

Dynamic sculpting of brain functional connectivity and mental rotation aptitude

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Abstract: Changes in long-range synchronization are considered a key mechanism for the integration and segregation of cortical regions mediating cognitive processes. Such synchronization or functional connectivity is reflected in human electroencephalographic (EEG) coherence and in steady-state visually evoked potential (SSVEP) coherence. In this chapter, the relationship between cognitive proficiency in the mental rotation task (MRT) and functional connectivity reflected in SSVEP event-related partial coherence is described. The capacity to estimate changing levels of functional connectivity with a relatively high temporal resolution makes it possible to examine the relationship between functional connectivity at various points in time and aptitude. In the current study, the relationships between functional connectivity and two mental rotation aptitude measures, mental rotation speed and mental rotation accuracy, are described. We observed that functional connectivity was correlated with proficiency and that this correlation was both positive and negative for various regions and points in time. It is suggested that cognitive aptitude is related to the brain's capacity to enhance functional connectivity or communication between cortical regions that are relevant to the cognitive demands while attenuating irrelevant communication. This capacity is termed *functional connectivity sculpting*, and it is proposed that *functional connectivity sculpting* may constitute an important functional component of the neural substrate of learning and aptitude.

Keywords: functional connectivity; synchronization; steady state visually evoked potential; partial coherence; mental rotation; aptitude

Oscillations and cortical integration, multiple frequencies, multiple spatial scales

It is now widely recognized that synchronous oscillations constitute an important mechanism for mediating both local interactions between neural networks and long-range interactions between cortical areas (for review see Schnitzler and Gross, 2005).

Such interactions appear to be mediated by synchronous or coherent oscillations between regions. Recent interest in this phenomenon was triggered

by the observations of Gray and Singer (1989) who demonstrated high-frequency (gamma range) synchronous firing in widely separated single units in the cat visual cortex in response to congruent visual stimuli that constitute a 'single object'. Such synchronous firing is now thought to play a critical role in 'perceptual binding', that is, the process whereby units responding to sensory stimuli are dynamically bound to yield a unitary percept (Engel et al., 2001). While gamma synchronization and its relationship to perceptual binding was originally described in terms of single cell activity, it has also been observed in local field potentials and scalp EEG (Tallon-Baudry and Bertrand,

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1999). Increased EEG gamma coherence has also been observed in perceptual and working memory tasks and in the process of associative learning (Miltner et al., 1999; Tallon-Baudry, 2003).

While numerous reports have focused on the gamma coherence changes, studies examining short-term memory processes and target detection tasks where an internal representation of the target is established have revealed increased coherence at lower EEG frequencies including the beta, alpha, theta, and delta ranges. For example, in an object working memory study, gamma coherence was increased during the perceptual component when the material to be held in working memory was present on the screen. When the material was being held in working memory, the gamma coherence increases were replaced with increases in the beta range (Tallon-Baudry, 2003). In an object recognition task where objects were presented as words (text), in an auditory form and pictorially, there was a consistent increase in intra-areal coherence in the beta and high-alpha frequency range. Specifically, this was observed between adjacent regions, that is, temporo-parietal or occipito-parietal regions. By contrast, in a working memory task, long-range coherence, for example, between frontal and parietal regions was observed in the theta frequency range (Sarnthein et al., 1998). Human EEG findings are complemented by animal studies. Cats trained to make a response to the appearance of a visual target exhibited increased gamma synchronization within cortical areas such as the visual cortex and also between cortical regions that are monosynaptically separated (such as areas 5 and 7). Increased synchronization between remote areas was also observed following the appearance of a target but this occurred at lower frequencies in the alpha and theta bands (von Stein et al., 2000).

Although the precise functional role of the EEG coherence at different frequency and spatial scales is not completely clarified, the suggestion of von Stein and Sarnthein (2000) seems plausible. That is, gamma synchronization or gamma coupling is primarily a reflection of intra-areal or local coupling where local is defined in terms of regions linked by monosynaptic rather than polysynaptic pathways. Inter-areal (polysynaptic) integration is

mediated by coupling in the alpha to beta band while long-range coupling is mediated by synchronized activity in the theta and delta frequency range (see von Stein and Sarnthein, 2000 for review). More generally, they suggest that perceptually driven processes or 'bottom-up' processes are mediated by gamma coupling operating on a local (monosynaptic) or intra-areal scale while 'top-down' processes such as selective attention and working memory are mediated by inter-areal and long-range (polysynaptic) functional connectivity in the beta, alpha, and theta band.

Cognitive aptitude and functional connectivity

If cognitive processes are mediated by changes in long-range functional connectivity that are reflected in EEG synchronization changes, then it is reasonable to assume that differences in ability may be reflected in variations in such functional connectivity. While few, a number of studies suggest that this is the case. Bhattacharya et al. (2001) examined changes in gamma coherence when a group of 20 subjects (10 musically trained and 10 not trained) performed the Shepard and Metzler (1971) mental rotation task (MRT). An interesting observation was that musically trained subjects produced significantly higher gamma band coherence than did the non musically trained subjects. While this study points to aptitude (that is, musical ability) being associated with increased gamma coherence during the task, this association was not reflected in differences in MRT performance between the groups.

Jausovec and Jausovec (2000) examined the relationship between IQ, creativity, and EEG parameters in a study involving 115 university students. Subjects were scored for IQ and creativity, and EEG was recorded while subjects counted backwards from 400. The authors observed a positive correlation between IQ and right hemisphere temporal-parietal coherence in the theta, alpha, and beta bands. By far the most robust effect was a negative correlation between creativity score and coherence in the alpha and beta bands. This effect was apparent at almost all scalp sites.

A study by Thatcher et al. (2005) examined the relationship between IQ score and eyes closed resting EEG in 442 subjects. They found that IQ was generally negatively correlated with coherence in the delta, theta, alpha, and beta ranges. Specifically, of the 169 electrode pairs where IQ was significantly correlated with coherence ($p < 0.05$), 165 of these coherence measurements were negatively correlated with full scale IQ. This effect was not a consequence of lower EEG signal to noise, as IQ was positively correlated with EEG power in the same frequency ranges.

