN), has been proposed to control the switching from DMN to task-relevant brain networks. Little is currently known about the extent of anticipatory processes subserved by DMN and SN during switching. We investigated anticipatory DMN and SN modulation using a novel cued-switching task of between-state (rest-to-task/task-to-rest) and within-state (task-to-task) transitions. Twenty healthy adults performed the task implemented in an event-related functional magnetic resonance imaging (fMRI) design. Increases in activity were observed in the DMN regions in response to cues signalling upcoming rest. DMN attenuation was observed for rest-to-task switch cues. Obversely, DMN was up-regulated by task-to-rest cues. The strongest rAI response was observed to rest-to-task switch cues. Task-to-task switch cues elicited smaller rAI activation, whereas no significant rAI activation occurred for task-to-rest switches. Our data provide the first evidence that DMN modulation occurs rapidly and can be elicited by short duration cues signalling rest- and task-related state switches. The role of rAI appears to be limited to certain switch types – those implicating transition from a resting state and to tasks involving active cognitive engagement.

Keywords: resting state, state-switching, task-switching, fMRI, default mode network, insula.

Abbreviations

ACC – anterior cingulate cortex.

ANOVA – analysis of variance.

BOLD – blood oxygent level dependent.

CTI – cue-target interval.

DMN – default mode network.

rFIC – right fronto insular cortex.

fMRI – functional magnetic resonance imaging.

GLM – general linear model.

HRF – haemodynamic response function.

ICA – independent component analysis.

MNI – Montreal Neurological Institute.

mPFC – medial prefrontal cortex.

PCC – posterior cingulate cortex.

rAI – right anterior insula.

ROI – region of interest.

RSN – resting state network.

RT – response time.

SmFG – superior medial frontal gyrus.

SN – salience network.

SPM – statistical parametric mapping.

1. Introduction

The brain at rest is characterized by coherent spontaneous low-frequency fluctuations across multiple discrete brain networks (i.e. resting state networks; RSNs) (Damoiseaux et al., 2006; De Luca et al., 2005). The default mode network (DMN) (Raichle et al., 2001) incorporates frontal and posterior midline regions, including medial prefrontal cortex (mPFC), and posterior cingulate cortex (PCC)/precuneus. This neural circuit controls internally-oriented, self-referential cognition (Buckner et al., 2008; Gerlach et al., 2011; Spreng and Grady, 2005). DMN activity increases during wakeful rest, and tasks of self-referential, introspective cognition, but is attenuated following the switch to externally-oriented attention-demanding tasks (Spreng et al., 2010; Spreng and Grady, 2010). Increase in cognitive load across a range of cognitive tasks, generally those, that do not involve social and/or self-referential processing, leads to enhanced DMN suppression (McKiernan et al., 2003; Pyka et al., 2009; Singh and Fawcett, 2008). Moreover, processing efficiency during those tasks is correlated with the degree of DMN attenuation (Greicius et al., 2003; Greicius and Menon, 2004; Meyer et al., 2012). According to the DMN interference hypothesis (Sonuga-Barke and Castellanos, 2007), insufficient DMN suppression during the switch to externally-oriented cognitively-demanding tasks interferes with task performance, producing periodic lapses of attention (Bendarski et al., 2011; Li et al., 2007; Weissman et al., 2006), and increased intra-individual behavioural variability (Sandrone and Bacigaluppi, 2012).

Comparatively little is known about the process, in contrast to the outcome, of these switches between resting and task related states. Initial research highlights the importance of preparatory processes occurring just prior to active task engagement controlling DMN attenuation. Sridharan et al. (2008) observed increased activation in right fronto-insular cortex (rFIC), (which together with anterior cingulate cortex (ACC) is part of the salience network [SN]), prior to both DMN attenuation and increased activation in neural circuits supporting task-specific processing. This led Menon and Uddin (2010) to propose the hypothesis that right anterior insula (rAI), is a critical hub initiating switches between DMN and brain networks of goal-directed, task-specific engagement. In addition, Bonnelle et al. (2012) have shown that effective DMN modulation depends on the structural integrity of SN.

