Department of Neuroscience and Biomedical Engineering

Brain basis of sharing and transmitting representations of social world

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Dmitry Smirnov

Aalto University

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Brain basis of sharing and transmitting representations of social world

Dmitry Smirnov

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Abstract

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Abstract

Social communication is a crucial element of human behavior. Every day we resolve conflicts, empathize with our peers, exchange opinions and observe other's behaviors. While the brain basis of these processes has been studied in single individuals, it remains unresolved how such complex patterns of social interaction are parsed in the brains of interacting humans.

This thesis addresses the brain basis of social communication in three domains: motor actions, language and emotions. These represent the main channels of human communication, and are tightly linked between each other. We used functional magnetic resonance imaging to collect the data, naturalistic stimulation as an experimental design principle and pseudo-hyperscanning to address the interaction in the experiments. We developed a novel hypeclassification approach, which combined pattern classification with functional realignment of data to investigate the shared neural codes between interacting individuals.

In the first study we compared the neural coupling across multiple observers during active simulation versus passive watching of naturalistic boxing match videos by computing the time-varying intersubject phase synchrony of multiple observers' brain activity. We have shown that shared perspective synchronized brain networks involved in action execution and observation.

In the second study we adopted a novel hyperclassification approach to investigate shared neural codes between action execution and observation in two individuals. We successfully showed that observed actions can be classified using the model trained on actor's data. The results revealed that action observation and execution share neural information in the brains of two interacting individuals.

In the third study we used pseudo-hyperscanning to investigate the neural "coupling" between individuals telling emotional stories, and listeners of these stories. We measured the synchronization of their brain activity time series and revealed that as the experienced emotions became stronger and more similar between speaker and listener, their neural synchronization in attentional, limbic, somatosensory and midline structures increased.

The fourth and final study investigated contextual effects on naturalistic speech comprehension. By manipulating context for a narrative, we addressed functional connectivity in the brain of listeners. Results of this study showed increase in functional connectivity in linguistic, attentional and error monitoring brain networks when individuals successfully understood speech in presence of relevant context.

These results provide evidence for significant role of intersubject neural synchronization and shared neural codes in social interaction. Such synchronization may provide a window into mind state of another individual and enhance one's ability to understand and predict behavior of others.

Keywords brain, fMRI, pattern classification, intersubject similarity, action, emotion, speech

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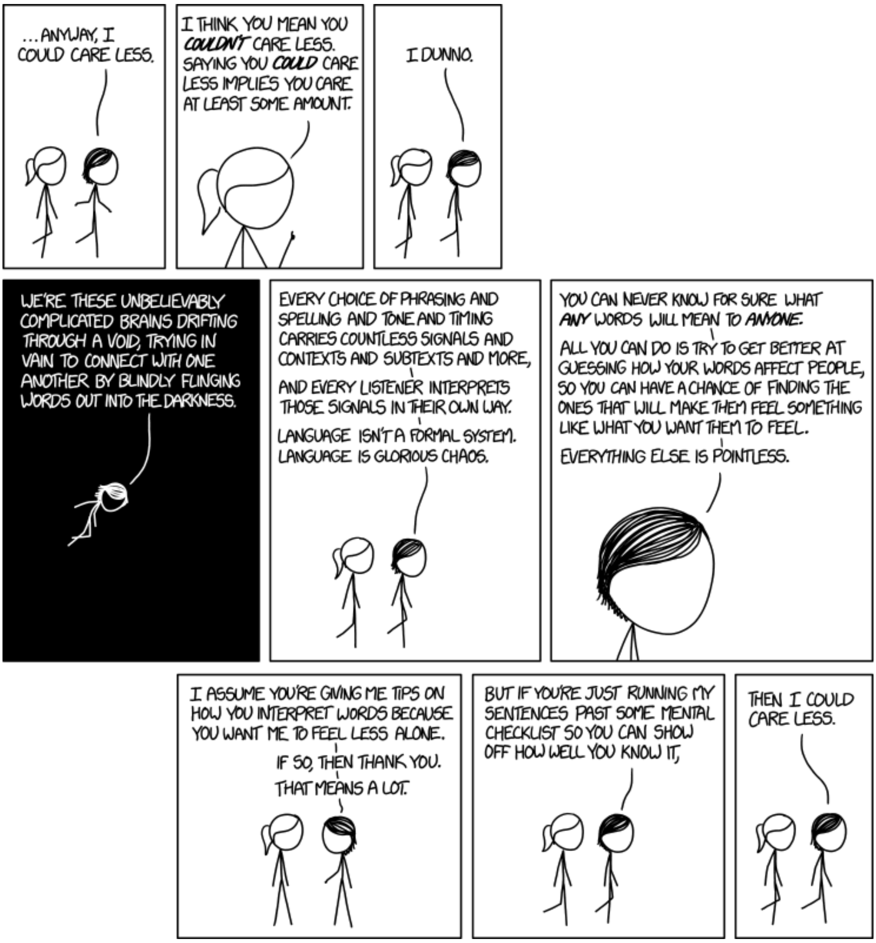

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Espoo, 15 November 2017
Dmitry Smirnov

Contents

List of Abbreviations and Symbols

ACC	Anterior cingulate cortex
AG	Angular gyrus
AON	Action-observation network
BCCA	Bayesian canonical correlation analysis
BOLD	Blood-oxygen-level dependent
EEG	electroencephalogram
FC	Functional connectivity
FDR	False discovery rate
fMRI	Functional magnetic resonance imaging
GLM	General linear model
HRF	Haemodynamic response function
IFG	Inferior frontal gyrus
INS	Insula
IPC	Inferior parietal cortex
IPL	Inferior parietal lobule
ISPS	Intersubject phase synchronization
ISC	Intersubject correlation
kNN	k-Nearest-Neighbors
LOC	Lateral occipital cortex
MFG	Middle frontal gyrus
MNI	Montreal neurological institute
MRI	Magnetic resonance imaging
MTG	Middle temporal gyrus
MVPA	Multi-voxel pattern analysis
PPI	Psycho-Physiological Interactions

RF	Radio Frequency
ROI	Region of interest
RSA	Representation similarity analysis
SBPS	Seed based phase synchronization
SEM	Standard error of the mean
SMA	Supplementary motor area
SMG	Supramarginal gyrus
SPL	Superior parietal lobe
STG	Superior temporal gyrus
STS	Superior temporal sulcus
TE	Echo time
TMS	Transcranial magnetic stimulation
TOM	Theory of mind
TPJ	Temporoparietal Junction
TR	Repetition time
V	Cerebellar lobule V
V1	Visual primary
V2	Secondary visual cortex
V3	Visual area V3
V4	Visual area V4
VIIIa	Cerebellar lobule VIIIa

List of Publications

This thesis comprises of three journal publications and one manuscript under review in scientific journal. Publications are referred to by their roman numerals.

I. Nummenmaa L, Smirnov D, Lahnakoski JM, Glerean E, Jääskeläinen IP, Sams M, Hari R (2014) Mental Action Simulation Synchronizes Action–Observation Circuits across Individuals. J Neurosci 34(3): 748–757.

II. Smirnov D, Lachat F, Peltola T, Lahnakoski JM, Koistinen OP, Glerean E, Vehtari A, Hari R, Sams M, Nummenmaa L (2017) Brain-To-Brain Hyperclassification Reveals Action-Specific Motor Mapping of Observed Actions in Humans. PLoS One 12(12): e0189508.

