BIAL Foundation

Final Report
Project no. 50/10 - 'Trance: Cortical Representations'

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1) Abstract (original proposal):

In recent years a number of independent neuroimaging studies about altered states of consciousness in healthy subjects during different kinds of religious and meditative states have shown that the subjective nature of the experience significantly influences the various levels of brain functioning (Beauregard, 2007, Peres et al., 2007, Moreira-Almeida and Koenig, 2008, Moreira-Almeida et al., 2008). Trance experiences are usually rich in dissociative behavior, hallucinations, feelings of being controlled by an external power, depersonalization, personality shifts, and alleged post-trance amnesia (Moreira-Almeida, 2009). There has been renewed interest in dissociative and hallucinatory experiences in people not suffering from mental disorders (Krippner, 1997, Moreira-Almeida and Koenig, 2006, Moreira-Almeida, 2009, Linden et al., 2010), such as schizophrenia. In ICD-10 trance states are classified as a psychiatric disorder only when they happen involuntarily or unwanted and outside of religious or culturally accepted context (F44.3). Trance and hallucinatory states are critically distinguished from imaginative states by lack of voluntary control and sense of reality (Moreira-Almeida, 2009). Thus the aim of the present study is to investigate possible differences in brain functions during trance states compared to imagined and meditative states. There are several possible definitions of trance, however, for the purposes of the present study we will define trance as a 'state of profound absorption during which the individual is experientially cut off from the outside world; it is frequently accompanied by vocal and motor automatisms, lack of responsive awareness and

amnesia' (Wulf, 2000). Therefore, we plan to study healthy subjects that are able to enter in trance (a self-controlled altered state similar to hallucination), but do not meet the ICD-10 criteria F44.3 and have no history of psychiatric disorders. We will combine different approaches to investigate the neural correlates of trance in fMRI. Firstly, we will investigate brain functional differences in trance compared to imagined and meditative states. Secondly, we will explore possible overlap of cortical areas supporting both trance, imaginative and meditative states. Our sample will be constituted of 32 healthy subjects (16 experts in trance; 16 naive subjects in trance states). A block design will be used with the following experimental tasks: a) trance (participants will be instructed to inform when the trance begins and ends by button press), b) mathematical equation (participants will perform a sequence of mathematical equations in order to wash out possible cognitive alterations caused by the altered states after trance); c) imagination (participants will be instructed to simulate by imagination in a non-trance state the same perceptual experiences they had during trance), d)meditative-relaxation (participants will be instructed to follow the oral instructions during a relaxation exercise focused on breathing). We expect similar activations at prefrontal and cingulate areas as those reported during psychopathological phenomena as found in dissociative states (Ludascher et al., 2010) and during hallucinations (Allen et al., 2007). Prefrontal areas also plays a key role during meditative states for experienced and naive practitioners (Baron Short et al., 2007). Therefore we hypothesized similar activation at cortical primary sensory areas during trance and imagined states for experts in trance. However a lack or diminished activation at sensory gating and prefrontal areas (cingulated and paracingulate areas) related to self-monitoring for trance states, as during trance there is a lack of voluntary control in comparison to imagined states (Linden et al., 2010). According to Baron Short et al (2007), we also expected that trance experts will show relatively stronger activations in prefrontal areas in comparison to naive participants during meditative states. Experts in trance might need higher self-control to sustain a meditative state apart from trance. Relaxation in meditative states could produce a state vulnerable to transition to trance. Therefore higher self-control might be needed in the trance experts group to keep themselves from getting into trance, this would be reflected in stronger prefrontal activation in the trance group during meditative state and additionally hints to the voluntary control they are able to exert over their trance experiences. In summary, studies using neuroimaging techniques could provide a complementary way to assess normal and altered states of consciousness. This could have relevant clinical implications concerning the neural correlates of psychopathological syndromes.

2) General Objectives (original proposal):

The principal aim of this project is to explore whether there are similarities and differences in functional brain networks during trance, meditative and imagined states to be able to differentiate these states on the basis of their functional brain activation pattern.

We hypothesized similar activation at cortical primary sensory areas during trance and imagined states for experts in trance (visual and auditory cortex). However a lack or diminished activation at sensory gating and prefrontal areas (cingulated and paracingulate areas) related to self-monitoring during trance states, as during trance there is a lack of voluntary control in comparison to imagined states (Linden et al., 2010). According to Baron Short et al (2007), we also expect that trance experts will show relatively stronger activations in prefrontal areas in comparison to naive participants during meditative states. Experts in trance might need higher self-control to sustain a meditative state apart from trance. Relaxation in meditative states could produce a state vulnerable to transition to trance. Therefore higher self-control might be needed in the trance experts group to keep themselves from getting into trance, this would be reflected in stronger prefrontal activation in the trance group during meditative state and additionally hints to the voluntary control they are able to exert over their trance experiences.

