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Research article

Higher interference susceptibility in reaction time task is accompanied by weakened functional dissociation between salience and default mode network

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ABSTRACT

Background: The relationship between task-positive and task-negative components of brain networks has repeatedly been shown to be characterized by dissociated fluctuations of spontaneous brain activity.

We tested whether the interaction between task-positive and task-negative brain areas during resting-state predicts higher interference susceptibility, i.e. increased reaction times (RTs), during an Attention Modulation by Salience Task (AMST).

Methods: 29 males underwent 3 T resting-state Magnetic Resonance Imaging scanning. Subsequently, they performed the AMST, which measures RTs to early- and late-onset auditory stimuli while perceiving high- or low-salient visual distractors. We conducted seed-based resting-state functional connectivity (rsFC) analyses using global signal correction. We assessed general responsiveness and salience related interference in the AMST and set this into context of the resting-state functional connectivity (rsFC) between a key salience network region (dACC; task-positive region) and a key default mode network region (precuneus; task-negative region).

Results: With increasing RTs to high- but not low-salient pictures dACC shows significantly weakened functional dissociation to a cluster in precuneus. This cluster overlaps with a cluster that correlates in its dACC rsFC with subjects' interference, as measured of high-salient RTs relative to low-salient RTs.

Conclusion: Our findings suggest that the interaction between salience network (SN) and default mode network (DMN) at rest predicts susceptibility to distraction. Subjects, that are more susceptible to high-salient stimuli – task-irrelevant external information – showed increased dACC rsFC toward precuneus. This is consistent with prior work in individuals with impaired attentional focus. Future studies might help to conclude whether an increased rsFC between a SN region and DMN region may serve as a predictor for clinical syndromes characterized by attentional impairments, e.g. ADHD. This could lead to an alternative, objective diagnosis and treatment of such disorders by decreasing the rsFC of these regions.

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1. Introduction

In the brain information is continuously processed and transported between structurally and functionally linked regions, forming a brain network [1]. Functional connectivity between remote regions can be defined as the temporal dependence of neuronal activity patterns of anatomically separated brain regions,

Abbreviations: AMST, Attention Modulation by Salience Task; RTs, reaction times; SN, salience network; DMN, default mode network.

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reflecting the level of functional communication between them [1–3]. Correlation of low frequency fluctuations, which may arise from fluctuations in blood oxygenation or flow, is a manifestation of functional connectivity of the resting brain [4]. As the brain, even in resting-state, is never completely at rest, resting-state networks are often called "intrinsic connectivity networks" [5]. With resting-state functional connectivity (rsFC) analysis several brain networks could be identified, e.g., the salience network (SN) [5] and the default-mode network (DMN) [6]. The SN consists mainly of dorsal anterior cingulate (dACC) and orbital fronto-insular cortices [5]. The DMN consists of functionally linked posterior cingulate cortex/precuneus, medial frontal and inferior parietal regions [1,6,7]. Task-positive regions like those from the SN routinely exhibit increased activity during attention demanding tasks, whereas task-negative regions from the DMN show decreased activity. This anticorrelation was reported for task as well as resting-state measurements [8].

"Salient" stimuli are stimuli with a special biological significance. These sudden events include novel stimuli, intense sensory stimuli, primary rewards, and arbitrary stimuli that are classically conditioned by association with primary rewards [9]. Generally, individuals differ in attention capacity, but attention is furthermore subject to heterogeneous susceptibility to interference depending on how salient stimuli in the environment are. Children show a higher interference susceptibility than adults [10]. On the pathological level, ADHD patients show an abnormally heightened processing of irrelevant information [11] whilst interference control is continuously compromised [12]. Furthermore, ADHD patients show a significantly less negative rsFC between dACC and precuneus than healthy controls reflecting increased functional coupling between SN and DMN [13]. With such a connectivity pattern, sleepiness and reaction times in a working memory task were shown to increase significantly [14]. Likewise, PTSD patients, who show disrupted attention, have an increased rsFC between SN and DMN regions [15]. Thus, the relation between the rsFC of SN and DMN regions and interference susceptibility/attention was already linked to clinically relevant disorders.