III. Smirnov D, Saarimäki H, Glerean E, Hari R, Sams M, Nummenmaa L (under review) Synchronized speaker-listener brain activity supports speech-driven emotional contagion.

IV. Smirnov D, Glerean E, Lahnakoski JM, Salmi J, Jääskeläinen IP, Sams M, Nummenmaa L (2014) Fronto-parietal network supports context-dependent speech comprehension. Neuropsychologia 64: 293-303.

Author's Contribution

Study I: Mental Action Simulation Synchronizes Action–Observation Circuits across Individuals

The candidate contributed to design of the experiment, acquired the data, contributed to the data analysis, and contributed to the writing of the manuscript.

Study II: Brain-To-Brain Hyperclassification Reveals Action-Specific Motor Mapping of Observed Actions in Humans

The candidate designed the experiment, gathered the data, designed and implemented the analysis approach, analysed the data and wrote the manuscript. All co-authors contributed valuable comments during the manuscript writing.

Study III: Synchronized speaker-listener brain activity supports speech-driven emotional contagion

The candidate contributed to the design of the experiment, gathered the data, designed and implemented the analysis approach, analysed the data and wrote the manuscript. All co-authors contributed valuable comments during the manuscript writing.

Study IV: Fronto-parietal network supports context-dependent speech comprehension

The candidate designed the experiment, gathered the data, analysed the data and wrote the manuscript. All co-authors contributed valuable comments during the manuscript writing.

1. Introduction

1.1 Brain basis of social communication

Social interaction is the cornerstone of human behavior. We convey our thoughts, emotions and actions to others with, for example, gestures, facial and vocal expressions. Human brain has evolved under the evolutionary pressure that supported social interactions and is wired for processing of social information. Multiple studies have shown that the relative size of the neocortex is expanded in humans versus other primates, and its volume correlates with indices of complexity of social behaviour (for reviews see Dunbar, 2003; Dunbar and Shultz, 2007). Species living in large groups face different social and cognitive demands than those living alone. To sustain group cohesion, individual group members must coordinate their behaviour with the other members of the group. This also requires being sensitive to potential conflicts and being able to predict how different social interactions develop (Dunbar and Shultz, 2007).

The better we can predict the behaviour of our peers, the more successful our interaction with them will be. Hence, one of the key functions of the social species' brains is the ability to make predictions in context of social interaction (Frith, 2007). Social cognition requires rapid and accurate recognition of and response to social stimuli, maintenance of long-term representations of social relationship status with different individuals, as well as emotional appraisal of the behaviour of conspecifics (Adolphs, 2009). Consequently, in the human brain there exist dedicated systems for face perception (Haxby et al., 2000) and social perception in general (Adolphs, 1999; Frith and Frith, 2010). Furthermore, some regions such as amygdala or posterior superior temporal sulcus (pSTS) may serve as higher-order "hubs" for social information processing (Lahnakoski et al., 2012a; Bickart et al., 2014). If we take a look at the meta-analytic map of brain regions which were activated in studies under keyword "social", we find that the regions included in that map are involved in various processes including conflict monitoring and resolution (ACC), memory (PCC), emotional processing (Amygdala) and others (Figure 1, based on the meta-analytic database Neurosynth.org; Yarkoni et al., 2012) As multiple evidence shows, social processes are at the core of our behaviour and are supported by sophisticated brain network.

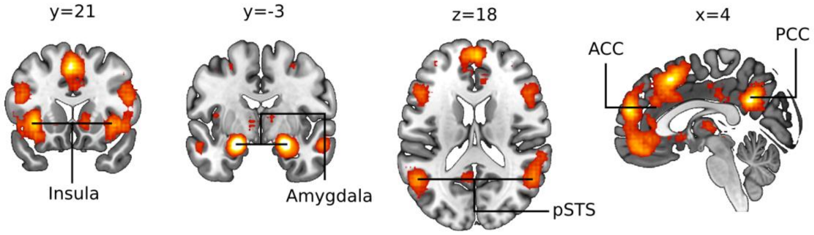

Figure 1. Brain regions mentioned in studies along the “social” keyword, extracted from Neurosynth.org database. The key areas include anterior and posterior cingulate cortex, insula, amygdala, pSTS, frontal and temporal poles and fusiform face area.

While brain mechanisms supporting social *perception,* actions and emotions are understood increasingly well, the brain basis of actual social *interaction* remains poorly understood. For example, it is not known how social information is exchanged between interacting individuals. Why is it sometimes so easy to understand the intentions, emotions and goals of individuals we interact with, and sometimes there is a vast distance between us, and we can barely understand what the person is trying to communicate? Similarity of perspectives and experiences enhance our ability to understand each other (Hari et al., 2016). It is easier to understand others, who read the same books, empathize with us and feel similar emotions. It could be speculated that if we would interact with an exact copy of ourselves, mutual understanding could be perfect because our own mental states would map exactly to mental states of our carbon-copy-interlocutor. Indeed prior research has shown that similarity in mental states is associated with similarity of neural activity (Hasson et al., 2004; Hasson et al., 2012), suggesting that such neural similarity might support social communication.

Verbal communication and observation of other's behavior are the key means to infer the thoughts, emotions, goals and intentions of our peers, yet the neural substrate of these processes in interaction remains unresolved. In the studies presented here, we investigated the brain basis of social communication from three different perspectives: action understanding, speech comprehension and emotional interaction. The overall theme we addressed in these studies concerned the role of similarity of brain activity in efficient social communication between individuals.

1.2 Studying brain function under naturalistic settings

Our brains have evolved in complex and dynamic world. It is thus not surprising that more complex, naturalistic stimuli, similar to what we experience in our normal everyday life, trigger stronger and more reliable cortical responses than highly controlled and simplified stimuli traditionally used in neuroimaging experiments (Fox et al., 2009; Schultz et al., 2013). Laboratory experiments have however most often utilized highly controlled stimulation models, where majority of spontaneous, variable aspects of human perception and / or behaviour are removed, and therefore allowing scrutiny of isolated functions and systems. It however remains unresolved whether models based on such simplified stimuli accurately represent the brain functioning when applied to realistic human social behaviour (Felsen and Dan, 2005). Social psychological phenomena are often impossible to fit into a fully controlled stimulus environment as they span multiple time scales (Hasson et al., 2008) and overlapping features (Lahnakoski et al., 2012a). Constructing a model that could explain a complex social process is prohibitive and alternative data driven approaches had to be developed.

Recent methodological developments in signal analysis and experimental designs have however enabled researchers to adopt highly naturalistic paradigms for brain imaging experiments. For example, data-driven intersubject similarity measures allow exploring the neural circuitry underlying human behavior by inspecting when and where is the neural activity similar across multiple subjects (Hasson et al., 2004; Jääskeläinen et al., 2008; Kauppi et al., 2010; Glerean et al., 2012). While controlled stimulation allows straightforward modeling of brain responses, naturalistic stimuli are high-dimensional and thus difficult to capture by specific stimulation models (Hari et al., 2016). When we are engaged in interaction, we see our interlocutors, hear their voice, and sometimes have tactile contact, that is, multiple events overlap in multiple modalities at the same time. However, with this tradeoff, naturalistic stimuli allow characterising neural response to such number of categories that would otherwise require multiple days with multiple experimental designs to collect (Huth et al., 2012; Lahnakoski et al., 2012a). For example, this type of studies have revealed that brains of speakers and listeners are spatially selectively synchronized when they successfully understand each other (Stephens et al., 2010), or when individuals share perspective on perceived behavior (Lahnakoski et al., 2012a).