Furthermore, this project is designed as first step to establish an international cooperation between researchers from RWTH Aachen, Sao Paulo University and Federal University of Juíz de Fora, the last two in Brazil. Once this first step has been taken the intentions of the group is to enlarge the cooperation, applying for financial support through international agreements between DFG (Germany), CNPq and FAPESP (Brazil) in order to develop new studies and an extensive cooperation in the field of neuroimaging between Aachen and the two universities in Brazil.

3) General Report

Twenty trance experts from the same religious group were contacted in 2011. However during the screening many of them met our exclusion criteria for fMRI [metal parts in body (tooth implant, knee band or tattoo, claustrophobia). During 2012 we get in contact with other 3 religious groups that share the same beliefs and similar approach to get into trance states. We screened 2 more experts in trance; however they also met our exclusion criteria for fMRI. Therefore our final simple was constituted of 8 experts in trance states all coming from the same religious group. Considering the difficulties to find experts in trance within the same kind of religious groups and our preliminary results presented last year, we decided to make some changes to our study design. In order to gain statistical power and nevertheless be able to pursue our original hypotheses in relation to relaxation-meditation state, we decided to create a second group, divided in 2 subgroups – experts and occasional practitioners of meditation (10 participants in each group). We get in contact with more the 50 persons who claimed to practice meditation – some of them practice on daily bases others occasionally. However, it was difficult to find volunteers with interest in take part of the study and/or able to practice their regular method of meditation hearing the scanner noise. Finally we tested 2 volunteers. However the results were not reliable.

In our original design experts in trance should performed 3 different tasks: relaxation-meditation, trance and imagination (control task). In fact our instruction to the relaxation-meditation task is quite similar to fMRI rest state (Gusnard and Raichle, 2001, Greicius et al., 2003, Raichle and Snyder, 2007): the participants were instructed to close their eyes, not focus in any particular content and relax. Therefore, control and trance group performed the same rest task. This procedure turned possible to explore the differences in rest state among experts and naïve subjects in trance states.

We presented the first results of the study at the DGPPN (Deutsche Geselschaft für Psychiatrie, Psychotherapie und Neurologie) in Berlin in 2012 (appendix A). The original paper is also in progress (appendix B).

3.1) Study

3.1.1) Participants

Eight right-handed, healthy participants experts in trance states were recruited from an experienced spiritual group and took part on the study (table 1). Four weeks prior the fMRI session an audio recording of the scanner noise was provided to the participants and they were instructed to trainee getting into trance while exposed to the scanner noise. We choose to introduce this procedure to the experts in trance in order to make them acquainted with the scanner noise during their process of trance self-induction and the timing of the trance condition during the scanner session. In order to test for possible differences concerning rest state between our experts in trance and general population, 5 matched healthy control subjects with no previous experiences in trance states were recruited from the staff of the RWTH University Hospital.

A battery of neuropsychological tests was administered in all participants in order to investigate possible cognitive factors that could influence the performance on the experiment: Wechsler Memory and verbal fluency test (RWT) (Aschenbrenner et al., 2000), working memory task (digit span forward and backward, WMS-R) (Härting et al., 2000), multiple-choice vocabulary test (MWTB), executive function (TMT-A and TMT-B) (Reitan, 1979) and Edinburgh

Inventory of Handedness (Oldfield, 1971). Besides the neuropsychological tests 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).

3.1.2) Experimental setup

All participants were scanned on the Siemens Trio 3 Tesla, located at the Aachen University Hospital, using standard gradients and a circular polarized phase array head coil. The participants were lying in supine position, while head movement were limited by foam padding within the head coil. A block design was used with the following experimental tasks: a) rest: participants were instructed to relax, not focus in any particular content and close their eyes; b) trance: participants were instructed to get into trance state as they do during their religious meetings and they should button press when they were achieving the state; c) mathematical equation: participants performed a sequence of 5 mathematical equations (3 digits each) to wash out possible cognitive alterations caused by the altered states after trance; d) control: the participants were instructed to simulate in a non-trance state the same experiences that they had during trance. Rest, trance and control blocks had 3 minutes length each and 30 seconds prior to the ending a loud sound informed the participants that they should end the task by opening their eyes. Each block was repeated 3 times always in the same order: rest, trance, mathematical equation and control (figure 1). The control group performed only the rest condition.