These findings, while suggestive, do not indicate a simple relationship between aptitude and EEG coherence. In fact, the Jausovec and Thatcher IQ, EEG coherence findings appear on the surface contradictory. This may be a consequence of differences in experimental design, for example, Jausovec subjects were engaged in a task (counting backwards) while the Thatcher subject were in an eyes closed 'resting state'. Another factor may be the impact of gender. A recent study by Jausovec and Jausovec (2005) reported that IQ was correlated with reduced frontal coherence in males and increased occipito-parietal coherence in females. If such drastic gender differences are confirmed, they may well constitute a significant source of experimental error in IQ — EEG studies and may account for some of the conflicting findings. Another contributing factor may be that the methods used to examine coherence may not have possessed adequate temporal resolution. This may be an important issue as animal studies have revealed that coherent or synchronized activity between regions can be established rapidly and just as rapidly terminated. A series of studies by Ding et al. (2000) examined changes in coherence in local field potentials recorded from dural electrodes in monkeys performing a target detection task. The appearance of the target was associated with a rapid but transient increase in coherence between the visual and motor cortex that was established in approximately 120 ms and returned to baseline levels after 280 ms.

As the level of coherent activity between cortical regions is continuously changing during a cognitive task (Varela et al., 2001), the correlation between aptitude and functional connectivity of

specific cortical regions may also vary with time. Thus, if the assessment of coherence does not possess the required temporal resolution, transient correlations between aptitude and coherence may be overlooked. A study utilizing steady-state visually evoked potential-event-related partial coherence (SSVEP-ERPC) to examine the relationship between information processing speed and functional connectivity undertaken in our laboratory would suggest this is the case (Silberstein et al., 2004a). In this study 41 subjects performed a pattern-matching task modeled on an IQ task termed Raven's Progressive Matrices. Shapes were presented for a fixed period of 3 s, and the individual mean reaction time varied from 647 to 1420 ms (population mean 1011 ms and SD 247 ms). When we calculated the correlation between processing speed (the inverse of reaction time) and SSVEP-ERPC, we found that the number of coherence estimates correlated with processing speed varied drastically over the 3 s trial duration. This number only started to deviate from zero at 0.7 s after the preceding response and peaking 0.8 s prior to the presentation of the next shape. All the observed correlations were positive (that is, faster processing speed associated with higher SSVEP-ERPC) and located primarily at right frontal and prefrontal sites.

We interpret the transient correlation between frontal SSVEP-ERPC and processing speed in the following manner: subjects with higher processing speed may be more efficient at refreshing the correct target image in working prior to the appearance of the following probe. More importantly, it illustrates the importance of temporal resolution of any methodology examining the relationship between aptitude and EEG coherence. Had we estimated coherence over the duration of the entire task, it is unlikely that we would have observed the transient but robust relationship between coherence and processing speed.

Mental rotation aptitude and functional connectivity

In the following section, we illustrate the use of high-temporal resolution coherence estimates such as SSVEP-ERPC to examine the relationship

between functional connectivity and aptitude for the MRT, a task involving the manipulation of mental imagery. We used a sequential version of the Shepard and Metzler (1971) MRT. In the sequential version of the MRT, the two images to be matched are presented sequentially with a blank screen interval interposed between the first and second images. This enables the task to be decomposed into a predominantly perceptual/encoding component during the first image, a working memory 'hold' component during the blank screen interval, and a mental rotation component that commences after the appearance of the second image.

Twenty-two male university students participated in the study that was approved by the Swinburne University of Technology Human Experimentation Ethics Committee. Each trial of the task commenced with a presentation of a 3D shape for 5 s. This was followed by a 3-s interval where the shape was replaced by blank screen and a small fixation cross and subjects were required to hold a representation of the originally viewed task in working memory. At the end of 3 s blank screen, another 3D shape was presented which was identical to either the original except for a rotation about the vertical axis or a mirror image that was likewise rotated. A typical trial is illustrated in Fig. 1. Thirty-five identical and 35 mirror reversed images were presented for each of the four rotation angles making a total of 220 presentations per individual.

The angular disparity between the shapes was either 0°, 60°, 120°, or 180° with equal representation of each angle. Details of the protocol have already been described (Silberstein et al., 2003), but briefly, subjects viewed the task through special goggles where a 13-Hz uniform visual flicker (160° horizontal, 90° vertical) was superimposed over the visual fields. The continuous visual flicker elicited a 13-Hz SSVEP.

For each subject, the SSVEP-ERPC was calculated for all 2016 distinct pairs of electrodes averaged across all *correct* trials. The partial coherence between each pair of electrode sites involves removal of the common contribution from the SSVEP stimulus and is considered a measure of *functional connectivity*. Subsequently in this chapter, the terms SSVEP-ERPC and functional con-

nectivity will be used interchangeably. SSVEP-ERPC during the 11-s trial epoch was calculated using a modified version of the event-related coherence technique (Andrew and Pfurtscheller, 1996; Nunez et al., 1999; Silberstein et al., 2003). Partial coherence varies between 0 and 1. Electrode pairs with high partial coherence indicate relatively stable SSVEP phase differences between electrode pairs across trials. This occurs even though SSVEP phase differences between each of the electrodes and the stimulus may be variable across trials. This result indicates that high SSVEP partial coherence between electrodes reflects a consistent synchronization between electrodes at the stimulus frequency and is not simply a consequence of two unrelated regions increasing their response to the common visual flicker.

We have previously demonstrated differences in functional connectivity specifically associated with the process of mental rotation. In essence, when comparing the most demanding MRT (180°) with the 60° condition, we found that statistically significant increases in functional connectivity were apparent during the rotation component, approximately 1 s after the presentation of the second shape. The most statistically robust increases were observed between prefrontal and parietal regions and especially between left frontal regions and right parietal regions (see Fig. 2).

To examine the relationship between functional connectivity and mental rotation aptitude, two aptitude measures were considered separately, *mental rotation speed* and *mental rotation accuracy*. Individual mental rotation speed was estimated from the individual line of best fit for the graph of mental rotation angle against reaction time while mental rotation accuracy was defined as the proportion of correct responses for 180° rotation trials. For each point in time in the 11 s trial interval and for each of the unique 2016 unique electrode pairs we calculated the correlation between the performance measure and functional connectivity. This yielded 2016 correlation coefficient time series where each time series described the correlation between one of the MRT aptitude parameters and functional connectivity. To explore the temporal variation in the strength of the correlation between aptitude measures and functional

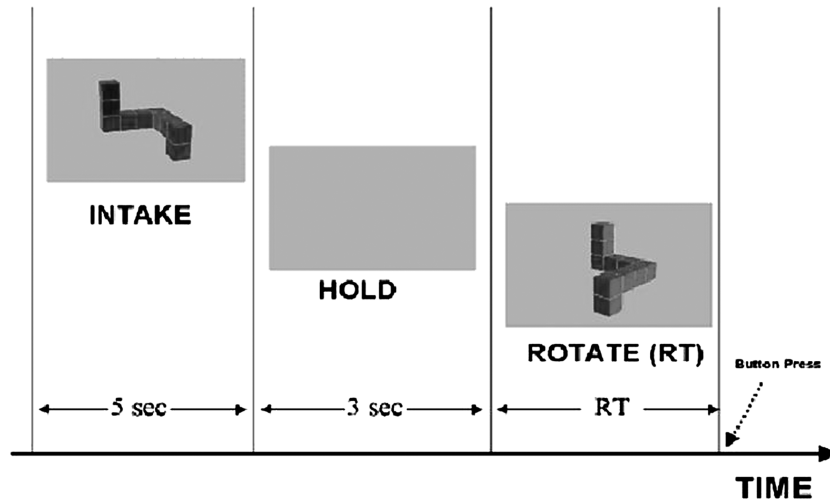


Fig. 1. Structure of sequential mental rotation task. Note all objects were rotated about the vertical axis.