The studies included in this thesis adopt the naturalistic stimulation paradigm to various extents to reveal the brain mechanisms subserving speech, emotional processing and action understanding during interaction in realistic environment. Naturalistic paradigm provides a powerful way for studying social and emotional processes, since these are inherently multimodal and they span long and variable time courses, thus they are hard to reduce to highly controlled stimuli. Actually, some aspects of brain functioning addressed in studies in this thesis are possible to study only in naturalistic setting. For example, contextual understanding of connected speech requires naturalistic narratives to assess how the comprehension is supported by the brain during actual conversation. Moreover, previous research shows that prolonged naturalistic stimulation enhances functional connectivity measures (Nummenmaa et al., 2014a). For similar reasons, to address neural synchronization during emotional interaction, rich and dynamic emotional content is required.

1.3 The role of shared mental states in social communication

Sharing knowledge, feelings and motor codes is fundamental to humans: observing emotions and actions of others has direct consequences for survival and enhances group cohesion. When we observe other people experiencing fear, emotional contagion ensures that we engage in the corresponding survival behaviour too. Therefore rapid inference of other people's emotional states is a crucial mechanism promoting survival (de Gelder, 2006). Strong feelings of arousal elicited by emotional videos synchronizes viewers' somatosensory cortex and attention networks, suggesting that highly stimulating experiences allow us to simulate bodily state of observed individual and enhance our joint attention towards salient features of environment (Nummenmaa et al., 2012). Joint attention guided by observing other individual allowed our ancestors to survive and possessing similar action knowledge allowed achieving goals as a group, therefore enhancing human abilities.

When we observe actions of others, we may automatically simulate them in our brains to predict consequences, and infer goals and intentions by putting ourselves in the shoes of other (Rizzolatti and Sinigaglia, 2010). Together with emotional information and sharing the perspective of individual, this combination of action and emotion processes enables one to efficiently interact and predict behaviour of others. Revealing neural coupling associated with social interaction thus may reflect an automatic process of finding the closest matching feeling or action program that would allow inference about mind state of other individual.

1.4 Brain basis of action understanding

Understanding others' actions is crucial for social interaction. Without being able to understand our peers' goals and intentions, we cannot infer whether a gesture is friendly or offensive. A fronto-parietal action–observation network (AON) has been proposed to support understanding others' actions and goals (Kilner, 2011). This network is activated both during action execution and observation, suggesting a tight link between perception and action in the human brain. Studies with monkeys and humans have shown that this link may be subserved by special kind of sensory-motor mirror neurons. It has been proposed that while viewing others' actions, the observer automatically mimics or “mirrors” some aspects of motor activity of the actor (Gallese et al., 1996; Hari et al., 1998; Rizzolatti and Craighero, 2004; Gazzola and Keysers, 2009; Rizzolatti and Sinigaglia, 2010). This shared sensorimotor information may subsequently enable the observer to simulate motor actions and sensations of another individual, possibly also supporting understanding of the other person's actions or action goals (Rizzolatti and Craighero, 2004; Hari and Kujala, 2009).

Multiple studies using functional magnetic resonance imaging (fMRI) have found overlapping neural activation for action execution and observation in brain regions homologous to those where mirror neurons were found in monkey studies (Kilner et al., 2009; Gazzola & Keysers, 2009; for review see Heyes, 2010; Molenberghs et al., 2012). Furthermore, pattern classification studies have found overlapping neural signatures in frontal and parietal cortices of individual subjects that encode both action execution and observation (Dinstein et al., 2008; Etzel et al., 2008; Oosterhof et al., 2010). However, it remains unresolved, whether these overlapping neural signatures are generalizable between individuals and whether they support action understanding. For example, direct matching hypothesis implies that action understanding is supported by simulating observed action in one's own motor cortex (Rizzolatti and Sinigaglia, 2010), suggesting that neural signatures for action execution and observation may be shared in the brains of interacting individuals. Several studies in other modalities suggest that such sharing mechanism is plausible. For example, brain responses during emotional experience in one subject's brain are predictive of activation in similar network in another perceiving subject perceiving the corresponding emotional expressions (Anders et al., 2011). Another study showed that somatosensory activation while being touched allowed accurate classification the type of observed touch (Keysers et al., 2004). Mirror neurons may be related to sensorimotor experience, which is primarily coming from interaction with others. This way, the mirroring systems could be a product, as well as a process, of social interaction (Heyes, 2010). While mirroring systems concern primary sensory-motor neurons, similar principle may work also in other modalities (Nishitani et al., 2005; Hari and Kujala, 2009).

1.5 Brain basis of emotional communication

Emotions are fundamental to human behaviour as they govern our actions in survival-salient encounters. Emotions are also social phenomena, and they are often communicated to others using facial expressions, postures, as well as semantics and prosody of speech. We also easily catch each other’s emotions: we cannot resist smiling when hearing newlyweds recalling how they fell in love with each other; similarly we often fail to hold back tears when hearing our friend telling us about the recent loss of a family member. When we observe other people experiencing fear, their faces and body postures immediately inform us about adequate adaptive behaviour. Therefore rapid recognizing of and responding to other people's emotional states is a crucial mechanism of survival (de Gelder, 2006). Indeed, high arousal during watching emotional videos synchronizes individuals' somatosensory cortex and attention networks, suggesting that highly stimulating experiences enhance our joint attention towards salient features of environment (Nummenmaa et al., 2012).

Catching others’ emotional states – coined emotional contagion – may be associated with automatic ‘mirroring’ of emotional expressions, behaviour and physiology, i.e. interacting individuals synchronize with each other in behavioural, psychological, physiological and even neural domain (Gallese, 2003; Lakin et al., 2003; Konvalinka et al., 2011). Such synchronization may enhance feelings of rapport and connectedness (Miles et al., 2009) and promote social bonding (van Baaren et al., 2004; Hove and Risen, 2009; Wiltermuth and Heath, 2009). Several studies have revealed neural activity in overlapping brain regions during observation and experience of various emotional states, including pain (Jackson et al., 2005; Singer et al., 2004), pleasure (Jabbi et al., 2007) and disgust (Wicker et al., 2003). These findings bear strong conceptual resemblance to those stemming from motor action mirroring studies, which shown coupling between action execution and observation (Rizzolatti and Sinigaglia, 2010). While ‘mirroring’ itself is primarily a motor phenomenon, emotional contagion is more somatic and the classical areas reported in mirroring studies are typically not observed in the emotion perception / contagion studies. The mapping between neural and emotional states across individuals may provide a shared framework, allowing individuals to infer feelings of others, and mentally synchronize with them (Hatfield et al., 1994; Nummenmaa et al., 2012). Emotional brain responses also become synchronized across the members of a group exposed to similar emotional events in movies and narratives (Nummenmaa et al., 2012; Nummenmaa et al., 2014a).

Such emotion-driven neural synchronization might be a candidate mechanism for explaining emotional contagion. Yet it remains unresolved whether similar synchronization actually occurs between interacting individuals transmitting and decoding each other’s emotional states. Previous studies involving verbal (Stephens et al., 2010) and non-verbal (Schippers et al., 2010; Anders et al., 2016) communication showed that successful communication is associated with increased neural synchronization across the communicating individuals. Revealing the brain regions where the interacting individuals synchronize during emotionally contagious events would also hint towards mechanisms that contribute to emotional contagion.