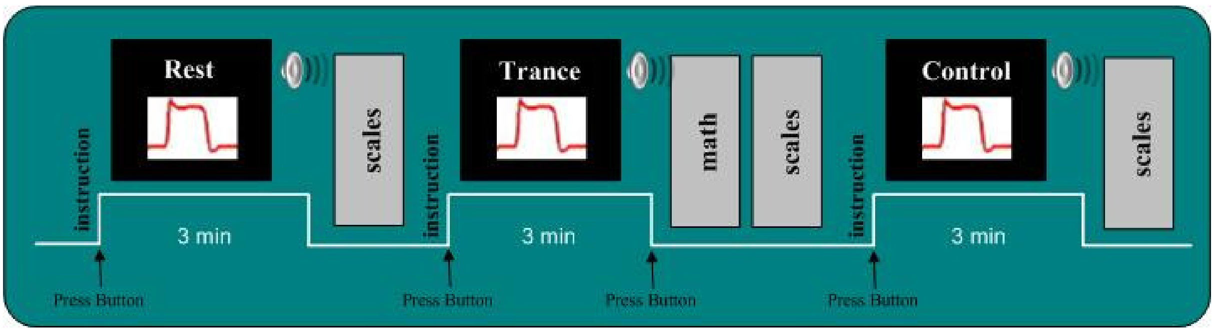

Figure 1: The sequence and duration of each block. Three sessions were performed and the blocks were presented always under the same sequence.

Subjective experiences during the three conditions were assessed by standardized questionnaires PANAS (Positive and Negative Affective Scale; (Watson et al., 1988) and ESR (Emotion Self-Rating; (Weiss et al., 1999, Schneider et al., 2006). In order to acquire relevant information concerning the intensity of the trance state, as well as the vividness of the control condition, we used two different questions after the respective task [trance: 'Concerning your experience, how deep was the trance?'; control: 'how vivid was the imagination?']. The participants should indicate their answer on a scale from 1 (not deep/not vivid) to 5 (very deep/vivid).

Functional scans covered the whole brain, including five initial dummy scans sagittal to the AC/PC line with the following parameters: IG = 0.30 mm; MS = 64 x 64; FOV = 240 x 240 mm; TR = 2.0 s; TE = 28 ms; FA = 77°; 34 slices (thickness: 3.5 mm, gap: 10 %) with a full coverage of the brain (voxel size 3.5 mm x 3.5 mm x 3.5 mm). 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=900ms; IG = 0 mm; FOV = 256 x 256 mm; voxel size = 1 x 1 x 1 mm).

3.1.3) Behavioral and fMRI data analysis

The behavioural statistical data analyses was performed using SPSS 15.0 and the level of significance was set at P = .05. Difference between groups concerning the neuropsychological tests, clinical interviews and scales were assessed using two-sample t-tests.

The fMRI data was analysed with FSL (www.fmrib.ox.ac.uk/fsl/;Smith et al., 2004). The following preprocessing was applied for each participant: head movement correction using MCFLIRT (Jenkinson et al., 2002); nonbrain 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 100 s was applied. All participants's 4D fMRI time series data were transformed into standard space at 2 X 2 X 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 semi-parametric estimation of residuals autocorrelation (Woolrich et al., 2001). A block design was employed using gamma hemodynamic response function (HRF) and 3 contrasts of interest [trance, control, others (scales)] were tested for statistical significance (against the null-hypothesis of zero effect size). Additionally, temporal derivative and movement parameters were also modelled. Finally, a group mean mixed effects Z statistic images were thresholded using clusters determined by $Z > 2.0$ and a corrected cluster significance threshold of $P < .0001$ 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): trance vs baseline (rest), trance vs control, control vs baseline (rest).

We also performed functional connectivity analyses to determine the impact of trance on the following networks: DMN, executive control, attention, visual and auditory systems. 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 it represents an explorative data analyses method that results in a number of spatially independent components which 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)]; 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 task and group were concatenated in three different multi-subject/session ICA: trance and rest task (trance group only), trance and control task (trance group only), rest task (trance and control group). A Pearson's Correlation of the unthresholded group spatial maps between the decomposed components and the RSN maps presented by Smith et al. (2009) was run to identify meaningful and reliably detectable RSNs from the group ICA components.

Finally a dual regression (DR) analyses ($P < .05$) was used in order to estimate significant differences between conditions and subjects (trance vs rest task; trance vs control task; trance group rest vs control group rest task). DR has three stages. First, the concatenated 4D data set is decomposed via ICA to identify patterns of functional connectivity over conditions and subjects. In the second DR step subject-specific temporal dynamics and associated spatial maps are identified within the individual data set. In the last step, the different component maps 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. The resulting contrast maps were corrected for multiple comparison based on the number of IC maps associated to RSNs. A Bonferroni correction was used.

3.2) Results

3.2.1) Behavioral data

We found no significant difference between naïve and experts in trance states concerning the structured clinical interviews and psychopathological scales. In relation to the neuropsychological battery we found a significant difference between experts and naïve participants only at the TMT-A (table 1).