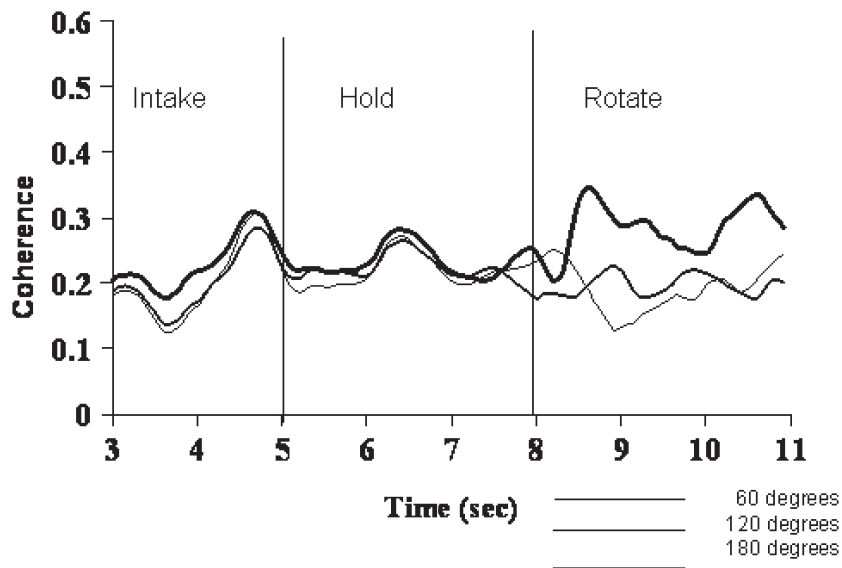


Fig. 2. Cross subject average of steady-state visually evoked potential event-related partial coherence (SSVEP-ERPC) between electrode 21 (left-frontal midway between F7 and T3) and P4 (right parietal) for all correct responses to matching trials. Labels indicate the angular disparity between first and second objects. Mean reaction time increased linearly from the 60° condition (RT = 2.19 s) to the 180° condition (RT = 3.21 s); see Silberstein et al. (2003).

connectivity, we determined the number of electrode pairs where the magnitude of the correlation coefficient exceeds 0.734, a threshold value corresponding to $p < 0.0001$ at each point in time.

Figure 3 illustrates the temporal variation in the number of electrode pairs where the correlation

coefficient between functional connectivity and mental rotation speed exceeds the threshold. Figure 4 illustrates the situation for the equivalent situation for mental rotation accuracy. Graphs illustrated in Figs. 3 and 4 are termed *correlation frequency curves*.

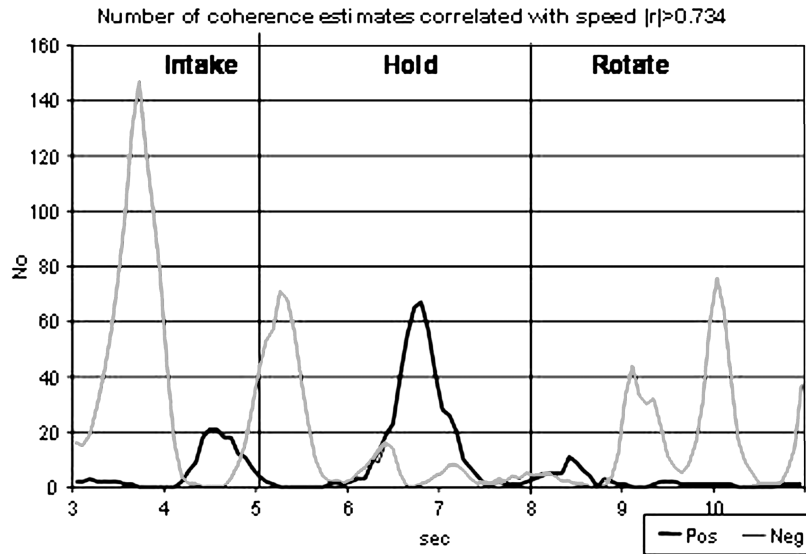


Fig. 3. *Correlation frequency curve* describing number of SSVEP-ERPC estimates that are correlated with individual mental rotation speed where the magnitude of the correlation coefficient exceeds the threshold value of 0.734, corresponding to $p < 0.0001$. Heavy line indicates number of coherence measurements positively correlated with mental rotation speed and the faint line the number negatively correlated. A permutation test was used to determine the number of coherence estimates correlated with mental rotation speed that could be expected by chance alone (Null hypothesis). At the threshold level of $r = 0.734$, the null hypothesis can be rejected at the $p = 0.01$ level if more than four coherence estimates are either positively or negatively correlated with mental rotation speed. The null hypothesis can be rejected at the more conservative $p < 0.001$ if more than 12 coherence estimates are correspondingly correlated.