The classical cognitive control experiments investigating preparatory processes during switching between tasks have shown a robust involvement of the fronto-parietal network in task set initiation (Monsell, 2003) along with anticipatory pre-activation of specific brain areas relevant for the execution of a particular upcoming task (Wylie et al., 2006). Such studies typically employ cued task-switching paradigms, consisting of a series of discrete trials on which participants perform one of a limited number of different tasks, i.e., on some trials they are prompted to repeat the immediately preceding task (non-switch trials), on others they are asked to perform a different task (switch trials) (Kiesel et al., 2010; Wylie et al., 2006). The use of anticipatory cueing in such paradigms enables the investigation of the preparatory cognitive and neural processes occurring before the actual initiation of goal-directed actions (Brass and von Cramon, 2002; Meiran et al., 2010). Although the role of the SN, specifically rAI, has generally not been the central focus of investigation in these studies, robust responses of both ACC and rAI have been commonly reported (Dove et al., 2000). Thus, the widespread functions of rAI suggest this region to be a general multimodal integration unit, which operates by gathering motivationally salient information, facilitating the appropriate neural reconfiguration and higher-level cognitive processing (Cauda et al., 2012; Chang et al., 2012; Downar et al., 2000, 2001, 2002; Kurth et al., 2010; Uddin et al., 2013). In turn, this highly coordinated processing is essential for effective cognitive control during different types of cognitive or mental switches.

Here we investigate the switch-related anticipatory processes with a task that extends the classical cued task-switching paradigm to also study state-to-state switches, i.e. switches from rest-to-task and vice versa. Crucially, this novel design enables the identification and comparison of the neural reconfiguration and associated network activations during the anticipation of both within- (task-to-task) and between-state switches.

The current study addresses three questions. First, from a methodological point of view we need to establish that our newly developed task provides a valid way of studying DMN attenuation during state-to-state switch anticipation. Thus, the first question is – *is the DMN, shown previously to be implicated in steady-state rest, responsive to cues signalling rest?* If so, is this DMN activity attenuated to cues of an upcoming task? Second, previous studies have only focused on DMN suppression following the switch from rest-to-task; here we raise the related question concerning the anticipation of switches in the opposite direction, i.e., *is there an up-*

regulation of DMN following the presentation of cues signalling an upcoming switch from task-to-rest? Finally, we examine the role of rAI during the anticipation of different switch types. Thus, the third question is – *is rAI equally involved in within- and between-state switch anticipation?*

To address these questions we developed a new paradigm and implemented it within an event-related experimental design in which visual cues signalled the nature of the following trial while fMRI was being acquired. We included rest trials and two different types of task trials. With regard to our three research questions we predicted that: (i) DMN will be activated in response to rest cues and that this activity will be attenuated by rest-to-task switch cues; (ii) cues signalling the switch from task-to-rest will elicit anticipatory DMN up-regulation; (iii) in keeping with the model of Menon and Uddin (2010), state-to-state switches requiring DMN disengagement will elicit the highest rAI response.

2. Materials and Methods

2.1. Participants

Twenty healthy adults with no prior history of neurological or psychiatric disease participated in the study. They all had an IQ in the average and above average range IQ (> 85) measured by the Ward 7-subtest short form of the Wechsler Adult Intelligence Scale-III (Pilgrim et al., 1999), mean IQ = 117.9 (SD = 11.2). Study participants were recruited via internet, magazine and internal university advertising. Two subjects had to be excluded from further analysis due to excessive head motion. The primary analysis included 18 subjects (10 female; mean age = 26.6 years; SD = 8.9; 3 left-handed) with normal or corrected to normal vision. All participants gave their written consent before entering the experiment and received a monetary reward for participation. The study was approved by the local ethical committee of Ghent University Hospital.