Table 1:Overview on demographical and neuropsychological characteristics of experts and naïve group in trance experience

	Experts	Naïve	*P* values
Demography			
Age	48.88(7.95)	51.2(5.63)	.582
Level of education	12.38(1.5)	13(2.55)	.585
Neuropsychology			
Verbal Intelligence (MWT-B)*	113.29(11.98)	113.8(22.3)	.966
Executive Functions (TMT-A)	23.88 (5.84)	16.14(4.86)	.031
Executive Functions (TMT-B)	49.63(22.42)	41 (14.95)	.466
Word Fluency – lexical	14.5 (3.74)	18.20 (5.45)	.172
Word Fluency – phonemic	15 (4.75)	15.2(6.68)	.951
Working Memory (WMS-R)	14.13(3.56)	16.2 (1.92)	.261
Global Assessment Scale	85.62 (4.95)	82(10.95)	.426
PANSS	34 (2 .2)	34(4.84)	1
Psychopathological Scale	18.29(1.6)	17.8(3.19)	.734

*one participant is a non-German native speaker. Therefore the test was suppressed as it is based on German language skills

Concerning the subjective experiences during the three conditions, the positive scale of PANAS was rated significantly higher for trance than control condition (t (8) = 2.83; P < .025). For the other conditions we found no significant differences [trance and rest condition (t (8) = -.11; P < .912); rest and control condition (t (8) = 1.71; P < .130)]. For the negative scale of PANAS we found no significant difference among all condition [rest versus trance condition (t (8) = -.29; P < .778); rest versus control condition (t(8) = .92; P < .929); trance versus control condition (t(8) = -,737; P < .485)]. In relation to the emotion self-rating scale (ERS), happy was significantly higher rated for trance than control condition (t (8) = 2.39; P < .048) and surprise was significantly higher rated for rest than control condition (t (8) = 2.64; P < .033). No significant differences were found among the other states. In relation to the deepness of the trance state and vividness ratings during trance and control condition, respectively, we found no significant differences among conditions and/or sessions.

After the fMRI measurement a short interview with each participant assessed the qualitative impression of the experiences during trance and control conditions. Almost all participants referred that it was not easy to 're-enact being in trance' because the re-enaction experience were not that vivid as during trance. In qualitative terms, the participants reported varying types of "spiritual contact" and reported feeling inspired during trance and/or being in a semi-conscious state: phrases came to them as if dictated as well as seen themselves "out of their bodies", "seen and/or hearing spirits" (human shape) and had no control over the content "elaborated by the spirit". Although the participants' experiences during trance state are phenomenological similar to dissociation, like delusions, auditory hallucinations and personality changes, they did not score for any mental disorders according to our neuropsychological tests and clinical interview (table 1).

3.2.2) fMRI Data

3.2.2.1) GLM analysis

We found stronger activations for trance in comparison to rest condition in the bilateral occipital pole, left middle temporal gyrus, temporal pole, middle frontal gyrus and frontal orbital cortex (table 2 and figure 2). Likewise we found significant activations for trance in comparison to control condition in the left lateral occipital cortex and posterior cingulate gyrus (table 2 and figure 3).

Table 2: Statistical information of clusters highlighted when comparing the BOLD response of trance and rest task as well as trance and control task

	side	Region	BA	MNI coordinates			*P* values
				X	Y	Z	
Trance > Rest							
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	
Trance > Control							
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	

