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Are emotions associated with activity during rest or interoception? An exploratory fMRI study in healthy subjects

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ABSTRACT

Imaging studies investigating the default-mode network (DMN) of the brain revealed the phenomenon of elevated neural responses during periods of rest. This effect has been shown to be abnormally elevated in regions of the DMN concerning mood disorders like major depressive disorder (MDD). Since these disorders are accompanied by impaired emotional functioning, this leads to the suggestion of an association between activity during rest conditions and emotions, which remains to be demonstrated in a healthy and clinical population. Controlling for interoceptive processing, a process often closely connected to emotional functioning, we here demonstrate in an fMRI study of 30 healthy subjects the connection between activity during rest conditions in regions of the DMN and emotions in a psychologically, regionally, and stimulus specific way. Our findings provide further insight into the psychological functions underlying rest activity. Our findings in healthy subjects may also have future implications for a better understanding of mood disorders.

The significance of the high level of activity displayed by certain regions of the brain during rest is a topic of increasing interest [26,34]. Central amongst these regions are those termed the default-mode network (DMN). This network consists mainly of cortical midline structures [17,35] and includes, for example, the perigenual anterior cingulate cortex (PACC), posterior cingulate cortex (PCC) as well as the ventro- and dorsomedial prefrontal cortex (VMPFC, DMPFC) [11,15,16]. The DMN displays a deactivation from its level of activity at rest in response to attention-requiring tasks (task-induced deactivations, TID).

Several studies have suggested that the DMN, or components of the DMN, are connected to emotional functioning [18,29]. This hypothesis is supported by the observation that a number of psychiatric disorders characterised by a deficit in emotional processing – such as major depressive disorder (MDD) and social phobia – are associated with an alteration in DMN functioning [14,39].

Emotional processing has, however, also been associated with interoceptive processing [6,7,27,31]. The attention-requiring nature of interoceptive tasks means that such processing can be assumed to induce a deactivation in the DMN (i.e., TID). This, in conjunction with the dual association of emotions with activity during rest and interoception, thus raises the question as to whether the link between emotion and activity in the DMN described above is due to a relationship between emotion and activity during rest itself, or whether the observed relationship is instead a result of emotion-induced interoceptive activity within the DMN.

In order to investigate this issue in an exploratory study with healthy subjects, we utilised a combination of fMRI and measures of emotions and bodily awareness. A well-established fMRI paradigm for interoceptive processing [8,32] was slightly modified to include an operationalisation of resting-state (via fixation cross) within an event-related design [39]. This design allowed the BOLD signal observed during rest, and intero-/exteroception (TID) to be related to the measures of emotions and bodily awareness.

Based on the DMN-related findings described above, it was hypothesised that emotional processing would be related to the level of rest activity within the DMN. In addition, it was further hypothesised that there would be no relationship between emotions and intero- or exteroceptive induced activity in these regions, as based on the assumption that it is the induced activity during rest itself in these regions that is tied to emotion, rather than any task-induced signal changes.

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We studied 30 subjects (15 females) with no psychiatric, neurological, or medical illness using fMRI. In order to evaluate the status of the subjects, they were questioned about psychiatric, neurological, or medical diseases as well as the use of psychoactive substances using a custom-made semi-structured clinical questionnaire. Participants were recruited from the University of Magdeburg and the local community. The study was approved by the local ethics committee and all participants gave written informed consent before participating in this study. Subjects were compensated for their participation.

The fMRI design was based on a paradigm introduced by Pollatos et al. [32] and Critchley et al. [8]. Subjects were presented with three separate conditions: an interoceptive task, an exteroceptive task, and rest periods (fixation) – in a pseudo-randomised order. For a detailed description of the paradigm, see Supplementary Fig. 1a or Wiebking et al. [39], where a separate dataset and independent analysis are presented.

Intelligence was assessed through the nonverbal LPS-3 [19] and verbal MWT-B [21] tests.

For investigating the ability to recognise emotions, we used the Florida Affect Battery (FAB) [3]. The FAB is a research tool that was designed to investigate disturbances in the perception of emotional signals (facial and prosodic affect) under a variety of task demands. In order to apply a comparable auditory emotional task in relation to the exteroceptive task in the scanner, we concentrated only on subtest 8a. This consists of a set of 15 semantically neutral sentences (e.g.: 'The chairs are made of wood') spoken in emotional tones of voice. The sentences are all approximately the same length and were recorded by an experienced actress in five different emotional intonations: happy, angry, sad, fearful and neutral. Each affect was presented three times. Subjects were asked to verbally label the emotional prosody of each item.

The Body Perception Questionnaire (BPQ) [33] was also used in order to test for the individuals' awareness and manner of processing bodily changes. It includes 4 subscales, e.g. for bodily awareness, with subjects scoring their answer on a 5-point scale (ranging from never to always). Since the resting-state network has been associated with depressive symptoms we also applied the 20-item Beck Hopelessness Scale (BHS) [1].