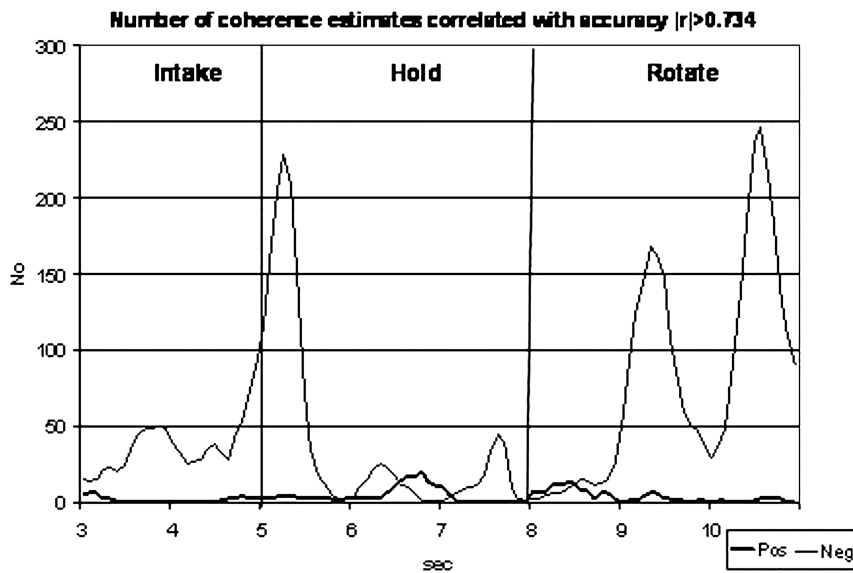


Fig. 4. *Correlation frequency curve* describing number of SSVEP-ERPC estimates that are correlated with individual mental rotation accuracy where the magnitude of the correlation coefficient exceeds the threshold value of 0.734, corresponding to $p < 0.0001$. See Fig. 3 legend for other details.

The multivariate permutation test was used to determine the statistical significance of the number of correlated electrode pairs. In this study, the null hypothesis can be rejected at the $p < 0.01$ level when the number of correlated coherence estimates conforming to the above criterion exceeds 4; correspondingly the Null hypothesis can be rejected at the $p < 0.001$ level when the number of correlated coherence estimates conforming to the above criterion exceeds 12. This estimation takes into account the correlation between electrode pairs and is applied separately for positive and negative correlations.

While these time series give us no information on the location of the coherent electrode pairs correlated with aptitude, they give an indication of the varying strength of the relationship between functional connectivity and aptitude. Two points should be noted: first, the correlation between functional connectivity and aptitude varies greatly over the time course of a trial. This reinforces the suggestion that inadequate temporal resolution may obscure time-varying relationships between aptitude and functional connectivity. Another point to note is that performance measures associated with the last 3 s of the trial when subjects are mentally rotating the shape are correlated with functional connectivity in earlier parts of the trial when subjects are observing the initial shape as well as during the interval when the screen is blank and subjects are required to hold the shape in working memory. This suggests that mental rotation aptitude (as reflected in performance during the rotation component) is dependent on the cognitive processing state in the earlier components of the trial. This may relate to the effectiveness of cognitive processes in earlier parts of the trial such as the initial visual intake and encoding component as well as the effectiveness of the working memory 'hold' component during the 3 s blank interval. These findings are consistent with the observations of Gevins et al. (1989) who examined the changes in event-related covariance during a bimanual visuo-motor judgment task. Accurate trials were associated with differing patterns of event-related covariance before the visual target for the trial was presented.

Functional connectivity topography correlated with aptitude

For purposes of brevity, discussion is limited to the four points in time corresponding to the first four peaks that are common to both accuracy and speed *correlation frequency curves*.

The first point to note is that the functional connectivity topography changes dramatically over the time course of a trial. At the point 3.8 s into the intake component (Figs. 5A and B) we see that higher mental rotation speed and higher mental rotation accuracy are negatively correlated with functional connectivity. The electrode pairs where functional connectivity is most strongly correlated with performance are located at prefrontal, frontal, and parietal and in the case of speed, temporal sites. The time at which this component peaks coincides with the drop in coherence observed at 3.8 s point in Fig. 2. The drop in coherence at this point in time is a feature of electrode pairs involving frontal, prefrontal, and parietal sites. In other words, the lower the coherence during this transient dip, the higher is the performance of the subject for both speed and accuracy.

At the beginning of the hold component (Figs. 5C and D), both speed and accuracy are negatively correlated with functional connectivity at prefrontal and frontal and central sites. In particular, speed also exhibits a negative correlation with functional connectivity between left temporo-frontal sites and central frontal sites. In addition to the negative correlation between performance and fronto-central sites, we note that accuracy alone is positively correlated with functional connectivity at left parieto-occipital sites at this time, although this just reaches significance at the $p < 0.01$ level. Approximately 1.5 s later during the middle of the hold component (Figs. 5E and F) the picture changes dramatically. Now, high mental rotation speed and accuracy are correlated with increased functional connectivity at right frontal and prefrontal sites. This coincides with the transient peak in coherence apparent at 6.7 s point in Fig. 2 at the time, a feature that was apparent in functional connectivity between all prefrontal and frontal electrode pairs.