1.6 Brain basis of contextual speech comprehension

Speech is a fundamentally human way for communication. When we get engaged in an already ongoing conversation, knowing the context in advance is crucial. Contextual knowledge of a narrative facilitates its comprehension and the effect of context on speech understanding has been established in several behavioural studies that show significant increase in recall and comprehension of narrative when pictorial or textual context clue was provided (Dooling and Lachman, 1971; Bransford and Johnson, 1972; Swinney, 1979). Speech comprehension recruits brain networks involved in auditory perception, attention, memory, phonological, syntactic and semantic processing. When we listen to a narrative, our mental lexicon is recruited, and word meanings are retrieved, selected and integrated into larger syntactic structures (unification), and attention is recruited to control for errors (MUC model; Hagoort, 2005). As new information becomes available, it is integrated with existing knowledge as early as possible (Wlotko and Federmeier, 2012), but as spoken discourse takes time to unfold, certain contextual information may not be immediately available, unless one already knows the context in advance. When we join a conversation without knowing the topic, it takes a significant effort to understand the meaning of sentences, even though speech is perfectly intelligible. However, when the contextual information is available, the sentences fall in place as a coherent narrative.

Human language processing network encompasses multiple regions, however Broca's area in the left inferior frontal gyrus, as well as Wernicke’s area encompassed by left inferior parietal cortex (IPC) together with left middle

(MTG) and superior temporal gyri (STG), are the key linguistic components (Binder et al., 2009). Multiple studies have shown that Broca's area is involved in phonological, syntactic and semantic functions (for review see Bookheimer, 2002). Wernicke′s area is involved in both semantic access and integration during discourse processing (Jung-Beeman, 2005; Binder et al., 2009). Both Broca's and Wernicke's area activity is implied in contextual understanding. For example, it was shown that anterior part of Broca's area is more active when processing sentences with high versus low ambiguity (Rodd et al., 2005), and lesions in Broca's area are associated with failure to use contextual information during word comprehension (Bedny et al., 2007). Activity in Wernicke's area on the other hand was reported when relevant context was present with the text (Martín-Loeches et al., 2008), or during tasks involving integration of prior experience, such as future planning (Binder et al., 1999), memorization of information (Hasson et al., 2007) and combinatorial processes (Humphries et al., 2007). It remains unresolved how the contextual information affects speech processing of naturalistic narrative. Revealing how the linguistic brain network is affected by lack or presence of contextually relevant information supports our efforts at revealing brain basis of social communication.

2. Goals

Brain basis of human social communication has been extensively investigated using highly controlled and simplified stimulation paradigms. However, findings from these studies may not necessarily translate to “real world” where individuals face multiple complex and overlapping social signals. Here we studied the brain basis of human social interaction in realistic settings, involving simulated (see methods for details) two-person social interactions. The overall goal of these studies was to test the idea that similarity of neural activity, shared prior knowledge, and shared neural encoding of actions between interacting individuals support social communication. The overall framework involves quantifying the similarity of two persons’ mental states by assessing the inter-subject similarity of their brain activity during real-world social perception or social communication. Simulated two-person interactions were used for studying the neural dynamics of information exchange between individuals during social communication.

Study I assessed whether mental simulation of others’ action synchronizes brains across observers viewing natural motor action sequences. It is known that simulation of mental and bodily states enhances understanding of others and helps to view the world in a similar fashion (Hari and Kujala, 2009; Nummenmaa et al., 2012). We expected that sharing a similar psychological perspective towards seen actions would lead to more similar experiences across observers, which would be reflected in increased synchronization of neural activation in action-observation network of observers.

Study II tested whether observing and executing hand actions elicits similar, actions-specific motor codes across individuals. Mirroring systems support both action execution and observation (Rizzolatti and Sinigaglia, 2010), yet it remains unresolved whether these systems contain action-specific neural codes that allow direct matching between actor’s and observer’s actions. We hypothesized that action-related neural signatures would be shared between individuals executing and observing the actions. We tested this hypothesis by developing novel “hyperclassification” approach, where we trained a pattern classifier to recognize executed actions from neural activity of a subject executing the actions, and then validated classifier’s performance on neural data collected from individuals observing the same actions. If such hyperclassification would be successful, it would confirm that neural signatures for executing and observing actions are similar across individuals.

Study III investigated whether similarity of emotional feelings between speaker and listener would result in increased neural coupling in brain’s emotion processing circuits. Previous studies show that viewing emotional events in movies or listening to emotional narratives elicits synchronized neural responses in the limbic system across the groups of subjects (Nummenmaa et al., 2012; Nummenmaa et al., 2014a) yet these studies have not actually measured transfer of emotional information from one brain to another. Such transfer of affective information between brains of interacting individuals might allow listeners to empathize with speaker. We hypothesized that stronger emotional feelings, indicated by subjective emotional valence and arousal, would enhance speaker-listener neural coupling in limbic and somatosensory circuits, as well as speech-related brain regions. We then tested this hypothesis in pseudo-hyperscanning approach, where we collected the data from speakers and listeners, and assessed how the intersubject similarity of their brain activity is modulated by felt emotions.

Study IV tested which functional brain networks mediate the use of prior knowledge during complex speech comprehension. Previous research has shown that context is crucial for speech comprehension (Bransford and Johnson, 1972). Comprehension of naturalistic narrative involves multiple components including speech processing nodes such as Broca’s area and Wernicke’s area, as well as error monitoring in anterior cingulate cortex (Hagoort, 2005; Binder et al., 2009). We expected knowing the context of the spoken narrative in advance would enhance semantic processing, promote comprehension and recall, and that this process will be accompanied with increase in functional connectivity of brain regions involved in semantic selection, integration and error monitoring.

3. Methods

3.1 Magnetic resonance imaging

Magnetic resonance imaging (MRI) was used to collect the neural data in all studies presented in this thesis. MRI is currently the dominant tool for non-invasive brain imaging in humans (see Huettel et al., 2004 for review). The most abundant element in human body is hydrogen, and it is used as main target for human MRI. Therefore presence of water molecules is a required property of the imaged tissue. In a nutshell, MRI measures the interaction of a tissue with an electromagnetic field. The signal recorded by MRI is related to spin, a property of elementary particles. Unpaired spins can have a magnetic moment, which aligns with external magnetic field. When no strong external magnetic field is applied, spins are oriented randomly. In MRI imaging, strong, constant and homogenous magnetic field (B0, currently typically between 1.5 – 7T) is introduced in the MRI scanner bore, which aligns spins in directions either parallel or anti-parallel to the magnetic field. A slightly exceeding number of spins will align with the field, resulting in net magnetization with external field. Stronger fields cause more spins to be aligned with external field, resulting in stronger signal.

While in this strong field, protons (hydrogen nuclei) precess around the direction of the external field with an angular frequency, also called Larmor frequency, which depends on the strength of external magnetic field and gyromagnetic ratio of atom. If an electromagnetic radio frequency (RF) pulse at Larmor frequency is applied, protons can absorb that energy. This RF pulse “flips” net magnetization by a certain angle (flip angle) relative to the main magnetic field. This process is called excitation. When the RF pulse ends, the absorbed RF energy will be emitted at the Larmor frequency, as the protons recover to the equilibrium state. This process is called relaxation and it happens at different rates in the longitudinal (spin-lattice relaxation) and transverse (spin-spin relaxation) directions in relation to the B0 field. The longitudinal recovery rate towards equilibrium is characterized by tissue-specific time constant T1. Because this rate differs across tissues, T1 is the source of nuclear magnetic resonance signal and can be used to differentiate between tissue types such as grey and white matter in the acquired brain images. The transverse recovery rate is characterized by tissue-specific time constant T2, which generally proceeds more rapidly than T1 recovery, and is useful for detecting white matter lesions.