2.2. Task

The cued-switching task was programmed using Presentation software package (Neurobehavioral Systems, www.neurobs.com). Visual stimuli were presented in the middle of a black screen viewed by the participants through a mirror attached to a head-coil. The behavioural responses were recorded using two MR-compatible response boxes, one positioned under each hand. Participants responded by pressing a response button with their right or left index finger, depending on task rules.

The cued-switching task was comprised of three types of trials: i) rest, ii) task1 and iii) task2 (Fig. 1). Trials alternated in pseudo-random fashion, so that the ratio of 1:3 was kept between switch (i.e., rest-to-task, task-to-rest, task-switch [task1-to-task2, task2-to-task1]) and repeat trials (task-repeat (task1-to-task1, task2-to-task2), rest-repeat [rest-to-rest]). Each trial started with the presentation of a fixation cross (+) for 500 ms in the middle of the screen followed by one of the predefined geometrical shape cues (a circle, a square or a triangle) counterbalanced across participants. The cue was presented for 500 ms and indicated trial type. During rest trials no stimuli followed the cue indicating rest and subjects were instructed to relax and rest with their eyes open until the next cue appeared. The duration of rest trials ranged from 6000 ms to

19200 ms. On task trials, number stimuli (ranging from 1 to 9, excluding 5) followed the cues and were presented in the centre of the screen for 500 ms. Depending upon the preceding cue, participants had to perform either a parity (task1) or a magnitude (task2) judgment task. In the parity judgment task participants had to decide whether the number presented was odd or even and in the magnitude judgment task, they had to decide whether the number presented was higher or lower than five. Parity and magnitude judgment tasks are two of the most commonly used tasks in task-switching experiments since they involve relatively abstract goal shifts, limited amount of attentional shifting and the same numeric stimulus modality (Kiesel et al., 2010). Subjects were instructed to respond as fast as possible by pressing the correct response button without sacrificing accuracy. The cue-target interval (CTI) was pseudo logarithmically jittered to separate anticipatory cue-related activity from target-related activity (De Baene and Brass, 2011). The jittering interval ranged from 200 ms to 6800 ms; 50% of the trials had a CTI ranging from 200 ms to 2000 ms. On 30% of the trials the CTI ranged from 2600 ms to 4400 ms. The remaining trials had the CTI in a range from 5000 ms to 6800 ms. The response-fixation cross interval was jittered in the same fashion as the CTI.

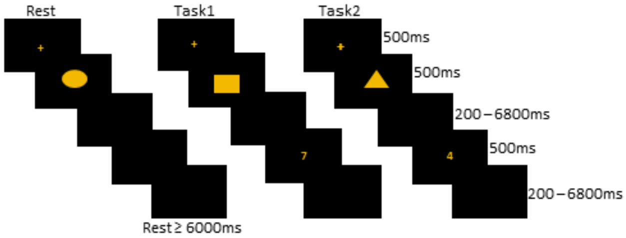

Figure 1. Outline of the cued switching task. Each trial starts with a fixation cross, followed by one of the three cues. The cue indicates the type of the trial: rest, task1 (parity judgment) or task2 (magnitude judgment). On task trials, after a jittered cue-target interval, a target appears on the screen and subjects have to respond by pressing a correct response button. Response-fixation cross interval is jittered in the same manner as cue-target interval. The minimum duration of rest trial is 6000 ms, no stimuli are presented, subjects are asked to relax and rest until the next trial indicating cue is presented.

Before the start of the experiment, subjects underwent a training session which was comprised of four blocks of trials. The first three included sequences of single-cue conditions. During the fourth block the cues were randomly intermixed and subjects had to alternate between performing the two tasks and rest trials. The task performed inside the scanner was comprised of a total of 300 trials, distributed over three runs. Every run started with an instruction screen informing the participants about cue-trial associations.

