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Does Generalized Linear Model Support Functional Default Mode Network Studies

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ABSTRACT

Introduction: A growing body of research has emerged on the resting state and the default mode of the brain. Functional connectivity studies, which lately dominate this research area, have confirmed that regions such as the cortical mid-line structures, as well as parietal-temporal regions are tightly interconnected within the default mode network (DMN). However, little is known about the activity patterns of resting state related brain regions detected in fMRI studies using the generalized linear model (GLM) in a whole brain analysis. The aim of the current study was to investigate the activity changes among brain regions identified through GLM during the transition from task to rest and the prolongation of rest.

Methods: A picture imagination task, as a controlled thought content task, was used in order to minimize confounding factors such as a visual stimulus or a motor response.

Results: The present study revealed a consistent fluctuating activation pattern of the dorsal anterior cingulate cortex (dACC), the posterior cingulate cortex (PCC), thalamus, primer motor area (PMA), insula, brain stem and bilateral putamen during the transition from task to the early phase of the resting state and the prolongation of the resting state. All regions showed increased activation during the detachment from task. However, this increased activation was not sustained during the extension of rest, replaced with a decreased activation at the late phase of rest. The increased activation of resting state regions might help with the detachment from the current task. Among these regions dACC, insula and putamen were correlated in all conditions.

Conclusion: These findings underline the importance of the activation increase of the cortical mid-line regions and insula in the transition from task to the resting state.

Keywords: Default mode network, mind wandering, cortical mid-line structures, GLM

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INTRODUCTION

The first attempts of understanding the baseline activity of the brain were conducted by Positron Emission Tomography (PET), which confirmed an activation of particular brain regions during a resting 'deactivation' state (1). In agreement with the previous PET meta-analysis studies (2, 3), Raichle et al. (1) was the first to postulate the 'default mode' of the brain. A large amount of research has been done in the last decade on the default mode, which refers to a set of interacting brain regions postulated to be activated during internally focused thoughts and to be deactivated during tasks requiring externally directed attention. The mid-line structures, including the medial prefrontal cortex (mPFC), the dorsal anterior cingulate cortex (dACC), the posterior cingulate cortex (PCC)/precuneus have been shown to be associated with the resting state. These cortical mid-line structures are suggested to be implicated in thought processes about one's self, mind wandering, self-referential thoughts, and resting state related spontaneous thoughts (4–6). The default mode is also referred to as a 'task negative network' (TNN), due to its deactivation during externally directed tasks (7), which is challenged by other research data (8).

Even though the first study that defined the default mode was a PET study (1), functional magnetic resonance imaging (fMRI) studies-started up by Greicius et al. (9) now dominate the research area. The study of Greicius et al. (9), a seed based connectivity study, introduced the term 'Default Mode Network' (DMN).

Since then, several advanced methodological approaches have been developed for investigating the neural basis of the network. The majority of DMN activity research is based on functional connectivity studies. Spatially distinct neuronal co-activation (blood oxygenation level dependent-BOLD-signals) is described as functional connectivity. These co-activation patterns have been shown to be continuously present during rest, anaesthesia, consciousness disturbances and cognitively demanding tasks (10, 11). A prominent indicator of functional connectivity was postulated to be the correlation based on the low frequency fluctuation (0.01–0.1 Hz) of the BOLD signal, which raised interest for spontaneous intrinsic slow wave oscillation (SISWO) studies.

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Previous work has demonstrated that slow wave fluctuation in resting state is strongly correlated within the DMN regions (7, 12). DMN studies also showed that the connectivity within the DMN regions reorganizes over time but also in response to the load of demanding tasks (12, 13). Connectivity studies are mainly focused on the ROI-based correlations within the default mode network regions, or are assessed by independent component analysis (ICA) methods (10, 14, 15).

ICA works on the whole data at once and identifies networks of event-related voxels to assess functional connectivity. However, it provides less information about the nature of the activity changes of particular brain regions among resting state and task. A huge amount of data collected from ICA connectivity studies of DMN provide information about the networks and the connectivity patterns, without supplying quantitative activity changes during the whole brain analysis. Seed-based DMN studies, on the other hand, have been mostly investigated through long resting state paradigms or through studies which compared the activity between rest and cognitive tasks. Seed-based DMN studies require a priori selection of particular brain regions, known to share the resting state network, which has been shown in previous PET default mode studies. Likewise, ICA-based DMN studies need the same a priori information for selecting the relevant network out of a number of identified networks (16).

