

## Neural correlates of psychotic-like experiences during spiritual-trance state



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### ABSTRACT

Recent studies indicate high levels of psychotic experiences in the general population. Here, we report a functional imaging study with 8 mentally healthy spiritual mediums and 8 matched controls. The mediums entered a mediumistic-trance state using a standardized manner by closing their eyes and actively seeking to ignore external and internal stimuli to achieve a ‘state of emptiness’; in a control condition, they were instructed to re-enact the same mediumistic experience that they had during the mediumistic-trance condition but in a non-trance state (imaginative-trance). Both mediums and controls took part in a resting state session. The results indicate stronger activation in the lateral occipital cortex, posterior cingulate cortex (PCC), temporal pole, middle temporal gyrus and orbitofrontal cortex during the mediumistic-trance state. We also observe increased functional connectivity within auditory and sensorimotor Resting State Networks (RSN) during mediumistic-trance compared to resting and imaginative-trance conditions. Comparing spiritual mediums and controls, no differences in RSN were found. These data show preserved engagement of prefrontal cortex and connectivity of the default-mode network that indicate maintained introspective control over non-pathological psychotic-like experiences.

### 1. Introduction

Hallucinations are prototypic psychotic symptoms whose clinical presence is often equated with a psychotic disorder. However, in a cross-national study on the prevalence of psychotic symptoms in the general population (52 countries; 250,000 participants), psychotic experiences were reported by 12.5% of the participants. Less than a 1/10 of those reporting psychotic experiences had a diagnosis of schizophrenia (Nuevo et al., 2012), which has increased interest in identifying factors determining the pathological or non-pathological nature of psychotic experiences. Different kinds of spiritual experiences (SE) [mystical experiences (Beauregard and Paquette, 2006), prayer (Newberg et al., 2003), glossolalia (Newberg et al., 2006), states of transcendence (Borg et al., 2003) and mediumistic-trance (Peres et al., 2012)] are described as presenting dissociative and psychotic characteristics but with non-pathological aspects, since the practitioners do not present psychiatric disorders. Thus, studies on SE might be a promising venue to more precisely understand the differential criteria of

psychotic states in the general and clinical population.

Mediumship is a spiritual phenomenon that has often been reported throughout human history and has been defined as a trance experience in which an individual claims to be in communication with, or under the control of, the mind of a deceased person or other nonmaterial being (Moreira-Almeida et al., 2008). Mediumistic experiences have dissociative and psychotic features, with motor, sensory or cognitive automatisms (e.g., hearing spirits or reporting body movements or thoughts caused by spirits) and alternate identity or possession (Peres and Newberg, 2013). Past studies on mediumship have contributed to enlarge our understanding of dissociation, the subliminal mind and psychotic experiences [Pierre Janet's classic 1889 study of dissociation examined several mediums; Carl Jung's doctoral thesis was a case study; William James did meticulous research on the medium Leonore Piper (Alvarado, 2002; Crabtree, 1993)]. Although it has received less attention from the scientific community in recent years, studies on mediumship might continue to provide important contributions to clinical psychiatry and neuroscience, providing interesting findings

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concerning hallucinations and psychotic states and their relation to cognitive mental control.

Studies of unconventional and spiritual experiences, such as mediumship, might enlarge our current understanding of the mind and its pathological states as well as provide possible alternative therapeutic approaches for mental disorders (Moreira-Almeida and Santos, 2012). Peres et al. (2012) performed the first and, to our knowledge, the only published functional neuroimaging study on mediumship. They investigated the neural correlates of mediumistic-trance writing in 10 mediums using single photon emission computed tomography (SPECT). The complexity of the text written under the mediumistic-trance was higher than the control writing (non-trance) for the whole sample. The experienced mediums showed lower levels of activity in the left inferior occipital gyrus, left anterior cingulate, right superior temporal gyrus and right precentral gyrus during the mediumistic state compared to their normal (non-trance) writing; the levels of brain activity showed an inverse correlation with the complexity of the text. These findings are not explainable by faking or role-playing. Planning-related neural networks would presumably be recruited to compose more elaborate texts if the subjects were faking trance states. However, the cognitive-processing regions involved in reasoning and planning written content showed decreased activity in the experienced mediums, who reported that they were not conscious of the text content and had no control over it.

Given these intriguing findings, we intended to expand and explore the neural correlates that differ during mediumistic-trance and resting state (baseline in mediums and a matched control group) and the imagined re-enactment of the mediumistic experience (imagined-trance). We hypothesized similar activations at prefrontal and cingulate areas for the mediumistic-trance state as those reported for pathological dissociative states (Ludascher et al., 2010) and hallucinations (Allen et al., 2007). We also expect similar activation at cortical primary sensory areas during mediumistic-trance and imagined-trance states but a lack or diminished activation at sensory gating and prefrontal areas (cingulate and paracingulate areas) related to self-monitoring for the mediumistic-trance state, as during trance there is a lack of voluntary control compared to imagined states (Linden et al., 2011). Finally, to enter a mediumistic-trance, mediums voluntarily clear their mind and refrain from directed thought, which shares some similarities with mindwandering. Thus, they might need higher self-control to sustain a resting state apart from mediumistic-trance state, reflected in stronger prefrontal activation in the mediums compared to matched controls in the resting state.

## 2. Methods

### 2.1. Participants

Eight right-handed mediums (3 males; 5 females) from an experienced German kardecist group took part in the study (Table 1). Kardecism is a spiritualistic movement developed in the 19th century in France that has spread around the world. Its practices strongly emphasize controlled psychotic and dissociative experiences called mediumship (Moreira-Almeida and Lotufo Neto, 2005; Moreira-Almeida et al., 2006). Kardecist mediums were chosen for methodological reasons. First, they are trained to control their body movements and vocalizations during a trance state, aspects that strongly improve the data quality of fMRI images. Second, all participants were trained within the same kardecist group, reducing inter-individual differences attributable to preparation and technique used to enter a mediumistic trance. In summary, we chose mediums from this group because this choice improved data quality and increased the homogeneity of our study sample, thus enabling us to isolate the phenomenon of mediumistic trance by controlling for a broad range of possible confounds. Additionally, a pilot study was performed with an experienced kardecist medium to adjust the amount of time for each experimental task as well

**Table 1**

Demographical and neuropsychological characteristics of mediums and control groups.

