Systems-level neural mechanisms of conscious perception in health and schizophrenia

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List of Abbreviations

ADP	Adenosine diphosphate
Ag	Angular gyrus
ATP	Adenosine triphosphate
BOLD	Blood-oxygen dependent signal
caS	Calcarine sulcus
CO	Cingulo-opercular system
CS	Central sulcus
DAN	Dorsal attention network
DMN	Default mode network
ER	Evoked response
FDR	False discovery rate
fEf	Frontal eye-field
fMRI	Functional magnetic resonance imaging
FPN	Fronto-parietal network
Fus	Fusiform face gyrus
EEG	Electro-encephalography
GLUT2	Glucose transporter isoform 2
iFG/S	inferior frontal gyrus/sulcus
INS	Insula
iPLV	Imaginary phase-locking value
iprCS	Inferior precentral sulcus
intPS	Intraparietal sulcus
iTG	Inferior temporal gyrus
mCi	Mid-cingulate
MEG	Magnetoencephalography
mFG/S	Mid-frontal gyrus/sulcus
mTG	Mid-temporal gyrus
MI	Primary motor area
MNE	Minimum norm estimate

MRI	Magnetic resonance imaging
NMDA	N-methyl-D-aspartate
Lim	Limbic system
OFA	Occipital face area
Opole	Occipital pole
pCi	Posterior cingulate
PET	Positron emission tomography
PFC	Prefrontal cortex
PLF	Phase-locking factor
PLV	Phase-locking value
POS	Parieto-occipital sulcus
PPC	Posterior parietal cortex
prCN	Precuneus
TPJ	Tempero-parietal junction
TSDT	Threshold of stimulus detection task
SI	Primary somatosensory area
SII	Secondary somatosensory area
SL	Stimulus locking
SM	Sensorimotor network
SMA	Supplementary motor area
sOG/S	Superior occipital gyrus/sulcus
sPG	Superior parietal gyrus
sprCS	Superior precentral sulcus
sTS/G	Superior temporal sulcus/gyrus
TF-ROI	Time-frequency region of interest
V1/V2	Primary/secondary visual areas
VAN	Ventral attention network
Vis	Visual system

Abstract

The interplay between senses and actions is one of the most crucial processes that takes place in the brain. The successful course from perception of a stimulus to a meaningful action requires coherent communication between different cortical areas. In humans, these events can be measured non-invasively outside the skull, for example by recording electric or magnetic fields that are produced by neuronal population activity on the cortex, with electroencephalography and magnetoencephalography (EEG and MEG). By combining MEG and EEG with simultaneous behavioural experiments, it is possible to extract neuronal activities that are correlated with perception and action. In this thesis, MEG recordings combined with advanced data-analysis techniques were used to study the role of cortical oscillations –brain rhythms – in coordinating conscious perception and action as well as their deficits in chronic schizophrenia.

In Study I and Study II, I investigated what the local and large-scale neuronal correlates of conscious somatosensory perception are, respectively. Healthy subjects were stimulated at their index fingers with somatosensory stimuli, adjusted individually at the threshold of detection, so that around half of the time the stimulus was detected. Concurrent MEG recordings and subsequent source-modelling revealed in Study I that perceived trials were correlated with strengthened evoked responses (ERs), phase-locking to stimulus onset (SL), and induced oscillation amplitude modulations. The most robust and widespread of these was SL that was sustained in the low-alpha (6-10 Hz) band. The strength of SL and to a lesser extent that of ER predicted conscious perception in the somatosensory, lateral and medial frontal, posterior parietal, and in the cingulate cortex.

In Study II, I investigated the role of large-scale synchronization in the conscious somatosensory perception. Perceiving and reporting of weak somatosensory stimuli were correlated with sustained strengthening of large-scale synchrony, concurrently in delta/theta- (3-7 Hz) and gamma- (40-60 Hz) frequency bands. In a data-driven network localization, I found this synchronization to dynamically connect the task-relevant, *i.e.* the frontoparietal, sensory and motor systems. The strength and temporal pattern of interareal synchronization were also correlated with the response times. These data showed that a rapid phase-reorganization and concurrent oscillation amplitude modulations in the specific areas play a key role in the emergence of a conscious decision-making, and subsequent actions. Furthermore, this study showed that perception is dependent on transient large-scale phase synchronization in the delta/theta and gamma bands.

In the third study, I investigated whether aberrant large-scale synchronization or dysconnectivity could underlie perceptual deficits in patients suffering from schizophrenia. To this end, I analysed MEG data from chronic schizophrenia patients and healthy control subjects recorded during a visual perception closure task. In schizophrenia patients, a reduction in gamma-band (30–120 Hz) oscillation amplitudes, accompanied by a pronounced deficit in large-scale synchronization at gamma-band frequencies characterized visual processing compared to healthy control subjects. Synchronization was reduced within visual regions, as well as between the visual and frontal cortex. Additionally, the reduction of synchronization correlated positively with clinical disorganization scores. Accordingly, these data imply that schizophrenia is associated with a profound disruption of transient synchronization. This observation provides critical support for the notion that the core aspect in the pathophysiology of schizophrenia arises from an impairment in coordination of distributed neural activity.

1 Introduction

1.1 An evolutionary perspective to biological oscillations

In nature, one of the very first movements that revolutionized the role of an ancient organism from a passive drifter to an active manipulator, was the development of the cilia and flagella. Rhythmic oscillatory and coordinated movements of the cellular protrusions like flagella and cilia, allowed organisms not only to move faster in a preferable direction (or away from the harmful one) but also to create local currents in the watery environments. Synchronous oscillations between these structures paved way for filter-feeding that is still seen in many multicellular sea-animals, such as in the primitive *Porifera* sponges (Fig. 1). The ability to control the frequency of these oscillatory movements was of paramount importance to keep the animal's fitness as optimal as possible in the changing surroundings. The mechanism that primitive organisms evolved to monitor their environment and the state of the protrusion, as well as to optimize their fitness in the given surroundings, is called a sensory system.

Senses are usually associated with neural activity. However, *Porifera* do not have a nervous system or even neurons. Later evolved coral animals *Cnidaria* with their nerve net structures are regarded as the first animals with a nervous system. They have also developed multi-cellular structures called tentacles or lophophores to manipulate their environment even more powerfully than the filter-feeders had done. In theory, these tentacles can be used in two ways to catch a prey: either by producing frequent oscillatory reach-and-grasp movements hoping to get something or by reaching out waiting to come across a proper prey, and to grasp or engulf only then. In the former strategy, the polyp might miss a plankter if it happens to come at the wrong phase of an action cycle. Nonetheless, it might be an apt approach if the flow of the resources is abundant. The latter strategy with reflexes is tailored for an environmental situation in which resources are scarce and their occurrence sporadic – the way nature appears to the predators most of the time. Physiologically, the fundamental difference between these two strategies is that the latter one requires feed-back information on the status of the tentacles to modulate the action generator and subsequent movements. Accordingly, investment in feed-back mechanisms has proven to be worth the cost as the previously described oscillatory and more expensive fixed movements are nowadays realized almost only in coral animals belonging to *Xeniidae* family (also known as pulse corals). They balance the cost of the pulse movements by increased oxygen repulsion to optimize photosynthesis of the symbiotic algae (Kremien et al., 2013).

Even though movements may not seem oscillatory anymore in the stimulus-driven behaviour of a preying *Cnidaria* -polyp, the underlying nervous system still acts on an oscillatory basis. Its level of excitation is suppressed for each cycle by inhibitory neurons and/or recurrent signals so that no movements are generated if the bottom-up, i.e. sensory stimulation is weak. A substantial amount of energy is spared when movements are optimized. Even more energy is saved when, at the same time, the reactive system is constantly kept at standby for an upcoming event. Namely, ignition from a low-level or zero base-line activity to a fully generated fixed action pattern, would take too much time (the prey escapes) and is metabolically costly (it is easier to keep a pendulum moving when it is already swinging). On the other hand, too high a level of excitation in lack of proper inhibition would lead to an excessive and unfavourable runaway reaction in the neuromuscular system, i.e. spasticity. Hereby, periodic oscillations are the solution to safely and frequently

manipulate cell excitability so that at certain phases it is easier to reach the required threshold than at other phases.

Because of the ecological one-upmanship provided by energy-saving oscillations, the nervous systems often work by constantly discharging their excitatory or inhibitory neurons, instantiating some more or less predictable rhythms. In the absence of any apparent external stimulus, such as a plankter falling into a tentacle, this waxing and waning systems-level neural activity is denoted as a spontaneous or endogenous top-down nervous activity. The balance between stimulus driven or bottom-up and top-down fluctuation states – in addition to the phase of the ongoing action cycle - determines whether a stimulus will be perceived. In *Cnidaria* and phylogenetically primitive animals there are relatively few such states.

As evolution can work only with the already existing solutions, this efficient oscillatory mechanism seen as an interplay between the sensory system and action generators of a primitive polyp has been applied to many other challenges over the course of time (Fig. 1). In a terrestrial multi-organ organism such as a human, increased physiological complexity, tissue specialization and organ function require communication and synchronized activity in different cells and tissues for a coherent and ideal overall reaction capacity. Ultimately, these same oscillatory strategies are applied to breathing, heart-beat, circulation, filtration, metabolism, endocrine cycles, circadian rhythms and to brain function as well.

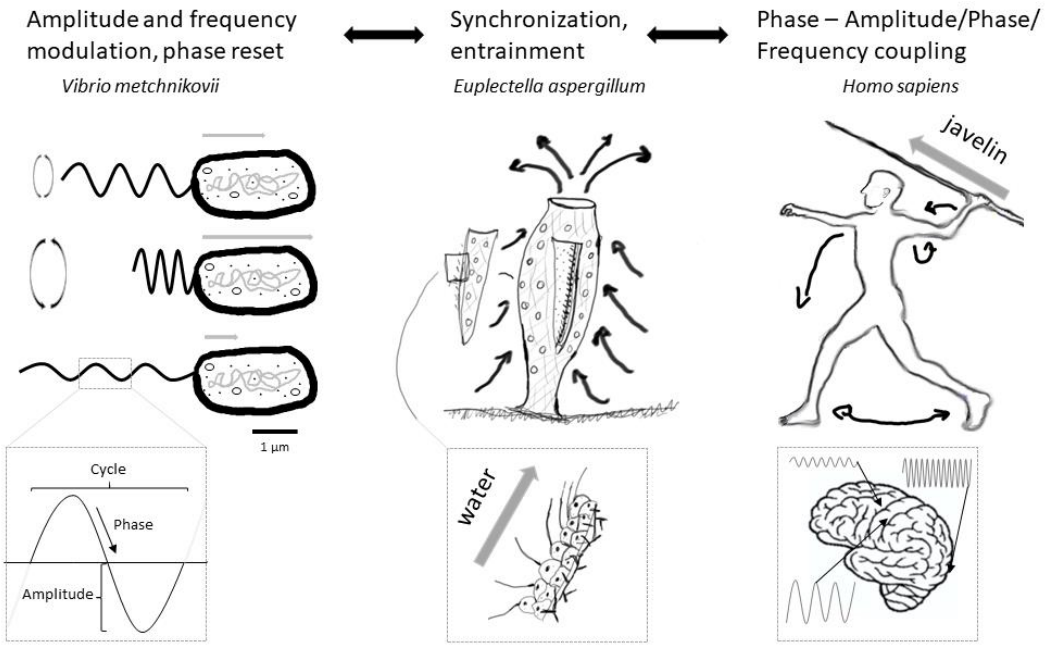

Figure 1: Examples of oscillatory mechanisms that produce and control movements.

1.2 Oscillations as means of synchronization – the same mechanisms from pancreas to brain

One noteworthy and relatively simple case where oscillations with alternating excitation and inhibition dynamics are manifested as an effective platform for coordinated bodily activity, is the regulation of glucose balance (Park et al., 2017). Glucose is the main energy source of all cellular metabolism and especially important for the nervous system that can poorly take advantage of other sources. Glucose concentration in the blood is elaborately controlled by hormones, of which the most important ones are glucagon and insulin. These hormones are produced by alpha and beta cells in the Langerhans islets of the pancreas. Additionally, there is a third kind of cells in these islets, namely delta cells that control the activity of alpha and beta cells via somatostatin secretion (Fig. 2A). There are around one million of these islets in the pancreas of a healthy adult human and each islet contains from 3,000 to 4,000 cells of which around 20, 65 and 10 % are alpha, beta and delta cells, respectively (the remaining 5 % is composed of PP cells that secrete pancreatic polypeptide). When these cells become depolarized as a response to paracrine or autocrine signalling from the neighbouring, or even from the same cell, they launch an action potential and secrete their signature hormones. In addition to the obvious systemic endocrine effect of these hormones mediated by the blood circulation, they also control each other in the Langerhans islets. They always do it in the same way, so that beta cells inhibit alpha cells, but excite delta cells, alpha cells excite both beta and delta cells, and delta cells inhibit both alpha and beta cells (Fig. 2A). In this case, the triad of directed communication could in theory have $3^6 = 749$ different motifs as per all possible intra-islet interaction combinations. Nevertheless, only the one with the previously presented anti-symmetric interactions is de facto realized in the body (Park et al., 2017).

This specific arrangement has the most optimal dynamics for sparing hormone consumption in intra-islet signalling, and at the same time for coordinating inter-islet synchronization, so that anti-phasic glucagon and insulin production (excitability in all other islets) can regulate normal blood glucose concentration fluctuations. Variations in islet-cell excitability and their synchronization create temporal windows, during which synchronized islet-cells can enhance information transfer between each other and simultaneously suppress information transfer with unsynchronized cells. Even more importantly, this inter-islet synchronization is not hyper-synchronized to a fixed regime but can in turn be entrained by high amplitude glucose oscillations so that the often-dangerous hypo- or hyperglycaemic states can be avoided. Disturbances in this fine-tuned islet synchronization pattern are observed when the blood glucose levels are continuously abnormal, compared to what they were evolved for, and may result in ever increasing occurrences of diseases, such as diabetes mellitus type 2 (often triggered due to modern Western eating habits).

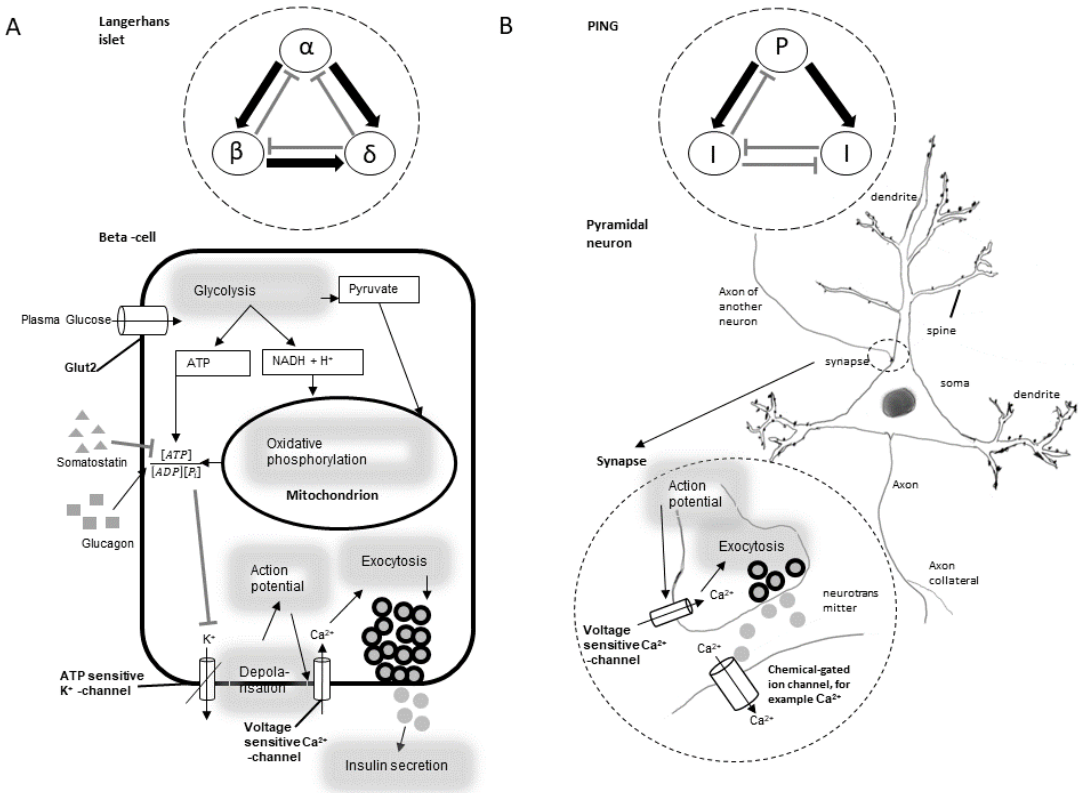

Figure 2: Cellular excitation-inhibition motifs and signal transduction in **A**) pancreas and **B**) brain cortex. PING (pyramidal-interneuron network gamma) is one mechanism for cortical gamma oscillations (Tiesinga and Sejnowski 2009). The Greek letters refer to alpha-, beta- and delta-cells in Langerhans islets.

In the brain, there are many areas with a small-world like population of pyramidal- and interneurons that can be thought to correspond to pancreatic islets. In fact, the pancreatic cells and neurons share many common traits and are closely related to each other (Arntfield and van der Kooy 2011; Eberhard 2013). However, the main difference is that pancreatic cells integrate their activities directly at the chemical level without the axons, dendrites or synapses that are seen in neurons. Not surprisingly, there is a growing body of evidence that synchronous oscillation facilitates and mediates the transfer of information across the brain areas (Engel et al., 2001; Singer and Gray 1995; Singer 1999). According to these findings, binding of perceptual features is related to synchronization of cell

assemblies that encode these distinct features (Singer 1999). On the contrary, unrelated features that are not part of a coherent object, are associated with uncorrelated firing activity and desynchronization. These ideas were originally obtained from studies where neurons representing different visual fields in the feline primary visual cortex were recorded when showing a single perceptual object to cats (Gray and Singer 1989). During a perception of coherently moving visual stimuli, the spiking dynamics of different neuronal assemblies became synchronized. On the other hand, when the visual stimuli moved into opposite directions, these neuronal assemblies became unsynchronized, even though the firing rates remained the same.

Later, communication through coherence theory proposed that oscillatory synchronization coordinates communication across neuronal assemblies (Fries 2005; Fries 2015). According to this theory, the information transfer and neuronal communication are achieved when the activity of different neuronal assemblies are synchronized, i.e. the assemblies are phase-coupled. This is because oscillations reflect fluctuations in neuronal excitability and because spiking is facilitated at one phase and suppressed at the opposite phase of the oscillatory cycle. The cycle length of gamma-band synchronization (30-100 Hz) has been proposed to mediate communication through this mechanism.