Another analytic approach, the general linear model (GLM), identifies activity changes for any condition (task/rest) on a single voxel basis, which provides a quantitative assessment of activity change in a spatiotemporal manner (16). Furthermore, GLM analysis based on the comparison of DMN (TNN) and a cognitive task-called the task-positive network (TPN), would enable the screening of the activity change patterns during the transition from TNN to TPN. Despite the large amount of connectivity studies assessing the nature of the resting state network/s, less is known about the activity changes during the transition from task to rest and the prolongation of rest in regions detected after a whole brain analysis, as it was demonstrated through PET studies (1–3). Quantitative analysis of brain regions during TNN-TPN transitions and the extension of TNN among regions identified through a whole brain analysis facilitate our understanding of the functional and anatomic aspects of DMN.

The aim of the current study was to investigate the nature of activity changes in a whole brain analysis during the transition from task to rest and the extension of rest. Previous work demonstrated that the thought content during internally focused thoughts/rest, might determine the extent of which brain regions are involved in the network. Furthermore, the demand of the given cognitive task seems to be one of the reasons of the inconsistent results among DMN regions. To address these questions we used a picture imagination task, a paradigm for assessing controlled thought content, which would have less confounding factors, since it requires no active motor response and no visual stimulus. This would allow us to demonstrate the pattern of the transition from a controlled thought state (non-wandering) to a mind wandering state.

MATERIALS AND METHODS

Participants

16 healthy adults (8 male and 8 female; mean age, 25.87±2.84, range, 24–33) participated in the study. All participants were university undergraduate students with normal vision and hearing. They had no history of neurological or psychiatric disorders. The study was approved by the local ethics committee and all participants gave written informed consent. The subjects were scanned using a 1.5 Tesla whole body imager (Infinion; Philips Medical Systems, Cleveland, OH) at the University of Kırıkkale, Department of Radiology. A calliper was built into the head coil for the immobilization of the subjects' heads. High-resolution T1-weighted anatomical scans were acquired in the axial plane using a gradient echo sequence (time to repeat/time to echo [TR/TE], 555/13 ms; flip angle, 69°; field of view (FOV), 230×230 mm; slice number, 36; slice thickness, 2 mm with 1 mm gap). Functional scans were obtained in the axial plane using twenty-two slices with a 0 mm gap and an echo-planar sequence (TR/TE, 4000/50 ms; flip angle, 90°; FOV, 224×224 mm; matrix, 64×64; slice thickness, 4 mm). The orientation of each functional scan was aligned with the anterior commissure-posterior commissure line. We obtained 105 TRs for each run (duration of each run was 420 s); subsequently the first five images were excluded from the analysis for signal equilibration.

Procedure

The study included a picture imagination task alternating with two different resting periods (20 and 40 s). Pictures on a card of a dog and an apple were shown to the volunteers before the scanning. Afterwards all subjects got directives in the scanner via a headphone from a pre-recorded audio CD as follows: 'imagine the apple' (Im1), 'imagine the dog' (Im2) or 'rest eyes closed' (R). Throughout the EPI scans, subjects were required to close their eyes. A blocked design was used, where each block lasted 20 s (5 TRs). Between the blocks of the imagination tasks, one (R1=20 s) or two (R1+R2=40 s) resting blocks were placed randomly (Figure 1). A total of 4 runs (each consisted of 20 blocks) were applied to all subjects, all runs contained equal numbers of both imagination and resting orders.

We used an imagination task directed by an external stimulus and we hypothesized that this task could allow us to demonstrate a mind wandering vs. controlled thought comparison, where less confounding factors, such as a lack of an external stimulus and a cognitive or motor response were present. We chose a picture imagination task as a cognitive control task in order to monitor the task positive regions detachment and the task negative regions changing patterns during different resting periods.

Image Processing and Data Analysis

Analysis of the data was performed using the Statistical Parametric Mapping software (SPM8 software, Welcome Department of Cognitive Neurology, London, UK) running in a MATLAB 2014a environment (Mathworks, Sherborn, Mass., USA). The pre-processing steps were slice timing, realignment, co-registration of mean image of the realigned EPI images with high-resolution anatomical T1 image, normalization and smoothing with an 8-mm full-width half-maximum Gaussian kernel. Statistical analysis was performed on the spatially smoothed fMRI data using the univariate GLM approach. In the individual level, the block design paradigm convolved with the canonical HRF function (17).