	Mediums (n = 8)	Controls (n = 8)	P values
<b>Demography</b>			
Age	48.88 (7.95)	51.2 (5.63)	0.724
Level of education	12.38 (1.5)	13.0 (2.55)	1.00
Years of mediumistic experience	15 (13.4)	–	–
<b>Neuropsychology</b>			
Verbal Intelligence (MWT-B)*	113.29 (11.98)	113.8 (22.3)	0.876
Executive Functions (TMT-A)	23.88 (5.84)	16.14 (4.86)	0.284
Executive Functions (TMT-B)	49.63 (22.42)	41.0 (14.95)	0.622
Word Fluency – lexical (RWT)	14.5 (3.74)	18.2 (5.45)	0.354
Word Fluency – phonemic (RWT)	15.0 (4.75)	15.2 (6.68)	0.833
Working Memory (WMS-R)	14.13 (3.56)	16.2 (1.92)	0.088
Global Assessment Scale	85.62 (4.95)	82.0 (10.95)	0.833
PANSS	34.0 (2.02)	34.0 (4.84)	0.724
Psychopathological Scale	18.29 (1.6)	17.8 (3.19)	0.755

as parameters for MRI acquisition to control for head movement and image post-processing (Additional material).

The mediums were indicated by the coordinator of the spiritist group, who has more than 40 years of experience in this kind of phenomenon. Four weeks prior to the fMRI session, an audio recording of the scanner noise was provided, and the participants were instructed to train to get into mediumistic-trance while exposed to the scanner noise. The mediums explained that to get into mediumistic-trance state they need to achieve a mental ‘state of emptiness’. We chose to introduce this procedure to acquaint the mediums with the scanner noise during their process of trance self-induction, optimizing the timing of the trance condition during the scanner session and reducing interference caused by the fMRI setup. To test for possible differences in resting state between the mediums and the general population, 8 matched control subjects with no previous experiences in trance states were recruited from the staff of the RWTH University Hospital and intern announcements. The groups were matched according to gender, age (+ or – 2 years) and level of education (+ or – 2 years) for each participant.

All participants were clinically assessed using the Structured Clinical Interview for DSM-IV (SCID German version (Wittchen et al., 1997), the Global Assessment Scale (Spitzer et al., 1976) and PANSS (Positive and Negative Syndrome Scale (Kay et al., 1987; Muller et al., 2000) conducted by an experienced clinical psychologist (NK). An additional battery of neuropsychological tests was administered, including tasks on verbal fluency (Regensburger Wortflüssigkeitstest, RWT, Aschenbrenner et al., 2000) working memory (Wechsler Memory Scale, WMS-R (Härting et al., 2000), verbal intelligence (multiple-choice vocabulary test MWVB), executive function (trail making test, TMT-A and TMT-B (Reitan, 1979) and handedness (Edinburgh Inventory of Handedness (Oldfield, 1971).

### 2.2. Functional magnetic resonance imaging

The participants were scanned in the Siemens Tim Trio (3 T) at the Aachen University Hospital using standard gradients and a circular polarized phase array head coil (Head Matrix). The participants were lying in supine position; head movement was limited by foam padding within the head coil. In a fMRI block design paradigm, the participants had to perform the following instructed experimental tasks (Fig. 1): a) resting: to relax with eyes closed; b) mediumistic-trance: to get into trance state as they do in their religious meetings; once they entered the trance state (about to lose conscious control) they should indicate the trance state by a button press; c) mathematical equation: after getting out of trance, participants performed a sequence of 5 mathematical equations (3 digits each) to wash out possible cognitive alterations caused by the altered states during trance; d) imaginative-trance: to

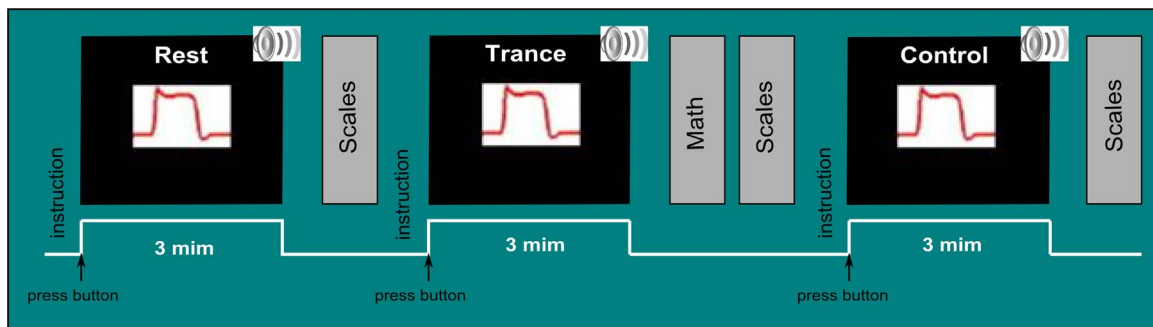


Fig. 1. Session with the duration of each task (block). Three sessions were performed, and the tasks were always presented in the same sequence.

mentally reenact the previous mediumistic-trance experience without getting into a trance state (non-trance state). The imaginative-trance task was chosen to compare similar perceptual, cognitive and motor processes during conscious self-directed imagination as those experienced while in trance. Resting, mediumistic-trance and imaginative-trance tasks were each 3 min long with eyes closed; 30 s prior to the task ending, a loud sound was played to inform the participants that they should end the task by opening their eyes. The session was repeated 3 times, and the tasks were presented always in the same order [resting, mediumistic-trance, mathematical equation and imaginative-trance task] due to the intrinsic characteristic of the paradigm. Subjective experiences during the conditions were assessed by standardized questionnaires after each task [PANAS (Positive and Negative Affective Scale; (Watson et al., 1988) and ESR (Emotion Self-Rating; (Schneider et al., 2006; Weiss et al., 1999)]. To acquire relevant information about the intensity of the mediumistic-trance state and the vividness of the imaginative-trance task, we asked two questions after the respective task [trance: ‘Concerning your experience, how deep was the trance?’; imaginative-trance: ‘how vivid was the imagination?’]. The participants should indicate their answer on a Likert scale (1- not deep/not vivid); 5 -very deep/vivid). The control group performed only the resting condition.