1.2.1 Mechanisms of gamma oscillations

Why do oscillations at gamma frequency play such a significant role in mediating interareal synchronization? One explanation is that oscillations in the gamma-band are fast enough to precisely, efficiently and selectively tap into the time-window at the length of approximately 3 ms that concurs before the recurrent perisomatic feedback inhibition, mainly carried out by GABAergic parvalbumin basket neurons (Fries 2015). Another mechanism that modulates gamma oscillations is the functioning of excitative glutamatergic NMDA receptors, blocking of which leads to increased gamma-band oscillations (Hong et al., 2010) and possibly dysfunctions in cortical integration (Pinault 2008). More recently, it has been found that gamma oscillations related to certain aspects of cognition are in fact composed of two distinct bands: slow (25-45 Hz) and fast ones (45-70 Hz) (Murty et al., 2018) where the slower ones are likely to be produced by inhibitory somatostatin (see pancreas example) interneurons, instead of the GABAergic ones related to higher gamma-band oscillations (Veit et al., 2017).

1.3 Neuronal long-range communication

It is still somewhat unclear how gamma band oscillations could integrate neuronal processing over long-distances, or even across hemispheres (Singer 2017). This is because at the longer distances, synchronization of neuronal activity becomes harder due to longer axonal conduction delays. Interestingly, synchronization in the lower frequencies is theoretically easier because the cycle length of these oscillations is wider (Siegel et al., 2012). Accordingly, some studies have found evidence that gamma-band synchronization is local, while alpha-band synchronization occurs over longer distances (von Stein and Sarnthein 2000).

Conduction delays may be partially overcome by myelination of the axons, which increases the conduction velocities, but only up to a certain limit. Growth of the myelin and white matter increases the brain volume, which is already at the maximum level in humans. In the case of long myelinated callosal projections, gamma-band oscillation can be synchronized across

hemispheres (Engel et al., 1991) via GABAergic connections and can then modulate local PING circuitry (Buzsaki and Wang 2012). However, this does not explain the observed distant connections within the hemispheres (Bastos et al., 2015; T. J. Buschman and Miller 2007; Gregoriou et al., 2009). The easiest solution would be to have either a cortical or sub-cortical common pace-making relay station between the two distant areas (Saalmann et al., 2012), but it is not necessary. Instead of a third source, fast oscillations can phase-lock to a slower background oscillation with cross-frequency coupling (Belluscio et al., 2012; Canolty et al., 2006; J. M. Palva et al., 2005). There are in theory three possibilities for the interareal cross-frequency synchronization: phase-phase, amplitude-amplitude and phase-amplitude couplings. Phase-amplitude coupling, or so called nested oscillations, happens when the amplitude of the faster oscillation follows the phase of the slower oscillation. For example, the phases of the pyramidal beta- and interneuronal gamma-band oscillations in a slice of the rat's hippocampus were seen to be locked to the amplitude of the high frequency stimulation in a 1 to 2 ratio of the frequency integers (Traub et al., 1999; Whittington et al., 1997). In the case of nested oscillations, the frequencies of the coupled oscillators are usually different because amplitude changes usually take more time than one cycle, but phase changes can exhibit sub-cycle dynamics within the same frequency. Nevertheless, within-frequency-phase-phase synchronization is a reasonable measure in assessing interareal communication in anatomically distributed neuronal networks. The benefits of the phase-phase synchronization to other coupling alternatives are that the phase shifts are quick and can entrain spiking activity without altering synaptic gains (S. Palva and Palva 2012). However, the actual bottom-up and top-down integration is probably carried out with either cross-frequency-phase-phase or phase-amplitude synchronization (J. M. Palva and Palva 2017).

1.4 Origins of neuronal activity in MEG

The constant flow or availability of glucose at the right concentration is especially important for the neurons of nervous tissue. Neurons consume a vast amount of energy to keep the ion gradients across the cell membrane steep enough for generating action, or graded potentials. Action potentials eventually propagate via axons and through synapses to the dendritic shafts of other neurons, where they become integrated from multiple inhibitory and excitatory sources and create post-synaptic potentials (Fig. 2B). Voltage difference between the dendrites and the cell soma results in decaying electrotonic intracellular ionic currents towards the soma (sink) of the neuron where it might trigger a new action potential. When many pyramidal neurons with their apical dendritic postsynaptic potentials are aligned in a laminar fashion as layers I-VI on a human brain cortex, they can generate population level electric and magnetic fields that are strong enough for sensors located outside the skull to capture them for EEG or MEG. The signals that are recordable with MEG are produced by a summed mass activity of cortical current dipoles. Brain oscillations at population level can be decomposed into sinusoidal rhythms, i.e. oscillations that have characteristics such as phase, amplitude and frequency (Hari et al., 2010).

1.5 Source-modelling of MEG data is necessary to make functional interpretations of the recorded activity

The sensor-level MEG data does not reveal the brain regions creating the activity observed at scalp-level. Moreover, signals that seem to be correlated at the sensor-level, might be uncorrelated in the source-level. The interpretation of recorded brain activity and its exact cortical location is impeded

by the ill-posed inverse problem. Since the mid-19th century it has been known that one cannot determine the exact current distribution in a circuit solely by knowing the properties of the generated electric or magnetic field (Helmholtz 1853). There is an infinite number of possible current distributions that can produce the observed changes in the fields. Furthermore, the inverse issue is underdetermined as there are fewer sensors than cortical sources to be modelled. Hereby, sensors located outside the scalp record a mixture of signals originating from different sources. Nonetheless, the inverse problem can be alleviated by creating a forward solution model from the known anatomical structures and volume conduction therein, which has a unique solution. Furthermore, the noise-patterns of the sensors can also be calculated (see methods 3.3). By combining the information from these well-posed sources and making minimal assumptions about the strength, orientation angles and localization of the current dipoles on the cortex, a source-model can be obtained. Minimum Norm Estimate (MNE) source-modelling is one approach for solving the inverse problem and it is used in the studies related to this thesis. MNE contains an assumption that the strength of source-dipoles is normally distributed (L2-norm) and the dipoles are perpendicular with respect to the brain surface (Hamalainen and Ilmoniemi 1994). Shortly, MNE returns the smallest possible current amplitude distribution for the given set of dipoles that can explain the recorded signals with the above mentioned auxiliary data.

1.6 Caveats in the analyses of MEG data

1.6.1 A need for individually optimized cortical parcellations

MNE based source-modelling yields 6,000-8,000 statistical source-dipoles from data usually measured with ~300 MEG sensors. However, because of the large source mixing due to the ill-posed and underdetermined inverse problem, the information carried out by each source dipole is redundant. Owing to the arrangement of the MEG sensors, the shape of the head and the brain being measured, the degree of source mixing varies in different areas and individuals. The poor source reconstruction accuracy of some cortical parcels limits the overall quality of all-to-all interaction analyses. In this study, I utilized a simulation-based method to assess the reliability of local source time-series reconstruction and interareal interaction estimates (Korhonen et al., 2014). Briefly, I used the subject cohort's source models, i.e. forward- and inverse-operators that were derived from real MEG recording, simulated independent parcel time series as the ground-truth data and then simulated a virtual MEG recording and source-reconstruction by forward- and inverse-modelling the ground-truth time series (for details, see methods 3.3). Thus, by assessing the correlations between simulated and reconstructed data, one can obtain quantitative estimates of the reconstruction accuracy and signal mixing between parcels. This reconstruction accuracy is called fidelity and is then used as weighting factor when averaging activity time-series of multiple source-dipoles into a coarser unit, i.e. parcel. The collapsing of source vertices into parcels by selecting the vertex-pairs with the highest fidelity yields a fathomable number of activity sites (a few hundred compared to 6,000-7,000). The collapsing also increases the signal-to-noise ratio as well as reduces the redundancy posed by a smaller number of sensors than cortical sources, hence leading to reduced artefactual synchronization. Finally, this method allows identifying those parcels that have low fidelity.

1.6.2 Estimating synchronization from MEG data

Phase synchronization between two neuronal signals means that their phase difference is stable over a certain period of time. In the studies related to the thesis work, interareal synchronization is

quantified as phase-locking values (PLV) and imaginary phase-locking values (iPLV) between all the cortical parcel pairs to reveal all-to-all connectivity (see methods 3.4 for details). PLV measures correlations at all phase lags, but among nearby parcels PLVs will be inflated by signal mixing and spatial leakage. Spatial leakage is what is left of signal mixing after source-modelling. Its degree depends on the choice of source-modelling method but cannot ever be completely abolished in the source models. The leaking of source activity across parcel borders is a critical aspect to consider, as neighbouring parcels can have very different functions in cognition. Contrary to PLV, imaginary PLV (iPLV) is insensitive to true zero- and π-lag phase couplings. iPLV thus does not produce artificial false positives like PLV. Nevertheless, spurious interactions, *i.*e. false positive connections between parcels adjacent to a pair of truly coupled parcels, do persist with both PLV and iPLV (S. Palva and Palva 2012). As the spurious synchronization has the same phase-lag distribution as the real synchronization, it is difficult to remove systematically. Fortunately, a recent article shows that the problem with the spurious connections can be remarkably alleviated with hyper-edge bundling (Wang et al., 2018). The goal for bundling is to hierarchically cluster connections into connection bundles that reflect isolable underlying true connections. In essence, hyper-edge bundling decreases the rate of false positive edges, i.e spurious interactions visible at the graph level with little loss of actual true connections. So, in this thesis work hyper-edge bundling correction was utilized as an informative visualization of the most central functional connections in graph theoretical analysis.

Finally, trial averaged neuronal activity and phase-resetting of the ongoing activity caused by external stimulation can bias any interaction metrics (S. Palva and Palva 2012). Here, this effect of the evoked responses is taken care of by creating trial shuffled surrogates for the comparison. Briefly, this method reconstructs the evoked components and their spatial spread caused by the signal mixing inherent to MEG/EEG and preserves local source topography changes, amplitude dynamics, and changes in auto-correlation structures that may constitute confounders (for details see 3.4). Hence, this new approach provides a good surrogate for selectively identifying the true induced interareal interactions, for which the conventional trial shuffling (Lachaux et al., 1999) is insufficient in the presence of signal mixing.

1.7 Neuronal correlates of conscious perception and action

Different oscillation frequencies have been linked to different cognitive functions. Oscillations are usually segregated into functionally distinct frequency bands: delta (<4 Hz), theta (4–7 Hz), alpha (8–12 Hz), beta (13–30 Hz) and gamma (> 30 Hz). Of these oscillations, gamma band oscillations that were shortly described above, are traditionally coupled to conscious perception (Fries et al., 1997; Meador et al., 2002; S. Palva et al., 2005; E. Rodriguez et al., 1999), perceptual switching during perception of bistable (Keil et al., 1999) and binocular rivalry figures (Tononi and Edelman 1998). Specifically, gamma oscillations have been shown to be correlated with bottom-up processes like content analysis and binding of stimulus features, both in EEG (Tallon-Baudry et al., 1996; Tallon-Baudry and Bertrand 1999) and MEG (Grutzner et al., 2010).

In contrast, alpha oscillations that were first observed at the beginning of the late twenties, were seen to be increased when the eyes are closed in contrast to being open (Berger 1929). Later, it was noticed that processing of sensory information in other modalities also modulated oscillations at the same frequency. In the sensorimotor (SM) region alpha rhythms were denoted as mu-rhythms (Gastaut and Bert 1954) and in the auditory cortex as tau-rhythms (Lehtela et al., 1997). Alpha oscillations have not been directly associated with perceptual functions but with attentional modulation of sensory stimuli (Jensen and Mazaheri 2010; Klimesch et al., 2007; S. Palva and Palva

2007; S. Palva and Palva 2011), either by facilitating processing of the attended information or suppressing the processing of the non-attended information. Furthermore, interareal alpha-band phase synchronization has been suggested to coordinate attentional and executive functions (S. Palva and Palva 2011). Recent work indeed supports this idea and shows that alpha-band synchronization predicts whether visual stimuli are attended (Lobier et al., 2017). In the somatosensory modality it was observed that reduced power in the alpha- (Weisz et al., 2014) and beta-band (Frey et al., 2016) oscillations before the stimulus onset preceded conscious perception. Moreover, beta-band power modulations also correlated with translation of perceptual information into goal-directed actions (Turella et al., 2016).

1.7.1 Cortical systems-level basis of the perception-action chain

It has been theorized that conscious perception is constituted by interactions between high order sensory areas and fronto-parietal network (FPN) system (Dehaene et al., 2006; Dehaene and Changeux 2011), as well as recurrent information flow between these regions (Lamme 2006; van Gaal and Lamme 2012). Experimental evidence from several previous studies using brain-imaging techniques, such as fMRI (Blankenburg et al., 2003; Boly et al., 2011; Dehaene and Changeux 2011; Li Hegner et al., 2015), human intracranial electroencephalography (Fisch et al., 2009; Gaillard et al., 2009) and non-invasive source-reconstructed EEG and MEG (Salti et al., 2015) has shown that neuronal activity in prefrontal (PFC) and posterior parietal cortex (PPC), along with that in occipitotemporal cortex (Grill-Spector et al., 2000; Hesselmann and Malach 2011; Hesselmann et al., 2011), is correlated positively with conscious perception (see Fig.3 for the areas). Furthermore, activity modulations of insula, anterior and posterior cortices and thalamus have been demonstrated to predict conscious perception (Boly et al., 2007; Marois et al., 2004; Sadaghiani et al., 2009).

Another domain of interest is to reveal the temporal dynamics behind different aspects leading to conscious perception for which fMRI has too poor a resolution. Earlier electrophysiological recordings with millisecond time-scales, such as EEG (Fahrenfort et al., 2007; Koivisto et al., 2008; Pins and Ffytche 2003; Sergent et al., 2005) and MEG data (Frey et al., 2016; S. R. Jones et al., 2007; Melloni et al., 2011; S. Palva et al., 2005) as well as intracranial EEG measurements (Fisch et al., 2009; Gaillard et al., 2009) have revealed that the magnitude of ER predicts conscious sensory perception. In addition to ER, also phase and amplitude dynamics, which regulate neuronal information processing (Cardin et al., 2009; Singer 1999; Womelsdorf and Fries 2007), are associated with conscious perception. Additionally, a recent study using a decoding approach of MEG data showed that the brain regions as well as temporal evolution of neuronal processing were distinct for perception, maintenance and visibility of seen and unseen visual stimuli (King et al., 2016)

More specifically, both MEG sensor-level results (S. Palva et al., 2005; Wyart and Tallon-Baudry 2008) and intracranial EEG analyses (Aru, Axmacher et al., 2012; Fisch et al., 2009; Gaillard et al., 2009; Vidal et al., 2014; Vidal et al., 2015) have manifested that especially the amplitudes of local gamma (30-120 Hz) band oscillations are correlated with conscious perception of visual stimuli. Moreover, it has been indicated that the strength of gamma oscillations also reflects visual content analysis or sensory evidence, rather than the conscious perception itself (Aru, Axmacher et al., 2012; Vidal et al., 2014).

Another different line of study is to investigate what processes before the stimulus onset there are that can lead to conscious perception. For example, moments before somatosensory stimulation leading to conscious perception were characterized by reduced alpha- and beta-band power in contralateral somatosensory (especially SII) and mFG regions (Frey et al., 2016; Weisz et al., 2014). Additionally, these prestimulus nodes were connected to each other but decoupled from precuneus, a part of DMN, when the oncoming stimulus was about to be consciously perceived (Weisz et al., 2014).

Perceptual decision making, i.e. the process for deciding to report the presence or absence of a stimulus, is associated with the changes in activity, at least in PPC and PFC in human (Donner et al., 2009a; Kaplan et al., 2017; Tosoni et al., 2008) mouse (Goard et al., 2016) and monkey (Siegel et al., 2015) local field potential data. More specifically, it has been hypothesized that the sensorimotor decision processes involve neuronal structures that influence the preparation of the closely associated actions. These areas include oculomotor regions of the parietal and prefrontal cortex in monkeys (Schall 2001; Yang and Shadlen 2007) and the response-related PPC regions and motor cortex in humans (Donner et al., 2009a; Gould et al., 2012; Kaplan et al., 2017; Medendorp et al., 2011; Tosoni et al., 2008). Finally, the last step of the chain, namely motor actions, affects dynamically the processing of sensory information (Gutteling et al., 2011; Wohlschlager 2000), and at the behavioural level, rhythmicity of visual perception is coupled with that of action (Tomassini et al., 2015). Entrainment of gamma-oscillation by stimulating parvalbumin interneurons optogenetically at 40 Hz turned out to enhance detection of weak tactile stimulus targeted at rat vibrissae 20-25 ms after the gamma entrainment (Lee et al., 2014). This is in line with the earlier assumption that attention facilitates gamma-band oscillations in sensory areas and subsequently perception of an oncoming stimulus (Fries 2015). Attention may also reduce response variability and noise-levels (R. Rodriguez et al., 2010).

This thesis aims to show in more detail whether the areas above play a role in the chain from conscious perception to an action as well as to reveal their local and interareal oscillatory dynamics.

1.8 Successful face perception requires interareal communication

The environment and its human-specific stimuli can be very complex by nature and neurons comparatively simple. How is this challenge of transforming certain physical features into meaningful and conscious mental representations solved in the brain? In literature this is denoted as the binding problem, the issue of binding elementary sensory input pieces into some relevant meaning or concept. This function has stemmed from the fact that neurons code only for very simple features, but the brain is able to create representations of quite abstracts objects. Take for example human faces as a natural stimulus. They have special meanings for different people. However, most of the faces have the same setup: two eyes, nose, mouth, lips, forehead, lashes, eyebrows, cheeks, jaw and two ears. These pieces of information are conveyed as alterations of light and contrast via optic nerves to visual cortex on the occipital part of the cerebrum (see caS in Fig. 3). There face properties are filtered and coded from simple features such as horizontal and vertical lines to successively more complex ones from primary visual cortex to secondary and higher order areas. A region called occipital face area (OFA) extracts different facial elementary parts (Gauthier et al., 2000). Then the information related to the faces gets more abstract and spatially dispersed the farther it propagates along the ventral visual stream. During this course it is all the time complemented by feed-back signalling from higher association areas. It has been suggested that synchronized activity especially at mid-gamma band (40-50 Hz) could underlie perceptual binding in primary visual cortex (see chapter 1.2).

Approximately after 150 milliseconds seeing a face, the signalling pathway activates among others a cortical structure called fusiform gyrus (Fus) (Halgren et al., 2000; Lin et al., 2018). Suffice activation of this area is required so that a person can claim to have recognized the picture to be a face (Miller et al., 2017). Then even more information and at a more abstract level can be decoded

from the faces, like age, gender or ethnicity of the face owner, the emotional states, his/her intentions, motivations and even health status if the observer is practised enough. For example, the activation of superior temporal sulcus (sTS) is thought to take care of encoding social facial contents such as gaze (Haxby et al., 2000; Puce et al., 1998). Together these three areas: OFA, FFA and sTS form core-face processing regions and exhibit selective activations during perception, in contrast to non-face objects (Tsao et al., 2006).