2.3. fMRI data acquisition and analysis

Subjects were positioned supine head first inside the scanner. Images were acquired with a 3T Siemens Magnetom Trio MRI system (Siemens Medical Systems, Erlangen, Germany) using a standard 32-channel head coil. For all participants structural high-resolution 1 mm^3 images were acquired using a T1-weighted 3D MPRAGE sequence. Whole brain functional images were collected with a T2*-weighted EPI sequence, sensitive to BOLD contrast (TR = 2000 ms, TE = 35 ms, acquisition matrix = 64 x 64, FoV = 224 mm, flip angle = 80^0, slice thickness = 3 mm, voxel size 3.5 x 3.5 x 3.5 mm^3, 30 axial slices). The first four EPI images of each run were discarded to reduce T1 relaxation artefacts

Images were preprocessed and analysed using the Statistical Parametric Mapping software (SPM8; http://www.fil.ion.ucl.ac.uk/spm/software/spm8/). Functional images were slice-time corrected and realined to the first EPI. Next, functional-to-anatomic coregistration was performed. Images were normalized to the Montreal Neurological Institute (MNI) template and smoothed with an isotropic full-width half-maximum (FWHM) Gaussian kernel of 8 mm. Head motion parameters were estimated separately for every run. A high-pass temporal filter with a 128 s cut-off was applied.

Single-subject event-related BOLD response amplitudes were estimated using the general linear model (GLM) implemented in SPM8. Event onset vectors were created based on the experimental conditions. To study cue and switch type-related anticipatory BOLD response, onset-time regressors of interest were computed based on all cue and switch types.

The current design allowed us to isolate cue-related BOLD responses from all other events of the paradigm (targets, responses), which together with error trials, were modelled as regressors of no interest. Onset vectors were convolved with the canonical haemodynamic response function (HRF) (Friston et al., 2003) and were used to compute the GLM design matrix. In addition, six head motion parameters (3 translational and 3 rotational) were included in the model to account for head movement variance.

2.4. Whole-brain analysis

The whole-brain analysis served two main goals. First, to answer the question whether rest cues in this task elicited the same brain DMN as has been shown in studies examining steady state rest. Second, to define the regions of interest (ROI) in an independent manner, thus to avoid "double dipping" (Kriegeskorte et al., 2009).

To establish whether rest cues elicit activation in the DMN, brain activity in response to rest cues was directly compared to activity in response to task cues (rest cue vs. task cue). In order to be sure that activity in the contrast map was related to the DMN, we masked this contrast with a DMN template (ref_default_mode) provided in the GIFT toolbox (http://mialab.mrn.org/software/gift/). To identify the common switch-related activity, single-subject whole brain activation contrasts were computed independent of any particular switch or repeat condition, i.e. collapsing across all switch conditions irrespective of the nature of the switch (state-to-state switches together with task-to-task switches), and contrasted with all repeat conditions (rest repeat and task repeat trials collapsed). To ensure that the resulting activation map corresponded to the SN, specifically rAI, it was inclusively masked with an SN mask comprised of bilateral insula and ACC computed using WFU Pickatlas automated anatomical labelling atlas (Kullmann et al., 2012; Seeley et al., 2007; Tzourio-Mazoyer et al., 2002).

All whole-brain single-subject contrasts were subjected to a second-level random effects analysis. Group whole-brain activation maps were generated using a one sample *t* test. Activations were reported as significant if they survived a family-wise error (FWE) correction at a cluster level ($p < .05$), based on an auxiliary voxel-wise height threshold ($p < .001$ uncorrected).

2.5. ROI analyses

To investigate the specific activation patterns associated with the anticipation of switches from rest-to-task, task-to-rest and task-to-task, ROI analyses were performed. To this end, one set of ROIs was derived from the group activation map directly contrasting rest cues with task cues, inclusively masked with the DMN “ref_default_mode” template (GIFT toolbox, http://mialab.mrn.org/software/gift/) to ensure the overlap of the activations. A second set of ROIs i.e. rAI, was derived from the group activation map comparing the collapsed switch conditions with collapsed repeat conditions. Thus, the definition of both sets of ROIs was independent of any specific comparison conducted in the ROI analysis (Kriegeskorte et al., 2009) and Bonferroni correction for multiple comparisons was applied. The parameter estimates (beta values) for every switch and repeat condition in each of the ROIs was extracted from a 10-mm sphere centered at the respective local activation maxima.