After the fMRI measurement, a short interview with each medium assessed the qualitative phenomenology of the experiences during mediumistic-trance and imaginative-trance conditions.

### 2.3. Data acquisition

Functional scans were acquired covering the whole brain sagittal to the AC/PC line with the following parameters: IG = 0.30 mm; MS = 64 × 64; FOV = 240 × 240 mm; TR = 2.0 s; TE = 28 ms; FA = 77°; 34 slices (thickness: 3.5 mm, gap: 10%) and a full coverage of the brain (voxel size 3.5 mm × 3.5 mm × 3.5 mm); 1620 volumes were acquired in total, divided in 3 runs of 15 min (approx.). For anatomical localization, we acquired high-resolution images with a T1-weighted 3D FFE sequence (TR = 1.9 ms; TE = 2.5 ms; NS = 176 (sagittal); TI = 900 ms; IG = 0 mm; FOV = 256 × 256 mm; voxel size = 1 × 1 × 1 mm).

### 2.4. Behavioral data analysis

Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS 15). Differences between groups on clinical interviews, psychopathological scales and neuropsychological tests were assessed by applying a Mann-Whitney test. Subjective experiences during the conditions were analyzed using full factorial Generalized Estimating Equations (GEEs) to account for their potentially non-normal distributions and/or violations of sphericity. The statistical models included main effects of the factors ‘ERS’, ‘PANAS’ and the conditions. Post hoc pairwise comparisons between conditions were performed using paired *t*-tests and Bonferroni correction. The level of significance was set at  $p = 0.05$  for both procedures.

### 2.5. fMRI data analysis

The fMRI data were analyzed with FSL [[www.fmrib.ox.ac.uk/fsl/](http://www.fmrib.ox.ac.uk/fsl/); Smith et al. (2004)]. The following pre-processing was applied for each participant: head movement correction using MCFLIRT (Jenkinson et al., 2002); non-brain removal using BET (Smith, 2002); spatial smoothing using a Gaussian kernel of full-width-at-half-maximum (FWHM) of 5 mm and spatial normalization to standard space using FLIRT [affine, 12 DoF (Greve and Fischl, 2009)]. In addition, high pass temporal filtering with a cut-off of 128 s was applied. All participants’ 4D fMRI time series data were transformed into standard stereotactic space at  $2 \times 2 \times 2$  mm resolution by using registration transformations derived as described above using FLIRT. Individual activation maps were produced using the general linear model analyses (GLM) carried out through FILM routines, which is based on a semi-parametric estimation of residual autocorrelation (Woolrich et al., 2001). A block design was employed using gamma hemodynamic response function (HRF), and 2 contrasts of interest [mediumistic-trance and imaginative-trance task] were tested for statistical significance (against the null-hypothesis of zero effect size). Additionally, temporal derivative, temporal filtering and movement parameters were also modeled. Subjective experiences (mediumistic-trance intensity and imaginative-trance vividness) were also included as covariates in the second level; however, no significant correlations were found. Finally, group mean mixed effects Z statistic images were thresholded using clusters determined by  $Z > 2.0$  and a corrected cluster significance threshold of  $p < 0.0001$  assuming a Gaussian random field for the Z-statistics (Beckmann et al., 2003; Woolrich et al., 2004). The following contrasts were tested for group statistical significance (against the null-hypothesis of zero effect size; FWE correction): mediumistic-trance vs. baseline (resting), mediumistic-trance vs. imaginative-trance, imaginative-trance vs. baseline (resting).

Second, a functional connectivity analysis was performed to determine the impact of mediumistic-trance on the following networks: default mode network (DMN), executive control, attention, visual and auditory systems (using template maps as published in Smith et al., 2009). Therefore, a second set of group activation maps was obtained by using independent component analysis (ICA). Unlike regression-based methods (i.e., GLM), ICA does not require a predefined model (design matrix) and represents an explorative data analysis method that results in several spatially independent components that are linearly mixed and spatially fixed. Similar procedures for the preprocessing as described above for the GLM analysis were used in the ICA: head movement correction using MCFLIRT (Jenkinson et al., 2002); non-brain removal using BET (Smith, 2002); spatial smoothing using a Gaussian kernel of full-width-at-half-maximum (FWHM) of 6 mm and spatial normalization to standard space using FLIRT [affine, 12 DoF (Greve and Fischl, 2009)]; and high pass temporal filtering with a cut-off of 100 s. The ICA was run using MELODIC (Beckmann and Smith, 2004).

All resulting datasets from each participant according to task and group were concatenated in three different multi-subject/session ICAs:

**Table 2**

Statistical information of clusters highlighted when comparing the BOLD response of mediumistic-trance and resting as well as mediumistic-trance and imaginative-trance conditions.

	side	Region	BA	MNI coordinates			P values
				X	Y	Z	
Trance > Resting							
Cluster 2	L	Occipital Pole	18	−32	−90	−10	< 0.000
	R	Occipital Fusiform Gyrus		24	−80	−18	
	R	Occipital Pole	17	14	−94	−8	
	R	Cerebellum		24	−78	−40	
Cluster 1	L	Temporal Pole		−54	20	−10	< 0.000
	L	Middle Temporal Gyrus		−52	−42	−2	
	L	Frontal Orbital Cortex	45	−42	30	−12	
	L	Middle Frontal Gyrus	6	−32	2	48	
Mediumistic-trance > imaginative- trance							
Cluster 1	L	Lateral Occipital Cortex	7	−12	−82	44	< 0.000
	L	Occipital Fusiform Gyrus	18	−10	−106	−4	
	L	Posterior Cingulate Gyrus		−2	−50	28	

Voxel coordinates are in MNI atlas space; FSL Anatomy tool box (Eickhoff et al., 2005).

mediumistic-trance and resting task (trance group only), mediumistic-trance and imaginative-trance task (trance group only), and resting task (trance and control group) with a fixed dimensionality of 30 components. A Pearson's correlation of the unthresholded spatial maps between the decomposed components and the mentioned canonical RSN maps resulting from the three multi-subject ICA was calculated (compare Smith et al., 2009 for details on the procedure). This was done to identify meaningful and reliably detectable RSNs from the group ICA components. The components with the highest correlation ( $r \geq 0.4$ ) to the canonical RSN maps were labeled according to the respective RSN label.