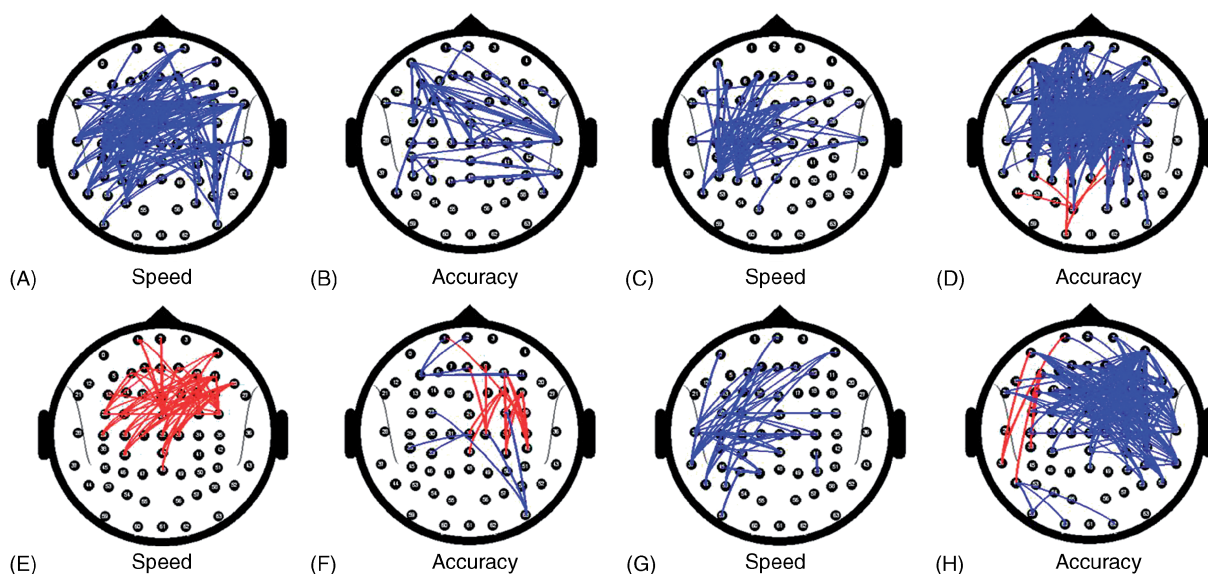


Fig. 5. (A–H) Location of electrode pairs where the mental rotation speed or accuracy are correlated with coherence. Blue lines indicate a negative correlation between aptitude and coherence, that is, high performance is associated with lower coherence. Red lines indicate the converse, high performance associated with higher coherence. (A) Illustrates the location of coherence estimates correlated with mental rotation speed at the point 3.8 s into the intake component of the trial corresponding to the first peak in Figs. 3 and 4. (B) Illustrates the location of coherence estimates correlated with mental rotation accuracy for the same point in time as (A). (C and D) Illustrate the equivalent distributions for speed (C) and accuracy (D) for point in time 5.4 s corresponding to the first peak in the hold component in Figs. 3 and 4. (E and F) Illustrate the equivalent distributions at the point 6.7 s into the trial corresponding to the second peak in the hold component seen most clearly in Fig. 3. (G and F) Illustrate the equivalent distributions at the point 9.1 s into the trial corresponding to the first major peak 1.1 s into the rotate component seen most clearly in Fig. 4. See Plate 5.5 in Colour Plate Section.

The occurrence of this peak in Figs. 3 and 4, in the middle of the working memory ‘hold’ component, and the location of the correlated functional connectivity measurements at right frontal and prefrontal sites suggest that both performance measures are dependent on working memory processes. This is consistent with neuroimaging and electrophysiological studies that indicate a central role for the prefrontal cortex in the operation of working memory (Goldman-Rakic, 1996). The predominantly right hemisphere of these correlated electrode pairs is also consistent with evidence pointing to the right prefrontal cortex contributing to object working memory (Courtney et al., 1998). The transient positive correlation between performance and right prefrontal functional connectivity may index the link between working memory efficiency (perhaps the refresh of working memory) and aptitude.

The suggestion that this peak represents the correlation between working memory efficiency

and aptitude is supported by a congruent observation in a different study. In this study (Silberstein et al., 2004a) (described earlier) we examined the relationship between functional connectivity and the cognitive processing speed in a task requiring subjects to classify shapes as matching a target or not. We found that the number of electrode pairs where functional connectivity was positively correlated with cognitive processing speed only occurred ~ 0.8 s prior to the appearance of a probe and was restricted to the same right frontal/prefrontal region illustrated in Fig. 5E. As this peak occurs prior to the appearance of the probe, we suggested that it may index the relationship between the efficiency of object working memory and cognitive processing speed.

At the point 1.1 s after the presentation of the second shape when shapes are presumably being mentally rotated, the pattern of correlation between coherent pairs and aptitude changes dramatically from the pattern observed in the working

memory interval (Figs. 5G and H). Mental rotation speed is negatively correlated with left temporal-frontal functional connectivity. By contrast, mental rotation accuracy is negatively correlated with left frontal to right parieto/temporal/frontal functional connectivity. The different patterns of correlation between speed, accuracy, and functional connectivity during the rotation period suggest that these aptitudes are dependent on different neural substrates at this time.

Strategy and effort as contributing factors

While both performance measures are positively correlated with right prefrontal functional connectivity during the working memory 'hold' component, by far the most common feature we have observed is a negative correlation between both performance measures and functional connectivity. While additional studies are needed to clarify this relationship, a number of possible contributing factors can be suggested. One potential factor may be the cognitive strategy used by the subjects. A number of researchers have suggested that the MRT can be performed using two distinct strategies: a gestalt strategy where the image is rotated as a whole and a serial or piecewise strategy where the image is mentally disassembled, sub-components individually rotated and reassembled (Bethell-Fox and Shepard, 1988; Corballis, 1997). Gestalt strategies are associated with faster mental rotation when compared with analytical strategies (Bethell-Fox and Shepard, 1988). Analytical strategies are known to preferentially engage the left hemisphere while gestalt strategies place more demands on right hemisphere processes (Corballis, 1997). An fMRI study by Jordan et al. (2002) examined gender differences in brain activity when a group of males and females, matched for performance, undertake the MRT. When comparing male and female brain activation pattern, they observed increased activation at the left inferior temporal gyrus in females but not males. They attribute this to the greater propensity for females to use an analytical or piecewise strategy when rotating a mental image. More generally, gender-related differences in EEG coherence during other

cognitive tasks such as auditory verbal retrieval have also been observed (Volf and Ruzumnikova, 2004).

The negative correlation we observed between left fronto-temporal functional connectivity and mental rotation speed may thus be a consequence of faster rotators being *less likely* to use a piecewise strategy and thus less likely to engage left temporo-frontal processes that are required to mediate such a piecewise strategy. A similar correlation is observed at the commencement of the working memory 'hold' component. Faster mental rotation speed is associated with reduced left temporal and frontal functional connectivity, suggesting that faster rotators are less likely to use a piecewise strategy when engaging the hold component of working memory. By contrast, during the rotation component, high-accuracy subjects demonstrated evidence of increased functional connectivity at left temporal and parietal sites. This would be consistent with the possibility that more accurate subjects are more likely to use an analytical stratagem that may be more accurate but slower.

Cognitive 'effort' may be another factor contributing to the negative correlation between aptitude and functional connectivity. There is considerable evidence that the level of mental effort in undertaking a cognitive task is influenced by the ability or aptitude of the subject in performing the task. Subjects with low aptitude or task proficiency will need to make a greater mental effort to perform the task than those with high proficiency or aptitude. This increased effort is reflected in an increase in the level and extent of task-related brain activity (Braver et al., 1997). Increased effort can also be associated with increased coherence or functional connectivity between scalp sites. Svoboda et al. (2002) reported increased alpha coherence during increased muscle contraction in an isometric task. The acquisition of a novel and demanding bimanual motor task is associated with increased alpha and beta 1 coherence over sensory motor cortex in the early stage of learning, presumably when effort is highest. As the task is mastered and the effort needed to perform the task reduced, the coherence also decreases (Andres et al., 1999).

If some coherence estimates are influenced by effort, we would expect that subjects with a higher proficiency would show a reduced ‘effort-related’ increase in functional connectivity leading to a negative correlation between functional connectivity and aptitude. This may be a contributing factor to the negative correlation between left frontal to right parietal functional connectivity and mental rotation accuracy observed during the rotation component illustrated in Fig. 5(H). In a previous publication based on this study, we observed a robust increase in left frontal to right parietal functional connectivity when we compared the demanding 180° rotation condition with the 60° rotation condition (Silberstein et al., 2003). The correlation data in the present study indicate that this functional connectivity increase became smaller as individual mental rotation accuracy increased. This particular pattern is consistent with the ‘effort’ hypothesis in that more accurate subjects may be exerting less effort at this point in the task and thus giving rise to a smaller ‘effort-related’ increase in left frontal to right parietal functional connectivity.

