

Where the BOLD signal goes when alpha EEG leaves

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Previous studies using simultaneous EEG and fMRI recordings have yielded discrepant results regarding the topography of brain activity in relation to spontaneous power fluctuations in the alpha band of the EEG during eyes-closed rest. Here, we explore several possible explanations for this discrepancy by re-analyzing in detail our previously reported data. Using single subject analyses as a starting point, we found that alpha power decreases are associated with fMRI signal increases that mostly follow two distinct patterns: either ‘visual’ areas in the occipital lobe or ‘attentional’ areas in the frontal and parietal lobe. On examination of the EEG spectra corresponding to these two fMRI patterns, we found greater relative theta power in sessions yielding the ‘visual’ fMRI pattern during alpha desynchronization and greater relative beta power in sessions yielding the ‘attentional’ fMRI pattern. The few sessions that fell into neither pattern featured the overall lowest theta and highest beta power. We conclude that the pattern of brain activation observed during spontaneous power reduction in the alpha band depends on the general level of brain activity as indexed over a broader spectral range in the EEG. Finally, we relate these findings to the concepts of ‘resting state’ and ‘default mode’ and discuss how – as for sleep – EEG-based criteria might be used for staging brain activity during wakefulness.

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Introduction

The functional connotation of the so-called alpha activity, i.e., the predominantly posterior 8–12 Hz oscillations that are the prominent characteristic in the human electroencephalogram (EEG) at eyes-closed rest, has remained in the focus of research

since its initial description by Hans Berger (Berger, 1929). In addition to the classical, posterior rhythm, different types of rhythmic activity in the alpha frequency band (8–12 Hz) have been topographically but also functionally distinguished (Niedermeyer, 1997). The Rolandic ‘mu-rhythm’, for instance, resembles posterior alpha frequency-wise but is linked to sensorimotor function, and the so-called ‘third alpha’, a mid-temporal alphoid rhythm that is usually not detectable on the scalp, may be modified by acoustical stimuli. Most studies, however, have investigated the Berger rhythm and related it to visual function but also to cognitive processing and vigilance (Berger, 1929; Niedermeyer, 1997).

Recently, electroencephalography (EEG) has been combined with functional magnetic resonance imaging (fMRI) to study blood oxygen level-dependent (BOLD) signal changes that are systematically associated with changes in power of the alpha rhythm. In summary, these studies have revealed two significant, but different patterns of brain areas where local activity as indexed by BOLD signal is associated with the power of activity in the alpha band. One pattern is characterized by occipital (and parietal) BOLD signal increases during alpha power decreases (Goldman et al., 2002; Moosmann et al., 2003), the other by respective increases in bilateral frontal and parietal cortices (Laufs et al., 2003a,b). From task-related activation studies, these latter areas are known to be involved in attentional control. While both patterns can claim some intuitive plausibility, it has remained puzzling how different results could be obtained in similar settings. Here, we report our findings from detailed re-analyses of the 22 EEG/fMRI data sets acquired during eyes-closed rest in our previous study.

Materials and methods

Subjects, basic EEG/fMRI analysis

We used the same data as reported in our previous study (Laufs et al., 2003a), and acquisition and post-processing of EEG and

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fMRI involved the same steps as detailed in that report (EEG: BrainAmp MR and Vision Analyzer, Brainproducts, Munich, Germany; fMRI: 1.5 T Siemens Vision, Erlangen, Germany; Statistical Parametric Mapping, SPM, <http://www.fil.ion.ucl.ac.uk/spm>; MATLAB, Mathworks, Inc., Sherborn, MA, USA). Twenty-two sessions were analyzed. Data from one subject that were excluded from our original analysis due to unsatisfactory correction of fMRI-induced EEG artifacts were successfully recovered for the present analysis by using more than one template for artifact subtraction.

All 11 subjects had undergone two 20 min sessions of simultaneous EEG and fMRI during resting wakefulness and no instruction other than to stay awake, keep the eyes closed and avoid moving. We determined the spontaneously fluctuating alpha power time course from the mean of the two occipital EEG leads O1 and O2 (referenced to FCz, 10–10 system, frequency/temporal resolution of short time Fourier Transform: 1 Hz/1 s, sliding average with 33% overlap). We convolved this time course with the hemodynamic response function (HRF). After down sampling to the middle of each image volume acquisition, the resulting time courses served as regressors of interest in a general linear model as implemented in SPM, alongside the six rigid body motion parameters, obtained during realignment, as confounds.

In the re-analysis presented here, we address the following possible intervening variables: effects of study duration, slow and fast alpha power modulations, peak alpha power variance and mean frequency band power.

Effects of study duration

To assess whether alpha power-associated fMRI maps varied systematically with time, the following analyses were performed based on individual session models (outlined above): (i) all pairs of subject sessions were analyzed together in a fixed effects and a second level random effects group analysis in which a linear combination of parameter estimates, reflected by a “contrast image”, from individual session analyses (general linear model) were taken to a second level by performing a voxel-based *t* test (Friston et al., 1999). The *t* test was performed on the contrast images related to the negatively weighted alpha regressor; (ii) all first sessions and 2nd sessions were analyzed separately (each forming one group); (iii) the 1st, 2nd and 3rd of each session were combined in one group each (fixed effects analysis).

Analysis of a temporal shift between EEG alpha power and the hemodynamic response

Convolution of the EEG power time series with the canonical HRF low-pass filters the time series and introduces a delay of approximately 6 s between the alpha power and the predicted hemodynamic response. To rule out that this shift might be decisive about which pattern would be detected, we created a flexible model comprising in parallel 5 regressors for each session convolved with a canonical shape of the HRF but shifted from negative 2 to positive 2 s in 1-s steps. For every session, by means of an *F* contrast (identity matrix across the 5), contrast estimates allowing any linear combination of the [highly correlated] 5 predictors per session were used to derive the estimated hemodynamic response function at every given

voxel as the sum of the products of the parameter estimates and the correspondingly shifted canonical HRF initially used when creating the regressor. At regions of interest (frontal left [−50, 37, 11], frontal right [44, 19, 30], parietal left [−44, −42, 46], parietal right [32, −68, 46], occipital left [−40, −79, −5], occipital right [42, −81, 6], [*x*, *y*, *z*] in mm and Talairach space), these estimated response functions were shifted against the canonical HRF and the correlation coefficients determined.

Power fluctuations within the alpha band

To test for different effects of alpha sub-bands, the 8–12 Hz alpha band was split into two halves, an 8–10 Hz and a 10–12 Hz band. From each band, a regressor was derived, and both were entered into one model as described above. Statistical parametric maps were evaluated for each band separately and for combinations of the two.