Finally, a dual regression (DR) analysis ( $p < 0.05$ ) was used to estimate significant differences between conditions and subjects (mediumistic-trance versus resting task; mediumistic-trance versus imaginative-trance task; trance group versus control group resting task). In dual regression, the input maps, which in our case are the components labeled by correlation with the canonical Smith RSN templates, are projected into the individual. For each of these components, subject-specific temporal dynamics and subject-specific spatial maps are identified from the individual's preprocessed 4D data during resting/mediumistic-trance/imaginative-trance. In the last step, the individual component maps (e.g., representations of the individual's connectivity of the particular RSN) are combined in one 4D file and tested voxel-wise for statistically significant differences between conditions and subjects. Non-parametric permutation testing is applied in the last step to determine statistical significance, and correction for multiple comparison within one volume is conducted via threshold-free cluster-extent (Smith and Nichols, 2009). The resulting contrast maps were corrected for multiple comparisons (Bonferroni) based on the number of IC maps associated with RSNs.

### 3. Results

#### 3.1. Behavioral data

We found no significant differences between mediums and controls in the structured clinical interviews and psychopathological scales (Table 1).

The GEE analysis showed no significant main effect for PANAS (Wald  $X^2(2) = 1.65$ ,  $p < 0.437$ ). However, the GEE analysis was significant for ERS: surprise (Wald  $X^2(1) = 10.780$ ,  $p < 0.005$ ) and happiness (Wald  $X^2(1) = 12.032$ ,  $p < 0.002$ ). Pairwise comparisons indicated significantly higher values for surprise in imaginative-trance compared to the resting condition ( $t = -2.949$ ;  $p < 0.033$ ) and for happiness in mediumistic-trance compared to the imaginative-trance condition ( $t = 2.393$ ;  $p < 0.048$ ).

The mediums reported different experiences during mediumistic-trance (Menezes et al., 2012) that can be summarized as follows: *spiritual seeing/clairvoyance* (described as the experience of seeing spirits: 'A man [spirit] came to me'; 'Two men [spirit] were standing beside me, near to my head'; 'Different spirits around me'; 'a person [spirit] wearing white clothes and I follow her'); *spiritual hearing* (described as the experience of hearing spirits or noises not produced materially: 'I heard voices'; 'someone says - you are strong, have faith'; 'I heard his [spirit] stertorous breathing'; 'a voice gives me instructions'; 'someone said: follow me'), *out-of-body experiences* (denotes the experience of feeling outside one's own body and/or feeling to go to other places: 'I was here and my body was there, lying'; 'someone came and took me into places'), *telepathy* (reporting the thoughts of others: 'I received their ideas mentally, telepathically'; 'words and sentences that came into my mind'). Seven subjects reported experiences of clairvoyance, spiritual hearing and telepathy in at least one of the three mediumistic-trance sessions; four subjects also reported out-of-body experiences in at least one of the three mediumistic-trance sessions.

#### 3.2. fMRI results

##### 3.2.1. GLM analysis

We found stronger activations for mediumistic-trance compared to resting conditions in the bilateral occipital pole, left middle temporal gyrus, temporal pole, middle frontal gyrus and frontal orbital cortex. Likewise, we found significantly higher activations for mediumistic-trance compared to imaginative-trance conditions in the left lateral occipital cortex and posterior cingulate gyrus (Table 2 and Fig. 2).

##### 3.2.2. ICA analysis

The first ICA decompositions were between control and trance groups during the resting condition. From the 11 independent component (IC) maps generated, 3 maps showed a sufficiently high correlation with 4 RSN maps ( $r > 0.40$ ): auditory, frontoparietal (1), visual (1, 2 and 3) and default mode network (DMN). However, we found no significant differences between groups in the DR for these RSNs.

Our second set of maps stem from ICA decompositions within the trance group, between the mediumistic-trance and imaginative-trance conditions. From the 14 IC maps generated, 2 maps were associated with 2 RSN maps ( $r > 0.40$ ): auditory and DMN. In the DR analysis, we found significant differences between the mediumistic-trance and imaginative-trance condition only in the auditory RSN map. For mediumistic-trance (mediumistic-trance > imaginative-trance) we found significant stronger connectivity within the posterior insula. On the other hand, we found no significant differences for the imaginative-trance task (Fig. 3A).