The following contrasts were computed for each participant at the first level analyses (all conditions minus the other three conditions):

Imagination1 minus Imagination2 and Rest1 and Rest2/3,

Imagination2 minus Imagination1 and Rest1 and Rest2/3,

Rest1 minus Imagination1 and Imagination2 and Rest2/3,

Rest2 minus Imagination1 and imagination2 and Rest1/3.

No significant activity differences have been detected between the two pictures (Im1 and Im2) based on the paired t-test in the second level group analyses. Therefore, the two imagination tasks were included as a single imagination (Im) condition. Within subject analysis of variance

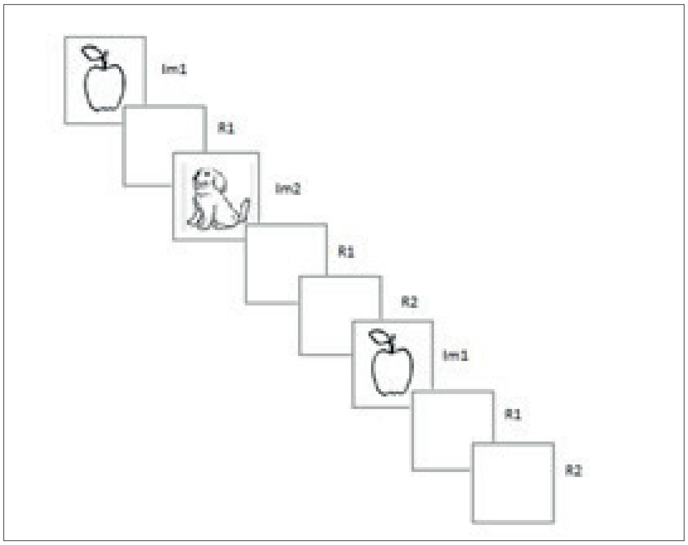

Figure 1. Outline of the picture imagination task and resting states. The imagination task was followed by two different alternating resting periods (20 and 40 s). Each square represents one block (5 TR=20 s). Directives via a headphone were as follows: 'imagine the apple' (Im1), 'imagine the dog' (Im2) or 'rest eyes closed' (R).

(ANOVA) of three conditions (Im, R1, R2) were performed in the second level group analyses [Im-(R1+R2)/2]. The threshold was set at p<0.05 for cluster level family-wise error (FWE) correction and clusters of at least 25 voxels. Activations above the threshold were reported as significant. The whole brain analysis allows us to define region of interest (ROI) in an independent manner. ROI analyses were performed, in order to identify the source of the significance and to determine the alternation pattern of the activation (increased or decreased activation) of the significant clusters. Percent signal change (%SC) was calculated for the voxel with maximum t value (Vtpeak) in the clusters of significant activity differences.

- Formulas below were used to calculate a time serie of %SC of i^{th} run for the voxel with the maximum t value ($\%SC_{i}\_V$) of clusters.
  - o Range=max(S)-min(S). Range is the maximum width of the signal in a run.
  - o Sc_k=Mean(S)-S_k. Sc is a time serie consisting signal's deviation from the mean in each TR. S_k is the signal value of the k^{th} TR.
  - o $\%SC_i\_V=(Sc_1,Sc_2,...Sc_k,...Sc_{100})$*range/100
- The means of the values of% SC_{i}_V that belongs to TR's of j^{th} condition (for four conditions: Im1, Im2, R1, R2) has been calculated ($m\%SC_{i}\_VC_{j}$).
- And finally, mean ($\%SC_{i}\_VC_{j}$) values have been accepted as %SC of the j^{th} condition for each subject.

%SC values of the conditions belonging to the significant clusters of each subject were added in the correlation analysis in order to estimate the connectivity of the regions. The criteria of selecting significant connectivity between clusters are as follows: if three correlation coefficients for each condition were significant, it has been accepted that there was a significant connectivity between these clusters.

RESULTS

Whole Brain Analysis

The first level analyses demonstrated no significant activity differences between the two pictures in the imagination task (Im1 and Im2) based on the paired t-test. Therefore, Im1 and Im2 were combined as one imagination condition (Im). Within subject ANOVA revealed significant differences in the following regions: the dorsal anterior cingulate cortex (dACC, BA24), the posterior cingulate cortex (PCC, BA23), the primary motor area (PMA, BA4), the insula, the brain stem, the thalamus and the putamen, bilaterally (Figure 2, 3). Accordingly, all regions, other than thalamus and left putamen, had significantly higher activity in R1 in comparison to R2 and the imagination task (R1 vs. all). The activity levels of thalamus and left putamen during the imagination task were different from the other 2 conditions (Im vs. all).