Determination of peak alpha frequency variance and mean frequency band power

To characterize the alpha oscillations more, for each 30 s epoch of EEG (in analogy to clinical EEG sleep staging), the peak frequency within the 8–12 Hz alpha band was determined resulting in a time series of the peak alpha frequency over time. Its variance was calculated as the square of its standard deviation. In an analogous fashion, the alpha, theta (4–7 Hz) and beta (13–30 Hz) band power session means (scalars) were calculated by taking the mean of the time series containing the sum of the respective band power values for every epoch.

Calculation of average group spectrograms and maps of alpha topography

To visualize differences between spectrograms of sessions assigned to different groups (see below), mean group spectrograms were calculated by averaging individual spectrograms. To create average group topographical alpha maps, a common average reference was calculated based on data from and for all scalp electrode positions except Fp1, Fp2, TP9, and TP10 which were excluded due to often sub-optimal data quality. Grand average maps

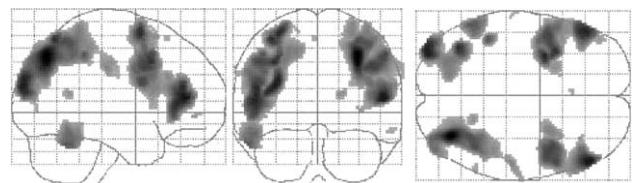


Fig. 1. Correlation of alpha power with fMRI time series leads to robust signal change in bilateral frontal and parietal cortices. Brain areas negatively correlated with alpha band power (i.e., brain areas that activate when alpha power decreases) of 22 sessions (11 subjects) are shown as projections on SPM ‘glass brains’. Statistical parametric maps (SPM{*t*}) are shown for a random effects group analysis ($P < 0.0001$ uncorrected for multiple comparisons). Coordinates [*x*, *y*, *z*] in approximate Talairach Space) and *Z* scores of cluster maxima: frontal left [−50, 37, 11], 5.3), frontal right ([44, 19, 30], 5.5), parietal left [−44, −42, 46], 5.4), parietal right ([32, −68, 46], 5.84).

are based on individual 8–12 Hz power maps normalized for occipital alpha power.

Regression at the second level

To demonstrate the dependency of the observed alpha-associated fMRI maps on neighboring frequency bands, based on the second level group analysis described above, a regression (correlation) was performed by extending the design matrix by two regressors. Corresponding to every contrast image, the respective theta (4–7 Hz) and beta (13–30 Hz) power session means were entered in to the second level regression model as implemented in SPM. This allowed us to test at which typically alpha power-associated voxels the parameter estimates were positively or negatively correlated with theta or beta power, respectively. Once the regressors have been mean-scaled, positive and negative

correlations can be understood as testing for higher and lower power, respectively.

Data-driven approach: eigenimage/principal component analysis

Singular value decomposition (principal component analysis) of the fMRI time series was performed using the multivariate linear models toolbox as implemented in SPM99 (Kherif et al., 2002) after removing the session mean and the variance explained by the realignment parameters. For each subject in the respective analysis, an individual eigenimage analysis was performed. In addition to all eigenvariate (one per image volume), the first 6 spatial modes (eigenimages) were calculated. The one which most resembled the alpha power-associated fMRI map as obtained by the single subject EEG/fMRI analysis was identified by choosing the first in the order of the 6 eigenimages whose corresponding eigenvariate