To enable encoding spatial information from MRI, smaller linearly varying magnetic fields, called gradient fields, are applied. There are three sets of gradients, each creating a magnetic field in X, Y or Z direction. These fields cause the magnetic moments of spins to precess around b0 field with different angular frequencies, depending on location of tissue within the field. Only protons that spin with the same frequency as the RF pulse will respond to that RF pulse. This allows designing RF-pulses in such a way that energy is deposited into specific locations and emitted from these locations at different RFs, allowing slice encoding.

3.2 Functional magnetic resonance imaging with BOLD contrast

The most common technique to measure brain function with MR imaging is the blood oxygenation level dependent (BOLD) contrast, where the MR images are made sensitive to the state of oxygenation of hemoglobin (Ogawa et al., 1990). The variation of the BOLD signal reflects the variations of the functional activity of neuronal populations (Logothetis et al., 2001). Hence, BOLD contrast can be used to map neuronal activity during various cognitive, motor and affective tasks. BOLD signal is based on the magnetic properties of hemoglobin. Hemoglobin is a molecule that is contained in blood and transports oxygen from lungs to the rest of the body. Oxygenated hemoglobin is diamagnetic thus it contains no unpaired spins that could have magnetic moment, resulting in null spin. Deoxygenated hemoglobin, on the contrary, is paramagnetic, having a non-zero magnetic moment. When MRI signal is measured from the brain, certain areas show higher MRI signal, indicating more Hb / dHb ratio. Neuronal activity requires oxygen, resulting in increased supply of oxygenated blood to the active brain regions. Consequently, BOLD can be used as an indirect measure of neuronal activity even though the signal comes from metabolic activity in the brain. While BOLD measures blood flow and blood volume, the dynamics of both of these phenomena are significantly slower than neuronal activity. Functional MR imaging requires multiple parameters to be taken into consideration, but perhaps the repetition time (TR) of the RF pulses that defines temporal resolution - time period between two successive excitations, and TE, which defines the time period between excitation and data acquisition, are the most important for data collection. Shorter TR provides higher sampling rates, allowing achieving higher temporal precision of collected data. The temporal precision of fMRI data has direct consequences for the statistical modeling of neural response, as higher precision enables more accurate models to be designed.

3.3 MR Data acquisition

MRI data for all studies were collected at the Advanced Magnetic Imaging (AMI) centre of Aalto University. Data for studies I and II were collected with General Electric Signa 3-Tesla MRI scanner. Data for studies III and IV were collected with Siemens Magnetom Skyra 3-Tesla MRI scanner. All data were collected with EPI pulse sequence sensitive to BOLD contrast with 64 x 64 matrix, slice thickness of 3-4 mm, TR ranging from 1700 to 2000 ms and TE 24 to 30 ms. High-resolution anatomical images with isotropic 1 x 1 x 1 mm^3 voxel size were collected using a T1-weighted MP-RAGE sequence.

3.4 Preprocessing of fMRI data

Preprocessing for all studies followed similar pipeline, with minor modifications related to smoothing kernels and high-pass filtering described in the original studies. Data were preprocessed using MATLAB (The MathWorks, Inc., Natick, Massachusetts, USA) and FSL (FMRIB's Software Library, www.fmrib.ox.ac.uk/fsl). After slice timing correction, the functional images were realigned to the middle scan by rigid-body transformations with MCFLIRT to correct for subject motion. Next, non-brain matter from functional and anatomical images was removed using Brain Extraction Tool (BET; Smith, 2002). Functional images were registered to the MNI152 standard-space template (Montreal Neurological Institute) with 2-mm resolution. The transformation parameters were acquired by first calculating transformations from structural MR image to standard space and from functional to structural space. Next, these transformation parameters were sequentially used to co-register functional datasets to the standard space. Both registration steps were performed using FLIRT (Jenkinson et al. 2002). Motion artefacts were cleaned from the functional data using 24 motion-related regressors (Power et al. 2014), signal from white matter, ventricles and cerebro-spinal fluid were also cleaned from the data as implemented in BraMiLa pipeline (https://git.becs.aalto.fi/bml/bramila). Finally, in studies I, II and IV additional spatial smoothing step with a Gaussian kernel of FWHM 8-10 mm was also applied. In study III spatial smoothing was not applied since pattern classification accuracy may suffer from losing information encoded in finer-grained patterns.

3.5 Modeling the brain response

The most ubiquitous analytic method used in fMRI data analysis is the univariate general linear model (GLM). In this method, stimulus model regressor is convolved with the canonical haemodynamic response function (HRF) and regressed against voxel-wise BOLD data. BOLD is an indirect measure of brain activity, since it measures metabolic changes associated with blood flow rather than actual neuronal activity. The relationship between BOLD and neuromodulatory processes on the neuronal population level is approximated by HRF, which is represented by a linear combination of two gamma functions and allows estimation of the BOLD response to stimulus events.

The standard approach to model task- and stimulus-related responses is a two-stage random effects model. The first stage stimulation models are fitted to individual subjects data, thus relating stimulus regressor time series to BOLD activation. The second stage computes the group-level statistics, by relating combined individual activation estimates to a group parameter, e.g. mean activation level. Such two-stage approach allows inferences on population level. GLM analyses presented here were implemented in either SPM12 (www.fil.ion.ucl.ac.uk/spm) or FSL (study IV).

GLM analysis is usually done independently for each voxel. A typical brain image contains more than 200000 voxels, therefore when a statistical test is performed for each of them, multiple comparisons need to be accounted for. A rather conservative Bonferroni correction is often used when number of comparisons is small, by dividing the p-value threshold by the number of comparisons. With fMRI data such test may be too conservative, so alternatives like false-discovery rate correction were proposed, which are designed to control the expected proportion of false positives (BH-FDR; Benjamini and Hochberg, 1995). Another approach is to simulate the null hypothesis by shuffling the data, which is also called permutation testing, and derive significance threshold from this simulated null distribution (Nichols and Holmes, 2002). Both of these approaches were used in all of the studies presented in this thesis.

3.6 Intersubject correlation

In contrast to GLM, inter-subject similarity metrics allow data-driven analysis of the brain activity patterns: they allow inference about brain regions involved in a task even when stimulation model is not specified or when it is unknown. This is achieved by assessing the similarity of regional neural activation across multiple individuals, revealing time-locked activity, for example when viewing movies or listening to narratives (Hasson et al., 2004; Wilson et al., 2008). As social interaction typically occurs in complex context and at multiple time scales, it is often impossible to represent it with specific stimulation models, hence ISC analysis is especially helpful in such cases. Mapping the brain areas where, for example, during emotional episodes the neural activity synchronizes across subjects, allows revealing the areas supporting some aspect of behavior that these subjects are involved in.