Region of Interest (ROI) Analysis

The mean and standard deviation (SD) of %SC values of the significant clusters are presented in Table 2. Averaged percent signal change (%SC) of Im and R2 are very close to each other, while a definite increase of %SC in R1 is observed. This is an indicator of a fluctuating pattern of activity from the task to rest2 in several regions which consist of cortical midline structures like BA24 and BA23.

Correlation analysis of the conditions' %SC values revealed a correlation between BA 24, right putamen and insula in all conditions. (Figure 4).

Table 1. Observed significant clusters, voxel sizes, F and p value of brain regions analysed with ANOVA

Post-Hoc	Region	BA	Hemisphere	Cluster Size	F	P	x	y	z
R1 vs. all	PCC	23	Left	93	40.35	<0.001	-26	-63	10
	Putamen		Right	62	34.34	<0.001	30	-10	6
	dACC	24	Right	125	32.85	<0.001	2	-18	50
	PMA	4	Left	41	32.02	0.004	-36	-18	38
	Insula		Left	48	30.75	0.002	-36	18	-10
	Brain stem		Left	29	28.55	0.019	-1	-35	-10
Im vs. all	Thalamus		Right	31	23.76	0.014	6	-21	2
	Putamen		Left	27	29.43	0.024	-22	0	10

PCC, posterior cingulate cortex; dACC, dorsal anterior cingulate cortex; PMA, primary motor area.

Table 2. %SC+SD of clusters showing significantly different activity in whole brain analysis

Region	Task	Rest1	Rest2	p
PCC	0.050+0.019	0.096+0.043	0.050+0.024	<0.001
dACC	0.076+0.0246	0.145+0.0454	0.071+0.012	<0.001
Insula	0.061+0.024	0.115+0.0474	0.060+0.0274	<0.001
L putamen	0.0474+0.02402	0.0908+0.04293	0.0457+0.019	<0.001
PMA	0.0657+0.02052	0.1239+0.04135	0.065+0.02236	<0.001
R putamen	0.05+0.01774	0.0961+0.03328	0.048+0.01483	<0.001
Thalamus	0.0636+0.02674	0.1261+0.05296	0.0634+0.0278	<0.001
Brain stem	0.0798+0.0367	0.1564+0.0688	0.0776+0.0305	<0.001

PCC, posterior cingulate cortex; dACC, dorsal anterior cingulate cortex; PMA, primary motor area; L, left; R, right.