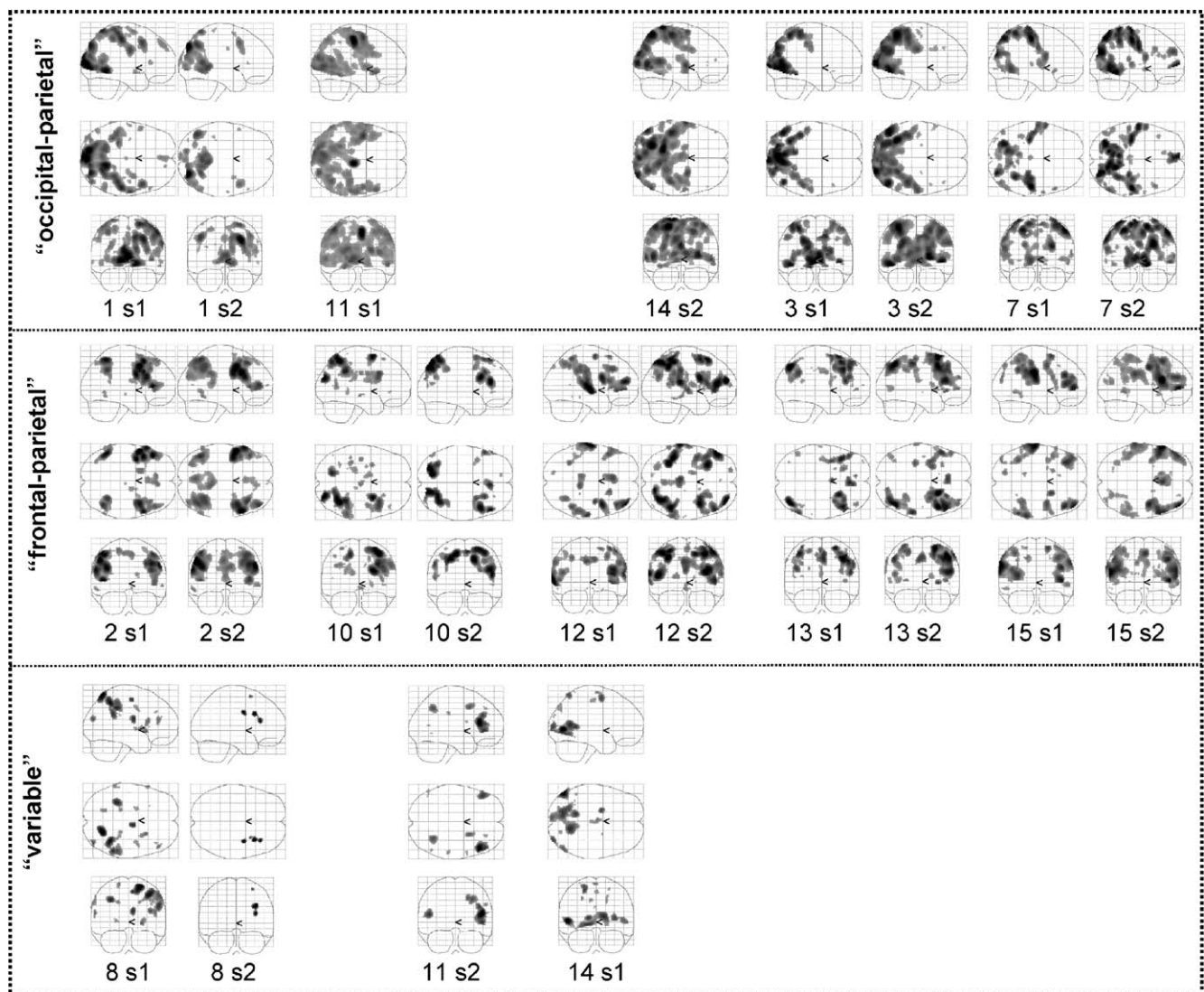


Fig. 2. Individual single session analyses allow visual classification of alpha-correlated deactivations into a “frontal–parietal”, an “occipital–parietal” and a group “variable”. Glass brain projections (compare Fig. 1; labeled with subject ID followed by “s” and session number) of statistical parametric maps of negative correlation between alpha power and BOLD signal for each of two sessions from 11 individual subjects ($P = 0.001$ uncorrected for multiple comparisons). Except for subject 11 and 14, session pairs each fall into the same group. The latter two may remotely resemble the “frontal–parietal” and “occipital–parietal” pattern, respectively.

showed any negative correlation (Pearson's R) with the alpha regressor used in the EEG/fMRI model.

Results

Decreases in alpha power during eyes-closed rest were associated with BOLD signal increases in bilateral frontal and parietal cortices. The reliability and generality of this finding were confirmed in a second level random effects group analysis (Fig. 1). In our previous publication, we analyzed all sessions pair-wise before taking one image per subject to the second level (Laufs et al., 2003a). Here, to account for intrasubject intersession differences, all individual sessions were subjected to the group analysis resulting in a qualitatively the same, but quantitatively slightly different map because of an overestimation of the degrees of freedom.

In spite of this robust result at the group level, visual assessment of the individual maps session by session revealed an occipital–parietal activation in 8 single sessions that was negatively correlated with alpha power and that resembled the pattern reported in other studies (Goldman et al., 2002; Moosmann et al., 2003). Our predominant group result with frontal–parietal activation could be identified in 10 of the single sessions. The remaining 4 individual sessions could not be classified with confidence due to weaker and more variable effects (Fig. 2). Usually, both sessions from each subject showed the same characteristic pattern except for two cases, where in one, the first session showed the “occipital–parietal”, the second a “variable” pattern and in the other vice versa.

Inspection of the single session results suggested that both patterns, the occipital–parietal and the frontal–parietal one, were present in our data set. They appeared to be distinct rather than forming a continuum. We therefore sought to identify further variables that might account for why some sessions expressed one rather than the other pattern. We found no systematic difference between first and second sessions, nor within sessions when splitting them into three segments (results not shown). Next, we tried to relate these patterns to higher vs. lower peak frequencies in the alpha band, and again found no explanation but that both the frontal–parietal and the occipital–parietal pattern were associated with the upper alpha sub-band (10–12 Hz, Fig. 3). Previously, we had tested whether different modulation frequencies of alpha power accounted for different topographical patterns and learned that the power modulations of the alpha band accounting for the negative correlation with brain BOLD activity are in a very low frequency range (Laufs et al., 2003a).

This is in accord with the observation that the exact time delay between the alpha power time series and the BOLD signal is not crucial. In fact, we found that the estimated hemodynamic responses at frontal, parietal and occipital regions of interest peaked around 2 s later than the canonical HRF (Fig. 4). This delay was region of interest-specific and was more pronounced at occipital regions, but did not distinguish between sessions showing the occipital– and the frontal–parietal fMRI pattern. Convolution of the EEG regressor with only the canonical HRF allowed to detect both occipital– and frontal–parietal regions (Fig. 2). Because of the observed intrasubject, intersession differences, we then hypothesized that different brain states might be responsible

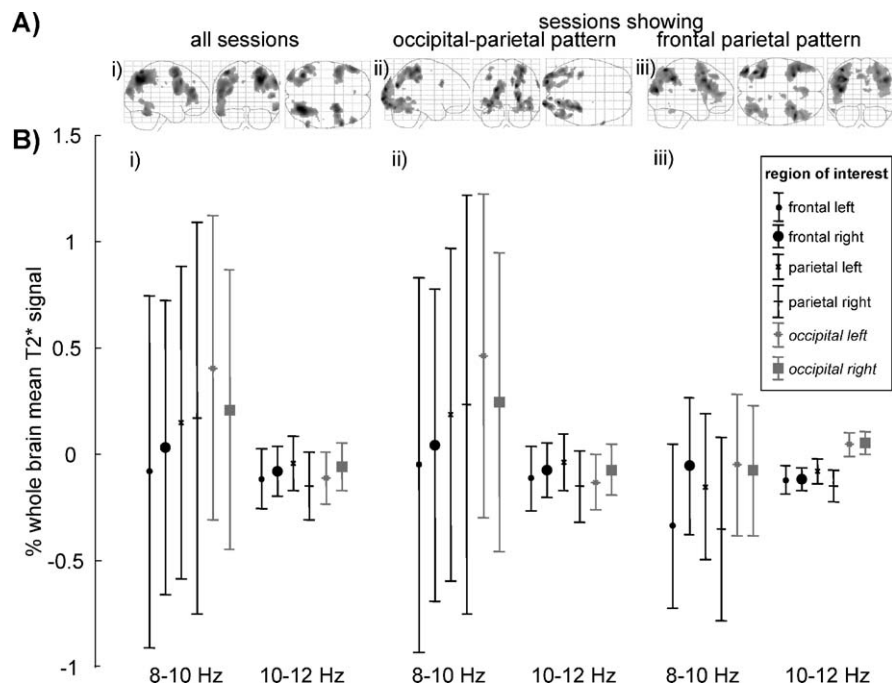


Fig. 3. Not low (8–10 Hz) but high (10–12 Hz) alpha band power is correlated with occipital–parietal and frontal–parietal BOLD signal changes. (A) Statistical parametric maps for BOLD signal changes negatively correlated with the high alpha band: random effects analyses ($P < 0.001$, uncorrected) of all 22 sessions (i) and those showing an occipital–parietal (ii) or frontal–parietal (iii) pattern with 8–12 Hz (compare Fig. 2); 8–10/10–12 Hz regressors were part of one fixed effects model. (B) Average parameter estimates with 90% confidence intervals for both low (8–10 Hz) and high (10–12 Hz) alpha band power for regions of interest, left and right frontal and parietal cluster maxima, respectively (compare Fig. 1) and – in light gray – occipital maxima ([42, –81, 6], [–40, –79, –5]) (compare A, ii). (i–iii) Same sessions as in panel A. Note narrower confidence intervals for high alpha band and generally negative means except for the occipital regions of interest in subjects showing the frontal–parietal pattern (iii).