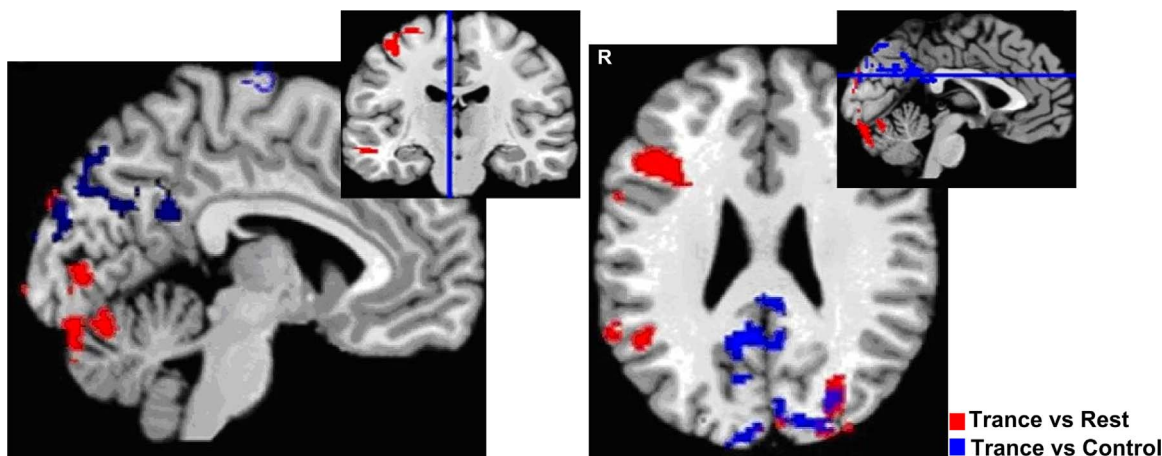


Fig. 2. Significant activation clusters for mediumistic-trance versus Resting (in red) and mediumistic-trance versus imagination (in blue).  $p < 0.0001$  corrected for multiple comparisons. FSL Anatomy tool box (Eickhoff et al., 2005). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Our final set of maps stem from ICA decompositions between resting and mediumistic-trance conditions within the trance group. From the 16 IC maps generated, 5 maps showed a sufficiently high correlation with 7 RSN maps ( $r > 0.40$ ): auditory, DMN, frontoparietal, sensorimotor, visual (1, 2 and 3). For the DR analysis, we found significant connectivity within the areas of sensorimotor RSN (intraparietal cortex and dorsal ACC) for mediumistic-trance (mediumistic-trance > resting) and within areas of DMN (posterior cingulate cortex) and medial visual (occipital cortex and retrosplenial cortex) RSN maps for resting (resting > mediumistic-trance) (Figs. 3B and C).

#### 4. Discussion

Our aim was to investigate the functional neural correlates of mediumistic-trance states compared to resting (the absence of a demanding cognitive task) and imaginative-trance conditions, which consisted of re-enacting a mediumistic-trance state. As expected, we found similar activation of cortical primary sensory areas during mediumistic-trance and imagined-trance states as well as in prefrontal areas (cingulate and paracingulate areas) related to self-monitoring for

the mediumistic-trance state. Mediumistic-trance shared auditory and visual subjective responses with psychotic hallucinations in schizophrenia. It seems to be a network involving sensory and frontal areas that are differentially correlated to mediumistic-trance compared to imaginative-trance and resting (Fig. 2 and Table 2). Mediums reported that the mediumistic experiences (e.g., “seeing and hearing spirits” and out-of-body experience) were as vivid as a contact with real person in everyday life, which is possibly associated with the enhanced activation in different cortical sensory areas for mediumistic-trance over imaginative-trance. These occipital and temporal areas have been found to be engaged in processing visual (Wandell et al., 2007) and auditory stimuli (Hwang et al., 2006) as well sensory mental imagery (Huijbers et al., 2011; Linden et al., 2011). Studies with schizophrenic patients have also shown sensory activation during hallucinations (Allen et al., 2007; Shergill et al., 2000). Furthermore, we found enhanced activation in the posterior cingulate cortex (PCC) for mediumistic-trance over imaginative-trance. The mediums stated that they actively seek to ignore external and internal stimuli, avoiding engaging in any cognitively demanding task to achieve a ‘state of emptiness’. Pearson et al. (2011) suggests that PCC neurons might track task engagement, with stronger

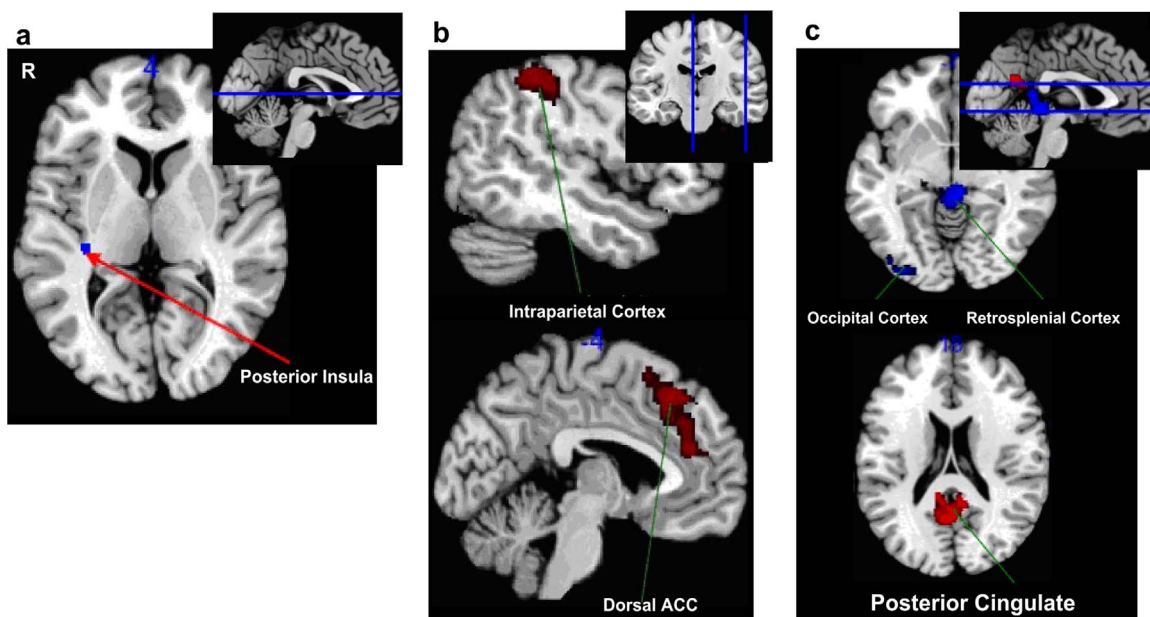


Fig. 3. Resting State Networks. A) mediumistic-trance versus imaginative-trance within the Auditory Network. B) mediumistic-trance versus Resting within the Sensorimotor Network. C) resting versus mediumistic-trance within the Medial Visual (blue) and Default Mode Network (red). FSL Anatomy tool box (Eickhoff et al., 2005). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

activation during the resting state (when no cognitive task engagement occurred) and diminished activation during cognitive task engagement. We suggest that the stronger activation of PCC during mediumistic-trance over imagined-trance reflects the sustained effort to not engage in any cognitively demanding task. Similarly, we found enhanced activity in the lateral orbitofrontal cortex (OFC) for mediumistic-trance over resting. Functionally and anatomically, the OFC is connected to temporal and parietal cortices, receiving connections from all regions associated with primary and secondary sensory modalities (Kringelbach and Rolls, 2004). Considering the description of the mediums to achieve the emptiness state and the functional and anatomical connections of the OFC, we suggest that this region might be involved in higher-order processes of integration, evaluation and regulation of sensory information.