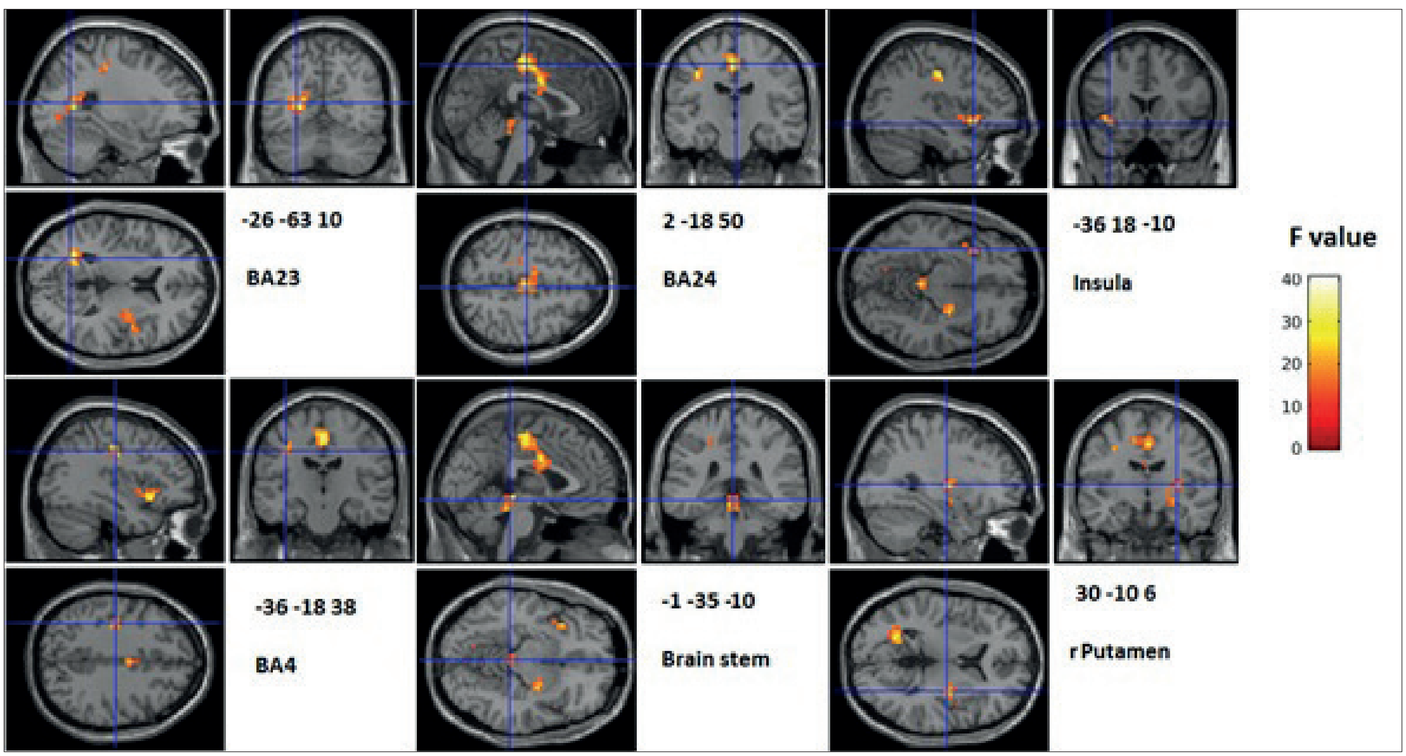

Figure 2. The regions displaying significant activity difference between Rest1 vs. all according to ANOVA. Crosshairs and coordinate indicates the voxel which has the highest activity difference within the cluster. The bar represents the F value. PCC (BA23), posterior cingulate cortex; dACC (BA24), dorsal anterior cingulate cortex; PMA (BA4), primary motor area; r Putamen.

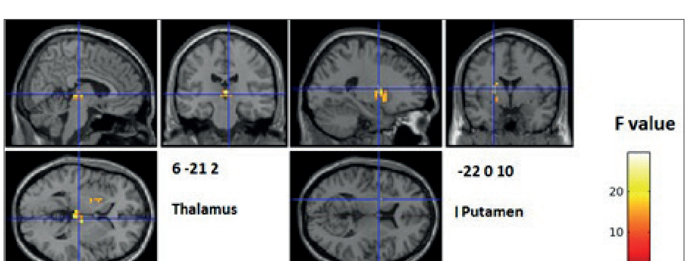

Figure 3. The regions displaying significant activity difference between Im vs. all according to ANOVA. Crosshairs and coordinate indicates the voxel which has the highest activity difference within the cluster. The bar represents the F value.

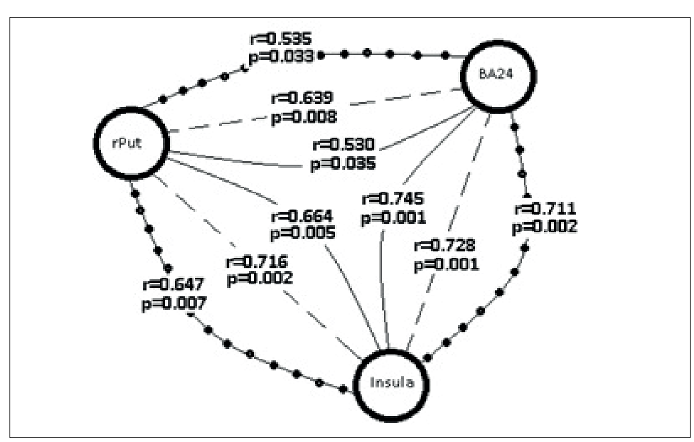

Figure 4. Pearson correlation analysis revealed three regions acting as a network in all conditions. BA24, PCC; BA23, dACC; PCC, posterior cingulate cortex; dACC, dorsal anterior cingulate cortex.