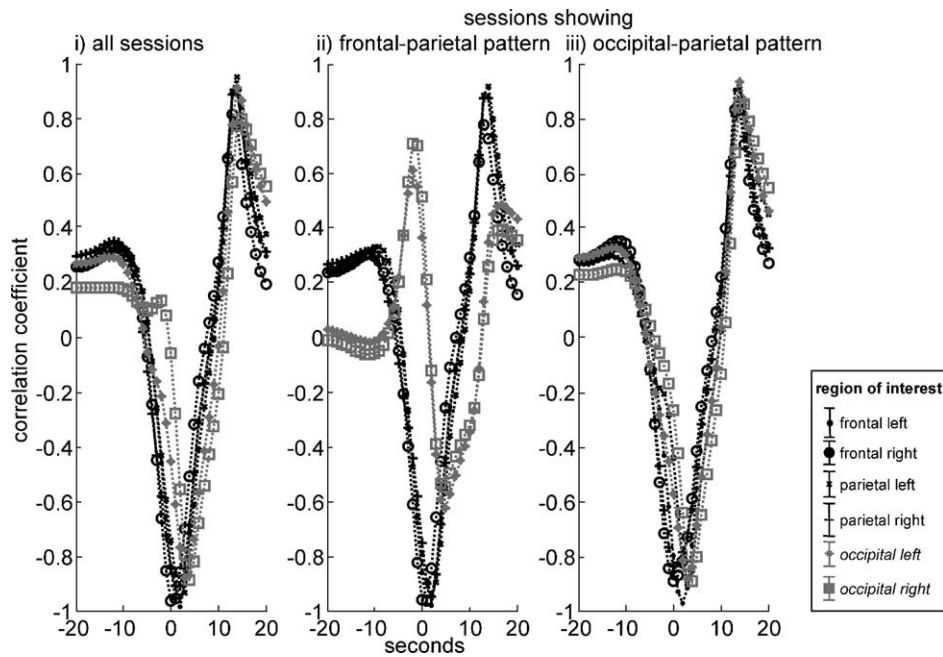


Fig. 4. A delay of the peak of the hemodynamic response to alpha power compared to the canonical hemodynamic response (HRF) is region of interest-specific but does not distinguish between the frontal- and the occipital-parietal fMRI patterns. Cross-correlation coefficients of the canonical HRF (as provided by SPM, peak at 6 s) shifted against estimated HRF at regions of interest (compare Materials and methods and Fig. 3 for coordinates; 0 s indicates no shift) for (i) all sessions (mean peak delay with respect to the canonical HRF at frontal and parietal regions): 1.5 ± 1 s excluding occipital regions (2.2 ± 1.3 s including occipital regions); at occipital regions 3.5 ± 2 s; (ii) sessions showing a frontal-parietal pattern at frontal and parietal regions: 1.75 ± 0.5 s excluding occipital regions (2.8 ± 1.7 s including occipital regions); at occipital regions 4.2 ± 2.7 s; (iii) sessions showing an occipital-parietal pattern at frontal and parietal regions: 1.25 ± 1.5 s excluding occipital regions (2.0 ± 1.7 s including occipital regions); at occipital regions 3.25 ± 2.5 s. Note: (1) The positive peaks reflect autocorrelation (peak at 11.5 s for the canonical HRF). (2) While the occipital regions of interest are only part of the occipital-parietal pattern as reflected by the ‘distorted’ graph (light gray, (i) and (ii)), the parietal – but also the frontal – regions of interest also show correlation with alpha power in sessions showing the occipital-parietal pattern (compare Fig. 2 and random effects group results, Fig. 1).

for the different alpha-related maps, in particular different states of vigilance. We therefore explored spectral content of the related EEG recordings beyond the alpha range. There was a significant difference between the session mean alpha power amplitudes. The group “occipital-parietal” had the lowest and the group “variable” the highest alpha power. More importantly, accounting for this absolute difference, we found that, in sessions where alpha power had been negatively correlated with occipital brain activity, the ratio of theta (4–7 Hz) over alpha (8–12 Hz) power was significantly higher than in sessions showing the “frontal-parietal” pattern (Fig. 5A, Table 1). Similarly, 13–16 (13–30) Hz beta power was significantly lower in the “occipital-parietal” vs. the “frontal-parietal” group, while a higher variance of the peak alpha frequency was observed in the former compared to the latter (Table 1). The sample size of the group with variable activation patterns (“variable”) was too small to perform reliable statistics. A summary fMRI map for each group was created based on the thresholded voxel-wise variance across the individual sessions’ ‘alpha maps’ (Fig. 5B). Alpha power topographical maps revealed a relatively higher frontal alpha distribution in the “occipital-parietal” compared to the “frontal-parietal” group, while in the “variable” group, a more central emphasis for alpha could be observed (Fig. 6).

To establish a link between this difference in EEG spectral properties and the fMRI data, we performed a regression analysis at the second level. Testing for a low beta and high theta content across all 22 sessions revealed bilateral occipital and parietal areas (Fig. 7A), whereas testing for a high beta and

low theta content showed bilateral frontal and parietal areas (Fig. 7B). This established the dependency of the different alpha-related fMRI patterns on theta and beta frequency power at the group level.

Eigenimage analysis (PCA)

As our findings had suggested the existence of two distinct patterns in relation to alpha power decreases and theta and beta EEG spectral content, we applied principal component analysis to our data set. Eigenimage analyses of all sessions revealed two distinct patterns corresponding to the two clusters of brain regions that changed their activity in relation to alpha power (Fig. 8, Table 2). Although not every session contained both cluster types, “visual” as well as “attentional” patterns could be found across most sessions. For seven out of eight sessions forming the “occipital-parietal” group, an eigenimage could be identified that resembled the statistical parametric map related to alpha power (Table 2). Similarly, 8 out of 10 eigenimages were identified in the “frontal-parietal” group (Table 2). The two identified spatial modes did not differ significantly in their correlation with the alpha regressor (-0.3 vs. -0.24 , see Table 2), but – whenever present – the eigenimages associated with the “occipital-parietal” alpha signature explained significantly more variance in the data (Table 2). In the “occipital-parietal” group, we also found eigenimages showing the “frontal-parietal” pattern (Fig. 8), but not vice versa. These eigenimages with frontal-parietal patterns were always lower in rank and explained less variance. Finally,