Normally, this ability to detect faces is so dominant that people see faces even where they do not exist, like in the clouds, trees, constellations or in perlin-noise in a simple neuropsychological experiment. This is a manifestation how endogenous species-specific brain activity influences in a feed-back manner the lower visual streams. However, in subjects suffering from schizophrenia this very humane skill is somewhat confounded. Namely, they have difficulties in seeing faces where healthy people see them (Butler et al., 2008; Chen et al., 2008). One reason for, or a manifestation of this shortcoming is that the patients suffering from schizophrenia often have reduced grey matter volumes in those above-mentioned core-face processing regions (Onitsuka et al., 2006). Moreover, functional analyses using fMRI have shown that activity in these areas indexed as face selectivity is reduced compared to healthy controls (Maher et al., 2016). However, the interplay of these and other cortical areas has remained somewhat unclear. Accordingly, it has been hypothesized that schizophrenic patients might have deficits in cortical interareal connectivity (Uhlhaas and Singer 2015) and their cortical excitation-inhibition balance seen as gamma-band changes might be altered (Lewis et al., 2005). Excitation-inhibition balance is largely influenced by the brain's neurochemistry and especially neurotransmitters such as dopamine, GABA, glutamate and acetylcholine that all have shown to be altered in patients suffering from schizophrenia (Haenschel and Linden 2011).

Research findings from MEEG imply that both the amplitude of high-frequency oscillations and their long-range synchronization during perceptual processing are confounded in patients suffering from schizophrenia (Uhlhaas 2015). Several earlier studies on integration of perceptual properties, such as face features, have shown that local neuronal synchronization, reflected by the amplitude/power of oscillatory activity, is associated with the reduction of oscillatory strength at beta and gamma-band frequencies along different stages of visual processing (Grent-'t-Jong et al., 2016; Grutzner et al., 2013; Spencer et al., 2003; Spencer et al., 2008; Sun et al., 2013; Uhlhaas and Singer 2006). Furthermore, there are pieces of evidence that demonstrate abnormalities in long-range synchronization of the schizophrenic patients during perceptual feature integration (Spencer et al., 2003; Uhlhaas and Singer 2006).

These lines of research are consistent with the idea that synchronization of high-frequency oscillations may be coupled to a formation of coherent object representations during normal brain functioning (Grutzner et al., 2010; Keil et al., 1999; E. Rodriguez et al., 1999), and that deviations specifically in the gamma-band synchronization could be the key of the pervasive perceptual deficits in schizophrenia (Uhlhaas and Mishara 2007; Uhlhaas and Singer 2015).

However, the exact details at source-level on the cortex and the mechanistic understanding have remained elusive. This thesis endeavours to elucidate some of those aspects with new experimental results.

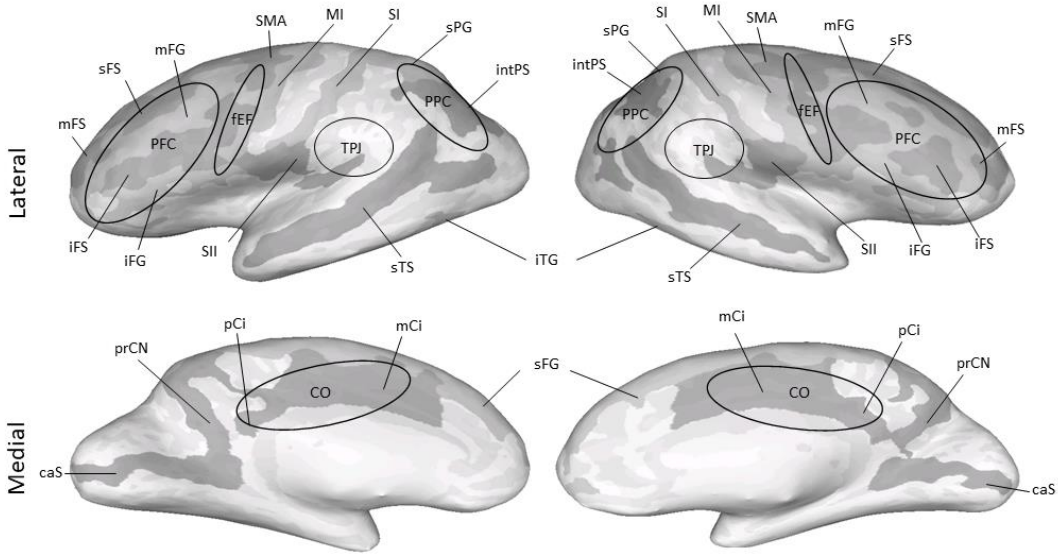

Figure 3: Cortical locations of some key parcels and areas discussed in this thesis. See the list of abbreviations for the full names.

2 Aims of the thesis

The primary goal of this thesis was to investigate the functional role of neural oscillations and synchronization in the conscious somatosensory and visual perception using MEG. The specific aims of the studies were to:

1. **Study I**. Characterize the functional role of local oscillation dynamics in conscious somatosensory perception of weak threshold-level stimuli and subsequent responses using MEG with source-modelling.

2. **Study II**. Characterize the functional role of interareal phase synchronization in conscious somatosensory perception of weak threshold-level stimuli and subsequent responses using MEG with source-modelling.

3. **Study III**. Characterize whether aberrant interareal phase synchronization underlies deficits in visual perception in chronic schizophrenia.

3 Methods

For detailed description of materials and methods used in this thesis work, the reader is referred to the original publications (I-III). An overview of the methodology is provided below:

3.1 Tasks and stimuli

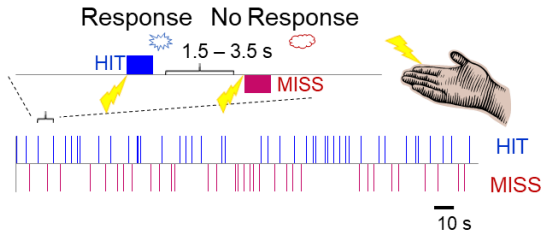

Figure 4: Schematic illustration on the experimental paradigm used in Studies I and II.

Somatosensory detection task: In Studies I and II, the course of becoming conscious of something, i.e from perception to the decision to make a movement, was probed with a simple threshold of stimulus detection task (TSDT) with concurrent MEG recording (see Fig. 4). We gave healthy human volunteers very weak somatosensory stimuli at the tip of the right index finger which they occasionally felt and sometimes did not, even though the intensity of the stimuli was always the same. The stimulation intensity was adjusted individually before the experiment so that the subjects perceived the stimulus half of the time. The subjects' task was to indicate with a thumb twitch when they had felt the stimulus. This was registered with EMG electrodes attached to thumb muscles. The stimulus onset asynchrony varied randomly between 1.5 and 4.5 seconds. The experiment was divided into two sets, each of which lasted 1,800 seconds. During that time the subjects sat relaxed with their eyes closed and responded whether they felt the stimulus. In total, data from 12 subjects were analysed for this thesis. On average, 1,073 ± 207 (mean ± standard deviation (SD), n = 12) trials were acquired per subject. No trials were rejected.

Visual closure task. In Study III, both healthy volunteers and patients suffering from schizophrenia were shown two-tone upright and inverted-scrambled Mooney faces (Fig. 5) during a simultaneous MEG recording. The pictures were shown for 200 milliseconds with a stimulus onset asynchrony of 3,500-4,500 milliseconds. The subjects were instructed to respond as quickly as possible and to fixate a central fixation cross during the interstimulus interval. The participants completed from three to six experimental runs, each of which was composed of 60 upright and 30 inverted-scrambled stimuli presented in a random sequence. On average, 411 ± 78 (mean ± standard deviation (SD), n = 35) trials were acquired per subject. The subjects responded by pressing a button if they saw a face and pressing another button if they did not see a face. Only data for correctly perceived inverted-scrambled and upright trials were used for amplitude and synchronization analysis. In other words, trials in which upright faces were not reported as faces and trials where inverted-scrambled faces were reported as faces were not analysed beyond psychophysical analysis, because of their exceedingly small number. Data from 19 healthy subjects and 16 patients were obtained for the analyses. All schizophrenia patients were on stable neuroleptic medication.

Figure 5: Examples of upright (left) and inverted-scrambled (right) Mooney faces, similar to those used in the experiment of Study III.

3.2 MEG recordings and pre-processing of MEG data

In Studies I and II, MEG recordings were carried out with a 306 channel MEG instrument composed of 204 planar gradiometers and 102 magnetometers (Elekta Neuromag, Helsinki, Finland) at 600 Hz sampling rate. In Study III, MEG data were recorded continuously using a 275-channel whole-head system (Omega 2005, VSM MedTech Ltd., BC, Canada) at a rate of 600 Hz in a synthetic third order axial gradiometer configuration (Data Acquisition Software Version 5.4.0, VSM MedTech Ltd., BC, Canada).

In all the studies, raw MEG time series were preprocessed with the temporal extension of the signal space separation method (Taulu et al., 2005), which was used to remove extracranial noise from the raw MEG recordings and to colocalize the recordings across sessions and subjects. Next, independent component analysis (Bell and Sejnowski 1995) was used to identify and exclude components associated with eye movements/blinks and cardiac artifacts. Followingly, the preprocessed MEG time-series data from each separate channel were then narrow-band filtered into 38 frequency bands, from 3 to 120 Hz by convolving
the sampled MEG signals with a family of Morlet wavelets. Finite impulse-response filter was used for broad-band filtering from 0.1 to 45 Hz (pass-band from 1 to 40 Hz) and Hilbert-transformation to obtain the signal phase time series. FreeSurfer software (http://surfer.nmr.mgh.harvard.edu/) was used for automatic volumetric segmentation of the MRI data, surface reconstruction, flattening, cortical parcellation, and labeling with the Freesurfer/Destrieux atlas (Dale et al., 1999; Destrieux et al., 2010; Fischl et al., 2002).

3.3 Source-modelling and filtering of the data

Based on the report by a thumb lift (Studies I and II) or button press (Study III), I segmented the whole experiment in the trials of perceived (Hit for Studies I and II, upright or inverted-scrambled correctly perceived for Study III) and unperceived (Miss for Studies I and II, upright or inverted-scrambled not correctly perceived for Study III) stimuli. I then applied MNE-based L2 source-modelling using individual brain structures obtained by magnetic resonance images (MRI) to reveal the exact brain areas correlating with the course from perception to action. The source models had dipole orientations fixed to the pial surface normals and a 7 mm source-to-source separation throughout the cortex, which yielded models containing 6,000 to 8,000 source vertices. To reconstruct ongoing cortical dynamics, I used minimum-norm estimate (MNE) inverse operators in the form of dynamic statistical parametric map (dSPM) operators (Dale et al., 2000) that were built by computing noise-covariance matrices from the baseline data, separately for the broadband and each wavelet filter frequency. In creating dSPMs, source-dipoles from MNE modelling are transformed into statistical measures of the diffuse current, by dividing the source-estimates by the estimated standard errors that rise from noise in each spatial location (Dale et al., 2000).

Collapsing of the source dipoles into a smaller number of brain areas (called parcels throughout the thesis) was done by first iteratively splitting the largest parcels of the Destrieux atlas along their most elongated axis, using the same parcel-wise splits for all subjects, and then using novel sparse-weight operators (see chapter 1.6 for introduction). In short, I used parcel *fidelity* (f_u) to describe source reconstruction accuracy of parcel u, and *infidelity* (i_{uv}) to quantify the amount of mixing between parcels u and v. Parcel *fidelity* (f_u) is defined as the real part of PLV between $x_u(t)$, the simulated parcel time series, and $x_u'(t)$, which is $x_u(t)$ after forward and inverse modeling. Parcel-to-parcel *infidelity* (i_{uv}) is defined as the real part of PLV between $x_u'(t)$, the forward-inverse modeled parcel time series of parcel u, and $x_v(t)$, the original true time series of any other parcel v on the cortex. Therefore, f_u reflects source reconstruction accuracy in parcel u, whereas i_{uv} describes the degree of signal leak from parcel v to parcel u.

The collapsed parcel-wise broad-band filter based inverse estimates of single trials were used for cortex-wide mapping of phase-locking of ongoing activity to the stimuli (stimulus-locking, SL), evoked responses (ER) and induced amplitude dynamics. SL was quantified with the phase-

locking value, PLF that was given for each parcel (Sinkkonen et al., 1995). PLF yields values between 0 and 1, so that with an increasing number of samples, PLF approaches 0 for a uniform phase distribution. The averaged event-related amplitude envelopes were computed for induced oscillations. The filtered evoked responses were obtained by averaging the real parts of the complex filtered parcel time series. Since in the ER the signal polarity might change in different sides of the sulci and hence across cortical parcels, I took the absolute value of the ERs before statistical analysis.

3.4 Phase synchrony estimation

For Studies II and III, all-to-all phase-coupling-based functional connectivity, *i.e.*, phase synchrony between all parcel pairs was estimated in reconstructed source-space for all 38 narrow-band time series. I first computed the complex-valued phase-locking value (cPLV) between all parcel pairs. Here I assessed phase synchrony both by using the phase-locking value (PLV), PLV = |cPLV|, and the imaginary part of cPLV (iPLV), iPLV = |*im*(*cPLV*)|, where *im* indicates the imaginary value operator. To compensate for the fact that both PLV and iPLV are biased by the number of samples, the numbers of Hit and Miss trials were balanced within subjects before the PLV/iPLV analyses by keeping only those events of the larger condition, which are closest to the onset latencies of the smallest condition. For each frequency, the cPLVs were obtained across samples in 100 ms time-windows with 50 ms overlap and across trials. See introduction chapter 1.6 for tools that were harnessed in validating the synchrony results.

Furthermore, to account for the artificial synchronization attributable by evoked responses and/or phase-locking of ongoing activity to the stimuli, I created trial-shuffled surrogate data. In order to reconstruct the effects of signal mixing at MEG acquisition and inverse modeling, I applied a novel forward-inverse-modeling based approach. For this I first used shuffled trials of source-modeled single-trial data in the 400-parcel parcellations as parcel time series in forward modelling, so that each source vertex of a parcel was simulated with the same parcel time series. Then I source reconstructed these sensor-level surrogate data with procedures identical to those used for real data. Phase correlation analyses were then performed with ten independent realizations for these surrogate source data in the same way as to those of real data.

3.5 Statistical tests

I used statistical testing across all parcels, frequency bands, and time windows to reveal the task-related amplitude and synchrony modulation. Before performing statistical group analyses for amplitude, individual data were baseline corrected parcel-by-parcel, by subtracting from all samples the mean amplitude of a baseline period. Significant differences between upright/inverted (Study III) or Hit/Miss trials (Studies I and II) and the baseline period, as well as between the upright and inverted or Hit and Miss trials were estimated with the Wilcoxon signed-rank test ($p < 0.05$). For the between-group comparisons in Study III, the Welch *t*-test was used separately for the Upright and Inverted conditions. In all the analyses of Study III, only trials with correct responses were used. To reduce the false discovery rate (FDR) for each contrast, I pooled significant observations across all samples, frequency bands, and cortical parcels and then discarded as many least-significant observations as were predicted to be false discoveries by the alpha-level used in the corresponding test.

3.6 Visualization of the data

To obtain a data-driven overview of all significant observations, I plotted for the amplitude data the fractions of parcels out of all 400 parcels exhibiting a statistically significant positive or negative effect (P_P^+ or P_P^-) for each time-frequency (TF) element in the peri-event TF plane. To identify the brain with the most prominent effects in the time- or time-frequency window-of-interest (TFROI), I displayed the fraction of significant TF-elements of all elements for each anatomical parcel, visualized on a representative inflated cortical surface (P_{TF}^+/P_{TF}^-). Functional intrinsic network borders based on population level fMRI resting state activity (Yeo et al., 2011) were overlaid on the inflated

surface as landmarks. Likewise, to assess the extent of large-scale synchronization in each frequency band and time-window, I defined connection density *K* to be the fraction of significant edges of all possible edges ($K = k / (N-1)N$, where k is the number of significant edges and N is the number of parcels, $N = 400$). Similarly to the amplitudes, the connection densities were visualized in the TF plane. Graph theory (Bullmore and Sporns, 2009) was then used to characterize the networks formed by statistically significant parcel-parcel phase synchrony. Here, parcels constitute the nodes and significant synchronization the edges of the network. The graphs corresponding to these data were then visualized so that most central connections were identified for the connected nodes (Rubinov and Sporns 2010). Subsequently, I applied a novel hyper-edge bundling approach to group raw metric (*i.e.* PLV, iPLV) edges into bundles by their adjacency in signal mixing, which is derived from the parcel-to-parcel fidelity function described earlier (Chapter 1.6) and see Wang et al., 2018. To improve the neuroanatomical resolution of the bundles, I discarded edges with low centrality (< 50%) within each bundle. To decrease the probability of reporting artificial and spurious synchronization due to poor source reconstruction accuracy, I first removed parcels with fidelity lower than 0.11. Briefly, fidelity represents the reliability of local source time-series reconstruction and interareal interaction estimates (Korhonen et al., 2014) (and see introduction 1.6). These parcels were located mostly in deep and/or inferior parts of the cortex and are known to generate weak signals in MEG. Next, I excluded cortical parcels close to the eyes because they are known to include oculomotor artefacts in MEG. These parcels are mostly located afar (*e.g.* > 5cm) from the sensors such as the orbital frontal, anterior and inferior temporal and medial structures. In addition, I also removed parcel-parcel interactions that connected any parcels with low fidelity, *i.e.* interactions that would be very unlikely to be observable with MEG. For analyzed data, these couplings would thus be much more likely to mirror signal-mixed interactions from other sources and thus yield false positives.

To estimate interactions between the seven functional subsystems (Yeo et al., 2011) in Study II, I morphed the original 400x400 adjacency matrices into 7x7 subsystem interaction matrices and evaluated *K* of connections among each subsystem. To test whether these *K*-values were greater than expected by chance, I computed 5,000 randomizations of the same 400x400 matrices keeping the numbers of significant edges constant. *K*-values of the original interaction matrices of subsystems were reported as significant if they exceeded the 95th percentile of the *K* values in the randomized graphs.

3.7 Anatomical distances in Study III

For Study III, I computed normalized Euclidean distances for each pair of cortical parcels to assess the anatomical distance distribution of observed synchronization in the time-frequency-windows of interest. I selected the synchronization distances for each significant parcel pair from the average cortical distance-map based on the population mean of all the subjects in the study ($n = 35$). The distance map comprised all the Euclidean distances derived from the RAS-space (Right, Anterior, Superior – a coordinate system used in Freesurfer software) for each possible combination of 400 parcels yielding in total 160,000 distance values**.** These values were normalized by the longest possible distance on the whole cortex and the normalized Euclidean distances were binned into five bins. I then estimated the distances for the significantly synchronized parcel-pairs and the proportion of synchronization in each bin. These data were compared against a surrogate distance distribution that was built by randomly taking 5,000 times the same number of edges and its 95 % -confidence intervals.