While the ‘effort hypothesis’ may be consistent with one particular set of observations and hence a contributing mechanism, it is unlikely to be sole mechanisms explaining all our observations. In particular, during the working memory ‘hold’ component a task-related increase in functional connectivity at right frontal and prefrontal sites is apparent. Had the ‘effort’ hypothesis applied to the right frontal functional connectivity, a negative correlation would be expected between aptitude and functional connectivity in this region. Yet the opposite effect was observed. Both speed and accuracy were positively correlated with functional connectivity at this point in the task.

Functional connectivity sculpting

While aptitude is sometimes positively correlated with functional connectivity, the most frequent observation is a negative correlation between these measures. Our observation of such a negative correlation is consistent with a number of other studies that report an association between improved

performance and reduced long-range functional connectivity as well as pathological conditions associated with increased long-range functional connectivity. Fell et al. (2001) examined gamma synchrony between rhinal cortex and hippocampus in a word memory task. Words that were subsequently recalled were associated with an initial biphasic increase in gamma coherence synchrony followed by a pronounced reduction in gamma synchrony. By contrast, words not subsequently recalled were not associated with these transient increases and decreases in gamma synchrony. An association between reduced functional connectivity and enhanced performance has also been observed in the alpha- and beta-frequency range. Gross et al. (2004) observed changes in beta functional connectivity between frontal, parietal, and temporal attentional networks during an attentional blink study. Compared with trials where subjects failed to detect the second of two successive targets (attentional blink), successful detection of the second target was associated with reduced coherence or functional connectivity prior to the appearance of the second target. Such transient reductions in functional connectivity in an attention task were first reported by Rodriguez et al. (1999) who observed a pronounced transient reduction in parieto-temporal gamma synchrony approximately 400 ms following the presentation of a facial image (“Mooney face”).

We have also observed a negative correlation between SSVEP-ERPC and full scale IQ. In this study, we examined the relationship between 13 Hz functional connectivity and IQ score when subjects were performing a cognitive task based on Raven’s Progressive Matrices. This required them to indicate whether two sets of images matched or not. We found that IQ was negatively correlated with frontal 13 Hz functional connectivity at the time subjects were making their response (Silberstein et al., 2004b).

An association between abnormally elevated long-range functional connectivity and pathology is most clearly seen in Parkinson’s disease where tremor and motor dysfunction are correlated with increased functional connectivity between basal ganglia and motor cortex (Williams et al., 2002).

It is suggested that the study reported in this chapter together with findings from our and other laboratories that have been briefly reviewed point to the importance of mechanisms that reduce or suppress long-range functional connectivity between neural networks. The fact that such functional connectivity suppression is associated with enhanced performance suggests that the suppressed functional connectivity was either irrelevant to the task or interfered with the establishment of brain states necessary to perform the cognitive or motor tasks. More specifically, it is suggested that the capacity to dynamically sculpt functional connectivity, that is to enhance functional connectivity relevant to the immediate cognitive/motor task while simultaneously attenuating irrelevant functional connectivity, may be a critical determinant of cognitive and motor aptitude. The importance of such decoupling is all the more apparent when one considers the disparity between the enormous structural interconnectedness of the cortex and the precision and specificity of synchronized networks that may be engaged in a cognitive or precision motor task. Many of the studies concerning functional connectivity and cognitive processes emphasize the establishment of synchronization or functional connectivity between cortical regions, a process that is frequently described in terms of ‘binding’. Our findings point to the importance of *decoupling* cortical regions whose interaction may interfere with cognitive or motor tasks. In other words, long-range ‘binding’ of certain cortical regions must be accompanied by ‘unbinding’ or decoupling of other regions. For purposes of brevity, this process of enhancing functional connectivity between certain cortical regions and suppression of others will be termed as ‘*functional connectivity sculpting*’.

Two of the mechanisms used to account for our observation of negative correlation between functional connectivity and aptitude are ‘cognitive strategy’ and functional connectivity sculpting. While these may appear distinct, it is suggested that they may constitute one and the same process. What constitutes an ‘irrelevant’ interaction between cortical regions that is to be suppressed is determined by the cognitive strategy adopted. For example, when adopting an analytical strategy,

functional connectivity between left hemisphere networks would be ‘relevant’ while functional connectivity involving the right-parietal cortex would be ‘irrelevant’. These categories would be reversed if a holistic visuo-spatial strategy was adopted. In summary, strategy effects could be considered a specific case of functional connectivity sculpting.

Given the similar behavior of 13 Hz SSVEP and the upper-alpha EEG (Silberstein et al., 2001) it is interesting to note that some of the findings described in this chapter concerning the relationship between functional connectivity and aptitude appear to be congruent with other EEG alpha findings. In particular, Klimesch (1999) and Doppelmayr et al. (2005) have reported that superior semantic memory performance and enhanced semantic performance are associated with larger upper-alpha event-related desynchronization (ERD) or a transient alpha amplitude reduction. Although speculative, the upper-alpha ERD may be an indication of a transient reduction in functional connectivity also observed via the SSVEP-ERPC.

The positive correlation between functional connectivity at right frontal sites during the ‘working memory’ hold component and mental rotation aptitude reported here may also be reflected in the behavior of the SSVEP and upper-alpha EEG. First, both the 13 Hz SSVEP amplitude (Silberstein et al., 2001; Perlstein et al., 2003) and EEG upper-alpha amplitude (Klimesch et al., 1999; Jensen et al., 2002) increase during the hold component of a short-term or working memory task. Furthermore, the increased upper-alpha amplitude is associated with enhanced memory performance and intelligence (Vogt et al., 1998; Doppelmayr et al., 2002) while the SSVEP amplitude during the ‘hold’ component of a face’s working memory task is positively correlated with performance on the working memory task (Perlstein et al., 2003). The relationship between upper-alpha amplitude and cognitive performance is unlikely to be coincidental or epiphenomenal in nature as neurofeedback training to increase upper-alpha amplitude improves cognitive performance (Hanselmayr et al., 2005) while the delivery of repetitive transcranial magnetic stimulation (TMS) at the individual

upper-alpha frequency also enhances cognitive performance (Klimesch et al., 2003).