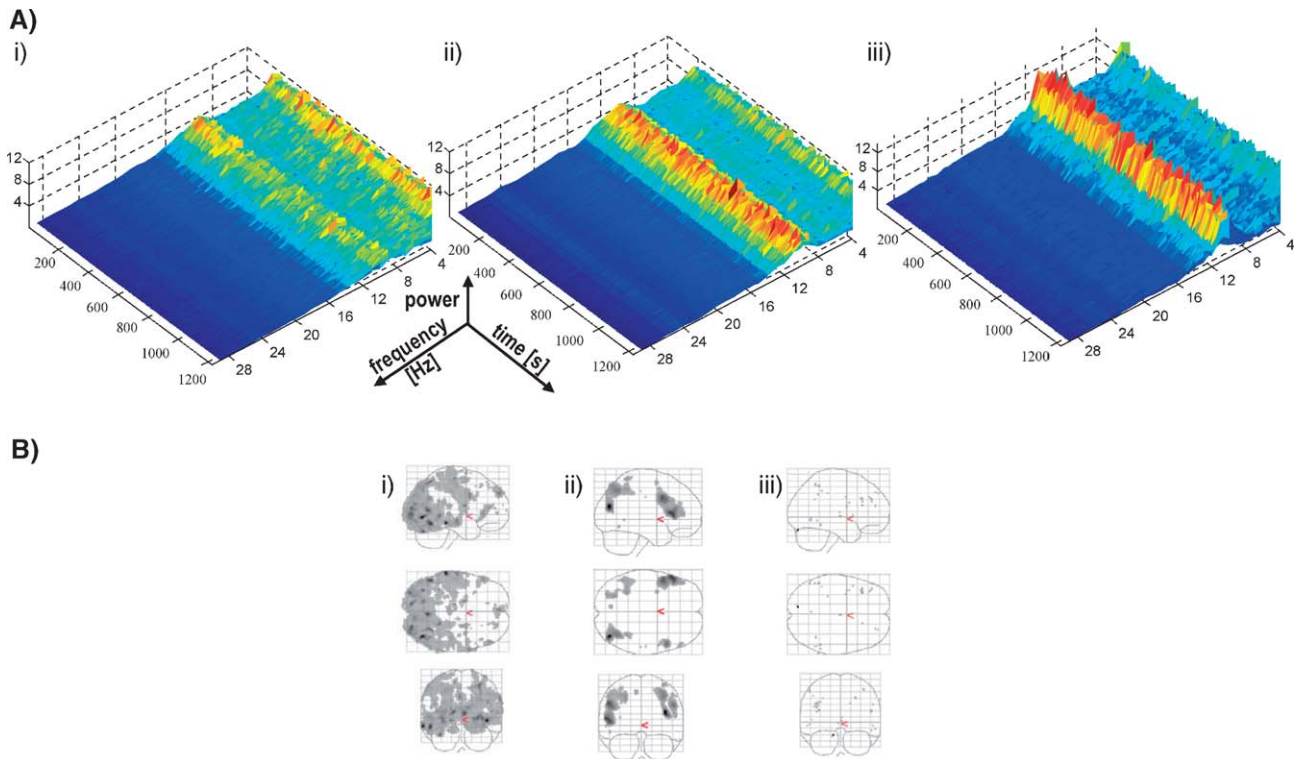


Fig. 5. Summary maps of individual sessions categorized into three groups differing both in their spectrograms (A) and fMRI pattern (B). (A) Mean normalized spectrograms corresponding to sessions grouped as: (i) “occipital–parietal”, (ii) “frontal–parietal”, (iii) “variable”. Normalized power is given in arbitrary units. (B) Brain areas negatively correlated with alpha band power (i.e., brain areas that activate when alpha power decreases) are shown as projections on SPM ‘glass brains’ (compare Fig. 1). Statistical parametric maps are thresholded at $P < 0.001$, uncorrected. (i) 8 sessions categorized as “occipital–parietal”, (ii) 10 sessions as “frontal–parietal”, (iii) 4 sessions as “variable”.

two sessions of the “variable” group showed eigenimages resembling the “frontal–parietal”, and one in addition the “occipital–parietal” pattern (Table 2).

Discussion

Three studies so far have investigated the correlation of BOLD signal and alpha band power on EEG during task-free, eyes-closed rest (Goldman et al., 2002; Laufs et al., 2003a; Moosmann et al.,

2003). The topography of BOLD signal increases during spontaneous 8–12 Hz alpha desynchronization has been controversial, with two studies mapping this effect mainly to the occipital lobe (Goldman et al., 2002; Moosmann et al., 2003) and our previous study observing signal changes centered in frontal and parietal cortices (Laufs et al., 2003a). Occipital deactivation was discussed as a result of synchronization and ‘idling’ of cortex or alternatively as linked to other functionally coupled processes, including vigilance (Moosmann et al., 2003). We interpreted the frontal–parietal activity, which increases as alpha power decreases in

Table 1
Group characteristics and statistical comparison of alpha, theta and beta EEG frequency content and heart rate

	A: occipital–parietal	B: frontal–parietal	C: variable	<i>t</i> test A vs. B
Number of sessions in group	8	10	4	
8–12 Hz alpha power mean	5.709 μV^2	13.061 μV^2	22.659 μV^2	<i>0.006</i>
8–12 Hz alpha power variance	0.924 μV^2	2.065 μV^2	3.165 μV^2	<i>0.011</i>
4–7 Hz theta power mean	4.808 μV^2	4.952 μV^2	5.962 μV^2	0.409
4–7 Hz theta power variance	0.753 μV^2	0.732 μV^2	0.883 μV^2	0.235
13–16 Hz beta power mean	1.36 μV^2	2.133 μV^2	3.42 μV^2	<i>0.02</i>
13–16 Hz beta power variance	0.26 μV^2	0.301 μV^2	0.40 μV^2	0.22
13–30 Hz beta power mean	0.39 μV^2	0.79 μV^2	1.09 μV^2	<i>0.02</i>
13–30 Hz beta power variance	0.10 μV^2	0.16 μV^2	0.21 μV^2	0.06
Mean theta power/mean alpha power	0.952	0.683	0.219	<i>0.001</i>
Alpha band peak frequency mean	9.95 Hz	10.22 Hz	10.48 Hz	0.181
Alpha band peak frequency variance	0.98 Hz	0.60 Hz	0.45 Hz	<i>0.005</i>
Heart rate mean	54.3/min	58.4/min	63.6/min	0.168

P values (right column) are printed in italics if below 0.05.