DISCUSSION

The main and noteworthy result of this study is a consistent fluctuating activation pattern of particular brain regions during the detachment from task to the early phase of the resting state and during the prolongation of the resting state. The whole brain analyses revealed the following regions to be involved: dACC, PCC, PMA, insula, brain stem, thalamus, and bilateral putamen. All regions have shown increased activity during the detachment from task and decreased activity during the course of rest. To our knowledge, this is the first study demonstrating a consistent fluctuating activation pattern of distinct brain regions related with the detachment from task and the extension of rest, as investigated with a minimally demanding task (controlled thought/non-wandering) with GLM in a whole brain analytic approach, without focusing on particular regions (ROI) known to be implicated in the DMN. This approach of the non-wandering/mind wandering comparison lead to the following findings we assume to be connected to the threshold of the statistical analysis (25 voxel-size and cluster-level FWE correction, $p<0.05$) we conducted:

Firstly, two of the brain regions observed to display activation changes were the PCC (BA23), and dACC (BA24), referred to as the mid-line structures, which are well-known to be implicated in resting state/DMN activity. In-line with previous research, the present study showed increased activity changes in both regions during the transition from task to rest. These structures, together with IPL, temporal structures and HF, are defined as the core DMN regions (1, 9, 18–20). No activity changes were detected in the other mentioned core DMN regions in the current study. Accumulating data support the view that the mid-line structures are the most DMN-correlated regions showing activation during internally directed cognition (as self-reference, episodic memory retrieval, mind wandering, etc.), and rapidly reducing activation during goal-directed tasks; these regions being associated with high glucose consumption/metabolic rate in comparison with the other cortical areas (1, 19, 21, 22). The failure to suppress activity in the DMN regions, such as the PCC is associated with momentary attentional lapses and the intrusion of internal mental activity into task performance (23). On the other hand, some studies have also demonstrated PCC to be implicated in externally directed attention, leading to the hypothesis of PCC's role on controlling the balance between internally and externally directed attention (22). These findings, together with other reports which show the involvement of DMN regions in externally directed cognitive processes, counter the notion of the distinction between task negative network and task positive network (8). The strength of the functional connectivity among the DMN regions may differ with age and sex, which needs to be considered for the understanding of normal variance (24). Moreover, the mid-line structures are also known to have a central role in self-referential mental activities. Several studies implicated both a commonality and dissociation between self-reference and resting state in the cortical mid-line structures (6, 25). The work of Whitfield-Gabrieli et al. (6) differentiate among the cortical mid-line structures by showing dorsal medial frontal cortex (dMFC) to be engaged in self-reference and dMFC/PCC to be engaged both in rest and self-referential processes. These results are strengthened by the study of Davey et al. (25), which demonstrated that PCC is a common region of rest and self-referential thinking, with increased activity when thinking explicitly about one's self. This substantiates the view that a commonality and a functional specialization during rest and self-referential cognition exist among the 'core' regions (25).

The present study also displayed a decreased activation in the same cortical mid-line regions during the prolongation of rest. These findings are in agreement with previous studies showing an attenuation of DMN regions for rest to task switch (26, 27). One study demonstrated that four different sub-networks are involved in the default mode network and that the latency of the transition to different DMN sub-networks varies from one sub-network to another (13). The fluctuating pattern demonstrated by the current study is in partial agreement with the work of van de Ville et al. (13). Furthermore, van de Ville et al. (13) demonstrated a gradual detachment from task to rest which progresses first from the anterior regions to the posterior, and afterwards from the dorsal to the ventral part of PCC. Additionally, the same study confirms that the cognitive demand of tasks is inversely proportional to the reactivation of attention related regions, compared to regions related to internally directed cognition.

Together with the cortical mid-line regions, PMA, thalamus, insula, brain stem and bilateral putamen also showed the same increased activation during the transition to rest in the current study. Even though striatum is not one of the core regions of DMN, Doucet et al. (28) found that putamen and caudate nucleus, bilaterally, were parts of one of three intrinsic sub-networks, shown to be activated during conscious resting state. The authors advocate that the first module of the three networks mediate the generation of self-related and spontaneous thoughts, and that the frontal/supramarginal/subcortical modules are related to activities such as cognitive control and switching. The latter module includes the striatum, the only subcortical brain region associated with resting state. This result is in agreement with our findings, showing a subcortical brain region involvement in conscious resting state network. In-line with the work of van de Ville et al. (13) that also demonstrated an increased activation in thalamus, which participates in one of the defined sub-networks, the current study observed an increase in the initial phase of rest, and afterwards a decreased activation in thalamus. Another brain region shown to be fluctuating in the present study is insula. It has been proposed that insula along with ACC plays a critical role in mediating the interaction between networks involved in externally oriented tasks-the central executive network (CEN)-and DMN (27, 29). The current study found also three of the eight fluctuating regions-insula, ACC and right putamen-to be interconnected in all conditions, which might strengthen the critical and causal role of insula and ACC in switching between the CEN and the DMN.