We see further support for the notion of increased non-pathological sensory input during mediumistic-trance from the connectivity analyses of the brain's resting state networks (RSN) (Smith et al., 2009). In the comparison between conditions within the medium group, the RSN connectivity analyses showed stronger associations in areas related to sensory and motor processing for mediumistic-trance (Fig. 3). We observed an increased connectivity within regions of auditory and sensorimotor RSN (Smith et al., 2009) for mediumistic-trance compared to imaginative-trance (posterior insula) and resting. The increased connectivity within these networks might be related to the vivid out-of-body and auditory experiences described by the mediums that resemble a hallucinatory state.

Resting, mediumistic-trance and imaginative-trance approaches are radically different concerning the subjective experience and the amount and quality of cognitive mental control. During mediumistic-trance, mediums actively seek to ignore external and internal stimuli to achieve a 'state of emptiness'. We found no differences between the medium and control groups in the resting condition. These findings indicate that RSN (Smith et al., 2009), especially the functional connectivity within DMN, is not altered in the medium group, indicating that the psychosis-like experiences presented in mediumistic-trance are not related to alterations in the DMN as in schizophrenic patients (Garrity et al., 2007; Rotarska-Jagiela et al., 2010; Skudlarski et al., 2010). We suggest that the preserved functional connectivity within the DMN regions might reflect the absence of any psychopathological state within the medium group.

There are a few methodological limitations in the present study. Although mediumship is a phenomenon presented in different cultures and religious traditions, the methods used to induce the trance state and the psychological experience are quite heterogeneous. In the present study, the sample was restricted to kardecist mediums from only one group. It is important to note that there are guidelines in the kardecism tradition for training and achieving the mediumistic trance state. Different fMRI studies have shown that training has an important effect to strengthen and/or shape the functional neural correlations for meta-cognitive awareness (Fox et al., 2016; McCaig et al., 2011). Therefore, to avoid possible confounds of differences in method and training, we chose to work with only one kardecist group. Originally, 16 mediums wanted to take part in the study, but 8 of them were excluded due to MRI exclusion criterion (metal attached to the bones, tattoo, claustrophobia, among others). Mediumistic trance is a rare phenomenon, yet the path into a trance state can differ tremendously between individuals. Therefore, we opted for a certain homogeneity in techniques over a possibly larger sample size, as this could possibly increase our power by reducing variability more than the inclusion of more individuals would. As the investigations on mediumistic trance are rare and border the esoteric, we aimed at implementing robust and well-explored techniques, such as a GLM approach to investigate differences in brain activation and a reference to canonical RSN for the investigation of different large scale brain networks. To limit methodological differences and potential biases, we adhered to similar procedures used by Smith et al. (2009) in the identification and characterization of the

canonical ICA components. However, our runs were shorter than conventional resting state scans, which was necessary due to the nature of the investigation. However, Hutchison et al. (2013) effectively compute the same or very similar metrics on much shorter time windows.

Religious and spiritual trance is present in different cultures and religious traditions; however, the methods used to induce the trance state are quite different. Hove et al. (2016) examined the brain-network configuration associated with trance state in experienced shamanic practitioners who listened to rhythmic drumming to achieve a trance state. Seed-based analysis revealed increased coactivation of the PCC (a default network hub involved in internally oriented cognitive states) with the dACC and insula (control-network regions involved in maintaining relevant neural streams). The authors discussed the brain pattern activation data, indicating that trance involves coactivation of DMN and control networks and decoupling of sensory processing (auditory network); however, there are no data about the shamanic practitioners' subjective experiences. Kardecist mediums and shamanic practitioners use different methods to achieve a trance state and might also have different subjective experiences. Kardecist mediums do not use any sound or other sensory stimulation to achieve a trance state, and they claim to be in contact with a deceased human being. Contrary to Hove et al. (2016), our results show increased functional connectivity within auditory and sensorimotor Resting State Networks (RSN) for the mediumistic-trance compared to resting and imaginative-trance conditions, compatible with kardecist mediums' subjective experiences. The neural correlate differences between our study and Hove et al. (2016) might be due to differences in the method used to achieve trance as well as to subjective experiences. There are no studies comparing different kinds of religious and spiritual trance states at neural and/or subjective levels. Meditation is also a spiritual practice and has received serious interest from the neuroscientific community in recent years. Fox et al. (2016) investigated 78 functional neuroimaging studies on meditation using activation likelihood estimation (ALE) meta-analyses to investigate brain patterns associated with meditation. They showed reliably dissociable patterns of brain activation and deactivation for four different styles of meditation (focused attention, mantra recitation, open monitoring, and compassion/loving-kindness) and suggestive differences for three other styles (visualization, sense-withdrawal, non-dual awareness practices). Moreover, the dissociable activation patterns were congruent with the psychological and behavioral aims of each practice. In sum, in future studies about the neural correlates of religious and spiritual trance, it might be relevant to compare practitioners from different religious and spiritual traditions, as well as include a description of the practitioners' subjective experiences.

In a nutshell our study suggests that people who experience hallucinations might be a heterogeneous group, with different clinical and neurofunctional implications. The main differences between the medium's non-psychiatric and schizophrenia's psychiatric experience is that mediums purposefully enter these states; whereas in schizophrenia, such states are involuntary. The activation pattern of sensory areas during a medium's psychosis-like experience share some neurofunctional similarities with the hallucinatory episodes of schizophrenic patients but differ in the involvement of prefrontal cortex. Additionally, mediums may have preserved DMN connectivity compared to the control group, which might explain the absence of psychiatric symptoms. However, the possibility remains that differences in DMN between normal controls and mediums exist and are stable but too subtle to be detected with our sample size.