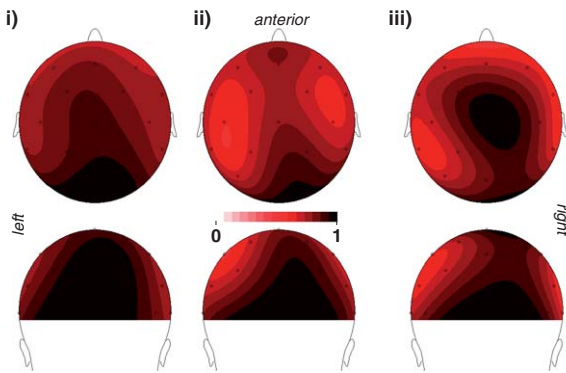


Fig. 6. Spatial distribution of alpha power. Grand average maps of 8–12 Hz power (normalized for O1/O2) distribution of the session averages of subjects grouped as (i) “occipital–parietal” (8 sessions), (ii) “frontal–parietal” (10 sessions), (iii) “variable” (4 sessions) based on fMRI maps. A common average reference was calculated based on data from and for all scalp electrode positions except Fp1, Fp2, TP9, TP10 (international 10–10 system) which were excluded due to often sub-optimal data quality (electrode positions indicated by tiny circles, interpolation by spherical splines; top (row one) and back view (row two)). In (i), relatively high alpha power extends to anterior compared with posterior regions, and in (ii) shows a different power gradient with less anterior alpha in lateral frontal regions, and in (iii), similar alpha power appears in occipital and central regions, declining towards the front and the sides.

relation to spontaneous fluctuations of attention (Laufs et al., 2003a). Here, we reanalyzed 22 EEG/fMRI sessions and found not only that both patterns could be identified in our data set but also that spectral EEG indices accounted for the prevalence of one over the other on a session-by-session basis.

While Moosmann et al. for the main part of their study used both the same MRI scanner and the same MR compatible EEG with the same reference as we did, the experimental set-up differed more for the Goldman et al. study. Nevertheless, those two studies produced similar results (Goldman et al., 2002; Moosmann et al., 2003). Our re-analysis allowed us to affirm that, in individual subjects, we could also obtain comparable results. This makes it unlikely that for instance the use of different EPI sequences or wavelet (Moosmann et al., 2003) vs. short time Fourier analysis of alpha oscillations led to discrepant results.

We also directly tested in our data set yet another hypothesis pertaining to differences in methodologies across these studies. Discrepant results might have been caused by different session lengths. Goldman et al. (2002) studied their subjects for 4.5 min or a breakdown of 9 min, whereas Moosmann et al. (2003) performed one 50 min and one 25 min session. Probing our data for such duration-dependent effects, we found no evidence in favor of this hypothesis. Finally, the average delay of the estimated BOLD response with respect to a canonical HRF (SPM) in our experiment (8.2 ± 1.3 s) was very similar to that determined by Moosmann et al. using NIRS (8.7 ± 2.5 s). This delay varied across regions of interest but did not distinguish between the occipital–parietal and the frontal–parietal pattern. Just like that of Moosmann, which by convolution with the canonical HRF (SPM) detected the occipital–parietal set, our model was sensitive to detect both sets of regions probably because low temporal frequency components of the spontaneous power fluctuations account for the correlation with BOLD signal (Laufs et al., 2003a; Leopold et al., 2003).

Varying experimental set-ups might potentially induce different cognitive states. Previous work has suggested that differences in

cognitive function are associated with frequency shifts between different alpha sub-bands (Petsche et al., 1997; Fink et al., 2005). We tested for such effects in our data but found that the different fMRI deactivation patterns associated with alpha power were both obtained predominantly in correlation with alpha activity in the high (10–12 Hz) alpha sub-band.

Still, we speculated that different resting brain states had dominated the study groups in the three published experiments. We therefore reanalyzed our findings on a session-by-session basis and found that even within our data set both aforementioned fMRI patterns and thus presumably both resting brain states that are associated with alpha desynchronization could be identified. Individual sessions were usually dominated by either one or the other of these two patterns. In a study of rest, we inevitably lacked behavioral parameters to discriminate the functional significance of these two patterns but instead investigated in more detail the spectral EEG content of individual sessions. In particular, in the absence of any ongoing ‘activation’ paradigm, we hypothesized to find characteristics of different brain states reflecting fluctuations in vigilance levels.

Different brain states

In addition to the alpha band, we determined oscillatory activity in the neighboring theta and beta bands. Theta oscillations are a prominent feature of the normal background EEG in the young population but are generally an indicator for reduced vigilance and early sleep stages in the adult population (Rechtschaffen and Kales, 1968; Himanen and Hasan, 2000). Age was not significantly different between the occipital–parietal and the frontal–parietal subjects (and in fact, sessions of the same subject could even fall into different groups, compare Fig. 2). We hence assessed theta power and its relation to alpha power to test whether the occurrence of different fMRI patterns during alpha desynchronization could be related to differences in vigilance. Aside from an increase in slower frequencies with decreasing vigilance (Loomis et al., 1935), slowing and thus increased variability of the alpha peak frequency is another indicator of decreasing vigilance (Ota et al., 1996). The

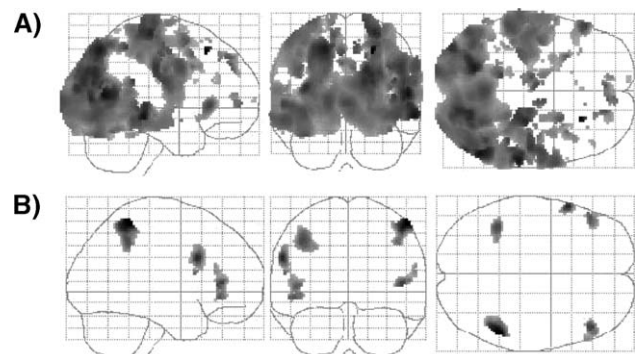


Fig. 7. Alpha power-associated deactivations in occipital–parietal regions are typical for high theta and less beta EEG frequency content (A), while alpha deactivations in frontal–parietal brain regions are typical for high beta and less theta power (B). A regression analysis was performed for all 22 sessions at the second level between the mean theta and beta power for each session and the respective “alpha deactivation maps” (negative contrast images corresponding to the HRF-convolved alpha regressor, see Fig. 2). An inclusive mask was applied, created by adding the binarized, thresholded summary maps as displayed in Fig. 5B, and results were thresholded at $P < 0.05$ uncorrected.