Neural mechanisms

The physiological mechanisms controlling long-range functional connectivity between cortical regions are not fully understood, although there is significant evidence pointing to an important role for the neurotransmitter dopamine (DA). This is most clearly seen in Parkinson's disease where the abnormal alpha and beta functional connectivity between basal ganglia and motor cortex is reduced or eliminated altogether with the administration of the DA precursor L-DOPA (Williams et al., 2002).

We have observed an analogous effect when examining the effects of a single dose of methylphenidate (MPD) on 13 Hz functional connectivity in boys diagnosed with attention deficit hyperactivity disorder (ADHD). MPD is a DA re-uptake blocker that increases the level of DA at receptor sites. 13 Hz functional connectivity was examined in boys performing the AX version of the continuous performance task, a commonly used visual vigilance task. We found that MPT caused a profound reduction in 13 Hz functional connectivity, and that these reductions were correlated with improvements in symptom score (Silberstein et al., 2005). It should be noted that the cognitive enhancing effects of MPD are consistent with the suggestion that aptitude is associated with the capacity to suppress irrelevant functional connectivity, or functional connectivity sculpting. The role of DA and nor-adrenaline as a decoupling agents was described in a neurophysiological model previously proposed by the author (Silberstein, 1995; Silberstein et al., 2001). In this model, cortico-cortico loops involving feed-forward and feed-back components mediate long-range cortical synchronization and contribute to low-frequency EEG rhythms in the theta, alpha, and beta ranges. DA and nor-adrenaline are thought to decouple long-range/low-frequency synchronization by inhibiting the feedback component originating in the deeper layers of the cortex such as layer V and terminating in the superficial layers I and II. These effects may be mediated, in part, by effects of DA on

excitatory D5 receptors located on inhibitory interneurons located in layers I and II (Gorelova et al., 2002).

Conclusion

Cognitive processes appear to be mediated by changes in functional connectivity across various spatial and temporal frequency scales. Task proficiency and aptitude appear to be a function of the effectiveness of functional connectivity sculpting. Such sculpting could play a crucial role in the effectiveness of cortical information processing and may constitute an important component of the neural substrate of learning and aptitude. It may also be useful to consider some disorders, such as ADHD as disorders of functional connectivity sculpting where the required increases or decreases in functional connectivity are not achieved.

References

- Andres, F.G., Mima, T., Schulman, A.E., Dichgans, J., Hallett, M. and Gerloff, C. (1999) Functional coupling of human cortical sensorimotor areas during bimanual skill acquisition. *Brain*, 122: 855–870.
- Andrew, C. and Pfurtscheller, G. (1996) Event-related coherence as a tool for studying dynamic interaction of brain regions. *Electroencephalogr. Clin. Neurophysiol.*, 98: 144–148.
- Bethell-Fox, C.E. and Shepard, R.N. (1988) Mental rotation: effects of stimulus complexity and familiarity. *J. Exp. Psychol. Hum. Percept. Perform.*, 14: 12–23.
- Bhattacharya, J., Petsche, H., Feldmann, U. and Rescher, B. (2001) EEG gamma phase synchronization between posterior and frontal cortex during mental rotation in humans. *Neurosci. Lett.*, 311: 29–32.
- Braver, T.S., Cohen, J.D., Nystrom, L.E., Jonides, J., Smith, E.E. and Noll, D.C. (1997) A parametric study of prefrontal cortex involvement in human working memory. *Neuroimage*, 5: 49–62.
- Corballis, M.C. (1997) Mental rotation and the right hemisphere. *Brain Lang.*, 57: 100–121.
- Courtney, S.M., Petit, L., Haxby, J.V. and Ungerleider, L.G. (1998) The role of prefrontal cortex in working memory: examining the contents of consciousness. *Philos. Trans. R. Soc. Lond. B Biol. Sci.*, 353: 1819–1828.
- Ding, M., Bressler, S.L., Yang, W. and Liang, H. (2000) Short-window spectral analysis of cortical event-related potentials by adaptive multivariate autoregressive modeling: data pre-processing, model validation, and variability assessment. *Biol. Cybern.*, 83: 35–45.