3. Results

Participants performed with a very high degree of accuracy (correct responses > 98% (SD = 1.28). A GLM repeated measures analysis of variance (ANOVA) revealed a main effect of switch type ($F_{(2,\ 34)} = 21.78$, $p < .001$). A task switching (task-to-task) cost was observed with slower response times (RT) on task switch than non-switch trials. The rest-to-task switch cost was smaller but still statistically significant (task-to-task switch: 873 ms, $p < .001$; rest-to-task switch: 809 ms, $p = .007$; task repeat: 738 ms).

3.1. *Do anticipatory rest cues rapidly activate the DMN and is it attenuated in response to cues signalling switches to a task?*

Fig. 2 (A) illustrates the brain regions differentially activated by rest cues compared to task cues (for the reverse contrast see "Insert Inline Supplementary Table 1, Fig.1 here"). Significant regions included superior medial frontal gyrus (SmFG) and precuneus (the regions that correspond to the frontal and posterior parts of the DMN) together with cuneus and lingual gyrus, regions that have been found co-activated with the DMN under eyes closed conditions, following spontaneous blinks and general change in luminance (Marx et al., 2004; Nakano et al., 2012). Fig. 2 (B) displays results of rest cue vs. task cue contrast for the ROIs, i.e., SmFG and precuneus (Bonferroni correction for multiple comparisons $p < .025$). A repeated measures ANOVA of the ROI-based parameter estimates (beta values) revealed a main effect of switch type in both DMN regions (SmFG: $F_{(4,\ 68)} = 9.88$, $p < .001$; precuneus: $F_{(2.24,\ 38.09)} = 13.22$, $p < .001$). Specific pairwise comparison (rest-to-rest (rest-repeat) vs. rest-to-task switch) demonstrated significant attenuation in the SmFG (i.e. frontal DMN region) during rest-to-task switch anticipation (Fig. 2 (B); $p = .024$). No difference between these conditions was observed in precuneus ($p = .620$).