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## References

- Allen, P., Amaro, E., Fu, C.H., Williams, S.C., Brammer, M.J., Johns, L.C., McGuire, P.K., 2007. Neural correlates of the misattribution of speech in schizophrenia. *Br. J. Psychiatry* 190, 162–169.
- Alvarado, C.S., 2002. Dissociation in Britain during the late nineteenth century: the society for psychical research (1882–1900). *J. Trauma Andm. Dissociation* 3, 29–33.
- Aschenbrenner, S., Tucha, O., Lange, K.W., 2000. Regensburger Wortflüssigkeits-Test. Hogrefe, Göttingen.
- Beauregard, M., Paquette, V., 2006. Neural correlates of a mystical experience in Carmelite nuns. *Neurosci. Lett.* 405 (3), 186–190.
- Beckmann, C.F., Jenkinson, M., Smith, S.M., 2003. General multilevel linear modeling for group analysis in fMRI. *Neuroimage* 20 (2), 1052–1063.
- Beckmann, C.F., Smith, S.M., 2004. Probabilistic independent component analysis for functional magnetic resonance imaging. *IEEE Trans. Med. Imaging* 23 (2), 137–152.
- Borg, J., Andree, B., Soderstrom, H., Farde, L., 2003. The serotonin system and spiritual experiences. *Am. J. Psychiatry* 160 (11), 1965–1969.
- Crabtree, A., 1993. From Mesmer to Freud: Magnetic Sleep and the Roots of Psychological Healing. Yale University Press, New Haven.
- Eickhoff, S.B., Stephan, K.E., Mohlberg, H., Grefkes, C., Fink, G.R., Amunts, K., Zilles, K., 2005. A new SPM toolbox for combining probabilistic cytoarchitectonic maps and functional imaging data. *Neuroimage* 25 (4), 1325–1335.
- Fox, K.C., Dixon, M.L., Nijeboer, S., Girn, M., Floman, J.L., Lifshitz, M., Emlam, M., Sedlmeier, P., Christoff, K., 2016. Functional neuroanatomy of meditation: a review and meta-analysis of 78 functional neuroimaging investigations. *Neurosci. Biobehav. Rev.* 65, 208–228.
- Garrity, A.G., Pearlson, G.D., McKiernan, K., Lloyd, D., Kiehl, K.A., Calhoun, V.D., 2007. Aberrant "default mode" functional connectivity in schizophrenia. *Am. J. Psychiatry* 164 (3), 450–457.
- Greve, D.N., Fischl, B., 2009. Accurate and robust brain image alignment using boundary-based registration. *Neuroimage* 48 (1), 63–72.
- Härting, C., Markowitsch, H.J., Neufeld, H., Calabrese, P., Deisinger, K., Kessler, J., 2000. Wechsler Gedächtnis Test, revidierte Fassung. Hans Huber Verlag, Bern.
- Hove, M.J., Stelzer, J., Nierhaus, T., Thiel, S.D., Gundlach, C., Margulies, D.S., Van Dijk, K.R., Turner, R., Keller, P.E., Merker, B., 2016. Brain network reconfiguration and perceptual decoupling during an absorptive state of consciousness. *Cereb. Cortex* 26 (7), 3116–3124.
- Huijbers, W., Pennartz, C.M., Rubin, D.C., Daselaar, S.M., 2011. Imagery and retrieval of auditory and visual information: neural correlates of successful and unsuccessful performance. *Neuropsychologia* 49 (7), 1730–1740.
- Hutchison, R.M., Womelsdorf, T., Allen, E.A., Bandettini, P.A., Calhoun, V.D., Corbetta, M., Della Penna, S., Duyn, J.H., Glover, G.H., Gonzalez-Castillo, J., Handwerker, D.A., Keilholz, S., Kiviniemi, V., Leopold, D.A., de Pasquale, F., Sporns, O., Walter, M., Chang, C., 2013. Dynamic functional connectivity: promise, issues, and interpretations. *Neuroimage* 80, 360–378.
- Hwang, J.H., Wu, C.W., Chen, J.H., Liu, T.C., 2006. The effects of masking on the activation of auditory-associated cortex during speech listening in white noise. *Acta Otolaryngol.* 126 (9), 916–920.
- Jenkinson, M., Bannister, P., Brady, M., Smith, S., 2002. Improved optimization for the robust and accurate linear registration and motion correction of brain images. *Neuroimage* 17 (2), 825–841.
- Kay, S.R., Fiszbein, A., Opler, L.A., 1987. The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizophr. Bull.* 13 (2), 261–276.
- Kringelbach, M.L., Rolls, E.T., 2004. The functional neuroanatomy of the human orbitofrontal cortex: evidence from neuroimaging and neuropsychology. *Prog. Neurobiol.* 72 (5), 341–372.
- Linden, D.E., Thornton, K., Kuswanto, C.N., Johnston, S.J., van de Ven, V., Jackson, M.C., 2011. The brain's voices: comparing nonclinical auditory hallucinations and imagery. *Cereb. Cortex* 21 (2), 330–337.
- Ludascher, P., Valerius, G., Stiglmayr, C., Mauchnik, J., Lanius, R.A., Bohus, M., Schmahl, C., 2010. Pain sensitivity and neural processing during dissociative states in patients with borderline personality disorder with and without comorbid posttraumatic stress disorder: a pilot study. *J. Psychiatry Neurosci.* 35 (3), 177–184.
- McCaig, R.G., Dixon, M., Keramatian, K., Liu, I., Christoff, K., 2011. Improved modulation of rostralateral prefrontal cortex using real-time fMRI training and meta-cognitive awareness. *Neuroimage* 55 (3), 1298–1305.
- Menezes Jr., A., Alminhana, L., Moreira-Almeida, A., 2012. Sociodemographic and anomalous experiences profile in subjects with psychotic and dissociative experiences in religious groups. *Rev. Psiqu. Clin.* 39 (6), 203–207.
- Moreira-Almeida, A., Lotufo Neto, F., 2005. Spiritist views of mental disorders in Brazil. *Transcult. Psychiatry* 42 (4), 570–595.