3.8 Correlations between graph strength and disorder severity in Study III

To explore the putative links between interareal phase synchrony and clinical scores in Study III, I tested whether graph strength in the mid-gamma (40–51 Hz) band response co-varied with PANSS-

ratings. To estimate individual graph strength values, I first computed individual weighted graphs by multiplying individual baseline corrected iPLV interaction matrices with a binary mask based on group graphs. Parcels and edges removed for low reconstruction accuracy or at-risk for oculomotor artifacts were excluded by masking from this analysis as well. Binary masks were defined for the mid-gamma (40–51 Hz) band and 125–325 ms time-window for the contrast of upright- vs. inverted Mooney stimuli and controls against patients. For each subject, I multiplied adjacency matrices with these masks and then summed over all parcel pairs. Graph strength values were then sorted according to clinical scores and plotted as a function of increasing scores. Pearson correlation was used to estimate the correlation and bootstrapping with 10,000 surrogates to estimate confidence limits.

4 Results

4.1 Local cortical oscillation dynamics during somatosensory TSDT (Study I)

4.1.1 Cortical broad-band evoked-response and stimulus-locking results

The findings in Study I show that perception of a weak somatosensory stimulus (henceforward called Hits throughout the thesis) were characterized by strengthened overall cortical evoked and stimulus-locked responses compared to the trials with unperceived stimuli (called Misses throughout the thesis). On average, ER was significant in 20 % of all the cortical parcels starting around 70 ms after the stimulus onset and lasting up to 300 ms (Fig. 6A). Source-modelling revealed that these parcels were located mostly within borders of fronto-parietal (FPN) as well as dorsal and ventral networks (DAN) (Fig. 6C). However, the strongest modulation was observed in the sensorimotor network. More specifically, activation was most prominent in the sensorimotor parcels, such as primary motor

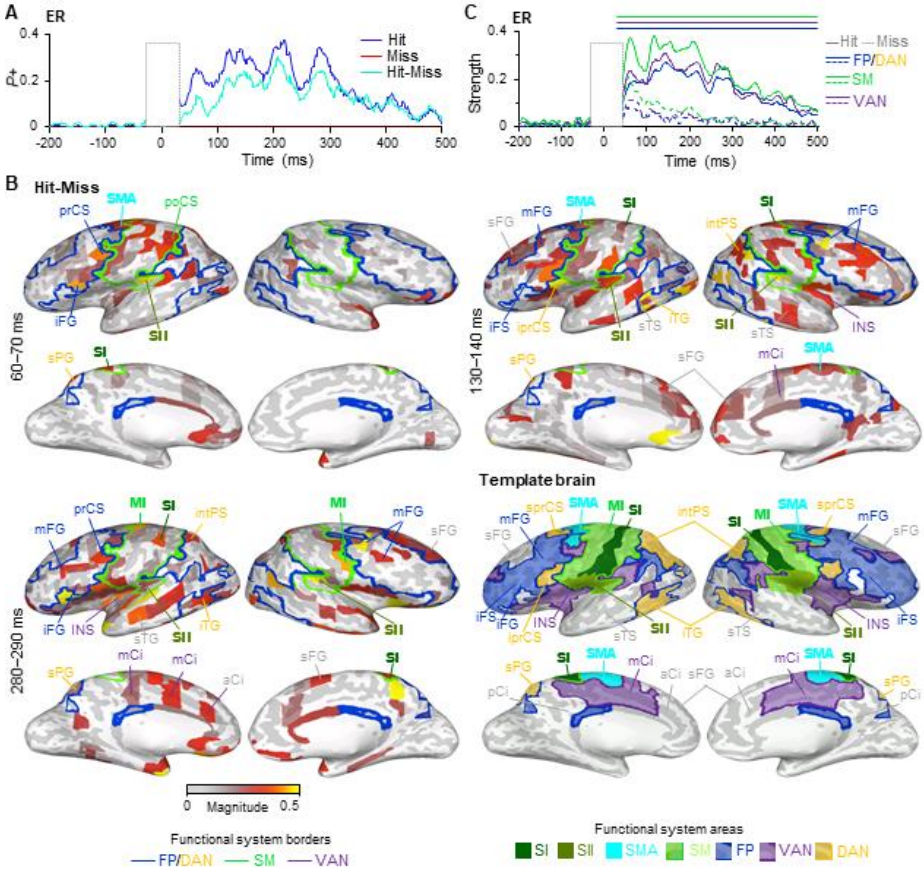

Figure 6: Evoked responses (ER) of broad-band (1 – 45 Hz) filtered MEG data perceived (Hit) and unperceived (Miss) stimuli. **A**) A fraction of the 400 brain areas (parcels) in which the ER was stronger (P+) than in the prestimulus baseline (BL) period separately for perceived stimuli (Hits (blue)) and unperceived stimuli (Misses (red) as well as for their difference (Cyan). The stimulus onset is at 0 ms. **B**) The cortical areas in which ER was stronger for the Hits compared to Misses displayed on inflated cortical surface. Colours of the parcels indicate average strength of the ER over a selected time-window. For the acronyms of the anatomical and functional brain areas, see the list of abbreviations. **C)** The strength of ER separately for Hits (solid line) and Misses (dashed line) averaged over contralateral SM (green), FP/DAN (blue), and VAN (purple). The lines above indicate significant difference between the Hit and Miss trials.

, secondary somatosensory area as well as frontal eye field (Fef) and supplementary motor areas contralaterally during the early latencies 60-70 ms. Later, after 100 ms, also ipsilateral areas became significantly modulated, but the most telling feature is the incorporation of frontal, temporal and parietal areas such as inferior and middle frontal gyrus (i/mFG), inferior temporal gyrus (iTG) and intraparietal sulcus (intPS) (Fig. 6B). Also parcels such as mid-cingulate (mCI) and medial suprafrontal gyrus (sFG) belonging to a so called cingulo-opercular saliency system (CO) exhibited local evoked response oscillation dynamics during the later latencies.

Also, for the phase-locking of the ongoing oscillations to the stimulus onset (SL), the proportion of significantly modulating parcels was on average ~30 % from 70 to 350 ms after the stimulus onset in the comparison of Hit-Miss. Along with the stronger modulation, the activation pattern included more frontal, parietal and CO parcels in addition to sensorimotor ones already at the earlier latencies than in the case of ER.

4.1.2 Broad- and narrow-band induced oscillation results

Induced oscillations, i.e. amplitude modulations, showed larger amplitudes in around 8 % of the cortical parcels from 70 to 230 ms after the stimulus onset and larger suppression, i.e. smaller amplitudes, than in the Miss condition in 30 % of the parcels at the latencies between 350 and 500 ms. This suppression at alpha and beta bands started from the sensorimotor, close parietal and mid-cingulate parcels and then spread to the frontal, farther parietal and temporal cortices. Increased amplitude at the earlier latencies were oscillating at delta and theta bands and transiently even at low beta.

4.1.3 Cortical narrow-band stimulus-locking results

The next question was to find out more in detail which narrow-band frequencies contributed to the observed and above described broad-band effects. Extraction of the spectral properties with Morlet wavelets revealed that the whole post-stimulus period in Hits was dominated by increased SL at theta-low alpha band centred on contralateral sensorimotor, bilateral frontal and intraparietal sulcus as well as ipsilateral CO areas. Hit-Miss comparison showed that the observed oscillation modulations at frequency bands from theta to low-alpha are in fact mostly focused on the low-alpha regime but reaches even up to high beta – though to a lesser extent.

4.1.4 Amplitudes and stimulus-locking for different reaction times

To investigate whether the oscillation phase and amplitude dynamics were related to response times, I compared SL and amplitudes averaged over sensorimotor and attentional networks separately for slow, intermediate and fast responses for Hits. It turned out that the PLF of SL was greater for the fast Hits than slow Hits in all the examined areas through the whole post-stimulus duration (Fig. 7B). Furthermore, also the early transient amplitude increase and a subsequent amplitude suppression were greater for the fast Hits than for the slow Hits (Fig. 7A).

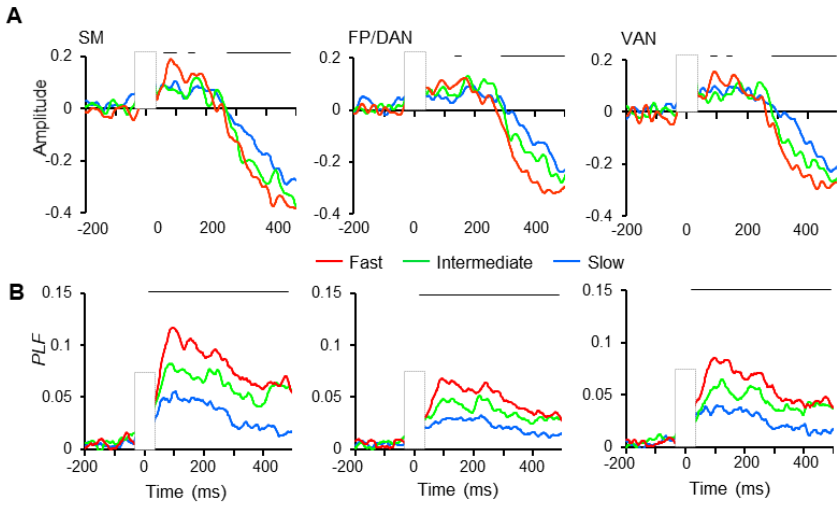

Figure 7: **A)** Oscillation amplitudes averaged over SM, FP/DAN, and VAN separately for trials with fast, intermediate, and slow RTs. Lines above indicate significant difference between fast and slow RT trials **B)** SL as in A.

4.1.5 Results from the LastMiss-before-Hit and FirstHit-after-Miss comparison

Finally, I showed that Hits and Misses were clustered throughout the length of the experiment and the magnitude of the ER (Fig. 8A) or SL (Fig. 8B) of Hit or Miss was not dependent on the position of that trial in a cluster. In other words, the difference between Hits and Misses was equally significant in spite of the identity of the following or the previous trial (whether Hit or Miss) and not attributable to gradual accumulation due to infra slow oscillations or attentional gain whatsoever.

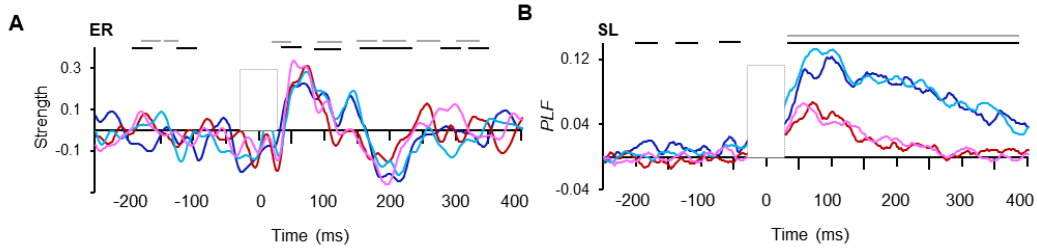

Figure 8: **A)** The relative strength of ER in the contralateral SI for Hits and Misses separately for stimuli in the different positions in the behavioural sequence. Colors as in A. Black lines indicate statistically significant difference between Hits and Misses in the middle of the sequence and grey lines between the first Hits and last Misses ($P < 0.05$, Wilcoxon signed rank test, FDR corrected). **B)** The relative strengths of SL for Hits and Misses in different positions in the behavioural series as displayed in C.

4.2 Interareal synchronization patterns in somatosensory TSDT (Study II)

Study II was based on the same data as Study I. Study II addressed the question of what the functional role of interareal phase-synchronization is in the coordination across brain regions during conscious somatosensory perception.

4.2.1 Synchronization at the whole cortex level

In comparison to Misses, I observed concurrent increased gamma-band synchronization from 170 ms onwards, and delta-theta band synchronization during the whole post-stimulus period exclusively for Hits. Additionally, a transient gamma-band desynchronization centred at 350 ms was seen for Misses only (Fig. 9A). Importantly, these results were present both with PLV and iPLV that are insensitive

to zero phase lag synchronization, meaning that the results likely do not reflect artificial synchronization. Additionally, surrogate subtraction from the actual data rendered the possibility of contamination by evoked responses likewise an unlike reason for the observed results. Furthermore, the strength of the synchronization was stronger for the actual measured data than for the surrogate data in all the frequency bands.

4.2.2 Synchronization at the subsystem-level

Mesoscale connectivity (connections between the subsystems) analysis revealed that the strongest connectivity occurred within attentional and sensorimotor networks, as well as between these two at delta-theta frequency band quite invariantly during the whole post-stimulus period (Fig. 9B). In comparison, gamma band synchronization was weaker but more variable as the proportion of different connections shifted from within-attentional to within-attentional and attentional-sensorimotor networks. Lastly, the proportion of different connections was composed of all the previous ones and connections between visual and default mode network (DMN). These changes of connection relations peaked at every 150 ms. Additionally, this connectivity pattern in different functional subsystems was a robust phenomenon as it survived single subject data statistics too.

4.2.3 Synchronization at the graph-level

Graph-level visualization of the most significant and central connections showed that the main ties at gamma-band were formed between contralateral sensorimotor hubs (such as SI, MI, SMA and SII) and ipsilateral fronto-parietal and attentional parcels such as mFG and intPS (Fig. 9D). Also, connections between cingulate hubs of CO and attentional areas, as well as cross-hemispheric edges from contralateral occipital (visual cortex) to ipsilateral frontal and SM vertices were a noteworthy pattern. Delta/theta band synchronization connected practically the whole contralateral SM with ipsilateral SII, mFG +iFG bilaterally, as well as ipsilateral visual areas (Fig. 9C).

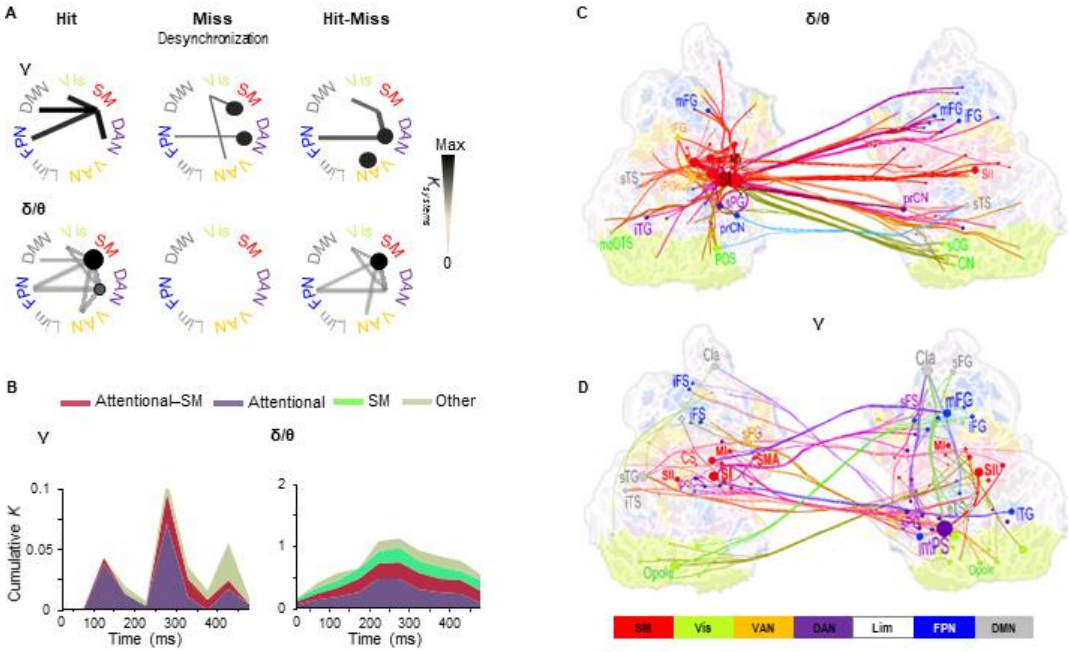

Figure 9: **A,** Connection densities of significant interareal mid-gamma- (40-60) Hz and delta/theta- (3-7 Hz) band synchronization among Yeo-atlas brain systems for Hits and Misses compared to baseline, and for their difference. The colour, line width and radius of circles of the system-system connections indicates the connection density of significant couplings ($K_{systems}$) within (circles) or between (lines) the functional systems in a time-window of 225-375 ms. **B**, time-resolved cumulative connection densities (K) of gamma- and delta /theta-band synchronization estimated separately for within-attentional (DAN, FNP and VAN), between-SM-and-attentional, and all-other functional subsystems. **C,** Graph of the significant differences in the strength of interareal phase synchrony as estimated with PLV between Hits and Misses in the delta/theta- (3-7 Hz) frequency band and in the time-window of 125-275 ms from stimulus onset. Lines connect the coupled parcels and line colours are determined by the parcel brain systems in Yeo-atlas (see below). **D**, Same as in **C** except for gamma (40-60 Hz) band synchronization. Graphs are displayed on an inflated and flattened cortical surface with 300 (**C**) and 200 (**D**) of the most central edges based on parcel PageRank centralities selected for visualization. For the acronyms of the anatomical and functional brain areas, see the list of abbreviations.

4.2.4 Synchronization for fast and slow reaction times

Lastly, I divided Hit trials into two categories as per their reaction times and applied the same synchrony metrics as in the results above. This analysis yielded stronger overall connectivity results for the fast Hits compared to the slow Hits at delta/theta band. As for the gamma band oscillations, this phase synchronization relation was varying so that at 300 ms connectivity was peaking for the fast Hits (mean RT for them being 350 ms) and then again at 500 ms. For the slow Hits (their mean RT being 590 ms) the first larger peak was observed at 500 ms instead.

4.3 Local and interareal oscillation deficits in schizophrenic patients (Study III)

Study III represents a different experiment from Studies I and II. Here chronic phase schizophrenia patients and healthy control subjects were shown black and white upright and inverted scrambled

Mooney face stimuli (Fig. 5). The patients had a significantly lower Hit rate for the upright face stimuli compared to the control subjects.

4.3.1 Local amplitude dynamics in time and frequency and their sources on the cortex

The results indicated that the healthy controls have stronger induced oscillation modulations for both correctly perceived upright and inverted-scrambled stimuli than the patients at low and high gamma bands. The high gamma band effect starts already at 100 ms after the stimulus presentation (Fig. 10A). During the latency period of 350-450 ms and at the frequency band of 60-120 Hz (high gamma) the strongest amplitude differences were noticed on bilateral fEF and mFG, as well as temporoparietal junction (TPJ) and superior temporal sulcus and gyrus (sTS/sTG) for the upright condition (Fig. 10B). In the temporal and parietal areas, such as intPS, the contrast was even stronger in the right than left hemisphere. In the inverted-scrambled condition, the patients had weaker activity, not only in the above-mentioned parcels but also in the early visual areas, though the contrast was much milder than in the upright condition overall. In addition to these high gamma effects, the patients had reduced amplitudes at mid-gamma (~40 Hz) as well, but only around 350 ms after the stimulus onset.