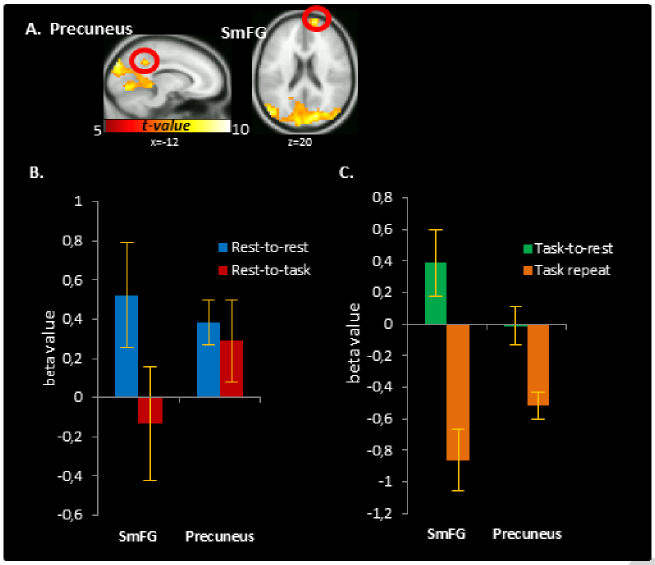

Figure 2. (A) Brain activation map averaged over 18 subjects depicting DMN areas exhibiting activation increases upon rest cues (rest cue vs. task cue), inclusively masked by "ref_default_mode" template (cluster level FWE-corrected $p < .05$). (B) Region of interest analysis on the frontal and posterior DMN regions showing more activation in response to rest cues compared to task cues during rest-to-rest (rest repeat) trials and to cues signalling the switch from rest-to-task anticipation. Average beta values (with SE) extracted from 10-mm spheres centered at the peak voxel coordinate for each area. Blue bars represent the activation in superior middle frontal gyrus and precuneus during rest-to-rest trials. Red bars depict the attenuated activation in those areas during rest-to-task switch trials. (C) Region of interest analysis on the frontal and posterior DMN regions showing more activation in response to rest cues compared to task cues during task-to-rest switch and task repeat trial anticipation. Average beta values (with SE) extracted from 10-mm spheres centered at the peak voxel coordinate for each area. Green bars represent increased activation in superior middle frontal gyrus and precuneus during task-to-rest switch trials, orange bars depict the attenuated activation in those areas during task repeat trials.

Table 1. The overview of peak activation coordinates for rest cue vs. task cue contrast inclusively masked by “ref_default_mode” template (p < .05, cluster-level FWE-corrected).

			MNI coordinates					
Region	Hemisphere	BA	x	y	z	Cluster extent	Z-value	FWE-corrected cluster p-value
Lingual gyrus	L	18	-18	-74	-12	1567	5.79	.000
Cuneus	L	19	-15	-91	34		5.75	
Middle temporal gyrus	L	-	-50	-80	16		5.68	
Superior medial frontal gyrus	R	10	13	63	20	120	5.34	.000
Superior frontal gyrus	R	9	16	42	44		4.64	
	R	9	20	60	34		4.53	
Precuneus	L	7	-12	-49	41	27	4.57	.005

3.2. *Do cues signalling an upcoming switch from task-to-rest elicit a preparatory increase in the DMN in contrast to the attenuation that typically follows rest-to-task switches?*

Fig. 2 (C) depicts differences in DMN activation levels elicited by task-to-rest switch and task repeat cues. As predicted, there was an anticipatory increase in activation in both SmFG ($p < .001$) and precuneus ($p = .001$) associated with task-to-rest switch cues (Bonferroni correction for multiple comparisons $p < .025$).

3.3. Is rAI implicated equally in task-to-task and state-to-state switching?

Fig. 3 (B) shows the patterns of rAI activation to cues signalling different types of switches based on a ROI analysis ($F_{(1.98,\ 33.6)} = 24$, $p < .001$). Specific pairwise comparisons between switch types revealed that rAI exhibited the strongest activation to rest-to-task switch cues which significantly differed from all other switch types (all p's < .001). rAI activation during task-to-task switches was less pronounced though significantly higher than during task-to-rest switches (p = .030), task repeats (p = .001) and rest-to-rest trials (p = .006). In contrast, task-to-rest switch cues did not yield significant increases in rAI activation as compared to task repeat (p = .706) and rest-to-rest trials (p = .820) (see Fig. 3 [B]).

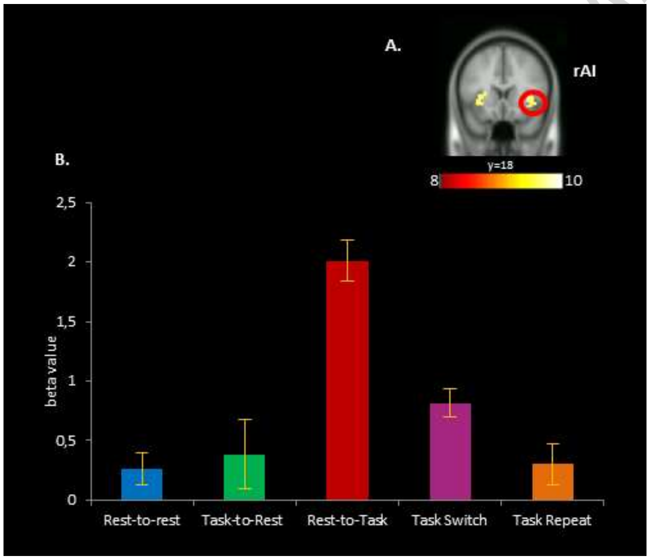

Figure 3. (A) Brain activation map averaged over 18 subjects depicting areas exhibiting higher activation for all switch trials compared to all repeat trials inclusively masked by SN template (cluster level FWE-corrected p < .05). (B) Region of interest analysis on rAI during state-to-state and task-to-task switches. Average beta values (with SE) extracted from 10-mm spheres centered at the peak voxel coordinate.