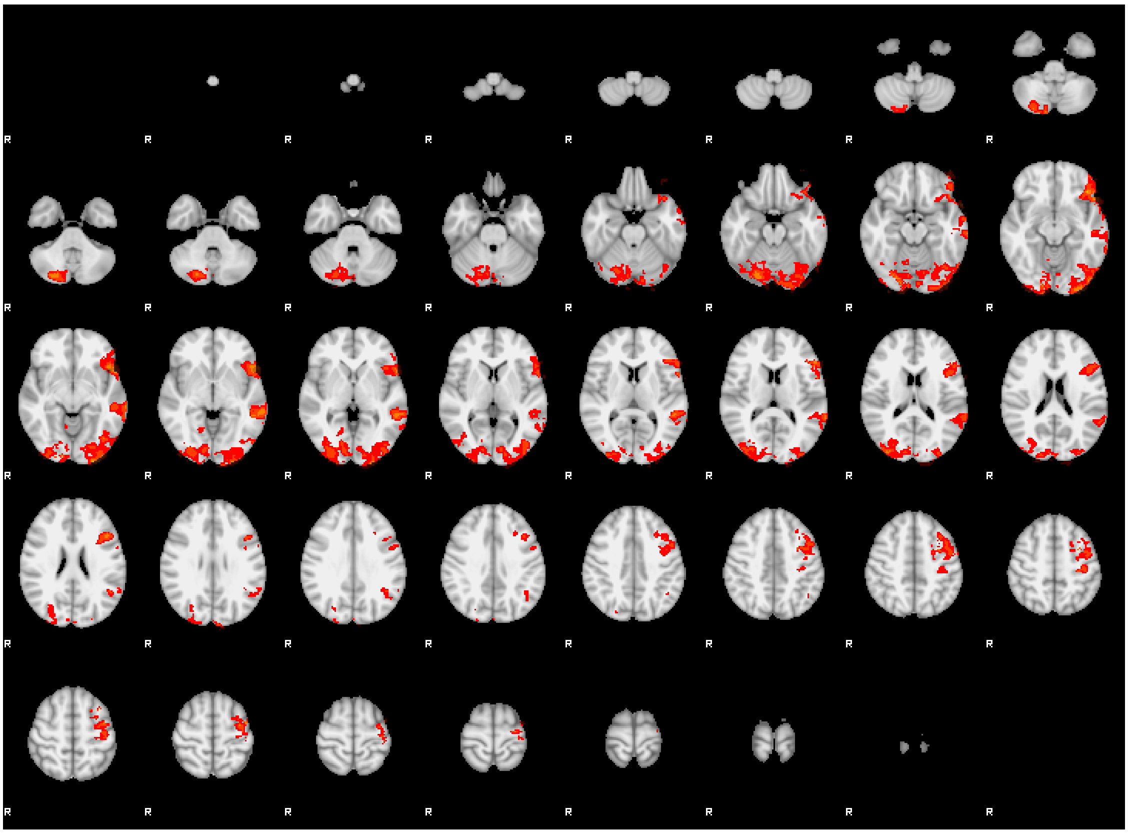

Figure 2 Significant activations for trance versus rest (trance > rest). Voxel coordinates are in MNI atlas space.

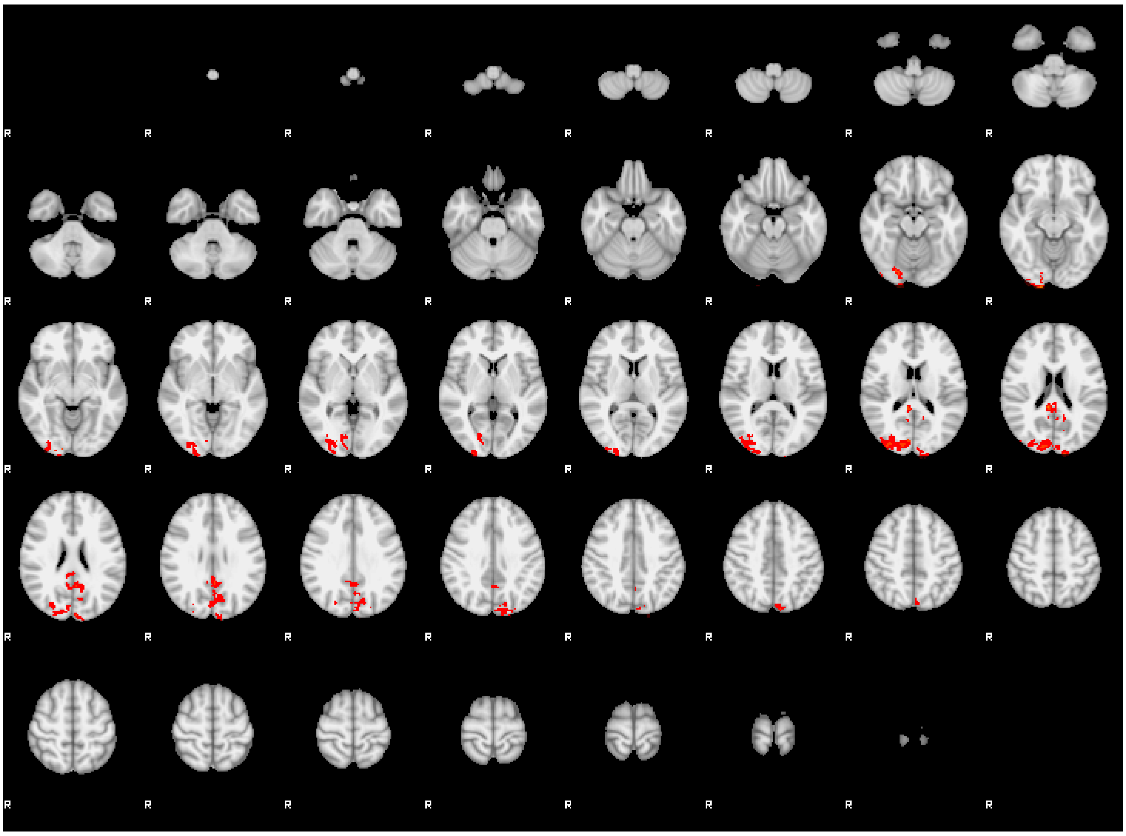

Figure 3. Significant activations for trance versus control (trance > control). Voxel coordinates are in MNI atlas space.