We investigated whether a less negative rsFC between the task-positive region, dACC, and the task-negative region, precuneus, correlate with higher interference susceptibility in healthy subjects. For this purpose we performed correlation analyses between the Attention Modulation by Salience Task (AMST; [16–18]), assessing interference susceptibility to salient stimuli, and the rsFC between dACC and precuneus in healthy subjects.

2. Material and methods

2.1. Participants

The sample consisted of 29 healthy males (mean age ± standard deviation = 29.10 ± 4.25 years). All subjects were right-handed and had normal or corrected to normal eyesight. An experienced psychiatrist excluded any psychiatric diagnoses prior to the scanning using the Mini International Neuropsychiatric Interview (M.I.N.I.; [19]). The study was approved by the institutional review board of the University of Magdeburg and all subjects gave written informed consent before inclusion.

2.2. Resting-fMRI acquisition

Functional magnetic resonance imaging (fMRI) data were acquired on a 3 T Siemens Magnetom Trio scanner with an eight-channel phase-array head coil. During an approximately ten-minutes fMRI data acquisition participants were instructed to lie still with their eyes closed and let their mind wander without engaging in any specific thought. The participants did not perform any task prior to the resting-state condition. A realistic estimate of the overall measurement duration is 80 min. A total of 488 volumes were acquired using an echo-planar image sequence. Acquisition parameters were: repetition time (TR) = 1250 ms, echo time (TE) = 25 ms, flip angle = 77°, field of view = 22 cm, bandwidth = 3665 Hz/pixel, acquisition matrix = 44 × 44, voxel size = 5 × 5 × 5 mm, 26 continuous axial slices covering the whole brain. Additionally, a T1-weighted structural image was acquired using a 3D-MPRAGE sequence (TE = 4.77 ms, TR = 2500 ms, T1 = 1100, flip angle = 7°, bandwidth = 140 Hz/pixel, matrix 256 × 256 × 192, voxel size = 1 mm^3).

2.3. Attentional interference assessment with AMST

In the subsequent behavioral part of the experiment, which was conducted between 15 min and 2 h after fMRI acquisition, subjects were seated in front of a computer screen in a quiet room with lights turned off, to rule out task-independent interference influences. First, the subjects did a three-minute reaction time pre-test, which was later used to normalize the AMST RTs. On a black screen the words "left" and "right" appeared in white color and the subjects were instructed to press the corresponding congruent (left or right) response button as quickly as possible. This reaction time pre-test was necessary to avoid carryover effects from previous salient stimuli.

In the AMST [18], subjects heard ascending (500–700 Hz) and descending (500–300 Hz) tones via headphones, which lasted 300 ms each. Tone modulations were created using MATLAB v7.1 R14SP3 [20]. Subjects were instructed to immediately press the left (right) response button with the right index (middle) finger upon hearing the ascending or descending tone, respectively. During this task subjects should focus on visual distractors presented on a screen. These visual distractors consisted of 40 photos taken from the International Affective Picture System (IAPS; [21]). The Photos – 20 photos each for high and low salience – have been validated in a previous study to assess values of subjective salience to sort high- and low-salient stimuli and pilot this behaviorally [16]. Salience has been explained to the subjects of this previous study as "a stimulus' inherent property to attract and maintain subjects' attention to it". Furthermore, the subjects from this pilot study rated the photo's valence as well as emotional and sexual intensity, for which the selected high- and low-salient photos were matched in the current study. Fig. 1 visualizes the paradigm and shows examples of a high-salient and a low-salient picture. The whole AMST included a second part with emotional and sexual visual distractors and took 12 min. In this study, only the first part dealing with salient distractors (6 min) has been analyzed according to the hypothesis of a relationship of interference susceptibility and rsFC between DMN and attention network. This part has been subdivided in 40 periods, each lasting about eight seconds. During each of this periods four tones were played while two visual stimuli were shown for four seconds: First a high- or low-salient distractor and afterwards a fixation cross. The tones were presented every 2 s, with an interstimulus interval jittered ±100 ms to prevent an adaptation effect. During this time interval, subjects had 2 s ±jittering time to respond.

The AMST and reaction time tasks were conducted using Presentation software v16.3 [22]. Accuracy and reaction time were recorded for each of the tones.

2.4. rsfMRI data processing

Resting-state data were preprocessed using Data Processing Assistant For Resting-State fMRI v2.3 (DPARSFA; [23]) including

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