Table 2. The overview of peak activation coordinates comparing all switch trials with all repeat trials, inclusively masked by SN template (switch trial vs. repeat trial; $p < .05$, cluster-level FWE-corrected).

			MNI coordinates					
Region	Hemisphere	BA	x	y	z	Cluster extent	Z-value	FWE-corrected cluster p-value
Anterior cingulate	R	32	6	35	20	46	5.51	.000
	L	-	-4	24	30		5.29	
	L	-	-12	32	24		5.24	
Anterior insula	L	-	-29	24	10	32	5.51	.000
	L	47	-36	18	-4		5.03	
	R	-	34	18	6	40	5.36	.000
	R	-	30	24	-4		5.26	

4. Discussion

The current study provides the first evidence of the rapid modulation of DMN and SN during state-to-state transitions using a cued-switching task.

4.1. Rest cue elicited rapid onset, anticipatory DMN activation and its attenuation during switches to task

Successful implementation of this novel cued-switching task was confirmed. The anticipatory rest cues induced activation in SmFG and precuneus – the regions that belong to frontal and posterior DMN. The expected DMN attenuation to task predicting cues was also observed. Current results provided the first evidence to support the idea that DMN activity, previously reported only during prolonged rest periods, can be elicited by short duration cues signalling upcoming circumscribed rest periods, suggesting that the neural rest-to-task modulations can occur in a relatively abrupt and rapid way early in the transitional process. It appears that the DMN reconfigures quickly in response to external stimuli signalling forthcoming mental states. The fact that the attenuation of neural activity only occurred in frontal DMN was surprising, given previous findings of posterior and frontal DMN to be among regions showing the highest activity during rest and robust attenuation following goal directed cognitive engagement (Greicius et al., 2004; Shulman et al., 1997). However, previous studies suggest the level of the frontal DMN suppression to be specifically related to enhanced performance and increasing cognitive demands (Gusnard et al., 2001; Lawrence et al., 2003; Shulman et al., 1997), while precuneus has also been shown to be involved in interpretation of and orientation in environment (Gusnard and Raichle, 2001; Hahn et al., 2006). Thus, the absence of attenuation in the posterior part of the DMN in the current study may represent cue-related attentional reorientation supported by precuneus.

4.2. Task-to-rest switch cue elicited DMN up-regulation

Our data also provided the first evidence for DMN up-regulation during switches from task-to-rest – the obverse of attenuation typically seen during rest-to-task switches. This finding fits well with the growing literature on states other than pure rest that can activate the DMN. Specifically, previous studies reported substantial increases in DMN activity during transitions from stimulus-driven to intrinsically oriented cognitive tasks, such as, autobiographic memory (Addis et al., 2007), internal mentation (Andrews-Hanna, 2012) and theory of mind (Buckner et al., 2008; Reniers, 2012; Spreng and Grady 2010), as well as representations of self and others (Mars et al., 2012; Tononi and Koch, 2007; Uddin et al., 2007). Moreover, Preminger et al. (2011) showed that activity in the DMN can be prompted and differentially modulated even in the absence of external stimuli, thus solely as a response to stimulus-free thoughts. Importantly, our results demonstrated that cue-related rest trial anticipation induced DMN up-regulation mimicking the sustained DMN response during isolated periods of self-referential engagement.