3.2.2.2) ICA Analysis

Our first ICA decompositions were between naïve and experts group during rest condition resulting in 11 ICs. From the 11IC maps generated, 3 maps were paired with 4 RSN maps ($r > .40$): Frontoparietal 2, visual (1 and 3) and default mode network (DMN). However we found no significant differences between groups in the dual regression analyses.

Our second set of maps stem from ICA decompositions between rest and trance condition (expert group) resulting in 16 independent component maps (IC). From the 16 IC maps generated, 5 maps were paired with 6 RSN maps ($r > .40$): visual (1 and 3), frontoparietal 1, sensorimotor, auditory and default mode network (DMN). For the dual regression analysis we found significant differences between trance and rest condition in the IC map 9 correlated with visual network 1 and 3 with stronger activations for rest in comparison to trance condition in the right primary motor cortex (BA4), superior parietal lobule (BA5) and left inferior parietal cortex and primary sensory cortex (BA1). Likewise for the reverse contrast we found stronger activations for trance bilaterally in the insular cortex, right premotor cortex (BA6) and frontal pole and left superior parietal lobule (BA7) and superior frontal gyrus (figure 4).

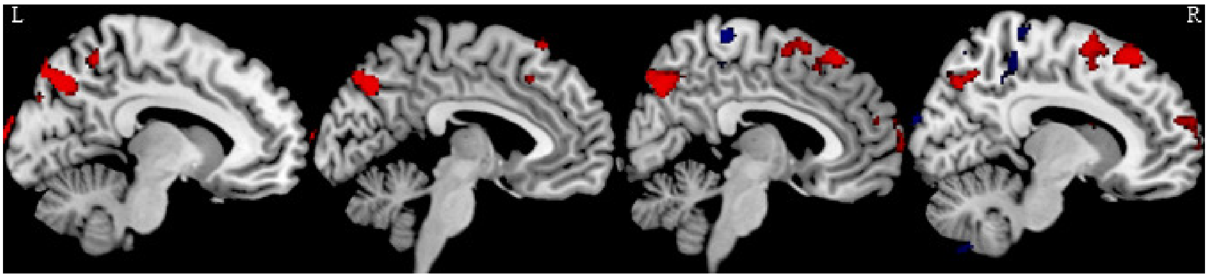

Figure 4. Significant activations rest versus trance (blue: rest > trance) and for trance versus rest (red: trance > rest). Voxel coordinates are in MNI atlas space.

Our final set of maps stem from ICA decompositions between trance and control condition (expert group) resulting in 14 ICs. From the 14 IC maps generated, 2 maps were paired with 2 RSN maps ($r > .40$): auditory and default mode network (DMN). For the dual regression analysis we found significant differences between trance and control condition only in the IC map 7 correlate to the auditory RSN map. We found significant stronger activations for trance in comparison to control condition (trance > control) in the left primary sensory cortex (BA 2 and 3) and primary motor cortex (BA4). On the other hand, we found significant stronger activations for control in comparison to trance condition in the bilateral superior parietal cortex (BA 5) and par operculares (BA 44), as well as right inferior parietal cortex (area Pft), premotor cortex (BA6) and primary sensory cortex (BA2) (figure 5).

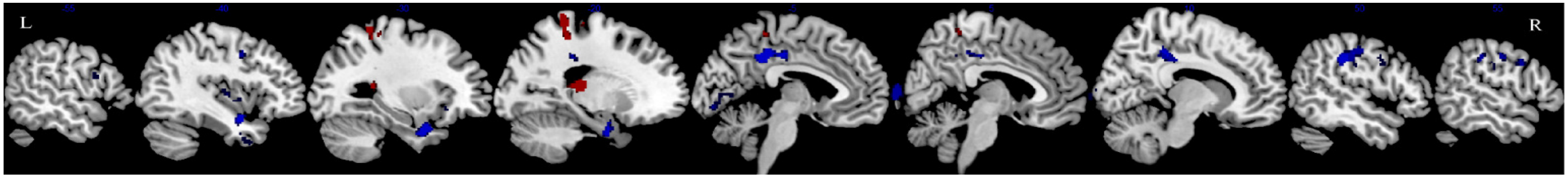

Figure 5. Significant activations for trance versus control (red: trance > control) and control versus trance (blue: control > trance). Voxel coordinates are in MNI atlas space.

3.3) Discussion

Our principal aim was to explore whether there are similarities and differences in functional brain networks during rest, trance and control condition (re-enacting trance state) to be able to differentiate these states on the basis of their functional brain activation pattern. First we demonstrated that cortical areas related to perceptual processing are more involved during trance than rest and control condition. The connections between prefrontal areas, occipital pole, middle temporal and temporal pole might explain why the perceptual experiences during trance states are interpreted as reality since these areas are related to auditory and visual processing. Second we showed intrinsic connectivity differences between trance and the other two conditions in key areas related to hallucinatory states, i.e. parietal e premotor cortex. Finally, we found no differences concerning rest condition between groups (naïve versus experts in trance states) as we hypothesized. This absence of difference in the rest state between groups is in accordance with our behavioral data which shows that the trance experts are mentally health and well adapted into their lives.