- Moreira-Almeida, A., Neto, F.L., Cardena, E., 2008. Comparison of Brazilian spiritist mediumship and dissociative identity disorder. *J. Nerv. Ment. Dis.* 196 (5), 420–424.
- Moreira-Almeida, A., Neto, F.L., Koenig, H.G., 2006. Religiousness and mental health: a review. *Rev. Bras. Psiquiatr.* 28 (3), 242–250.
- Moreira-Almeida, A., Santos, S.F., 2012. Exploring Frontiers of Mind-Brain Relationship. Springer, New York.
- Muller, M.J., Rossbach, W., Davids, E., Wetzel, H., Benkert, O., 2000. [Evaluation of standardized training for the "Positive and Negative Syndrome Scale" (PANSS)]. *Nervenarzt* 71 (3), 195–204.
- Newberg, A.B., Pourdehnad, M., Alavi, A., d'Aquili, E.G., 2003. Cerebral blood flow during meditative prayer: preliminary findings and methodological issues. *Percept. Mot. Skills* 97 (2), 625–630.
- Newberg, A.B., Wintering, N.A., Morgan, D., Waldman, M.R., 2006. The measurement of regional cerebral blood flow during glossolalia: a preliminary SPECT study. *Psychiatry Res.* 148 (1), 67–71.
- Nuevo, R., Chatterji, S., Verdes, E., Naidoo, N., Arango, C., Ayuso-Mateos, J.L., 2012. The continuum of psychotic symptoms in the general population: a cross-national study. *Schizophr. Bull.* 38 (3), 475–485.
- Oldfield, R.C., 1971. The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia* 9 (1), 97–113.
- Pearson, J.M., Heilbronner, S.R., Barack, D.L., Hayden, B.Y., Platt, M.L., 2011. Posterior cingulate cortex: adapting behavior to a changing world. *Trends Cogn. Sci.* 15 (4), 143–151.
- Peres, J., Newberg, A., 2013. Neuroimaging and mediumship: a promising research line. *Rev. Psiquiatr. Clin.* 40 (6), 225–232.
- Peres, J.F., Moreira-Almeida, A., Caixeta, L., Leao, F., Newberg, A., 2012. Neuroimaging during trance state: a contribution to the study of dissociation. *PLoS One* 7 (11), e49360.
- Reitan, R.M., 1979. Trail Making Test. Hogrefe-Verlag, Bern, Göttingen.
- Rotarska-Jagiela, A., van de Ven, V., Oertel-Knochel, V., Uhlhaas, P.J., Vogeley, K., Linden, D.E., 2010. Resting-state functional network correlates of psychotic symptoms in schizophrenia. *Schizophr. Res.* 117 (1), 21–30.
- Schneider, F., Gur, R.C., Koch, K., Backes, V., Amunts, K., Shah, N.J., Bilker, W., Gur, R.E., Habel, U., 2006. Impairment in the specificity of emotion processing in schizophrenia. *Am. J. Psychiatry* 163 (3), 442–447.
- Shergill, S.S., Brammer, M.J., Williams, S.C., Murray, R.M., McGuire, P.K., 2000. Mapping auditory hallucinations in schizophrenia using functional magnetic resonance imaging. *Arch. Gen. Psychiatry* 57 (11), 1033–1038.
- Skudlarski, P., Jagannathan, K., Anderson, K., Stevens, M.C., Calhoun, V.D., Skudlarski, B.A., Pearlson, G., 2010. Brain connectivity is not only lower but different in schizophrenia: a combined anatomical and functional approach. *Biol. Psychiatry* 68 (1), 61–69.
- Smith, S.M., 2002. Fast robust automated brain extraction. *Hum. Brain Mapp.* 17 (3), 143–155.
- Smith, S.M., Fox, P.T., Miller, K.L., Glahn, D.C., Fox, P.M., Mackay, C.E., Filippini, N., Watkins, K.E., Toro, R., Laird, A.R., Beckmann, C.F., 2009. Correspondence of the brain's functional architecture during activation and rest. *Proc. Natl. Acad. Sci. USA* 106 (31), 13040–13045.
- Smith, S.M., Jenkinson, M., Woolrich, M.W., Beckmann, C.F., Behrens, T.E., Johansen-Berg, H., Bannister, P.R., De Luca, M., Drobnjak, I., Flitney, D.E., Niazy, R.K., Saunders, J., Vickers, J., Zhang, Y., De Stefano, N., Brady, J.M., Matthews, P.M., 2004. Advances in functional and structural MR image analysis and implementation as FSL. *Neuroimage* 23 (Suppl 1), S208–S219.
- Smith, S.M., Nichols, T.E., 2009. Threshold-free cluster enhancement: addressing problems of smoothing, threshold dependence and localisation in cluster inference. *Neuroimage* 44 (1), 83–98.
- Spitzer, R.L., Gibbon, M., Endicott, J., 1976. Global assessment scale (GAS). In: Guy, W. (Ed.), ECDEU Assessment Manual for Psychopharmacology. National Institute of Health. Psychopharmacology Research Branch, pp. 583–585.
- Wandell, B.A., Dumoulin, S.O., Brewer, A.A., 2007. Visual field maps in human cortex. *Neuron* 56 (2), 366–383.
- Watson, D., Clark, L.A., Tellegen, A., 1988. Development and validation of brief measures of positive and negative affect: the PANAS scales. *J. Pers. Soc. Psychol.* 54 (6), 1063–1070.
- Weiss, U., Salloum, J.B., Schneider, F., 1999. Correspondence of emotional self-rating with facial expression. *Psychiatry Res.* 86 (2), 175–184.
- Wittchen, H.U., Wunderlich, U., Gruschwitz, S., Zaudig, M., 1997. Strukturieretes Klinisches Interview für DSM-IV. Hogrefe-Verlag, Göttingen.
- Woolrich, M.W., Behrens, T.E., Beckmann, C.F., Jenkinson, M., Smith, S.M., 2004. Multilevel linear modelling for fMRI group analysis using Bayesian inference. *Neuroimage* 21 (4), 1732–1747.
- Woolrich, M.W., Ripley, B.D., Brady, M., Smith, S.M., 2001. Temporal autocorrelation in univariate linear modeling of fMRI data. *Neuroimage* 14 (6), 1370–1386.