4.3. Anticipatory rAI response was dependent on switch type

rAI activation was triggered to different degrees by different types of switch cues. More specifically, rAI response to cues signalling an upcoming switch from rest-to-task was larger than for all other switch types. Activation levels were next largest for task-to-task switches, while task-to-rest switches did not yield a significant activation of rAI. This finding is in line with the model of Uddin and Menon (2010) and the findings of Sridharan et al. (2008) where rAI was suggested to play a central role controlling those large scale shifts in brain network dynamics, involved principally in DMN disengagement and the subsequent activation of task specific brain regions. The fact that we saw greater increase in rAI activity during rest-to-task switches, compared to task-to-task switches, suggests a special role for this region in the modulation of resting brain states. Furthermore, the results indicate that rAI is preferentially involved in a certain type of state-to-state transitions where it is associated with down-regulation and not the augmentation of the DMN. This is a crucial finding because it provides a highly novel insight into DMN functional modulation by rAI. The results are also in line with the findings of Bonnelle et al. (2012) where rAI or SN integrity in general has been found to predict the efficacy of the DMN modulation. In addition, lately there has been an emerging number of studies implicating the more dorsal part of the rAI, in higher cognitive operations (Cauda et al., 2012; Chang et al., 2012; Uddin et al., 2013). This is consistent with the extension of activation into this region seen in the current study. Given that our data provide no evidence for rIA as a generic state switching hub, it is on the face of it, still difficult to distinguish between the notion of rIA as a specialised (rest-to-task) switching hub and the classical notion that its primary role is signalling the salience of upcoming events – provided that cues of an upcoming task when one is in a resting state are more salient than when one is already performing a task (Crottaz-Herbette and Menon, 2006; Dosenbach et al., 2006; Dove et al., 2000; Medford and Critchley, 2010; Seeley et al., 2007). Moreover, rAI has been implicated in regulation of autonomic bodily functions, such as blood pressure, heart and respiratory rate, etc. Thus, during the anticipation of rest-to-task switches, rAI may operate to prepare the body for the greater upcoming challenges than those when switching between tasks or from task-to-rest (Craig, 2009; Ullsperger et al., 2010).

The disturbance of this dynamic balancing between DMN and task-specific brain networks, controlled by rAI, has been implicated in various psychopathological conditions, such as depression, schizophrenia, autism, anxiety and attention deficit hyperactivity disorder (Chen et al., 2013; Menon, 2011). Thus, being validated in a sample of healthy participants, the current cued-switching paradigm is a promising tool to be applied in studies on different psychopathological conditions. Importantly, targeting the anticipatory DMN and SN modulation during state-to-state switching, the current task can aid in revealing and understanding disorder-specific DMN and SN alterations.

4.4. Limitations

The inclusion of state-to-state switches in the experimental design was challenging per se, in that it incorporates both task trials and rest periods. One potential constraint in this regard is the limited temporal differentiation between cued anticipatory processes preceding rest trials and the initiation of the rest phase itself. While task anticipation and initiation were separated by the appearance of a target, rest was not. Thus, rest anticipation and initiation could not be clearly differentiated. However, even taking this into account our finding of cue-related DMN attenuation during rest-to-task switches provides initial support for rapid anticipatory DMN modulation during state-to-state switching.

4.5. Conclusions

The present data support the rapid modulation of the DMN regions following short duration anticipatory cues signalling rest-to-task and task-to-rest switches. The findings extend the understanding of rAI during the anticipation of different types of cognitive switches. Only transitions to active cognitive engagement yielded significant levels of rAI activity, with the largest rAI response during switches from rest-to-task.

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Highlights

- A cued-switching task was used to study anticipatory processes in state switching.
- Briefly presentecd rest-cues elicited activation in the DMN.
- Between-state (rest-to-task) switch cues elicited anticipatory DMN attenuation.
- Task-to-rest cues yielded DMN up-regulation.
- The core hub of the SN – rAI is the most responsive to switches from rest.