In general our results show an increased activation in cortical sensory areas during trance state. The middle temporal gyrus, which contains the auditory cortex, was activated during trance versus rest condition. The middle temporal gyrus is also involved in language comprehension and is suggested to be a key area related to auditory hallucination in psychotic patients (Northoff and Qin, 2011). We also found stronger activation on trance condition in comparison to the other two conditions on structures related to visual processing, i.e. posterior cingulate cortex, occipital cortex, occipital pole and occipital fusiform gyrus. Different studies have shown that visual information is largely processed through two pathways: an object pathway from visual cortex to the temporal cortex (ventral stream) and a spatial pathway to the parietal cortex (dorsal stream). Both paths are functionally connected to the prefrontal cortex (Takahashi et al., 2012). Imaging studies of meditation have generally found increased frontal lobe activity (Wang et al. 2011; Davanger et al., 2010), which is similar to what we observed in our data. Although meditative states do not necessarily involve dissociation and the phenomenological expressions are different compared to mediumship, a recent study suggested that meditation practices improve the efficiency of brain functioning (Kozasa et al., 2012) so the mediums might be able to manage in a different way their attention resources. Taking all together it seems that during trance state important neural areas responsible for perceptual bottom up processes are strongly engaged fitting to the perceptual qualitative description of our participants.

We also found the posterior cingulated cortex (PCC) more engaged during trance condition in comparison to control condition. PCC has been found to be involved in many different social cognitive process [i.e. episodic memory (Szpunar et al., 2009), self-reflection(Northoff and Bermpohl, 2004), mentalizing (Majdandzic et al., 2012) among others] as well as in conscious awareness and it has a pivotal role in certain epilepsy cases and vegetative states (Stillova et al., 2012). PCC is also part of the DMN which is a network consisted found altered in different psychiatric disorders [i.e depression (Zhu et al., 2012); schizophrenia (van der Meer et al., 2012)]. Additionally, in different studies using fMRI-real time technique it has been shown that it is possible to increase posterior cingulated cortex activation by training (Van De Ville et al., 2012, Zhang et al., 2012). Due to its lack of cognitive specificity and profuse connections PCC has been considered the brain hub. We suggest that the involvement of PCC in mediumistic states is related to its profuse connections, modulating the connectivity between frontal and posterior areas of the brain. However, further investigations would be necessary to disentangle the actual role of PCC in non-pathological dissociative states like mediumship.

Intrinsic Connectivity (ICA)

The mediums claimed to achieve the mediumistic state by creating a similar condition as in fMRI rest state: with eyes closed they voluntarily do not fixate their attention in any information (internal or external). FMRI rest state has been defined as the absence of external stimuli and/or attention demanding tasks. In general it is assumed that when the brain is not engaged in a specific attention-demanding or stimulus dependent task, it switches gears into a default mode of stimulus-independent thought that is detached from the external environment and is characterized by mental explorations based on personal introspection, autobiographical memories and thoughts of the future (Buckner et al., 2008). Although rest and mediumistic approaches share some similarities, they are radically different concerning the subjective experience of cognitive mental control. The key difference between both is that during rest the subjects permit themselves to engage in mental explorations based on personal introspection, autobiographical memories and thoughts of the future while during trance they intentionally avoid this kind of process.

In general we observed increased connectivity within the regions of visual and auditory resting state networks (RSN; Smith et al., 2009) for mediumistic state compared to rest and re-enaction of medumistic state. The DMN was identified in all conditions and in the comparison between conditions. However, contrary to our expectations, we found no variation in the connectivity within the regions of DMN among the conditions (mediumistic vs rest; mediumistic vs re-enaction). Moreover, in the comparison between mediums and matched controls both in the rest condition, DMN was also identified but we found no significant differences in the DMN functional connectivity between groups. This data indicates that the functional connectivity within DMN is preserved during rest and mediumistic states, suggesting that the dissociative characteristics presented in mediumistic state are not related to alterations in the DMN. The different effects of DMN on pathological and non-pathological dissociative and hallucinatory states have not been yet fully explored. Currently there are some hints in the literature concerning the effects of rest state networks in verbal hallucination. Northoff and Qin (2011) proposed an explanation for the verbal auditory hallucinations suggesting that the alterated functional connectivity of the DMN interacts with the aberrant activation of the auditory cortex presented in patients with auditory verbal hallucinations. Rotarska-Jagiela et al. (2010) investigated brain rest state in 16 paranoid schizophrenic patients and matched controls. The results show that schizophrenia patients present an aberrant functional connectivity in the default-mode network, which correlated with severity of hallucinations and delusions. Furthermore, the severity of positive symptoms correlated with functional connectivity of fronto-temporal and auditory networks. They also found decreased connectivity in the DMN, including posterior cingulate cortex and hippocampus. In our study, the mediums referred 'seeing and hearing spirits' during the mediumistic trance (see the results section). We found increased functional connectivity in visual and auditory networks during trance but no alterations in DMN. We suggest that the preserved functional connectivity within the DMN regions might be responsible for the absence of pathological dissociative and hallucinatory states between the mediums. However our results are not conclusive and further investigations on mediumistic states compared to pathological delusions and hallucinatory states or drug induce temporary dissociation (psychoactive drugs) would provide more evidences to disentangle the effects of DMN in pathological and non-pathological dissociative and hallucinatory states.