In ISC analysis, correlation between the voxelwise time series is computed for every pair of individuals, separately for each voxel. Voxelwise correlations are subsequently averaged to produce group-level ISC maps. These maps show the regional reliability of the brain responses during particular stimulation. ISC also can be computed over sliding windows, providing time series of intersubject similarity in brain activity. Since correlation requires more than just one time point to be computed, windowed approach reduces the temporal resolution of data in comparison with BOLD GLM, as each timepoint in the new ISC time series contains correlation computed over multiple timepoints. In these studies we used ISC analysis as implemented in the ISCToolbox (Kauppi et al., 2008), which uses Pearson correlation coefficient with non-parametric tests for statistical significance. ISC analysis was used in the study II to quantify the similarity of the brain activation before and after the hyperalignment (see 3.12. for details) and in the study IV to quantify the similarity of brain activity with vs without contextual queues.

3.7 Intersubject phase synchrony

ISC computed over sliding windows allows addressing dynamic changes in intersubject similarity of neural activity and reveal the brain regions where individual brains are activated more or less similarly depending on time-specific stimulation parameters. However, the temporal accuracy of ISC suffers from computing the ISC within a temporal sliding window to warrant sufficient SNR. ISC approach has thus been developed further into inter-subject phase synchrony (ISPS), which allows increasing temporal accuracy up to 1 TR (Glerean et al., 2012). In these studies phase synchrony analysis was implemented using FUNPSY toolbox (Glerean et al., 2012). It uses analytic signal which is acquired by rearranging the frequency content of the original time series using Hilbert transform. This analytic signal is converted into a product of amplitude and phase signals using Euler's equation. The Hilbert transform requires signal to be narrow-band, hence band-pass filtering with the frequency range of 0.04 – 0.07 Hz is applied. This band is least affected by physiological noise and contains majority of useful signal in BOLD (Glerean et al., 2012). After Hilbert transform, phase synchrony time series is computed between every pair of experimental subjects. The resulting time series provides a measure of dynamic (i.e. moment-to-moment) inter-subject similarity that can be modeled like any other signal with, for example, task regressor (Figure 2). ISPS method was used in study I to quantify the similarity of the brain activation across the viewers of the videos, and in study III to quantify the similarity of brain activation between speakers and listeners.

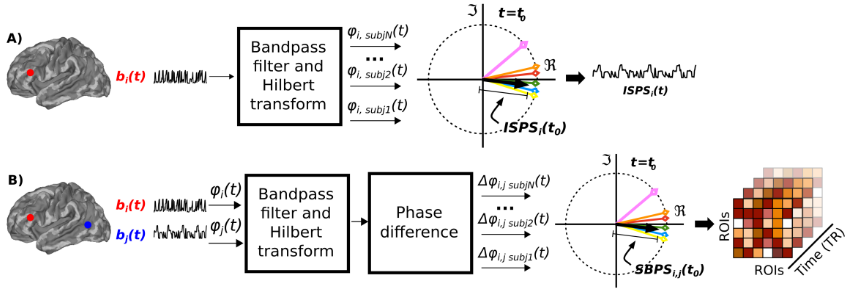

Figure 2. (A) Blueprints of ISPS analysis pipeline and (B) and instantaneous SBPS analysis. t: Time; ϕ: phase; PS: phase synchrony; i,j: seed regions; b: BOLD signal. Adapted from Glerean et al., 2012.

3.8 Functional connectivity analyses

While the GLM reveals how each brain area separately responds to certain stimulation, functional connectivity analysis allows quantifying the task-driven changes in neural interactions between brain areas. Such functional connectivity analysis is motivated by studies demonstrating that almost every cognitive function is supported by interaction of multiple brain structures involved in distinct processes (Sporns et al., 2004; Bullmore and Sporns, 2009).

In the study IV, we analyzed task-dependent functional connectivity using psycho-physiological interactions (PPIs; Friston et al., 1997; see also more recent review in O'Reilly et al., 2012). PPI identifies brain regions whose activity depends on the interaction between psychological factors (the stimulation or task) and physiological factors (the neural activity time-series of a ROI). PPI assumes that if two areas are interacting, the level of activity in these areas will correlate over time. PPI analysis begins by defining (typically a single) “seed” ROI. Next, activity time course is extracted from this region by using the first eigenvariate from all raw voxel time series in ROI. The psycho-physiological interaction regressor (a PPI effect) is constructed as an element-by-element product of the mean-centered task or stimulation time course and the ROI time course. Finally, this PPI effect time series is used as a regressor in a GLM analysis to reveal the voxels where a task-specific increase in the relationship between brain regions (a PPI effect) is associated with a task-specific increase in the correlation, or exchange of information between the regions. PPI as a method has limitations: it does not make inferences about the causality, or direction of information flow between brain regions. Instead, PPI indicates task-specific increases in relationship between a seed region and the rest of the brain, and makes no implication whether the seed is the driver rather than the driven area (O'Reilly et al., 2012).

In study I we also used phase synchronization to estimate functional connectivity using seed-based phase synchronization (SBPS). In SBPS, first the difference between phase signals of two ROIs is calculated for every subject, and then the phase synchrony across all subjects is computed to represent the similarity or consistency between a pair of ROIs across the group (see Glerean et al., 2012 for details). SBPS preserves maximal temporal resolution of the data, as the phase synchronization is computed for each time point, rendering it especially useful for inferring task-dependent functional connectivity changes.

3.9 Representational similarity of emotional and neural time series

Revealing that similarity of neural states is paralleled by similarity of subjective mental states would provide additional evidence that perceiving the world in similar manner really is associated with more similar neural functioning. Such neural and mental synchronization could support social interaction by providing interacting individuals with shared emotional and somatomotor framework. We investigated such representational similarity (RS; Kriegeskorte et al., 2008) between the synchronization of emotional states and neural synchronization across speaker-listener pairs in the similar methodological approach as done by Nummenmaa et al. (2014). In Study III we used ISPS as the similarity metric for neural activity, and ISPS of continuous ratings of valence and arousal as the similarity metric for emotions. Two-stage approach was implemented in the analysis. In the first level analyses we used Pearson correlation coefficient to estimate voxel-wise similarity between time series of neural and emotional synchronization for each speaker-listener pair. The voxel intensities on resulting maps reflect the degree to which brain-to-brain similarity between speaker and listener was associated with similarity of their emotional feelings. Subsequently, mass-univariate t-tests were used in the second-level analyses to estimate similarity at the population level.

3.10 Two-person ‘pseudo-hyperscanning’

We wanted to study the human brains during the actual social communication process, however, MR imaging of two individuals at the same time is a challenging and often technically impossible task. The process of scanning multiple subjects at the same time is called hyperscanning. While mostly done with EEG (for review see Babiloni and Astolfi, 2014), a handful of fMRI hyperscanning studies were also performed in various contexts, e.g. interaction games (Montague et al., 2002), flow of affective information during facial communication (Anders et al., 2011), gestural communication (Schippers et al., 2010) and verbal communication (Stephens et al., 2010).To acquire the neural activity data matched in time between the subjects, we adopted “pseudo-hyperscanning” paradigm, where we scanned subjects as pairs to address how the brains of interacting individuals subserve mutual understanding and sharing of the emotions. This involved scanning the subjects transmitting and receiving information sequentially: during the first session one participant’s brain activity is recorded while she, for example, performed hand actions (study II) or narrated short autobiographical events (study III). Video and audio were recorded, and subsequently presented to the next participant in an independent MR scan. This way, fMRI data of the individual transmitting the information is matched in time with brain data of the individual receiving the information, and only one fMRI scanner is required for the data acquisition.