Scans were performed on a 3-T whole body MRI system (Siemens Trio, Erlangen, Germany) using an eight-channel head coil. Slices were acquired parallel to the AC-PC plane in an odd-even interleaved acquisition order. Thirty-two T2*-weighted echo planar images per volume with BOLD contrast were obtained (matrix: 64×64; FoV: 224×224 mm; spatial resolution: $3.5 \times 3.5 \times 4$ mm; TE = 30 ms; TR = 2000 ms; flip angle = 80°). Functional data were recorded in four scanning sessions containing 290 volumes per session for each subject. The first five volumes were discarded due to saturation effects.

The fMRI data were pre-processed and statistically analysed by the general linear model approach [13] using the SPM2 software package (spm2, http://www.fil.ion.ucl.ac.uk) and MATLAB 6.5 (The Mathworks Inc., Natick, MA, USA). For a detailed description of the pre-processing see Wiebking et al. [39].

All three conditions (rest, intero-/exteroception) were included in the SPM model as separate events without their response phases. Regionally specific condition effects were tested by employing linear contrasts for each subject and different conditions. The resulting contrast images were submitted to a second level random-effects analysis. Here, one-sample t-tests were used on images obtained for each subjects' volume set and different conditions. To control for the multiple testing problem we performed a familywise error rate correction [2,25]. The anatomical localisation of significant neural responses in our main contrast [rest > intero-/exteroception] ($P < 0.01$, FWE-corrected, $k > 10$) was assessed with reference to the standard stereotactic atlas by superimposition of the SPM maps on a standard brain template provided by SPM2.

In a second step, the BOLD signals were analysed. Applying sphere-shaped regions of interest (ROI, radius 5 mm), we extracted fMRI signal timecourses from regions of the DMN, as identified using the contrast [rest > intero-/exteroception] (VMPFC: −2, 52, −4, DMPFC: −2, 52, 40, PCC: 6, −48, 24) using the MarsBaR toolbox (http://www.sourceforge.net/projects/marsbar). Using a custom PERL script, fMRI signals were corrected for baseline shifts (applying a linear baseline correction algorithm) as well as normalised (dividing each value through the average fMRI signal of the time from −6 s to 30 s). The normalised average fMRI signal of the timepoints −2 s and 0 s was then subtracted from each single fMRI value. This procedure ensured that all timecourses start from 0% signal change at 0 s. For each subject, mean fMRI signal changes for each of the three conditions were calculated by averaging the normalised fMRI signal values from 4 s to 10 s. For inter-subject statistical analysis, these values were Pearson-correlated (SPSS 17.0) with subjects' behavioural scores.

Following the recommendations of Kriegeskorte et al. [20], we also used independent coordinates (midline rather than right or left as criterion; except the DMPFC, see Table 1a). As described above, we calculated percent signal changes in similar regions found to be involved in mind-wandering and Pearson-correlated them with the behavioural test results. Independent coordinates were taken from Christoff et al. [5] and transferred from Talairach in MNI coordinates using the WFU-pickatlas [22,37].

The group of 30 subjects had a mean age of 33.73 years (±11.62 SD) and a mean time in education of 16.05 years (±2.42 SD), with no sex differences. Their mean score for verbal intelligence was 114.23 (±13.56 SD) and for nonverbal intelligence 118.40 (±14.53 SD). Emotional tests included the BHS and the FAB_8a, with mean scores of 4.6 (±3.9 SD) and 91.78 (percent correct answers ±8.87 SD), respectively. The BPQ showed a total score of 199.03 (±50.24) and for the subscale of bodily awareness a score of 107.80 (±38.78).

We firstly tested the validity of our paradigm by analysing the contrast [interoception > exteroception] ($P < 0.05$, FWE corrected, $k > 10$), comparing relevant regions with those obtained from the same contrast by Critchley et al. [8]. As detailed in Supplementary Table 1b, this yielded almost identical regions, demonstrating that our modified paradigm can be considered to be valid.

Since we included the rest condition as a separate condition, we were able to calculate in a second step the main contrast [rest > intero-/exteroception] ($P < 0.01$, FWE corrected, $k > 10$), which showed significant signal changes in the VMPFC, DMPFC, and PCC (see Fig. 1 and Supplementary Table 1a) mirroring regions implicated in the DMN (Table 1a).

With the rest periods used here being rather short in comparison to the periods used in the majority of resting-state studies, we compared the regions identified by the main contrast with those obtained in a study by Fox et al. [12], which measured activity during rest over a time interval of 5 min. In addition, we compared our regions with the ones obtained in a comparable study by Christoff et al. [5]. Corresponding regions provide evidence that our rest periods show an acceptable representation of the resting-state (Table 1a).

Calculating percent signal changes in regions of the DMN obtained by the main contrast revealed task-induced deactivations (TID) during both intero- and exteroceptive processing (Supplementary Table 1a). Small positive BOLD responses (PBR) were observed in these regions during the rest condition (see also BOLD curves in Fig. 1).

The observed signal changes in the regions identified in the main contrast were then correlated with the results of the emotion-related psychological tests. This revealed negative correlations between signal changes during rest (i.e., PBR) with scores of the