CONCLUSION

The discussion above leads to the conclusion that the cortical mid-line structures, dACC-PCC, as well as insula mediate the transition from the external world to the self. These structures are tightly interconnected with the other known core regions of the DMN, as documented in numerous connectivity studies. However, together with the findings of the current study, accumulated data reveals primarily the importance of the posterior structures within the DMN regions for the transition to self-referential cognition. The study of Jack et al. (30) provides evidence for the anti-correlation of DMN and task-positive networks during rest, suggesting a reciprocal inhibition among these networks. These findings strengthen the hypothesis that the detachment from a task to end the current cognitive activity emerges not in a passive manner; rather, it requires the activation of the DMN. DMN helps the TPN for its detachment, during the transition to resting state. The results of the present study support this hypothesis, by demonstrating the activation of PCC, dACC and insula during the detachment from task to rest. PCC has been shown to play a central role in the generation of the DMN. The cognitive demand determines the activation/deactivation pattern of particular regions implicated in externally/internally directed attention. Fox et al. (4) hypothesized that during mind wandering, a specific temporal sequence of activation of particular brain regions is required. Among the brain regions, some may contribute to the initiation of thoughts and other brain regions to their subsequent evaluation. The results of the present study strengthen this idea by showing consecutive activation/deactivation of distinct brain regions during the prolongation of the resting state. Moreover, to define the different states of mind only as, "complete externally directed cognition" and "an absolute resting state, namely internally directed cognition" seems to be an oversimplification.

The intrusion of internally focused cognition to an externally directed process is more likely. It seems that the resting state does not have a homogenous nature. An activation increase in the DMN regions might be required in order to detach from the previous externally oriented task, as well as an attenuation in the same regions seems to be involved for effective performance of the oncoming cognitive task.

Ethics Committee Approval: The study was approved by the local ethics committee.

Informed Consent: All participants gave written informed consent.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - OMK; Design - OMK, YK; Supervision - YK, MI; Resource -OMK, SVB; Materials - OMK, YK, SVB; Data Collection and/ or Processing - OMK, YK, MI; Analysis and/or Interpretation - OMK, HOR; Literature Search -OMK, HOR; Writing - HOR, OMK; Critical Reviews - OMK, HOR.

Conflict of Interest: No conflict of interest to declare.