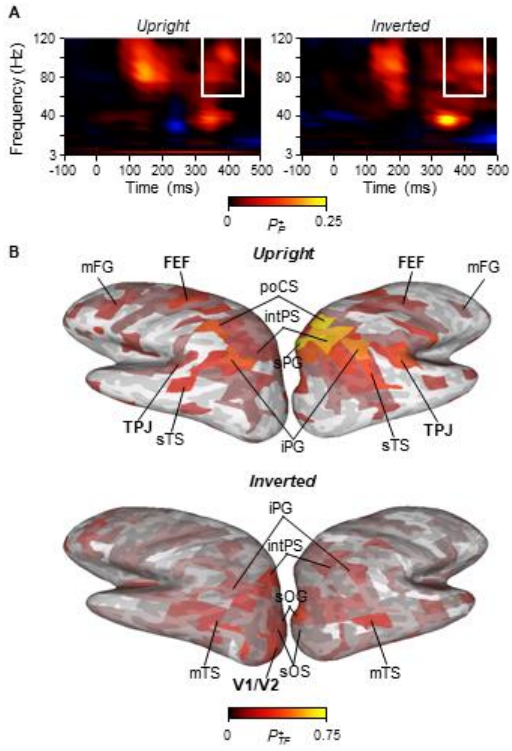

Figure 10: Time frequency representations and cortical localizations of significant oscillation amplitude modulations. **A**, Difference in oscillation amplitudes between the controls and schizophrenic patients for the correctly perceived upright and inverted-scrambled stimuli. Colour scale indicates the fraction of cortical parcels with a significant positive control-patient difference. **B**, Parcels in which significant differences in oscillation amplitudes between the controls and patients were observed for the selected time-frequency region of interest indicated by white rectangles in **A** for upright and inverted stimuli displayed on inflated cortical surfaces. Colours of the parcels indicate the fraction of time-frequency elements with significant modulation in the parcel. For the acronyms of the anatomical and functional brain areas, see the list of abbreviations.

4.3.2 Interareal synchronization on the whole cortex, at the graph-level and correlation with disorder severity

Interareal phase synchronization was quantified with iPLV between all cortical parcels, time-windows and between all frequencies from 3 to 120 Hz. To remove the effect of evoked activity on synchronization, a novel surrogate approach was used (See 3.3). This analysis was made for each condition for both control subjects and patients, as well as for their differences. The output measure was cortical connectivity i.e. the proportion of significant synchronization parcel pairs out of all possible pairs in the given TF-ROI.

The connectivity was reduced in the patients in all analysed frequencies below 20 Hz during the whole post-stimulus epoch. Nonetheless, the most interesting differences in the cortical connectivity values were seen around 350 ms after the stimulus onset (or 150 ms after the stimulus

offset) at low-gamma band. Both in the upright and inverted-scrambled conditions, the control subject had greater connectivity in that TF-ROI but in inverted-scrambled condition the connectivity was decreased for the controls at mid-gamma band. In the inverted-scrambled condition, the most central connections at 350 ms and 20 Hz were located mainly between intra- and cross-hemispheric visual areas and extending to the parietal parcels with intPS and superior posterior gyrus (sPG). In the upright condition, the increased connectivity in controls did cover the same areas, but also more widely frontal and temporal regions such as iFG/iFS and s/mTG. Visual hubs comprised primary and higher visual areas such as fusiform face gyrus (Fus), especially on the right hemisphere.

The next question was to identify those parcels and frequency bands that were exclusively attributable to face perception. After subtracting iPLVs in the inverted-scrambled condition from the upright condition, I found that mid-gamma synchronization at 275-400 ms after the stimulus onset was the most prominent remaining time-frequency-feature (Fig. 11A). The most central face related connections were localized to both temporal and frontal areas, though main hubs being right sTS/G and mFG, as well as SMA (Fig. 11B). Overall, control subjects had more mid- and long-range connections and even slightly fewer short-range connections than the patients in that mid-gamma time-window.

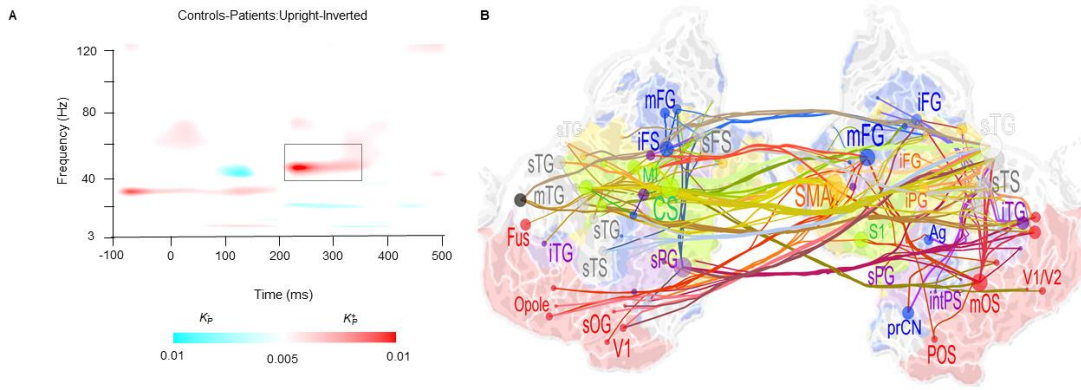

Figure 11: Time-frequency representation and cortical localizations of the most central connections for the difference between control and patient groups in the upright-inverted contrast. The rectangle in **A** indicates the region of interest selected for visualization in **B**. **B**, Mid-gamma-band (40–50 Hz) network for the upright-inverted contrast that was stronger for control than patient group in the 200- to 300-ms time-window. For acronyms for the anatomic and functional brain areas, see the list of abbreviations.

Finally, I investigated how network strength in the difference of upright and inverted-scrambled conditions is related to the severity of the disease. It turned out that the scores in the disorganization test were positively correlated with the lower mid-gamma band network strength (the higher the scores, the more severely ill).

5 Discussion

In this thesis work, two separate projects with three studies are summarized in pursuit of elucidating neuronal correlates of sensory perception and related actions. The experiment in Studies I and II was designed to address a question of what kind of cortical activity patterns are correlated with the perception of a weak somatosensory stimulus when it is either perceived or unperceived. The most central findings indicated that changes in locally evoked, induced and stimulus-locked responses in several cortical regions associated with sensory processing, as well as those associated with attentional coordination and awareness correlated with conscious perception of the stimulus. Furthermore, interareal synchronization in the delta/theta bands was stronger for Hits than Misses. In the gamma-band synchronization was exclusively present for the perceived trials only.

Study III investigated neuronal correlates of Gestalt closure perception, using two-tone Mooney face stimuli (Fig. 5) in patients suffering from schizophrenia and healthy controls. The results showed that the schizophrenia patients had suppressed gamma-band amplitude modulations to these stimuli compared to controls. The patients also had reduced interareal synchronization during visual face recognition. Moreover, the severity of the disease disorder was correlated with the degree of the synchronization reduction. Also, the remaining cortical connections at mid-gamma band were on average shorter than in the healthy subjects.

5.1 Perception-action chain in somatosensory stimulation

A big portion of the literature concerning the different aspects and moments of conscious perception come from studies where visual experiments have been used. Despite many studies, there is a lot of heterogeneity across the results that report the time courses from stimulus sensation to action, in the endeavour to hunt neuronal correlates of consciousness (Rutiku et al., 2016). The research goes on to reach a consensus on the processes and at which latencies they belong – for example to neural prerequisites or neural consequences, or what does the proper correlate of consciousness look like (Aru, Bachmann et al., 2012). Meanwhile, related topics in somatosensory modality are much less investigated, especially with source-modelling in conjunction with millisecond temporal precision provided by MEG. Somatosensory stimuli, such as the ones used in Studies I and II of this thesis work, have a weaker effect on the cortex as they have simpler contents than visual stimuli and the subjects had their eyes closed. These properties could in theory provide complementary and missing information in obtaining an overall picture of the different processes pertaining many steps from stimulus presentation to the response given.

5.1.1 Motivational background of Study I

In a prior MEG sensor-level study, it was observed that the earliest correlate predicting conscious somatosensory perception and subsequent responses was stimulus-locking already at 30-70 ms from stimulus onset in sensors over the somatosensory, frontal and parietal areas (S. Palva et al., 2005). This effect was present in theta, alpha, beta and gamma bands, but alpha-band oscillations were most dominant and widespread. Because of the lack of source-reconstruction, the cortical regions underlying these effects remained unknown. In essence, Study I is a follow-up study of the previous Palva et al., 2005 study. The aim is to reveal the cortical regions underlying the modulations of

oscillatory activities during conscious perception, using MEG combined with MNE based source-modelling (see Methods section).

Additionally, the 2005 study was criticised for not considering the possible effect of the subjects' prestimulus attentional states (Schubert et al., 2006). According to Schubert et al., 2006, these states "*could fluctuate during the recording session and might be responsible for effects on early evoked activity as well as the failure of perception*." A prior study had indeed shown that detected trials segment into scale-free clusters of Hits and Misses, which is correlated with the phase of infra-slow fluctuation (< 0.01 Hz) (Monto et al., 2008). Hence, the phase of the infra-slow fluctuation could theoretically predict the gradual increase in the strength of ER and SL as a function of infra-slow fluctuation cycle position. To test this possibility, I analysed evoked and stimulus-locked responses separately for Hit and Miss trials in different cluster positions. Then I separated Hits that followed a Miss and vice versa and compared these to all other Hits and Misses.

In short, Study I showed that strengthened SL, ER, and induced oscillations amplitude modulations all were associated with conscious somatosensory perception. The most robust and widespread of these effects was SL that was sustained in the low-alpha (6–10 Hz) band. The strength of SL and to a lesser extent magnitude of ER preceded conscious perception in the somatosensory, lateral and medial frontal, posterior parietal, and in the cingulate cortex. The results of Study I hence corroborated those in Palva et al., 2005, and other related research that has used EEG (Koivisto et al., 2008; Pins and Ffytche 2003) and MEG (S. R. Jones et al., 2007) and has shown that the magnitude of ER is positively correlated with conscious sensory perception. Additionally, results in Study I were not explained by infra-slow fluctuations as discussed above.

5.1.2 Perception-action chain and local modulations of its components

One of the key questions in neuroscience is to understand how perceptions of surroundings are translated into coherent mental representation in the brain and then executed as purposeful actions. According to the perception-action cycle concept, signals on the cortex reverberate in a circular flow with feed-back at every level, from posterior sensory areas to frontal executive structures (Fuster 2004; Lamme 2006). Particularly, the prefrontal cortex of higher association cortices has the greatest role in integrating signals from varying temporal origins in a complex top-down guided behaviour (Koechlin et al., 2003). Then subsequent actions manipulate the environment and give new perceptions in a cyclic manner (Fuster 2004). In this thesis, I reduce the concept of a cycle to a chain as the experiment setup in Studies I and II allows only one-way throughput, from given stimulus to executed response. Furthermore, the focus of the perception-action chain is to reveal the time-lineage and oscillatory mechanisms behind the processes, starting from stimulus sensation and ending in motor response.

In earlier studies, it has been shown that premotor cortical areas are anatomically connected to relatively early sensory areas, whereas more frontal areas have links to parietal association sites (Cavada and Goldman-Rakic 1989; E. G. Jones and Powell 1970). Moreover, there are pieces of evidence that show existing efferent connections from prefrontal cortex to premotor cortex (Bates and Goldman-Rakic 1993; Luppino et al., 1993). In short, the main tenet is that the processing from perception to action is achieved by co-operation between sensory areas together with frontoparietal attentional networks. Intriguingly, also increased activity in 'task-negative' systems, such as default mode network (DMN) or the network of another sensory modality have been found to enhance perception (Esterman et al., 2012).

In Study I, I observed that the difference in waveforms for Hits and Misses can be distinguished at relatively early latency. ERs were stronger for the Hits than Misses already at 70 ms after the stimulus onset. This difference peaked at 130 and 280 ms. Source-modelling revealed that the regions of activation were shifted during these peaks from sensory areas to higher association areas. The reason for the temporal propagation of the activity centres could be that it reflects different stages within the perception-action chain. This is supported by the findings from studies using backward masking that have shown only the P300 component to be correlated to conscious perception (Del Cul et al., 2007; Fahrenfort et al., 2007; Koivisto et al., 2017; Melloni et al., 2011; Sergent et al., 2005). The earlier components (M70) observed in Study I could be related to early feed-forward push from the sensory areas that are eliminated in backward-masking experiments, rather than to the neuronal correlate of consciousness itself as proposed by the recurrent processing theory (Lamme and Roelfsema 2000; Lamme 2006; van Gaal and Lamme 2012). In visual modality, similar results seen as the discrepancy of the earlier and later components are theorized to reflect preconscious processes that allow the stimulus to access consciousness (Koivisto and Grassini 2016; Koivisto et al., 2017; Revonsuo and Koivisto 2010).

Along with the prior MEG experiments using source-modelling to map neuronal activity, specifically the parcels involved in FPN such as mFG and intPS could be involved in conscious perception (Dehaene et al., 2006; Dehaene and Changeux 2011) or perceptual decision making (Donner et al., 2009b; Goard et al., 2016; Hegner et al., 2016; Kaplan et al., 2017; Siegel et al., 2015; Tosoni et al., 2008). Accordingly, these are the parcels that are missing from the early M70 ER component as per the source-model results. Instead, earlier activated parcels in medial (mCi), superior (sFG, SMA) and inferior frontal (iFG) areas might play a role in conscious access of sensory stimuli (Brancucci et al., 2011; Salti et al., 2015). In contrast to ER and induced amplitudes, SL dynamics were a more widespread phenomenon and appeared earlier. In particular, parcels that were supposedly related to conscious perception were present already around 80 ms after the stimulus onset on a wide-ranged area of dorsal and ventral prefrontal cortices in addition to intPS. Furthermore, the effect was once again stronger for faster than slower Hits. These results suggest that the reorganization of phase-dynamics might precede following ER and amplitude modulations. This fits well along with the suggestion that phase-dynamics are crucial in contributing to the emergence of conscious sensory perception possibly by influencing the information flow across the brain areas, or by stabilizing neuronal activity (Schurger et al., 2015). Alternatively, changes in SL values could be distorted by the modulations of evoked responses rather than phase-perturbation of the ongoing oscillations (van Diepen et al., 2015).

A fourth possible component involved in the perception-action chain is the preparation of the motor responses. This might be reflected in the results as an early increased ER in SMA followed by a later ER in preMI and MI. These effects are observed both in broad-band ER and transiently (75-175 ms) in induced beta-band amplitudes for Hits. Additionally, amplitudes in SM and in other task-positive networks (DAN/FP and VAN) were higher at early latencies and on the other hand more suppressed at late latencies, when comparing trials with faster reaction times to slower ones.

5.1.3 Trial position in the behavioural series does not affect neuronal amplification

Finally, one more thinkable component influencing Hits is attention as already suggested by Schubert et al., 2006. Undeniably, there is an effect of attention as the Study I results show oscillation

modulation for Hits in the parcels belonging to Fef, sPG and TPJ, i.e. belonging to attentional networks DAN and VAN. However, attention is unlikely to have a dominant role in determining whether a somatosensory TSDT stimulus will eventually be perceived or not, i.e. whether becoming Hit or Miss. This claim is motivated by the results from above described FirstHit-after-LastMiss and LastMiss-before-FirstHit analysis that yielded no difference for the contrast Hit-Miss regardless of their position in a cluster and suggesting that attentional fluctuations cannot explain differences in neuronal activity between Hit and Miss stimuli.

5.1.4 Delta/theta- and gamma-band synchronization characterizes interareal communication from perception to action

In Study II, I investigated the role of large-scale interareal phase synchronization in the transition from sensory perception to action generation. The main finding was that Hits were characterised by increased sustained synchronization after the stimulus onset in the delta/theta band (3-8 Hz) and cyclically in the mid gamma-band (40-50 Hz). In the delta/theta band, the contralateral SM had connections within itself and fronto-parietal and attentional nodes bilaterally. This cortical connectivity pattern seen at delta/theta band corroborated similar results from earlier publications that have suggested a close link and dynamic interactions between perceptual (Gutteling et al., 2011; Wohlschlager 2000) and decision-making processes (Donner et al., 2009b; Gould et al., 2012; Kaplan et al., 2017; Tosoni et al., 2008) in conjunction of motor actions. Delta/theta-band synchronization could thus underlie the coordination of neuronal processing, achieved collectively in motor and sensory cortices (here both bilateral SM and ipsilateral visual). However, the temporally stable profile of delta/theta band synchronization in SM, together with an increment in the strength of synchronization, but not a change in temporal profile in response to faster RTs, suggest that delta-band synchronization more likely is related to evidence accumulation of sensory information and coordination of motor actions but not to achieving perceptual decisions per se.

In contrast, for the gamma-band synchronization, the key connections were observed between ipsilateral mFG, sFS and intPS and contralateral SI and SII. It has been observed previously, both using the whole-brain as well as subsystem analyses that these nodes belong to FPN and DAN systems (Murakami and Okada 2006; Power et al., 2011; Spadone et al., 2015). These FPN/DAN nodes were also reciprocally linked in both hemispheres, implying that gamma-band synchronization could here mediate neuronal communication particularly within the attentional system and between the attentional and sensory systems. The fact that the visual system was consistently connected with the sensorimotor system, both in delta/theta and gamma bands, may reflect the responsiveness of the visual cortex also to the somatosensory stimulation (Nordmark et al., 2012) and/or complementary representation of the perceived somatosensory stimuli in the visual cortex (Orlov et al., 2010), which could make sense as the subjects had their eyes closed during the measurements.

Intriguingly, I found gamma-band oscillations to be desynchronized below baseline levels for Misses. Furthermore, the desynchronization pattern for Misses was qualitatively and genuinely distinct from synchronization to Hits. The connections that were desynchronized for Misses comprised edges within SM and DAN systems as well as between DAN and FPN. Solely for Hits, SM was the main hub that was connected to other subsystems. The suppression of gamma oscillations for Misses in SM is well in line with prior fMRI research, reporting negative BOLD fMRI signal responses in contralateral SI, SII, and SMA for subthreshold somatosensory stimuli (Blankenburg et al., 2003; Nierhaus et al., 2015; Taskin et al., 2008). In Study II, the suppression of synchronization may reflect active uncoupling of task-relevant cortical areas to block conscious access from subliminal stimuli, or it may reflect non-conscious stop-signals to interrupt motor responses (van Gaal et al., 2008).