Another important variable to consider in the context of our study is training effects. Peres et al (2012) found that the experienced mediums show lower brain activity during mediumistic state; similar effects were also found in experienced meditators (Pagnoni et al., 2008) and also the meditation training improves brain functions (Kozasa et al., 2008, Kozasa et al., 2012, Sato et al., 2012). Due to the size of our simple we were not able to explore the effects of training. However, the mediums and the director of the spiritual group reported that according to their experience consistent and regular use of the mediumship capacities helps the mediums to get into deeper and stable mediumistic states.

4) **Research Group Meeting in Aachen**

The visit from Prof. Dr. Moreira de Almeida and Dr. Peres in Aachen last January was very fruitful. While their visit, work meetings and talks were planned and they were able to visit our neuroimaging research center facilities and also the whole psychiatric services of the Aachen University Hospital as well as getting in contact with other professors and researcher from the department. Prof. Moreira de Almeira presented a talk 'Scientific Studies of Spiritual Experiences: Exploring the Relationship between Brain, Mind and Soul' based on his book (Moreira-Almeida and Santos, 2012). Dr. Peres gave two talks: one in the IRTG International Graduate School (in cooperation with the University of Pennsylvania - USA) entitle 'Neuroimaging Studies about Spirituality and Trance: Methodological Challenges' and a second one 'Neuroimaging Studies about Posttraumatic Stress Disorder (PTSD)' to the fMRI Group (a meeting where researchers, physicians and students who have interest in fMRI methods take part). During our work meetings news ideas for future research in the field were discussed as well as possible funding to support not just research but also exchanges of students and professors from both countries in order to share expertise about spirituality and mental health in the field of neuroscience.

Currently Prof. Dr. Moreira de Almeida and Ms. Mainieri are planning to develop of a new neuroimaging center at the Federal University of Juiz de Fora (UFJF). Prof. Dr. Habel, Prof. Dr. Dr. Schneider and Prof. Dr. Dr. Mathiak are supporting the initiative sharing their expertise and experience in the field. Prof. Dr. Moreira-Almeida was invited by Prof. Dr. Dr. Schneider to come back to Aachen and perform a workshop about mental health and spirituality which will take place during the second semester of 2013. Likewise, Prof. Dr. Habel is planning to visit UFJF in order to acquire more familiarity with the phenomena of mediumship and the current investigations in the field of spirituality and mental health developed by NUPES (Núcleo de Pesquisa em Espiritualidade e Saúde). Prof. Dr. Moreira de Almeida and Prof. Dr. Habel have both recently received the Theodore-Kármán Fellowship from the RWTH Aachen University to support both visits .

6) Conclusions and future steps

The principal aim of this project was to explore whether there are similarities and differences in functional brain networks during trance, rest and imagined states to be able to differentiate these states on the basis of their functional brain activation pattern. Our results suggest activation at cortical primary sensory areas during trance (visual and auditory cortex) as we predicted. However, we do not find lack or diminished activation at sensory gating and prefrontal areas (cingulated and paracingulate areas) during trance states; on the contrary, it seems that ACC is more strongly involved in trance states. This is the first fMRI study about trance states and we are currently submitting our paper to publication. Larger sample sizes to draw more specific hypotheses about the dissociative sates comparing healthy participants able to get into trance states and clinical population would be a very valuable contribution to the comprehension of pathological and non-pathological dissociative states.

From a methodological perspective, FSL offers better tools to denoise the data as well as certain tools better suited for the analysis of longer blocks. The decision to change the software package was made concerning our subsequent analysis plan, including the analysis of resting state. The opportunity to take part in a seminar about resting state in Magdeburg (Germany) as well as in the

FSL course in Bristol (UK) helped us to develop more expertise which will be used in our next studies.

The research team has already submitted a new proposal to different funding institutions in order to extend the results from the present study to clinical application. We will implement a novel comparative approach in which we will investigate the neural correlates of working memory in patients who suffer from pathological delusions (schizophrenia) and participants whose Spiritual Experience are not classified as a mental disorder according to DSM-IV-R and ICD-10 (Mediumship).

__________________________________ Aachen, 25 April 2013.

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