- Doppelmayr, M., Klimesch, W., Stadler, W., Pollhuber, D. and Heine, C. (2002) EEG alpha power and intelligence. *Intelligence*(30): 289–302.
- Doppelmayr, M., Klimesch, W., Hodlmoser, K., Sauseng, P. and Gruber, W. (2005) Intelligence related upper alpha desynchronization in a semantic memory task. *Brain Res. Bull.*, 66: 171–177.
- Engel, A.K., Fries, P. and Singer, W. (2001) Dynamic predictions: oscillations and synchrony in top-down processing. *Nat. Rev. Neurosci.*, 2: 704–716.
- Fell, J., Klaver, P., Lehnertz, K., Grunwald, T., Schaller, C., Elger, C.E. and Fernandez, G. (2001) Human memory formation is accompanied by rhinal-hippocampal coupling and decoupling. *Nat. Neurosci.*, 4: 1259–1264.
- Gevens, A.S., Cuttillo, B.A., Bressler, S.L., Morgan, N.H., White, R.M., Illes, J. and Greer, D.S. (1989) Event-related covariances during a bimanual visuomotor task. II. Preparation and feedback. *Electroencephalogr. Clin. Neurophysiol.*, 74: 147–160.
- Goldman-Rakic, P.S. (1996) Regional and cellular fractionation of working memory. *Proc. Natl. Acad. Sci. U.S.A.*, 93: 13473–13480.
- Gorelova, N., Seamans, J.K. and Yang, C.R. (2002) Mechanisms of dopamine activation of fast-spiking interneurons that exert inhibition in rat prefrontal cortex. *J. Neurophysiol.*, 88: 3150–3166.
- Gray, C.M. and Singer, W. (1989) Stimulus-specific neuronal oscillations in orientation columns of cat visual cortex. *Proc. Natl. Acad. Sci. U.S.A.*, 86: 1698–1702.
- Gross, J., Schmitz, F., Schnitzler, I., Kessler, K., Shapiro, K., Hommel, B. and Schnitzler, A. (2004) Modulation of long-range neural synchrony reflects temporal limitations of visual attention in humans. *Proc. Natl. Acad. Sci. U.S.A.*, 101: 13050–13055.
- Hanslmayr, S., Sauseng, P., Doppelmayr, M., Schabus, M. and Klimesch, W. (2005) Increasing individual upper alpha power by neurofeedback improves cognitive performance in human subjects. *Appl. Psychophysiol. Biofeedback*, 30: 1–10.
- Jausovec, N. and Jausovec, K. (2000) Differences in resting EEG related to ability. *Brain Topogr.*, 12: 229–240.
- Jausovec, N. and Jausovec, K. (2005) Sex differences in brain activity related to general and emotional intelligence. *Brain Cogn.*, 59: 277–286.
- Jensen, O., Gelfand, J., Kounios, J. and Lisman, J.E. (2002) Oscillations in the alpha band (9–12 Hz) increase with memory load during retention in a short-term memory task. *Cereb. Cortex*, 12: 877–882.
- Jordan, K., Wustenberg, T., Heinze, H.J., Peters, M. and Jancke, L. (2002) Women and men exhibit different cortical activation patterns during mental rotation tasks. *Neuropsychologia*, 40: 2397–2408.
- Klimesch, W. (1999) EEG alpha and theta oscillations reflect cognitive and memory performance: a review and analysis. *Brain Res. Rev.*, 29: 169–195.
- Klimesch, W., Doppelmayr, M., Schwaiger, J., Auinger, P. and Winkler, T. (1999) ‘Paradoxical’ alpha synchronization in a memory task. *Brain Res. Cogn. Brain Res.*, 7: 493–501.
- Klimesch, W., Sauseng, P. and Gerloff, C. (2003) Enhancing cognitive performance with repetitive transcranial magnetic stimulation at human individual alpha frequency. *Eur. J. Neurosci.*, 17: 1129–1133.
- Miltner, W.H.R., Braun, C., Arnold, M., Witte, H. and Taub, E. (1999) Coherence of gamma-band EEG activity as a basis for associative learning. *Nature*, 397: 434–438.
- Nunez, P.L., Silberstein, R.B., Shi, Z., Carpenter, M.R., Srinivasan, R., Tucker, D.M., Doran, S.M., Cadusch, P.J. and Wijesinghe, R. (1999) EEG coherence II: experimental comparisons of multiple coherence measures. *Clin. Neurophysiol.*, 110: 469–486.
- Perlstein, W.M., Cole, M.A., Larson, M., Kelly, K., Seignourel, P. and Keil, A. (2003) Steady-state visual evoked potentials reveal frontally-mediated working memory activity in humans. *Neurosci. Lett.*, 342: 191–195.
- Rodriguez, E., George, N., Lachaux, J.P., Martinerie, J., Renault, B. and Varela, F.J. (1999) Perception’s shadow: long-distance synchronization of human brain activity. *Nature*, 397: 430–433.
- Sarnthein, J., Petsche, H., Rappelsberger, P., Shaw, G.L. and von Stein, A. (1998) Synchronization between prefrontal and posterior association cortex during human working memory. *Proc. Natl. Acad. Sci. U.S.A.*, 95: 7092–7096.
- Schnitzler, A. and Gross, J. (2005) Normal and pathological oscillatory communication in the brain. *Nat. Rev. Neurosci.*, 6: 285–296.
- Shepard, R.N. and Metzler, J. (1971) Mental rotation of three-dimensional objects. *Science*, 171: 701–703.
- Silberstein, R.B. (1995) Neuromodulation of neocortical dynamics. In: Nunez, P.L. (Ed.), *Neocortical Dynamics and Human EEG Rhythms*. Oxford University Press, New York, pp. 591–627.
- Silberstein, R.B., Danieli, F. and Nunez, P.L. (2003) Frontoparietal evoked potential synchronization is increased during mental rotation. *Neuroreport*, 14: 67–71.
- Silberstein, R.B., Farrow, M., Park, W. and Nunez, P.L. (2005) Effects of methylphenidate on dynamic changes in cortical connectivity in attention deficit hyperactivity disorder (ADHD) (abstract). 16th International Congress of the International Society for Brain Electromagnetic Topography, Bern, Switzerland.
- Silberstein, R.B., Nunez, P.L., Pipingas, A., Harris, P. and Danieli, F. (2001) Steady state visually evoked potential (SSVEP) topography in a graded working memory task. *Int. J. Psychophysiol.*, 42: 125–138.
- Silberstein, R.B., Song, J., Nunez, P.L., and Park, W. (2004b) Verbal and performance IQ scores are correlated with different patterns of cortical synchronization, (abstract). 34th Annual Meeting of Society for Neuroscience, San Diego, CA, USA.
- Silberstein, R.B., Song, J., Nunez, P.L. and Park, W. (2004a) Dynamic sculpting of brain functional connectivity is correlated with performance. *Brain Topogr.*, 16: 249–254.
- Svoboda, J., Sovka, P. and Stancak, A. (2002) Intra- and inter-hemispheric coupling of electroencephalographic 8–13 Hz

- rhythm in humans and force of static finger extension. *Neurosci. Lett.*, 334: 191–195.
- Tallon-Baudry, C. (2003) Oscillatory synchrony and human visual cognition. *J. Physiol. Paris*, 97: 355–363.
- Tallon-Baudry, C. and Bertrand, O. (1999) Oscillatory gamma activity in humans and its role in object representation. *Trends Cogn. Sci.*, 3: 151–162.
- Thatcher, R.W., North, D. and Biver, C. (2005) EEG and intelligence: relations between EEG coherence, EEG phase delay and power. *Clin. Neurophysiol.*, 116: 2129–2141.
- Varela, F., Lachaux, J.P., Rodriguez, E. and Martinerie, J. (2001) The brainweb: phase synchronization and large-scale integration. *Nat. Rev. Neurosci.*, 2: 229–239.
- Vogt, F., Klimesch, W. and Doppelmayr, M. (1998) High-frequency components in the alpha band and memory performance. *J. Clin. Neurophysiol.*, 15: 167–172.
- Volf, N.V. and Razumnikova, O.M. (2004) Gender differences in hemispheric spatiotemporal EEG patterns upon reproduction of verbal information. *Hum. Physiol.*, 30: 274–280.
- von Stein, A., Chiang, C. and Konig, P. (2000) Top-down processing mediated by interareal synchronization. *Proc. Natl. Acad. Sci. U.S.A.*, 97: 14748–14753.
- von Stein, A. and Sarnthein, J. (2000) Different frequencies for different scales of cortical integration: from local gamma to long range alpha/theta synchronization. *Int. J. Psychophysiol.*, 38: 301–313.
- Williams, D., Tijssen, M., Van Bruggen, G., Bosch, A., Insola, A., Di Lazzaro, V., Mazzone, P., Oliviero, A., Quartarone, A., Speelman, H. and Brown, P. (2002) Dopamine-dependent changes in the functional connectivity between basal ganglia and cerebral cortex in humans. *Brain*, 125: 1558–1569.