The temporal pattern of gamma-band connectivity evolution suggests that the attentional system indeed influences sensory perception (see discussion above). Along this line, it has been reported that fMRI BOLD signal fluctuations in the attentional but not in the sensory system are correlated with perceptual performance in TSDTs, like in Studies I and II (Sadaghiani et al., 2009). Furthermore, as PFC and PPC coordinate both perceptual decisions (Donner et al., 2009b; Goard et al., 2016; Hegner et al., 2016; Kaplan et al., 2017; Siegel et al., 2015; Tosoni et al., 2008) and conscious perception (Dehaene and Changeux 2011; Gaillard et al., 2009; Li Hegner et al., 2015; Salti et al., 2015) I speculate that the gamma-band synchronization during the later time-windows (see Fig. 12) could affect conscious perceptual decisions of the weak somatosensory stimuli.

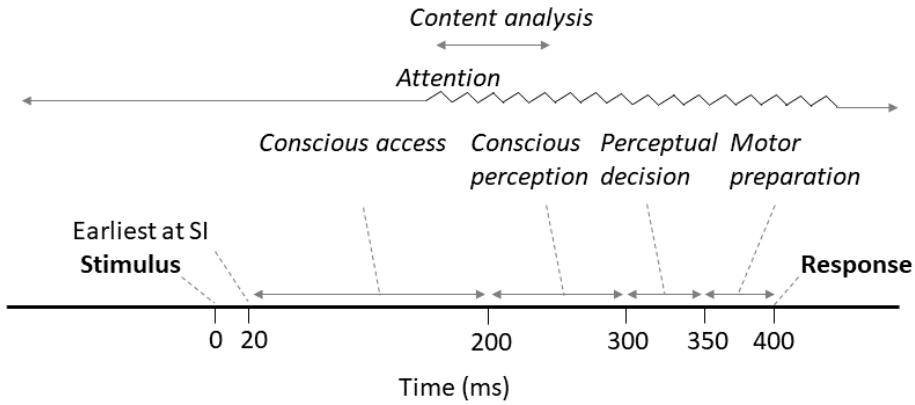

Figure 12: Schematic illustration of the hypothetic components in perception-action chain.

Conversely, large-scale functional network results from Study II support the idea that neuronal synchronization between frontoparietal attentional networks and sensory areas plays a key role in the emergence of conscious sensory perception (Dehaene and Changeux 2011; Engel and Singer 2001; Tallon-Baudry 2012) and sensorimotor decisions (Donner et al., 2009b; Engel and Fries 2010). Specifically, the hypothesis that gamma-band synchronization could coordinate perceptual decisions was supported by the distinct observed temporal profiles of synchronization for fast and slow actions. In conclusion, the neuroanatomical and temporal patterns of gamma-band synchronization could reflect a sequence of network reconfigurations that occurs during the transitions from sensory decisions to the coordination of motor actions (Fig.12).

5.2 Oscillations in schizophrenia

Study III is a follow-up of a study, in which chronic schizophrenia patients under antipsychotic medication were recorded concurrently when viewing Mooney faces (Fig. 5) (Grutzner et al., 2013). In this prior study, it was observed that schizophrenic patients had a pronounced reduction of gamma oscillations between 60 and 120 Hz. Furthermore, the disease severity was negatively correlated with the power in the gamma-band. A later study showed that especially activity in Fus was significantly lower in patients than in controls when indexing face selectivity (Maher et al., 2016).

In study III, I advanced these findings by using source-level analysis for estimating the cortical localization of oscillation amplitude modulation, as well as quantified the functional role of interareal phase synchronization in visual perception in schizophrenia.

5.2.1 Local amplitude dynamics in the gamma-band are reduced in schizophrenic patients

Gamma oscillation amplitudes showed stronger modulations for the control subjects than for schizophrenic patients in the high- (60-120 Hz) and mid-gamma (~40 Hz) band in response to face perception, i.e. higher amplitudes for the upright than inverted stimuli. These results are congruent with those observed in the prior analyses of the same data (Grüetzner et al., 2013), indicating that amplitude reductions are a robust finding characterizing deficits of schizophrenic patients in perceiving incomplete facial traits.

Source-modelling of gamma-amplitude difference revealed that particularly those brain areas that have been traditionally associated with face perception (sTS), perception in general (mFG, intPS) and attention (fEF), showed most of the enhanced activity in the upright condition for the healthy controls. In patients this activity was reduced instead. Indeed, it has been known for a while that especially dorsolateral prefrontal cortex (such as mFG here) show increased dysconnectivity in the schizophrenic patients as a function of local blood-flow measures (Weinberger et al., 1988). Furthermore, one of the brain's major integrative and attention sites: TPJ that has been reported to be hypoactive in schizophrenic patients (Vercammen et al., 2010), had bilaterally decreased activity in the patient group compared to healthy controls. For the inverted condition, activity was mainly reduced to early visual areas. This suggests that the decrement in gamma-band oscillations in the patient group could be caused by defects at later stages of visual hierarchy. This is in agreement with the earlier research showing that perceptual closure (Gestalt property studied with the Mooney faces) involves higher visual areas (Grutzner et al., 2010) that exert top-down control of visual sensory information processing (T. Buschman and Kastner 2015; Corbetta and Shulman 2002; Corbetta and Shulman 2011; Womelsdorf and Everling 2015).

5.2.2 Schizophrenic patients have weaker interareal phase synchronization between attention, awareness and face perception areas

The interest in the main aspect of Study III, namely interareal phase synchronization, is inspired by a hypothesis according to which schizophrenia is associated with a dysconnectivity syndrome (Friston and Frith 1995; Stephan et al., 2009). More specifically, some earlier research has preliminarily shown that the oscillatory long-range synchronization could be impaired in schizophrenia (Spencer et al., 2003; Uhlhaas et al., 2006). However, these results were obtained at sensor-level and were not corrected for the non-neuronal artifacts and the effect of the volume conduction which have severe effects on the detection of true neuronal synchronization (see chapter 1.5). Study III addressed these previous short-comings. Thus, I carried out an analysis of large-scale synchronization from source-localized MEG data. These data showed in line with prior studies that large-scale synchronization is aberrant in the patient group. First, the patients had an overall post-stimulus reduction in synchronization in low-frequencies in the delta and theta (3-7 Hz) bands. This reduction could be due to impaired temporal parsing of the evoked responses, or some process related to initial coordination of motor responses, or action monitoring as well as task-specific regulation of executive control (Schmiedt et al., 2005). Nonetheless, these findings are in line with earlier results showing deviant delta-band activity in schizophrenic patients (Alfimova and Uvarova 2007; Sekimoto et al., 2011).

Second, gamma band synchronization, especially in mid-gamma range 300-400 ms after the stimulus onset, was reduced in schizophrenic patients. Connections were reduced between early visual areas and Fus that underlies face perception, and between the visual system and the key nodes in FPN and DAN that are involved in the coordination of visual attention (Corbetta and Shulman 2002; Fox et al., 2005). Additionally, visual system and frontoparietal key areas were connected to hubs on the right TPJ, and especially to sTS/sTG, when comparing upright condition to inverted ones. This comparison should leave only those elements that are associated to face perception

per se. sTS is often linked to multisensory processing capabilities especially in the context of social perception (Grossman and Blake 2001; Senkowski et al., 2008) and even face recognition (Van Lancker and Canter 1982). Also, sTG appears to play a role among other functions in face perception, especially in emotion decoding (Bigler et al., 2007; Radua et al., 2010). More specifically, anterior and dorsal parts of sTG have been observed to influence information processing related to several changeable features of a face (Bigler et al., 2007). Finally, structural neuroimaging studies have shown that schizophrenia patients have a reduction in gray-matter volume in their sTG (Kasai et al., 2003), which could be the reason for the weakening in the functional connectivity as seen here in Study III.

Moreover, Study III revealed that those mid gamma-band connections that were reduced in schizophrenia patients were composed of medium- and long-distance connections. This supports the notion that schizophrenia is characterized by defects in the temporal coordination of distributed neural activity at global cortical scales. Furthermore, decrements in network strength were positively correlated with the severity of the clinical symptoms as quantified by disorganization points. In principle, this means that coordination failures in the context of dysconnectivity may emerge gradually, and thus manifested as distinct clinical symptoms from milder to more severe.

5.2.3 Suggested directions for future studies

Given the apparent oscillation and synchronization effects at low delta-alpha frequencies and on the other hand the observed mid-gamma synchronization, one is easily led to consider cross-frequency synchronization. It is hypothesized that deviations in excitation-inhibition balance could lead to the decrements of oscillation activity in these frequency bands (Uhlhaas and Singer 2015). Some preliminary results have shown that there are changes in the cross-frequency coupling (Siebenhühner et al., 2013). Another study reports intact coupling in the patients (Kirihara et al., 2012). More studies with source-modelling and elaborate interaction measures (see chapter 1.5 and 1.6) are needed to validate these.

There is a growing body of evidence that synchronization findings in high frequency oscillations are closely associated to higher cognitive functions in the healthy brain (Kim et al., 2016; Michalareas et al., 2016). As parvalbumin-positive interneurons and NMDA receptors have been coupled to gamma-band oscillations (Fries 2015), it is plausible that impairments in these structures could give rise to lower gamma-band amplitudes and synchronization reductions observed in schizophrenia (Kantrowitz and Javitt 2010). Interestingly, there is a genetic component involved, too, as genes coding for calcium-binding protein parvalbumin and GABA producing gene GAD 65, all crucial components for generating gamma-band oscillations, are observed to be downregulated in these parvalbumin basket cells (Lewis et al., 2005; Lewis et al., 2012). Taken together, Study III, renders robust correlative support for the hypothesis that clinical symptoms and cognitive impairments in schizophrenia are associated with a dysconnection syndrome (Friston 1998; Uhlhaas and Singer 2012; Uhlhaas and Singer 2015; Voytek and Knight 2015). However, more studies are needed to overarch the relationship between molecular/genetical deviations and the apparent systems-level neural deficits in the schizophrenic patients.

5.3 Conscious perception is a manifestation of highly evolved oscillatory mechanisms

In the cases of *Cnidaria* and the pancreas it was explained with a few sentences what oscillations and their synchronization can contribute to. As for the brain, this is less straightforward. Namely, the human brain has 100 billion neurons, ten times of that glial cells (such as astrocytes which process glucose into lactate and feed that to the neurons) and 100 trillion synapses. Hereby, the number of possible combinations for theoretical cell interaction motifs is much bigger than that 749 of the pancreas described in the introduction. Unlike to pancreatic cells, neurons can excite or inhibit other neurons directly over longer distances and more accurately, as well as faster than the chemical gradients created in the paracrine Langerhans cell communication. Moreover, the brain is highly

connected – up to 70 % of all the possible connections are *de facto* realized in the brain's connectome (Bullmore and Sporns 2009). This means that any node in the cortex can be reached with a relatively small number of intervening nodes. The outcome of this property is that the brain can carry out an astronomical number of different neuronal activity combinations in a short time. Faced by this enormous communication complexity, it might indeed be easier to fathom and disentangle some mechanisms of the human brain by researching populational neuron mass activity, its filtered oscillations and dynamics, for example with MEG, than mapping each of these single connections with its weight. In addition to being beyond computational capacity for the time being, some existing properties might not even be detectable at the neuronal level. Several properties such as complex brain networks at systems-level and consciousness at the behavioural level have been suggested to emerge from this immensely complex arrangement (Varela et al., 2001). Here oscillatory mechanisms play a key role in integrating different pieces of information and units over many distances on the cortex, so that more and more advanced functions can emerge. For example, synchronized communication between posterior parietal, occipital and temporal associative cortices has been shown to be the most likely seat of phenomenal consciousness, whereas the frontoparietal network is involved in attention and task execution, reporting and monitoring (Koch et al., 2016), such as in Mooney face perception task or somatosensory TSDT, as shown in this thesis work.

6 Conclusions

In this thesis work, results from three separate MEG studies are brought together in a pursuit of explaining how oscillations and their different mechanisms affect perceptual processes in health and schizophrenia.

In Studies I and II, perceptual processes in a perception-action chain were investigated. In this chain, stimulus sensation arrival at the primary somatosensory cortex eventually leads to behavioural report, i.e. thumb twitch about the presence of a stimulus. This whole cascade is very fast and takes time, on average 400 milliseconds. During this time, neuronal activation spreads from sensorimotor cortex to attentional and frontoparietal networks. The most significant cortical systems-level neural mechanisms that in the given data mediated these different stages of the perception-action chain, were oscillations at delta/theta- and gamma-bands. Delta/theta -band oscillations were present both for the perceived and unperceived trials, although being significantly stronger for the perceived trials. Delta-band synchronization can partly be related to evoked responses. However, even after controlling for the evoked response, delta-band synchronization was much stronger for the perceived than unperceived trials, suggesting that they may be related to regulation of neuronal excitability fluctuations of attended information. In contrast, gamma-band oscillations were completely exclusive for the consciously perceived stimuli. Particularly, gamma-band synchronization was not only instrumental in linking contralateral sensorimotor cortex to ipsilateral attentional and frontoparietal networks in early latencies, but also for instantiating the transition to visual and default mode areas at later stages of the perception-action chain. For unperceived trials, a transient desynchronization was observed instead. This suggests that desynchronization could reflect active uncoupling of task-relevant cortical areas to suppress conscious access from subliminal stimuli, or it may reflect non-conscious stop-signals to interrupt motor responses.

In Study III, conscious perception was involved in seeing a face vs not seeing a face in images with equal visual two-tone complexity. These two kinds of trials were contrasted between the schizophrenic patients and healthy controls. Results of the study showed that gamma-band oscillations again were the main factor behind increased oscillation amplitudes and longer distances in large scale synchronization on the healthy cortex. Specifically, stronger gamma-band amplitude modulations in frontoparietal cognitive and attentional networks, as well as supratemporal areas along with temporoparietal junction, characterized the healthy performance. Right supratemporal social areas were also the main hubs governing connections to other above mentioned cortical sites in addition to visual areas, such as the fusiform face area when focusing on the better face perception in healthy people, compared to the patients. Furthermore, network strength in these areas in the mid-gamma band correlated negatively with the disease severity as defined in terms of disorganization scores. Taken together, deviations in gamma-band network values of the above mentioned cortical areas could be used as a biomarker in early onset clinical schizophrenia screening.

Studies in this thesis work are limited to correlational inferences, albeit with good spatial and temporal resolution rendered possible with source-modelling of MEG data. Prospects as to a continuation of these studies would go further to investigate causal relationships of different aspects of perceptual processes. Transcranial magnetic or current stimulation of key nodes/regions could be one option, but one could also apply effective connectivity tools to the existing data to go beyond current functional connections. Moreover, cross-frequency synchrony analysis would be of

particular interest as the increased gamma-band synchronization appears to go hand in hand with lower frequencies such as delta and theta as a function of enhanced conscious perception.

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References

Alfimova, M.V. and Uvarova, L.G. (2007). Changes in the EEG spectral power during perception of neutral and emotionally salient words in schizophrenic patients, their relatives and healthy individuals from the general population. *Zhurnal Vysshei Nervnoi Deiatelnosti Imeni I P Pavlova, 57*, 426-436.

Arntfield, M.E. and van der Kooy, D. (2011). Beta-cell evolution: How the pancreas borrowed from the brain: The shared toolbox of genes expressed by neural and pancreatic endocrine cells may reflect their evolutionary relationship. *BioEssays : News and Reviews in Molecular, Cellular and Developmental Biology, 33*, 582-587.

Aru, J., Bachmann, T., Singer, W., Melloni, L. (2012). Distilling the neural correlates of consciousness. *Neuroscience and Biobehavioral Reviews, 36*, 737-746.

Aru, J., Axmacher, N., Do Lam, A.T., Fell, J., Elger, C.E., Singer, W., Melloni, L. (2012). Local category-specific gamma band responses in the visual cortex do not reflect conscious perception. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience, 32*, 14909-14914.

Bastos, A.M., Vezoli, J., Bosman, C.A., Schoffelen, J.M., Oostenveld, R., Dowdall, J.R., De Weerd, P., Kennedy, H., Fries, P. (2015). Visual areas exert feedforward and feedback influences through distinct frequency channels. *Neuron, 85*, 390-401.

Bates, J.F. and Goldman-Rakic, P.S. (1993). Prefrontal connections of medial motor areas in the rhesus monkey. *The Journal of Comparative Neurology, 336*, 211-228.

Bell, A.J. and Sejnowski, T.J. (1995). An information-maximization approach to blind separation and blind deconvolution. *Neural Computation, 7*, 1129-1159.

Belluscio, M.A., Mizuseki, K., Schmidt, R., Kempter, R., Buzsaki, G. (2012). Cross-frequency phase-phase coupling between theta and gamma oscillations in the hippocampus. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience, 32*, 423-435.

Berger, H. (1929). Über das elektrenkephalogramm des menschen. *European Archives of Psychiatry and Clinical Neuroscience, 87*, 527-570.

Bigler, E.D., Mortensen, S., Neeley, E.S., Ozonoff, S., Krasny, L., Johnson, M., Lu, J., Provencal, S.L., McMahon, W., Lainhart, J.E. (2007). Superior temporal gyrus, language function, and autism. *Developmental Neuropsychology, 31*, 217-238.

Blankenburg, F., Taskin, B., Ruben, J., Moosmann, M., Ritter, P., Curio, G., Villringer, A. (2003). Imperceptible stimuli and sensory processing impediment. *Science (New York, N.Y.), 299*, 1864.

Boly, M., Garrido, M.I., Gosseries, O., Bruno, M.A., Boveroux, P., Schnakers, C., Massimini, M., Litvak, V., Laureys, S., Friston, K. (2011). Preserved feedforward but impaired top-down processes in the vegetative state. *Science (New York, N.Y.), 332*, 858-862.

Boly, M., Balteau, E., Schnakers, C., Degueldre, C., Moonen, G., Luxen, A., Phillips, C., Peigneux, P., Maquet, P., Laureys, S. (2007). Baseline brain activity fluctuations predict somatosensory perception in humans. *Proceedings of the National Academy of Sciences of the United States of America, 104*, 12187-12192.

Brancucci, A., Franciotti, R., D'Anselmo, A., Della Penna, S., Tommasi, L. (2011). The sound of consciousness: Neural underpinnings of auditory perception. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience, 31*, 16611-16618.

Bullmore, E. and Sporns, O. (2009). Complex brain networks: Graph theoretical analysis of structural and functional systems. *Nature Reviews.Neuroscience, 10*, 186-198.

Buschman, T.J. and Miller, E.K. (2007). Top-down versus bottom-up control of attention in the prefrontal and posterior parietal cortices. *Science (New York, N.Y.), 315*, 1860-1862.

Buschman, T. and Kastner, S. (2015). From behavior to neural dynamics: An integrated theory of attention. *Neuron, 88*, 127-144.

Butler, P.D., Tambini, A., Yovel, G., Jalbrzikowski, M., Ziwich, R., Silipo, G., Kanwisher, N., Javitt, D.C. (2008). What's in a face? effects of stimulus duration and inversion on face processing in schizophrenia. *Schizophrenia Research, 103*, 283-292.