3.11 Multivariate pattern classification

Pattern classification methods are generally used for discovering the regularities in multivariate data that enhance the predictive power of models, compared to univariate models. In some experimental settings, the differences in brain responses in single voxel are often not large enough between experimental conditions to detect different effects for those experimental conditions within a region (Kragel et al., 2012). The pioneering work by Haxby et al., (2001) demonstrated that a multivariate classifier can predict, after learning the pattern of brain activity during object observation, which object category the participant is currently viewing. Inspecting multiple voxel time series jointly allows pattern classifiers to substantially increase the amount of information that can be derived from brain activity, increasing accuracy in classification between brain states (Mitchell et al., 2004; Haynes and Rees, 2006; Norman et al., 2006; Pereira et al., 2009), and a wide range of pattern classification algorithms has been introduced to fMRI data analysis (Haynes, 2015).

Pattern classifiers typically are models that are trained to discriminate between the spatial activity patterns corresponding to a range of experimental conditions. The trained classifier is subsequently validated or “tested” against new data not used in the training to avoid overfitting. For the classifiers that we used in study II, we evaluated the performance of the classification model in leave-one-run-out cross-validation framework, where one run was left out for testing, and all remaining runs were used to train the classifier, and the process was repeated iteratively for each run and separately for each subject.

There are multiple different frameworks or pattern classification. Here we used logistic regression based approach, where the model predicts log-odds of dichotomous outcome variable as a linear combination of predictors. In multi-class situations, where the predicted variable has more than two possible outcomes, usually one outcome *versus* all classification is done iteratively. Specific implementation used in this work was Bayesian logistic regression with a sparsity promoting Laplace prior (Williams, 1995; van Gerven et al., 2010). In this model, each individual voxel weight was given a univariate Laplace prior distribution with a scale hyperparameter, which was optimized over multiple candidate values by maximizing the average accuracy over the subjects in leave-one-subject-out cross-validation (Lamnisos et al., 2012). Such model attempts to avoid overfitting, and results in a smaller set of voxels contributing to the predicted label. When testing the classifier performance, the data of a single subject were left out from the optimization. The multivariate posterior distribution was approximated using the expectation propagation algorithm (van Gerven et al., 2010) implemented in the FieldTrip toolbox (Oostenveld et al., 2001). The classification performance was tested by collecting the class probabilities for each pattern in the testing set using the binary classifiers, and assigning the class with the maximum probability to each pattern.

Statistical significance of classification accuracy was tested by comparing mean (across subjects) accuracy against theoretical chance level, here defined as 100% divided by the number of class labels (such approach is valid only when the number of examples per class is balanced). Since empirical chance level accuracy can differ from theoretical chance level (Combrisson and Jerbi, 2015), we verified it by constructing the null distribution by randomly shuffling class labels to inspect accuracy produced by random classifier. As the classification accuracies were approximately normally distributed, the confidence intervals for their means were obtained from Student's t-distribution.

3.12 Functional realignment with Bayesian canonical correlation analysis

Individuals differ in the functional and structural organization of the cerebral cortex; therefore it is not feasible to assume that activity in the anatomically identical region across two brains would necessarily reflect an identical underlying perceptual or cognitive process. Recent work has indeed shown that, for example, individual differences in functional and anatomical organization of the ventral visual cortex can be accommodated with a high-dimensional common-space (“hyperalignment”) model (Haxby et al., 2011; Yamada et al., 2015) that improves group-level estimates of hemodynamic responses and significantly improves the accuracy of pattern classification results in comparison with those acquired with anatomical alignment and spatial smoothing.

We adopted a similar functional realignment approach, where we acquired a common functional space between two independent modalities: motor action and action observation. This approach aimed at improving the classification of seen actions on the basis of executed actions. Multiple methods can be used to find matching between two datasets, but intuition behind these methods is in general the same – we assume that both of the datasets contain some dataset-specific information, and some shared information. These datasets can be viewed also as “rotations”, or transformations of some “unobserved” original dataset. This way, if the transformations are acquired, one dataset can be transformed into another, and such transformation can be validated by, for example, classification task.

To account for differences in functional localization of action execution and observation across individuals in study II, we implemented this additional functional realignment step in our preprocessing pipeline. We used Bayesian canonical correlation analysis (BCCA; Klami et al., 2013) to perform the realignment step prior to hyperclassification. BCCA was implemented using R CCAGFA package (Virtanen et al., 2012; Klami et al., 2013). The BCCA model separates the correlation patterns in the simultaneous brain-activity spaces of the individual who executes an action and the individual who observes it into three types of components, also called views: actor-specific, observer-specific, and shared. The shared components provide a low-rank linear mapping for the realignment of the brain-activity spaces. The view-specific variation has to be modeled to avoid misinterpretation of strong view-specific components as shared effects (Klami et al., 2013). For each actor–observer pair, the total number of components was optimized together with scale hyperparameter for classifier over multiple candidate values. The model automatically assigns the components to the three types via a group-wise sparse automatic relevance determination prior (Klami et al., 2013). BCCA was done for each ROI in the cross-validation framework, where the mapping was estimated using four runs from both the actor and the observer, and, in the left-out runs, the shared activation was mapped into actor's space to produce representation of observer's data and used for testing the classifier. Classifier was trained on the actor's data from the four runs and tested on functionally realigned observer's runs.

3.13 Validation metrics

In hyperclassification framework, functional realignment is used to map data of one individual to another individual. Functional realignment may work and show above chance-level classification accuracy even when there is no real shared signal between two datasets. Simulations show that random noise filtered with BOLD spectra can be transformed by some functional realignment methods (like procrustean transform) in a strongly overfitted way. We used three validation approaches to ensure that realignment achieved with BCCA and the subsequent improvements of classifier performance do not reflect merely realignment of the noise present in the data:

1. Temporal misalignment: properly working BCCA mapping should lead to chance-level hyperclassification when BOLD time series of training and testing data are temporally misaligned. On the contrary, if hyperclassification accuracy stays above chance level for temporally misaligned data, the BCCA is realigning task-independent noise across the data sets.
2. Realigning and classifying surrogate data: we also trained and tested the classifier with BCCA-aligned random noise filtered with BOLD spectra that were acquired from actual data recorded during the experiment. Data of real subject were used in training the classifier, and surrogate data were used in testing. While surrogate data retain the characteristics of real BOLD signals, they lack the temporal structure of the actual experiment. In case the BCCA remapping would introduce a nonexistent temporal structure to the data, this approach would result in above-chance-level classification accuracy.
3. Realigning and testing classification in control ROI data: finally, if functional realignment would allow successful classification in a region unrelated to stimulus or task of interest, the model would not be robust against noise. Functional remapping between these regions should not give above-chance-level accuracy for hyperclassification. Consequently, ROIs for these regions were generated using the Jülich Histological Atlas in FSL (Eickhoff et al., 2007), and hyperalignment and classification were then attempted for this set of ROIs.

3.14 Visualization of functional realignment consequences

Visualization of components involved in functional realignment of two datasets is complicated and requires additional work and research. However, we used two approaches that allow to some extent to characterize how the functional realignment improved the data used for testing the classifier. We first calculated ISC between the brain signals of individuals, whose data was realigned, before and after realignment, assuming that successful realignment would increase ISC in brain regions where shared information between individuals increased. Because we allowed remapping of voxel activation to any place within the ROI, this step allowed us to quantify whether remapping would be specific to some regions or randomly distributed across the multinode ROI. In the latter case the realignment model would be theoretically meaningless as, correlation would increase and decrease randomly across the brain. Pearson correlation coefficient was used to calculate the intersubject correlation for each voxel for each actor–observer pair before and after the realignment. The resulting R-statistic maps were Fisher transformed and compared using t-test to show which regions became statistically significantly more similar after the realignment.