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REFERENCES

1. Raichle ME, MacLeod AM, Snyder AZ, Powers WJ, Gusnard DA, Shulman GL. A default mode of brain function. Proc Natl Acad Sci U S A 2001;98:676–682. [CrossRef]
2. Mazoyer B, Zago L, Mellet E, Bricogne S, Etard O, Houdé O, Crivello F, Joliot M, Petit L, Tzourio-Mazoyer N. Cortical networks for working memory and executive functions sustain the conscious resting state in man. Brain Res Bull 2001;54:287–298. [CrossRef]
3. Shulman GL, Fiez JA, Corbetta M, Buckner RL, Miezin FM, Raichle ME, Petersen SE. Common Blood Flow Changes across Visual Tasks: II. Decreases in Cerebral Cortex. J Cogn Neurosci 1997;9:648–663. [CrossRef]
4. Fox KCR, Spreng RN, Ellamil M, Andrews-Hanna JR, Christoff K. The wandering brain: meta-analysis of functional neuroimaging studies of mind-wandering and related spontaneous thought processes. Neuroimage 2015;111:611–621. [CrossRef]
5. Qin P, Northoff G. How is our self related to midline regions and the default-mode network? Neuroimage 2011;57:1221–1233. [CrossRef]
6. Whitfield-Gabrieli S, Moran JM, Nieto-Castañón A, Triantafyllou C, Saxe R, Gabrieli JD. Associations and dissociations between default and self-reference networks in the human brain. Neuroimage 2011;55:225–232. [CrossRef]
7. Fox MD, Snyder AZ, Vincent JL, Corbetta M, Van Essen DC, Raichle ME. The human brain is intrinsically organized into dynamic, anticorrelated functional networks. Proc Natl Acad Sci U S A 2005;102:9673–9678. [CrossRef]
8. Spreng RN. The fallacy of a "task-negative" network. Front Psychol 2012;3:145. [CrossRef]
9. Greicius MD, Krasnow B, Reiss AL, Menon V. Functional connectivity in the resting brain: a network analysis of the default mode hypothesis. Proc Natl Acad Sci U S A 2003;100:253–258. [CrossRef]
10. Boly M, Phillips C, Tshibanda L, Vanhaudenhuyse A, Schabus M, Dang-Vu TT, Moonen G, Hustinx R, Maquet P, Laureys S. Intrinsic brain activity in altered states of consciousness: how conscious is the default mode of brain function? Ann N Y Acad Sci 2008;1129:119–129. [CrossRef]
11. van den Heuvel MP, Hulshoff Pol HE. Exploring the brain network: a review on resting-state fMRI functional connectivity. Eur Neuropsychopharmacol 2010;20:519–534. [CrossRef]
12. Fransson P. How default is the default mode of brain function? Further evidence from intrinsic BOLD signal fluctuations. Neuropsychologia 2006;44:2836–2845. [CrossRef]
13. van de Ville D, Jhooti P, Haas T, Kopel R, Lovblad KO, Scheffler K, Haller S. Recovery of the default mode network after demanding neurofeedback training occurs in spatio-temporally segregated subnetworks. Neuroimage 2012;63:1775–1781. [CrossRef]
14. Barkhof F, Haller S, Rombouts SARB. Resting-state functional MR imaging: a new window to the brain. Radiology 2014;272:29–49. [CrossRef]
15. Northoff G, Qin P, Nakao T. Rest-stimulus interaction in the brain: a review. Trends Neurosci 2010;33:277–284. [CrossRef]
16. Ashby FG. Statistical Analysis of fMRI Data. The MIT Press. Cambridge Massachusetts, London, England: MIT Press; 2011.
17. Friston KJ, Jezzard P, Turner R. Analysis of functional MRI time–series. Hum Brain Mapp 1994;1:153–171. [CrossRef]
18. Mayer JS, Roebroeck A, Maurer K, Linden DE. Specialization in the default mode: Task-induced brain deactivations dissociate between visual working memory and attention. Hum Brain Mapp 2010;31:126–139. [CrossRef]
19. Buckner RL, Andrews-Hanna JR, Schacter DL. The brain's default network: anatomy, function, and relevance to disease. Ann N Y Acad Sci 2008;1124:1–38. [CrossRef]
20. Utevsky AV, Smith DV, Huettel SA. Precuneus is a functional core of the default-mode network. J Neurosci 2014;34:932–940. [CrossRef]
21. Gusnard DA, Raichle ME. Searching for a baseline: functional imaging and the resting human brain. Nat Rev Neurosci 2001;2:685–694. [CrossRef]
22. Leech R, Sharp DJ. The role of the posterior cingulate cortex in cognition and disease. Brain 2014;137:12–32. [CrossRef]
23. Weissman DH, Roberts KC, Visscher KM, Woldorff MG. The neural bases of momentary lapses in attention. Nat Neurosci 2006;9:971–978. [CrossRef]
24. Mak LE, Minuzzi L, MacQueen G, Hall G, Kennedy SH, Milev R. The Default Mode Network in Healthy Individuals: A Systematic Review and Meta-Analysis. Brain Connect 2017;7:25–33. [CrossRef]
25. Davey CG, Pujol J, Harrison BJ. Mapping the self in the brain's default mode network. Neuroimage 2016;132:390–397. [CrossRef]
26. Singh KD, Fawcett IP. Transient and linearly graded deactivation of the human default-mode network by a visualdetection task. Neuroimage 2008;41:100–112. [CrossRef]
27. Sridharan D1, Levitin DJ, Menon V. A critical role for the right fronto-insular cortex in switching between central-executive and default-mode networks. Proc Natl Acad Sci U S A 2008;105:12569–12574. [CrossRef]
28. Doucet G, Naveau M, Petit L, Delcroix N, Zago L, Crivello F, Jobard G, Tzourio-Mazoyer N, Mazoyer B, Mellet E, Joliot M. Brain activity at rest: a multiscale hierarchical functional organization. J Neurophysiol 2011;105:2753–2763. [CrossRef]
29. Menon V, Uddin LQ. Saliency, switching, attention and control: a network model of insula function. Brain Struct Funct 2010;214:655–667. [CrossRef]
30. Jack AI, Dawson AJ, Begany KL, Leckie RL, Barry KP, Ciccia AH, Snyder AZ. fMRI reveals reciprocal inhibition between social and physical cognitive domains. Neuroimage 2013;66:385–401. [CrossRef]