Buzsaki, G. and Wang, X.J. (2012). Mechanisms of gamma oscillations. *Annual Review of Neuroscience, 35*, 203-225.

Canolty, R.T., Edwards, E., Dalal, S.S., Soltani, M., Nagarajan, S.S., Kirsch, H.E., Berger, M.S., Barbaro, N.M., Knight, R.T. (2006). High gamma power is phase-locked to theta oscillations in human neocortex. *Science (New York, N.Y.), 313*, 1626-1628.

Cardin, J.A., Carlen, M., Meletis, K., Knoblich, U., Zhang, F., Deisseroth, K., Tsai, L.H., Moore, C.I. (2009). Driving fast-spiking cells induces gamma rhythm and controls sensory responses. *Nature, 459*, 663-667.

Cavada, C. and Goldman-Rakic, P.S. (1989). Posterior parietal cortex in rhesus monkey: II. evidence for segregated corticocortical networks linking sensory and limbic areas with the frontal lobe. *The Journal of Comparative Neurology, 287*, 422-445.

Chen, Y., Norton, D., Ongur, D., Heckers, S. (2008). Inefficient face detection in schizophrenia. *Schizophrenia Bulletin, 34*, 367-374.

Corbetta, M. and Shulman, G.L. (2011). Spatial neglect and attention networks. *Annual Review of Neuroscience, 34*, 569-599.

Corbetta, M. and Shulman, G.L. (2002). Control of goal-directed and stimulus-driven attention in the brain. *Nature Reviews.Neuroscience, 3*, 201-215.

Dale, A.M., Fischl, B., Sereno, M.I. (1999). Cortical surface-based analysis. I. segmentation and surface reconstruction. *NeuroImage, 9*, 179-194.

Dale, A.M., Liu, A.K., Fischl, B.R., Buckner, R.L., Belliveau, J.W., Lewine, J.D., Halgren, E. (2000). Dynamic statistical parametric mapping: Combining fMRI and MEG for high-resolution imaging of cortical activity. *Neuron, 26*, 55-67.

Dehaene, S. and Changeux, J.P. (2011). Experimental and theoretical approaches to conscious processing. *Neuron, 70*, 200-227.

Dehaene, S., Changeux, J.P., Naccache, L., Sackur, J., Sergent, C. (2006). Conscious, preconscious, and subliminal processing: A testable taxonomy. *Trends in Cognitive Sciences, 10*, 204-211.

Del Cul, A., Baillet, S., Dehaene, S. (2007). Brain dynamics underlying the nonlinear threshold for access to consciousness. *PLoS Biology, 5*, e260.

Destrieux, C., Fischl, B., Dale, A., Halgren, E. (2010). Automatic parcellation of human cortical gyri and sulci using standard anatomical nomenclature. *NeuroImage, 53*, 1-15.

Donner, T.H., Siegel, M., Fries, P., Engel, A.K. (2009a). Buildup of choice-predictive activity in human motor cortex during perceptual decision making. *Current Biology : CB, 19*, 1581-1585.

Donner, T.H., Siegel, M., Fries, P., Engel, A.K. (2009b). Buildup of choice-predictive activity in human motor cortex during perceptual decision making. *Current Biology : CB, 19*, 1581-1585.

Eberhard, D. (2013). Neuron and beta-cell evolution: Learning about neurons is learning about beta-cells. *BioEssays : News and Reviews in Molecular, Cellular and Developmental Biology, 35*, 584.

Engel, A.K. and Fries, P. (2010). Beta-band oscillations--signalling the status quo? *Current Opinion in Neurobiology, 20*, 156-165.

Engel, A.K. and Singer, W. (2001). Temporal binding and the neural correlates of sensory awareness. *Trends in Cognitive Sciences, 5*, 16-25.

Engel, A.K., Fries, P., Singer, W. (2001). Dynamic predictions: Oscillations and synchrony in top-down processing. *Nature Reviews.Neuroscience, 2*, 704-716.

Engel, A.K., Konig, P., Kreiter, A.K., Singer, W. (1991). Interhemispheric synchronization of oscillatory neuronal responses in cat visual-cortex. *Science, 252*, 1177-1179.

Esterman, M., Noonan, S.K., Rosenberg, M., Degutis, J. (2012). In the zone or zoning out? tracking behavioral and neural fluctuations during sustained attention. *Cerebral Cortex (New York, N.Y.: 1991), .*

Fahrenfort, J.J., Scholte, H.S., Lamme, V.A. (2007). Masking disrupts reentrant processing in human visual cortex. *Journal of Cognitive Neuroscience, 19*, 1488-1497.

Fisch, L., Privman, E., Ramot, M., Harel, M., Nir, Y., Kipervasser, S., Andelman, F., Neufeld, M.Y., Kramer, U., Fried, I., Malach, R. (2009). Neural "ignition": Enhanced activation linked to perceptual awareness in human ventral stream visual cortex. *Neuron, 64*, 562-574.

Fischl, B., Salat, D.H., Busa, E., Albert, M., Dieterich, M., Haselgrove, C., van der Kouwe, A., Killiany, R., Kennedy, D., Klaveness, S., Montillo, A., Makris, N., Rosen, B., Dale, A.M. (2002). Whole brain segmentation: Automated labeling of neuroanatomical structures in the human brain. *Neuron, 33*, 341-355.

Fox, M.D., Snyder, A.Z., Vincent, J.L., Corbetta, M., Van Essen, D.C., Raichle, M.E. (2005). The human brain is intrinsically organized into dynamic, anticorrelated functional networks. *Proceedings of the National Academy of Sciences of the United States of America, 102*, 9673-9678.

Frey, J.N., Ruhnau, P., Leske, S., Siegel, M., Braun, C., Weisz, N. (2016). The tactile window to consciousness is characterized by frequency-specific integration and segregation of the primary somatosensory cortex. *Scientific Reports, 6*, 20805.

Fries, P. (2015). Rhythms for cognition: Communication through coherence. *Neuron, 88*, 220-235.

Fries, P. (2005). A mechanism for cognitive dynamics: Neuronal communication through neuronal coherence. *Trends in Cognitive Sciences, 9*, 474-480.

Fries, P., Roelfsema, P.R., Engel, A.K., Konig, P., Singer, W. (1997). Synchronization of oscillatory responses in visual cortex correlates with perception in interocular rivalry. *Proceedings of the National Academy of Sciences of the United States of America, 94*, 12699-12704.

Friston, K.J. (1998). The disconnection hypothesis. *Schizophrenia Research, 30*, 115-125.

Friston, K.J. and Frith, C.D. (1995). Schizophrenia: A disconnection syndrome? *Clinical Neuroscience (New York, N.Y.), 3*, 89-97.

Fuster, J.M. (2004). Upper processing stages of the perception-action cycle. *Trends in Cognitive Sciences, 8*, 143-145.

Gaillard, R., Dehaene, S., Adam, C., Clemenceau, S., Hasboun, D., Baulac, M., Cohen, L., Naccache, L. (2009). Converging intracranial markers of conscious access. *PLoS Biology, 7*, e61.

Gastaut, H.J. and Bert, J. (1954). EEG changes during cinematographic presentation; moving picture activation of the EEG. *Electroencephalography and Clinical Neurophysiology, 6*, 433-444.

Gauthier, I., Tarr, M.J., Moylan, J., Skudlarski, P., Gore, J.C., Anderson, A.W. (2000). The fusiform "face area" is part of a network that processes faces at the individual level. *Journal of Cognitive Neuroscience, 12*, 495-504.

Goard, M.J., Pho, G.N., Woodson, J., Sur, M. (2016). Distinct roles of visual, parietal, and frontal motor cortices in memory-guided sensorimotor decisions. *eLife, 5*, 10.7554/eLife.13764.

Gould, I.C., Nobre, A.C., Wyart, V., Rushworth, M.F. (2012). Effects of decision variables and intraparietal stimulation on sensorimotor oscillatory activity in the human brain. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience, 32*, 13805-13818.

Gray, C.M. and Singer, W. (1989). Stimulus-specific neuronal oscillations in orientation columns of cat visual cortex. *Proceedings of the National Academy of Sciences of the United States of America, 86*, 1698-1702.

Gregoriou, G.G., Gotts, S.J., Zhou, H., Desimone, R. (2009). High-frequency, long-range coupling between prefrontal and visual cortex during attention. *Science (New York, N.Y.), 324*, 1207-1210.

Grent-'t-Jong, T., Rivolta, D., Sauer, A., Grube, M., Singer, W., Wibral, M., Uhlhaas, P.J. (2016). MEG-measured visually induced gamma-band oscillations in chronic schizophrenia: Evidence for impaired generation of rhythmic activity in ventral stream regions. *Schizophrenia Research, 176*, 177-185.

Grill-Spector, K., Kushnir, T., Hendler, T., Malach, R. (2000). The dynamics of object-selective activation correlate with recognition performance in humans. *Nature Neuroscience, 3*, 837-843.

Grossman, E.D. and Blake, R. (2001). Brain activity evoked by inverted and imagined biological motion. *Vision Research, 41*, 1475-1482.

Grutzner, C., Uhlhaas, P.J., Genc, E., Kohler, A., Singer, W., Wibral, M. (2010). Neuroelectromagnetic correlates of perceptual closure processes. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience, 30*, 8342-8352.

Grutzner, C., Wibral, M., Sun, L., Rivolta, D., Singer, W., Maurer, K., Uhlhaas, P.J. (2013). Deficits in high- (>60 hz) gamma-band oscillations during visual processing in schizophrenia. *Frontiers in Human Neuroscience, 7*, 88.

Gutteling, T.P., Kenemans, J.L., Neggers, S.F. (2011). Grasping preparation enhances orientation change detection. *PloS One, 6*, e17675.

Haenschel, C. and Linden, D. (2011). Exploring intermediate phenotypes with EEG: Working memory dysfunction in schizophrenia. *Behavioural Brain Research, 216*, 481-495.

Halgren, E., Raij, T., Marinkovic, K., Jousmaki, V., Hari, R. (2000). Cognitive response profile of the human fusiform face area as determined by MEG. *Cerebral Cortex (New York, N.Y.: 1991), 10*, 69-81.

Hamalainen, M.S. and Ilmoniemi, R.J. (1994). Interpreting magnetic fields of the brain: Minimum norm estimates. *Medical & Biological Engineering & Computing, 32*, 35-42.

Hari, R., Parkkonen, L., Nangini, C. (2010). The brain in time: Insights from neuromagnetic recordings. *Annals of the New York Academy of Sciences, 1191*, 89-109.

Haxby, J.V., Hoffman, E.A., Gobbini, M.I. (2000). The distributed human neural system for face perception. *Trends in Cognitive Sciences, 4*, 223-233.

Hegner, Y.L., Lindner, A., Braun, C. (2016). A somatosensory-to-motor cascade of cortical areas engaged in perceptual decision making during tactile pattern discrimination. *Human Brain Mapping, .*

Helmholtz, H. (1853). Ueber einige gesetze der vertheilung elektrischer StrÃ¶me in kÃ¶rperlichen leitern, mit anwendung auf die thierisch-elektrischen versuche (schluss.). *Annalen Der Physik, 165*, 353-377.

Hesselmann, G. and Malach, R. (2011). The link between fMRI-BOLD activation and perceptual awareness is "stream-invariant" in the human visual system. *Cerebral Cortex (New York, N.Y.: 1991), 21*, 2829-2837.

Hesselmann, G., Hebart, M., Malach, R. (2011). Differential BOLD activity associated with subjective and objective reports during "blindsight" in normal observers. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience, 31*, 12936-12944.

Hong, L.E., Summerfelt, A., Buchanan, R.W., O'Donnell, P., Thaker, G.K., Weiler, M.A., Lahti, A.C. (2010). Gamma and delta neural oscillations and association with clinical symptoms under subanesthetic ketamine. *Neuropsychopharmacology : Official Publication of the American College of Neuropsychopharmacology, 35*, 632-640.

Jensen, O. and Mazaheri, A. (2010). Shaping functional architecture by oscillatory alpha activity: Gating by inhibition. *Frontiers in Human Neuroscience, 4*, 186.

Jones, E.G. and Powell, T.P. (1970). An anatomical study of converging sensory pathways within the cerebral cortex of the monkey. *Brain : A Journal of Neurology, 93*, 793-820.

Jones, S.R., Pritchett, D.L., Stufflebeam, S.M., Hamalainen, M., Moore, C.I. (2007). Neural correlates of tactile detection: A combined magnetoencephalography and biophysically based computational modeling study. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience, 27*, 10751-10764.

Kantrowitz, J.T. and Javitt, D.C. (2010). N-methyl-d-aspartate (NMDA) receptor dysfunction or dysregulation: The final common pathway on the road to schizophrenia? *Brain Research Bulletin, 83*, 108-121.

Kaplan, R., King, J., Koster, R., Penny, W.D., Burgess, N., Friston, K.J. (2017). The neural representation of prospective choice during spatial planning and decisions. *PLoS Biology, 15*, e1002588.

Kasai, K., Shenton, M.E., Salisbury, D.F., Hirayasu, Y., Lee, C.U., Ciszewski, A.A., Yurgelun-Todd, D., Kikinis, R., Jolesz, F.A., McCarley, R.W. (2003). Progressive decrease of left superior temporal gyrus gray matter volume in patients with first-episode schizophrenia. *The American Journal of Psychiatry, 160*, 156-164.

Keil, A., Muller, M.M., Ray, W.J., Gruber, T., Elbert, T. (1999). Human gamma band activity and perception of a gestalt. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience, 19*, 7152-7161.

Kim, H., Ahrlund-Richter, S., Wang, X., Deisseroth, K., Carlen, M. (2016). Prefrontal parvalbumin neurons in control of attention. *Cell, 164*, 208-218.

King, J.R., Pescetelli, N., Dehaene, S. (2016). Brain mechanisms underlying the brief maintenance of seen and unseen sensory information. *Neuron, 92*, 1122-1134.

Kirihara, K., Rissling, A.J., Swerdlow, N.R., Braff, D.L., Light, G.A. (2012). Hierarchical organization of gamma and theta oscillatory dynamics in schizophrenia. *Biological Psychiatry, 71*, 873-880.

Klimesch, W., Sauseng, P., Hanslmayr, S. (2007). EEG alpha oscillations: The inhibition-timing hypothesis. *Brain Research Reviews, 53*, 63-88.

Koch, C., Massimini, M., Boly, M., Tononi, G. (2016). Neural correlates of consciousness: Progress and problems. *Nature Reviews Neuroscience, 17*, 307-321.

Koechlin, E., Ody, C., Kouneiher, F. (2003). The architecture of cognitive control in the human prefrontal cortex. *Science (New York, N.Y.), 302*, 1181-1185.

Koivisto, M. and Grassini, S. (2016). Neural processing around 200 ms after stimulus-onset correlates with subjective visual awareness. *Neuropsychologia, 84*, 235-243.

Koivisto, M., Grassini, S., Salminen-Vaparanta, N., Revonsuo, A. (2017). Different electrophysiological correlates of visual awareness for detection and identification. *Journal of Cognitive Neuroscience, 29*, 1621-1631.

Koivisto, M., Lahteenmaki, M., Sorensen, T.A., Vangkilde, S., Overgaard, M., Revonsuo, A. (2008). The earliest electrophysiological correlate of visual awareness? *Brain and Cognition, 66*, 91-103.

Korhonen, O., Palva, S., Palva, J.M. (2014). Sparse weightings for collapsing inverse solutions to cortical parcellations optimize M/EEG source reconstruction accuracy. *Journal of Neuroscience Methods, 226C*, 147-160.

Kremien, M., Shavit, U., Mass, T., Genin, A. (2013). Benefit of pulsation in soft corals. *Proceedings of the National Academy of Sciences of the United States of America, 110*, 8978-8983.

Lachaux, J.P., Rodriguez, E., Martinerie, J., Varela, F.J. (1999). Measuring phase synchrony in brain signals. *Human Brain Mapping, 8*, 194-208.

Lamme, V.A. (2006). Towards a true neural stance on consciousness. *Trends in Cognitive Sciences, 10*, 494-501.

Lamme, V.A. and Roelfsema, P.R. (2000). The distinct modes of vision offered by feedforward and recurrent processing. *Trends in Neurosciences, 23*, 571-579.

Lee, A.T., Vogt, D., Rubenstein, J.L., Sohal, V.S. (2014). A class of GABAergic neurons in the prefrontal cortex sends long-range projections to the nucleus accumbens and elicits acute

avoidance behavior. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience, 34*, 11519-11525.

Lehtela, L., Salmelin, R., Hari, R. (1997). Evidence for reactive magnetic 10-hz rhythm in the human auditory cortex. *Neuroscience Letters, 222*, 111-114.

Lewis, D.A., Hashimoto, T., Volk, D.W. (2005). Cortical inhibitory neurons and schizophrenia. *Nature Reviews.Neuroscience, 6*, 312-324.

Lewis, D.A., Curley, A.A., Glausier, J.R., Volk, D.W. (2012). Cortical parvalbumin interneurons and cognitive dysfunction in schizophrenia. *Trends in Neurosciences, 35*, 57-67.

Li Hegner, Y., Lindner, A., Braun, C. (2015). Cortical correlates of perceptual decision making during tactile spatial pattern discrimination. *Human Brain Mapping, 36*, 3339-3350.

Lin, J.L., Silva-Pereyra, J., Chou, C.C., Lin, F.H. (2018). The sequence of cortical activity inferred by response latency variability in the human ventral pathway of face processing. *Scientific Reports, 8*, 5836-018-23942-x.

Lobier, M., Palva, J.M., Palva, S. (2017). High-alpha band synchronization across frontal, parietal and visual cortex mediates behavioral and neuronal effects of visuospatial attention. *NeuroImage, 165*, 222-237.

Luppino, G., Matelli, M., Camarda, R., Rizzolatti, G. (1993). Corticocortical connections of area F3 (SMA-proper) and area F6 (pre-SMA) in the macaque monkey. *The Journal of Comparative Neurology, 338*, 114-140.

Maher, S., Ekstrom, T., Holt, D., Ongur, D., Chen, Y. (2016). The core brain region for face processing in schizophrenia lacks face selectivity. *Schizophrenia Bulletin, 42*, 666-674.

Marois, R., Yi, D.J., Chun, M.M. (2004). The neural fate of consciously perceived and missed events in the attentional blink. *Neuron, 41*, 465-472.

Meador, K.J., Ray, P.G., Echauz, J.R., Loring, D.W., Vachtsevanos, G.J. (2002). Gamma coherence and conscious perception. *Neurology, 59*, 847-854.

Medendorp, W.P., Buchholz, V.N., Van Der Werf, J., Leone, F.T. (2011). Parietofrontal circuits in goal-oriented behaviour. *The European Journal of Neuroscience, 33*, 2017-2027.