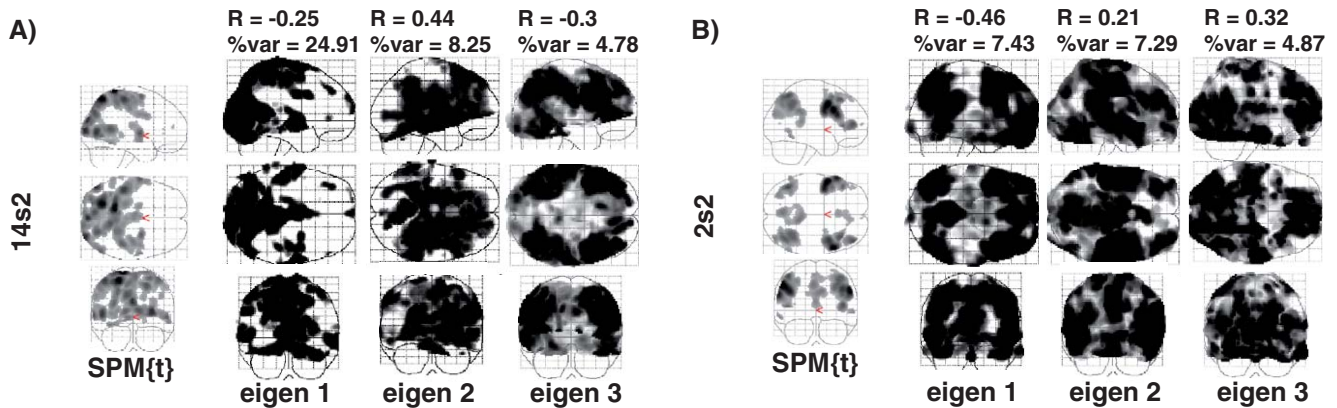


Fig. 8. Eigenimage examples for one session showing activations in occipital–parietal cortices with decreasing 8–12 Hz alpha power (A) and one showing respective bilateral frontal and parietal activations (B). SPM{t} indicates the statistical parametric maps as obtained by the general linear model SPM analysis (compare subjects with ID 14s2 and 2s2 in Fig. 2, respectively). eigen 1, 2 and 3 indicate the first three spatial nodes (eigenimages). In panels A and B, eigen 1 was judged to show the highest resemblance with the SPM{t}. *R*: Pearson's correlation between the alpha regressor used to obtain the SPM{t} and the eigenvariate of the respective spatial mode (negative values reflect inverse relationship between alpha power and BOLD signal changes); %var: percent variance explained by the respective spatial mode. Note that in panel A, the eigenvariate corresponding to eigenimage 3 is highly correlated with the alpha regressor in association with a bilateral frontal and parietal pattern. The variance explained by eigen 3, however, is much lower.

mean amplitude of the alpha power peak in the “occipital–parietal” group was significantly lower than that in the “frontal–parietal” group, and the variance of the peak alpha frequency was significantly higher in the “occipital–parietal” group than in the “frontal–parietal” group (Table 1). Finally, there were significantly more oscillations faster than alpha in the “frontal–parietal” group than the “occipital–parietal”. There was a trend of an increasing mean heart rate from the “occipital–frontal” over the “frontal–parietal” to the “variable” group (Table 1). Together, these findings are best accounted for by different vigilance levels.

In this context, it is noteworthy that in the Goldman et al. study only selected epochs were analyzed. To be included, these had to exceed a certain ratio of the epoch's standard deviation over the average alpha power. Given a constant standard deviation (numerator), a relatively low average alpha power (denominator) will facilitate meeting the threshold criterion, which might have biased their analysis towards one brain state. It is also conceivable that session lengths of up to 50 min (Moosmann et al., 2003) resulted in overall lower levels of vigilance. Finally, topographically, posterior alpha present during the awake state shifts more anteriorly with decreasing vigilance (Zschocke, 1995). Both Moosmann's and our choice of the reference (FCz) facilitated sensitivity to frontal alpha power. In fact, the average alpha topography of those individual sessions showing an occipital–parietal pattern reflected a relatively higher anterior alpha prominence than that of the other groups (Fig. 6). This would be in keeping with a potential reduction in vigilance in those subjects—although a pure trait effect could also explain this observation.

A solution: linking broader EEG spectral content to BOLD data

By complementing the information from alpha power with that from the theta and beta bands of the EEG spectrum, we found that these neighboring frequency bands enabled us to dissect the BOLD activation maps associated with alpha power decreases: the “occipital–parietal” could be distinguished from the “frontal–parietal” pattern when pooling all 22 sessions in one second level

group analysis and performing a regression with each session's mean theta and beta power content. When mean beta was high and theta power low, the frontal–parietal pattern was revealed, and vice-versa the occipital–parietal pattern (Fig. 7).

Recently, Kilner et al. proposed a ‘heuristic’ linking EEG to hemodynamic measures. Stated simply, BOLD deactivations were speculated to be associated with a shift in the EEG spectral profile to lower frequencies, and BOLD activations with a shift in the opposite direction (Kilner et al., 2005). With alpha power dominating the spectrum (Fig. 5A), this is in line with our prominent alpha-associated BOLD deactivations with an increasing theta/alpha ratio while they cease when the latter ratio decreases and the beta/alpha ratio increases (Table 1, Fig. 7).

A different perspective on BOLD signal decreases associated with alpha power

Based on the observation that alpha is the prominent rhythm during relaxed wakefulness (Berger, 1929), we propose the following perspective on the relation between EEG alpha activity and the topography of associated brain activity changes. Brain areas that are less active during high alpha power – in reverse – are more active during epochs of decreased alpha power (Pfurtscheller et al., 1996). In other words, associated with higher alpha power, we identify brain areas that have been active ‘before’ and ‘after’ epochs of higher alpha power. The intermittent epochs of high alpha power can be seen as an intermediate state, or baseline, between states of either higher degrees of vigilance and activity (characterized by low theta power) or states characterized by lower degrees of vigilance and activity (high theta power) (Loomis et al., 1935, 1937; Kinnari et al., 2000). Hence, it is conceivable to find different topographies of activations when the ‘resting alpha state’ is left, namely as a function of the direction of this change. Cantero and colleagues suggested “that electrophysiological features of human cortical oscillations in the alpha frequency range vary across different behavioral states, as well as within state, reflecting different cerebral phenomena with probably dissimilar functional meaning” (Cantero et al., 2002).