Melloni, L., Schwiedrzik, C.M., Muller, N., Rodriguez, E., Singer, W. (2011). Expectations change the signatures and timing of electrophysiological correlates of perceptual awareness. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience, 31*, 1386-1396.

Michalareas, G., Vezoli, J., van Pelt, S., Schoffelen, J., Kennedy, H., Fries, P. (2016). Alpha-beta and gamma rhythms subserve feedback and feedforward influences among human visual cortical areas. *Neuron, .*

Miller, K.J., Hermes, D., Pestilli, F., Wig, G.S., Ojemann, J.G. (2017). Face percept formation in human ventral temporal cortex. *Journal of Neurophysiology, 118*, 2614-2627.

Monto, S., Palva, S., Voipio, J., Palva, J.M. (2008). Very slow EEG fluctuations predict the dynamics of stimulus detection and oscillation amplitudes in humans. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience, 28*, 8268-8272.

Murakami, S. and Okada, Y. (2006). Contributions of principal neocortical neurons to magnetoencephalography and electroencephalography signals. *The Journal of Physiology, 575*, 925-936.

Murty, D.V.P.S., Shirhatti, V., Ravishankar, P., Ray, S. (2018). Large visual stimuli induce two distinct gamma oscillations in primate visual cortex. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience, .*

Nierhaus, T., Forschack, N., Piper, S.K., Holtze, S., Krause, T., Taskin, B., Long, X., Stelzer, J., Margulies, D.S., Steinbrink, J., Villringer, A. (2015). Imperceptible somatosensory stimulation alters sensorimotor background rhythm and connectivity. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience, 35*, 5917-5925.

Nordmark, P.F., Pruszynski, J.A., Johansson, R.S. (2012). BOLD responses to tactile stimuli in visual and auditory cortex depend on the frequency content of stimulation. *Journal of Cognitive Neuroscience, 24*, 2120-2134.

Onitsuka, T., Niznikiewicz, M.A., Spencer, K.M., Frumin, M., Kuroki, N., Lucia, L.C., Shenton, M.E., McCarley, R.W. (2006). Functional and structural deficits in brain regions subserving face perception in schizophrenia. *The American Journal of Psychiatry, 163*, 455-462.

Orlov, T., Makin, T.R., Zohary, E. (2010). Topographic representation of the human body in the occipitotemporal cortex. *Neuron, 68*, 586-600.

Palva, J.M. and Palva, S. (2017). Functional integration across oscillation frequencies by cross-frequency phase synchronization. *European Journal of Neuroscience, 0*.

Palva, J.M., Palva, S., Kaila, K. (2005). Phase synchrony among neuronal oscillations in the human cortex. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience, 25*, 3962-3972.

Palva, S. and Palva, J.M. (2012). Discovering oscillatory interaction networks with M/EEG: Challenges and breakthroughs. *Trends in Cognitive Sciences, 16*, 219-230.

Palva, S. and Palva, J.M. (2011). Functional roles of alpha-band phase synchronization in local and large-scale cortical networks. *Frontiers in Psychology, 2*, 204.

Palva, S. and Palva, J.M. (2007). New vistas for alpha-frequency band oscillations. *Trends in Neurosciences, 30*, 150-158.

Palva, S., Linkenkaer-Hansen, K., Naatanen, R., Palva, J.M. (2005). Early neural correlates of conscious somatosensory perception. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience, 25*, 5248-5258.

Park, D.H., Song, T., Hoang, D.T., Xu, J., Jo, J. (2017). A local counter-regulatory motif modulates the global phase of hormonal oscillations. *Scientific Reports, 7*, 1602-017-01806-0.

Pinault, D. (2008). N-methyl d-aspartate receptor antagonists ketamine and MK-801 induce wake-related aberrant gamma oscillations in the rat neocortex. *Biological Psychiatry, 63*, 730-735.

Pins, D. and Ffytche, D. (2003). The neural correlates of conscious vision. *Cerebral Cortex (New York, N.Y.: 1991), 13*, 461-474.

Power, J.D., Cohen, A.L., Nelson, S.M., Wig, G.S., Barnes, K.A., Church, J.A., Vogel, A.C., Laumann, T.O., Miezin, F.M., Schlaggar, B.L., Petersen, S.E. (2011). Functional network organization of the human brain. *Neuron, 72*, 665-678.

Puce, A., Allison, T., Bentin, S., Gore, J.C., McCarthy, G. (1998). Temporal cortex activation in humans viewing eye and mouth movements. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience, 18*, 2188-2199.

Radua, J., Phillips, M.L., Russell, T., Lawrence, N., Marshall, N., Kalidindi, S., El-Hage, W., McDonald, C., Giampietro, V., Brammer, M.J., David, A.S., Surguladze, S.A. (2010). Neural response to specific components of fearful faces in healthy and schizophrenic adults. *NeuroImage, 49*, 939-946.

Revonsuo, A. and Koivisto, M. (2010). Electrophysiological evidence for phenomenal consciousness. *Cognitive Neuroscience, 1*, 225-227.

Rodriguez, E., George, N., Lachaux, J.P., Martinerie, J., Renault, B., Varela, F.J. (1999). Perception's shadow: Long-distance synchronization of human brain activity. *Nature, 397*, 430-433.

Rodriguez, R., Kallenbach, U., Singer, W., Munk, M.H. (2010). Stabilization of visual responses through cholinergic activation. *Neuroscience, 165*, 944-954.

Rubinov, M. and Sporns, O. (2010). Complex network measures of brain connectivity: Uses and interpretations. *NeuroImage, 52*, 1059-1069.

Rutiku, R., Aru, J., Bachmann, T. (2016). General markers of conscious visual perception and their timing. *Frontiers in Human Neuroscience, 10*, 23.

Saalmann, Y.B., Pinsk, M.A., Wang, L., Li, X., Kastner, S. (2012). The pulvinar regulates information transmission between cortical areas based on attention demands. *Science (New York, N.Y.), 337*, 753-756.

Sadaghiani, S., Hesselmann, G., Kleinschmidt, A. (2009). Distributed and antagonistic contributions of ongoing activity fluctuations to auditory stimulus detection. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience, 29*, 13410-13417.

Salti, M., Monto, S., Charles, L., King, J.R., Parkkonen, L., Dehaene, S. (2015). Distinct cortical codes and temporal dynamics for conscious and unconscious percepts. *eLife, 4*, 10.7554/eLife.05652.

Schall, J.D. (2001). Neural basis of deciding, choosing and acting. *Nature Reviews.Neuroscience, 2*, 33-42.

Schmiedt, C., Brand, A., Hildebrandt, H., Basar-Eroglu, C. (2005). Event-related theta oscillations during working memory tasks in patients with schizophrenia and healthy controls. *Brain Research.Cognitive Brain Research, 25*, 936-947.

Schubert, R., Blankenburg, F., Lemm, S., Villringer, A., Curio, G. (2006). Now you feel it--now you don't: ERP correlates of somatosensory awareness. *Psychophysiology, 43*, 31-40.

Schurger, A., Sarigiannidis, I., Naccache, L., Sitt, J.D., Dehaene, S. (2015). Cortical activity is more stable when sensory stimuli are consciously perceived. *Proceedings of the National Academy of Sciences of the United States of America, 112*, E2083-92.

Sekimoto, M., Kato, M., Watanabe, T., Kajimura, N., Takahashi, K. (2011). Cortical regional differences of delta waves during all-night sleep in schizophrenia. *Schizophrenia Research, 126*, 284-290.

Senkowski, D., Schneider, T.R., Foxe, J.J., Engel, A.K. (2008). Crossmodal binding through neural coherence: Implications for multisensory processing. *Trends in Neurosciences, 31*, 401-409.

Sergent, C., Baillet, S., Dehaene, S. (2005). Timing of the brain events underlying access to consciousness during the attentional blink. *Nature Neuroscience, 8*, 1391-1400.

Siebenhühner, F., Weiss, S.A., Coppola, R., Weinberger, D.R., Bassett, D.S. (2013). Intra- and inter-frequency brain network structure in health and schizophrenia. *PLoS ONE, 8*, e72351.

Siegel, M., Buschman, T.J., Miller, E.K. (2015). Cortical information flow during flexible sensorimotor decisions. *Science (New York, N.Y.), 348*, 1352-1355.

Siegel, M., Donner, T.H., Engel, A.K. (2012). Spectral fingerprints of large-scale neuronal interactions. *Nature Reviews.Neuroscience, 13*, 121-134.

Singer, W. (2017). Neuronal oscillations: Unavoidable and useful? *The European Journal of Neuroscience, .*

Singer, W. (1999). Neuronal synchrony: A versatile code for the definition of relations? *Neuron, 24*, 49-65, 111-25.

Singer, W. and Gray, C.M. (1995). Visual feature integration and the temporal correlation hypothesis. *Annual Review of Neuroscience, 18*, 555-586.

Sinkkonen, J., Tiitinen, H., Naatanen, R. (1995). Gabor filters: An informative way for analysing event-related brain activity. *Journal of Neuroscience Methods, 56*, 99-104.

Spadone, S., Della Penna, S., Sestieri, C., Betti, V., Tosoni, A., Perrucci, M.G., Romani, G.L., Corbetta, M. (2015). Dynamic reorganization of human resting-state networks during visuospatial attention. *Proceedings of the National Academy of Sciences of the United States of America, 112*, 8112-8117.

Spencer, K.M., Niznikiewicz, M.A., Shenton, M.E., McCarley, R.W. (2008). Sensory-evoked gamma oscillations in chronic schizophrenia. *Biological Psychiatry, 63*, 744-747.

Spencer, K.M., Nestor, P.G., Niznikiewicz, M.A., Salisbury, D.F., Shenton, M.E., McCarley, R.W. (2003). Abnormal neural synchrony in schizophrenia. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience, 23*, 7407-7411.

Stephan, K.E., Friston, K.J., Frith, C.D. (2009). Dysconnection in schizophrenia: From abnormal synaptic plasticity to failures of self-monitoring. *Schizophrenia Bulletin, 35*, 509-527.

Sun, L., Castellanos, N., Grutzner, C., Koethe, D., Rivolta, D., Wibral, M., Kranaster, L., Singer, W., Leweke, M.F., Uhlhaas, P.J. (2013). Evidence for dysregulated high-frequency oscillations during sensory processing in medication-naive, first episode schizophrenia. *Schizophrenia Research, 150*, 519-525.

Tallon-Baudry, C. (2012). On the neural mechanisms subserving consciousness and attention. *Frontiers in Psychology, 2*, 397.

Tallon-Baudry, C. and Bertrand, O. (1999). Oscillatory gamma activity in humans and its role in object representation. *Trends in Cognitive Sciences, 3*, 151-162.

Tallon-Baudry, C., Bertrand, O., Delpuech, C., Pernier, J. (1996). Stimulus specificity of phase-locked and non-phase-locked 40 hz visual responses in human. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience, 16*, 4240-4249.

Taskin, B., Holtze, S., Krause, T., Villringer, A. (2008). Inhibitory impact of subliminal electrical finger stimulation on SI representation and perceptual sensitivity of an adjacent finger. *NeuroImage, 39*, 1307-1313.

Taulu, S., Simola, J., Kajola, M. (2005). Applications of the signal space separation method. *Ieee Transactions on Signal Processing, 53*, 3359-13.

Tiesinga, P. and Sejnowski, T.J. (2009). Cortical enlightenment: Are attentional gamma oscillations driven by ING or PING? *Neuron, 63*, 727-732.

Tomassini, A., Spinelli, D., Jacono, M., Sandini, G., Morrone, M.C. (2015). Rhythmic oscillations of visual contrast sensitivity synchronized with action. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience, 35*, 7019-7029.

Tononi, G. and Edelman, G.M. (1998). Consciousness and complexity. *Science (New York, N.Y.), 282*, 1846-1851.

Tosoni, A., Galati, G., Romani, G.L., Corbetta, M. (2008). Sensory-motor mechanisms in human parietal cortex underlie arbitrary visual decisions. *Nature Neuroscience, 11*, 1446-1453.

Traub, R.D., Whittington, M.A., Buhl, E.H., Jefferys, J.G., Faulkner, H.J. (1999). On the mechanism of the gamma --> beta frequency shift in neuronal oscillations induced in rat hippocampal slices by tetanic stimulation. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience, 19*, 1088-1105.

Tsao, D.Y., Freiwald, W.A., Tootell, R.B., Livingstone, M.S. (2006). A cortical region consisting entirely of face-selective cells. *Science (New York, N.Y.), 311*, 670-674.

Turella, L., Tucciarelli, R., Oosterhof, N.N., Weisz, N., Rumiati, R., Lingnau, A. (2016). Beta band modulations underlie action representations for movement planning. *NeuroImage, 136*, 197-207.

Uhlhaas, P.J. (2015). Neural dynamics in mental disorders. *World Psychiatry : Official Journal of the World Psychiatric Association (WPA), 14*, 116-118.

Uhlhaas, P.J. and Singer, W. (2015). Oscillations and neuronal dynamics in schizophrenia: The search for basic symptoms and translational opportunities. *Biological Psychiatry, 77*, 1001-1009.

Uhlhaas, P.J. and Singer, W. (2012). Neuronal dynamics and neuropsychiatric disorders: Toward a translational paradigm for dysfunctional large-scale networks. *Neuron, 75*, 963-980.

Uhlhaas, P.J. and Mishara, A.L. (2007). Perceptual anomalies in schizophrenia: Integrating phenomenology and cognitive neuroscience. *Schizophrenia Bulletin, 33*, 142-156.

Uhlhaas, P.J. and Singer, W. (2006). Neural synchrony in brain disorders: Relevance for cognitive dysfunctions and pathophysiology. *Neuron, 52*, 155-168.

Uhlhaas, P.J., Linden, D.E., Singer, W., Haenschel, C., Lindner, M., Maurer, K., Rodriguez, E. (2006). Dysfunctional long-range coordination of neural activity during gestalt perception in schizophrenia. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience, 26*, 8168-8175.

van Diepen, R.M., Cohen, M.X., Denys, D., Mazaheri, A. (2015). Attention and temporal expectations modulate power, not phase, of ongoing alpha oscillations. *Journal of Cognitive Neuroscience, 27*, 1573-1586.

van Gaal, S. and Lamme, V.A. (2012). Unconscious high-level information processing: Implication for neurobiological theories of consciousness. *The Neuroscientist : A Review Journal Bringing Neurobiology, Neurology and Psychiatry, 18*, 287-301.

van Gaal, S., Ridderinkhof, K.R., Fahrenfort, J.J., Scholte, H.S., Lamme, V.A. (2008). Frontal cortex mediates unconsciously triggered inhibitory control. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience, 28*, 8053-8062.

Van Lancker, D.R. and Canter, G.J. (1982). Impairment of voice and face recognition in patients with hemispheric damage. *Brain and Cognition, 1*, 185-195.

Varela, F., Lachaux, J.P., Rodriguez, E., Martinerie, J. (2001). The brainweb: Phase synchronization and large-scale integration. *Nature Reviews.Neuroscience, 2*, 229-239.

Veit, J., Hakim, R., Jadi, M.P., Sejnowski, T.J., Adesnik, H. (2017). Cortical gamma band synchronization through somatostatin interneurons. *Nature Neuroscience, 20*, 951-959.

Vercammen, A., Knegtering, H., den Boer, J.A., Liemburg, E.J., Aleman, A. (2010). Auditory hallucinations in schizophrenia are associated with reduced functional connectivity of the temporo-parietal area. *Biological Psychiatry, 67*, 912-918.

Vidal, J.R., Perrone-Bertolotti, M., Kahane, P., Lachaux, J.P. (2015). Intracranial spectral amplitude dynamics of perceptual suppression in fronto-insular, occipito-temporal, and primary visual cortex. *Frontiers in Psychology, 5*, 1545.

Vidal, J.R., Perrone-Bertolotti, M., Levy, J., De Palma, L., Minotti, L., Kahane, P., Bertrand, O., Lutz, A., Jerbi, K., Lachaux, J.P. (2014). Neural repetition suppression in ventral occipito-temporal cortex occurs during conscious and unconscious processing of frequent stimuli. *NeuroImage, 95*, 129-135.

von Stein, A. and Sarnthein, J. (2000). Different frequencies for different scales of cortical integration: From local gamma to long range alpha/theta synchronization. *International Journal of Psychophysiology : Official Journal of the International Organization of Psychophysiology, 38*, 301-313.

Voytek, B. and Knight, R.T. (2015). Dynamic network communication as a unifying neural basis for cognition, development, aging, and disease. *Biological Psychiatry, 77*, 1089-1097.

Wang, S., Lobier, L., Siebenhühner, F., Puoliväli, T., Palva, S., Palva, J. (2018). Hyperedge bundling: A practical solutin to spurious interactions in MEG/EEG connectivity analyses. *NeuroImage, S1053-8119*, 0056.

Weinberger, D.R., Berman, K.F., Illowsky, B.P. (1988). Physiological dysfunction of dorsolateral prefrontal cortex in schizophrenia. III. A new cohort and evidence for a monoaminergic mechanism. *Archives of General Psychiatry, 45*, 609-615.

Weisz, N., Wuhle, A., Monittola, G., Demarchi, G., Frey, J., Popov, T., Braun, C. (2014). Prestimulus oscillatory power and connectivity patterns predispose conscious somatosensory perception. *Proceedings of the National Academy of Sciences of the United States of America, 111*, E417-25.

Whittington, M.A., Traub, R.D., Faulkner, H.J., Stanford, I.M., Jefferys, J.G. (1997). Recurrent excitatory postsynaptic potentials induced by synchronized fast cortical oscillations. *Proceedings of the National Academy of Sciences of the United States of America, 94*, 12198-12203.

Wohlschlager, A. (2000). Visual motion priming by invisible actions. *Vision Research, 40*, 925-930.

Womelsdorf, T. and Everling, S. (2015). Long-range attention networks: Circuit motifs underlying endogenously controlled stimulus selection. *Trends in Neurosciences, 38*, 682-700.

Womelsdorf, T. and Fries, P. (2007). The role of neuronal synchronization in selective attention. *Current Opinion in Neurobiology, 17*, 154-160.

Wyart, V. and Tallon-Baudry, C. (2008). Neural dissociation between visual awareness and spatial attention. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience, 28*, 2667-2679.

Yang, T. and Shadlen, M.N. (2007). Probabilistic reasoning by neurons. *Nature, 447*, 1075-1080.

Yeo, B.T., Krienen, F.M., Sepulcre, J., Sabuncu, M.R., Lashkari, D., Hollinshead, M., Roffman, J.L., Smoller, J.W., Zollei, L., Polimeni, J.R., Fischl, B., Liu, H., Buckner, R.L. (2011). The organization of the human cerebral cortex estimated by intrinsic functional connectivity. *Journal of Neurophysiology, 106*, 1125-1165.