Table 2
Eigenimage analysis results

Subject ID	Eigenimage resembling “occipital–parietal”	Cross-correlation with 8–12 Hz power	% variance explained by eigenimage	Eigenimage resembling “frontal–parietal”	Cross-correlation with 8–12 Hz power	% variance explained by eigenimage
Occipital–parietal						
1s1	2	−0.21	7.96	3	−0.24	5.58
1s2	2	−0.11	7.18	n/a		
3s1	1	−0.03	26.10	n/a	−0.20	5.74
3s2		n/a		n/a	0.38	7.39
7s1	1	−0.36	23.89	n/a		
7s2	1	−0.47	14.72	3		
11s1	1	−0.64	20.22	3		
14s2	1	−0.25	24.91	2	−0.30	4.78
Mean		−0.30	17.85		−0.09	5.87
Frontal–parietal						
2s1	n/a			n/a		
2s2	n/a			1	−0.46	7.43
10s1	n/a			4	−0.23	4.10
10s2	n/a			1	−0.28	8.61
12s1	n/a			3	−0.31	5.57
12s2	n/a			n/a		
13s1	n/a			1	−0.23	7.47
13s2	n/a			1	−0.20	6.62
15s1	n/a			2	−0.11	6.99
15s2	n/a			2	−0.11	8.28
Mean					−0.24	6.88
Variable						
8s1	n/a			3	−0.28	6.36
8s2	n/a			3	0.08	5.34
11s2	n/a			n/a		
14s1	1	−0.09	28.07	3	−0.01	7.32
Mean		−0.09	28.07		−0.07	6.34
Grand mean		−0.27	19.13		−0.17	6.50
Grand <i>t</i> test						
Occipital–parietal vs. frontal–parietal		Cross-correlation with 8–12 Hz			Variance explained	
<i>P</i> value		0.13			0.001	

Among the first six eigenimages, those were identified which matched either the frontal–parietal or the occipital–parietal activation pattern by comparing it with the individual session SPM{t}. The group summary map was used for comparison to identify the pattern if it was not expressed in the individual’s SPM (e.g., “the occipital–parietal” pattern in subjects of the “frontal–parietal” group and vice versa, and both patterns for “variable” subjects). Columns 2 and 5 refer to the rank of the eigenimage, columns 3 and 6 to Pearson’s *R* between the respective eigenvariables and the alpha power regressor.

In summary, we have identified within a single data set two different modes of brain activity to which the brain can move from baseline alpha activity. This reconciles our findings with those obtained in other studies and moreover suggests the mechanisms that can account for this variability. We found one pattern of alpha-correlated brain activity changes that is coupled with a high amount of theta activity in the EEG spectrum (“occipital–parietal”) whereas the other pattern is associated with significantly less power in that band (“frontal–parietal”). It may be that the former state occurs during reduced vigilance compared to alpha baseline as is supported further by the slower and more variable peak alpha frequency (the brain ‘climbs back up to alpha’).

Vigilance states

In contrast, apart from significantly less theta activity, the frontal–parietal set of brain areas was paired with more activity in the beta band which is characteristic for a higher degree of vigilance and activity (and from which the brain ‘falls back down to alpha’)

(Ota et al., 1996). If different degrees of vigilance were the causal factor, the brain state reflected by the occipital–parietal pattern would resemble “stage I” sleep (Rechtschaffen and Kales, 1968) or “stage A” with “trains” as classified by Loomis et al. (1935, 1937). In contrast, the state represented by the “frontal–parietal” set of brain areas would appear to be a state of higher vigilance for which fewer classifications exist than for sleep stages (Kinnari et al., 2000). The group of sessions with variable patterns was associated with even higher content of beta oscillations and less slow activity. Oscillations in the beta band have often been linked to higher order mental processing (Ray and Cole, 1985; Neuper and Pfurtscheller, 2001). It is conceivable that, in this group, during epochs of reduced alpha power – when not ‘in alpha mode’ – subjects were engaged in various different mental activities (very alert). These were not reflected when contrasted against activity during alpha power because they were too variable to reveal brain areas significantly and homogeneously active. The high amount of variance explained by the “occipital–parietal” pattern in the eigenimages would finally support the notion of a more homogenous (and thus less complex) brain state associated with high theta power (drowsy). In contrast,

brain states occurring in association with the “frontal–parietal” pattern may exclusively share transiently heightened attentional levels as their only commonality while the actual content of the ‘atoms of thought’ (Lehmann and Koenig, 1997) might be more variable.

Alpha states and the “default mode” of brain function

Neither of the two presented typical sets of brain areas associated with alpha power changes show the characteristic “default mode” brain areas. This concept has mainly been proposed by Raichle and colleagues and refers to the observation that the retrosplenial, temporo-parietal and dorso-medial prefrontal cortices are more active during rest both compared to sleep and to perception and action (Mazoyer et al., 2001; Raichle et al., 2001). Recently, the analysis of resting state fluctuations has shown functional coupling in the default mode network (Greicius et al., 2003; Laufs et al., 2003b) but also at least one further tightly coupled network that is de- (Laufs et al., 2003b) or anti-correlated (Fransson, 2005) with respect to activity in the default mode system. It has been proposed that intrinsic brain activity such as the interplay between the two is modulated rather than determined by changing contingencies (Fox et al., 2005). Alpha power changes might be linked to such modulations and in fact frontal and parietal regions were prominent among the “anti-correlated nodes” identified by Fox et al. (2005) and Fransson (2005). While activity in “default mode” brain regions decreases during states of reduced vigilance (Laureys et al., 2004), we have previously demonstrated that its dynamics during resting wakefulness are associated with beta oscillations (Laufs et al., 2003b). This may indicate that activity in these regions is related to a more complex set of variables than mere alpha power, a view that would explain why they did not appear in our “negative alpha”-oriented analyses. However, it is noteworthy that “default mode” regions as the precuneus did appear on some eigenimages within the “frontal–parietal” group (Fig. 8).

Conclusion

We have demonstrated the existence of two prominent and distinct alpha power-associated BOLD signal patterns during eyes-closed rest as well as the occurrence of cases that resist classification into either category. The occurrence of either of the two distinct patterns could be related to oscillations in frequency bands adjacent to that of alpha. We hence propose that BOLD patterns during alpha desynchronization depend on where brain activity is heading. This can be towards a relatively stable, more homogenous, globally organized brain state in association with slower (4–7 Hz theta) oscillations on one end, reflected by occipital BOLD signal increases. Conversely, on the other end, the brain states with the strongest EEG acceleration appear to be too heterogeneous to yield consistent BOLD patterns. Finally, an intermediate pattern – and overall the most reliable one in our sample – corresponds to a state where the onset of generic attention-demanding cognitive processes dominates and results in the activation of frontal and parietal areas. These observations suggest that analysis of the entire spectral EEG information in conjunction with fMRI may permit to delineate neuroanatomically defined sub-stages of brain activity during resting wakefulness.

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