Second, to reveal brain regions where realignment would increase hyperclassification accuracy, we used a k-nearest-neighbour (kNN) classifier (Fix and

Hodges, 1951; Lahnakoski et al., 2014) based on ISC matrices of spherical searchlights, containing 19 voxels (6 mm^3) over three TRs, with k-values ranging from 1 to 120 with a step of 6. We used mean classification accuracy over all k-values to control for possible sensitivity of kNN classifiers to noise at low k-values (Mitchell et al., 2004). We calculated hyperclassification accuracy for spherical neighbourhood of each voxel before and after functional realignment and tested the difference using permutation-based t-test. Statistical threshold was set at $p < 0.05$, FDR-corrected (Benjamini and Hochberg, 1995). Resulting statistical maps show brain regions where searchlight classification accuracy increased after functional realignment. In principle, any classification algorithm could be used for this step, and our choice is guided just by the convenience of implementation.

3.15 Eye-tracking data

Eye-tracking data was recorded for studies I and IV with a SMI 60Hz Eye Track long-range eye tracking system (Sensomotoric Instruments GmbH, Germany). A five-point calibration and validation was performed prior to the experiment. In study IV, eye-tracking was used to collect pupil size data as a marker of cognitive load. Participant’s pupil size was measured as an index of attention and cognitive load. To get an absolute scale for pupil diameter, we used a reference “fake pupil”, a piece of paper with a black circle of known diameter painted on it. This fake pupil was placed in front of participants’ eye at the beginning of the experiment, and a conversion factor was acquired. This conversion factor was subsequently used to convert the pupil diameter from pixels to millimeters. In study I, the eye-tracking data was used to investigate the spatiotemporal intersubject synchronization of eye movements.

4. Summary of the original studies

4.1 Study 1: Mental action simulation synchronizes action-observation circuits across individuals.

4.1.1 Aims of the study

Study I investigated how active mental simulation (“empathizing”) of seen actions synchronizes action-observation network in the brain across multiple individuals during attending to natural stimuli. We used videos of boxing matches as stimuli, as they contain large clear limb motions and strong emotional feelings.

4.1.2 Materials and methods

Twenty right-handed healthy volunteers viewed short video clips depicting professional boxing matches during fMRI and concurrent eye movement recording. Before each trial, participants were instructed to either view the video passively, or to mentally simulate a pre-specified boxer (Figure 3). The clips depicted typical highlights of the matches, in which one boxer was clearly winning and causing pain to the losing boxer with his punches. All movies were presented with sound. Participants watched the films in a fixed, pseudorandom order; two different counterbalanced orders of the instruction screens were used to control for possible order effects.

ISPS analysis was used to analyze synchronization of brain activation across individuals and compare active simulation conditions to passive observation. The experimental-condition regressors were convolved with gamma function ($\theta = 1$, $k = 6$) and used to predict voxelwise ISPS time courses in the general linear model (GLM). In addition, we analyzed functional connectivity within the AON. To this end, we estimated dynamic functional connectivity of regional time courses using instantaneous seed-based phase synchrony (SBPS; Glerean et al., 2012). Regions of interest (ROIs) were selected from meta-analyses of the brain basis of action observation (Paus, 1996; Caspers et al., 2010) and AAL atlas (Tzourio-Mazoyer et al., 2002). Spheres of 6 mm diameter were drawn around these ROIs. SBPS was used as a group-level time-varying connectivity measure between each pair of regions. The gamma-convolved experimental-condition regressors were used to predict each connection's time series in the GLM to assess the effects of simulation on AON connectivity. To test the statistical significance of the ISPS maps and SBPS connections, we performed a fully nonparametric voxelwise permutation test for the r statistic (Wilson et al., 2008; Kauppi et al., 2010).

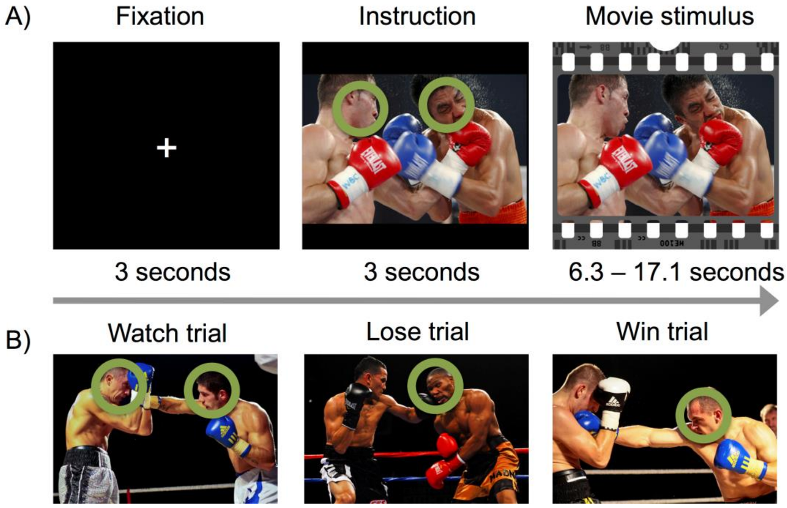

Figure 3. Overview of the trial structure and illustrations of the stimuli.

Because calculation of all possible time-shift combinations would be computationally prohibitive, we approximated the full permutation distribution with A = 1,000,000 realizations. Sampling was randomized over every brain voxel and shifting point without any restrictions.

To test whether active simulation would enhance intersubject synchronization of functional brain networks, the core intrinsic networks were delineated using seed-voxel correlation. Seeds were anatomical foci routinely used in seed-voxel correlation analysis (visual, sensorimotor, auditory, default-mode, dorsal attention, and executive control networks). Spherical ROIs with 6 mm radius were generated around these coordinates, and mean time-series were extracted for each ROI and participant. Means of each participant's regionwise time series were subsequently used to identify individual correlation maps for each of the six networks by correlating seed region time series with time series of all other voxels in brain. To analyze whether the regional synchronization in each network would be modulated by the simulation task, a spatially averaged ISPS time series was extracted for each statistically thresholded network ROI. These time series were correlated with the experimental time series of explicit simulation versus passive viewing.

In addition, a two-stage random-effects model was implemented to estimate regional effects of passive viewing and simulation conditions. At the first level, GLM with boxcar regressors was used to assess task-dependent BOLD activation for each participant. Model included three experimental conditions (watch, lose, win) and effects of no interest (motion realignment parameters). The second-level analysis was used to generate group-level statistical parametric maps. Statistical threshold was set at $T > 3.0$ and $p < 0.05$, FDR corrected at cluster level.

Spatiotemporal intersubject synchronization of eye movements was measured by computing subjectwise heatmaps for each trial. Mean intersubject correlation index was computed for a sliding window (length 1 s, step size 100 ms), and average intersubject similarity scores were computed for the different experimental conditions (lose, win, watch). This synchronization time series was also used to predict cerebral ISPS to test whether synchronization of visual attention across subjects would be associated with enhanced intersubject synchrony of brain activation.

4.1.3 Results

Brain activity during passive observation was similar across subjects only in lower-level sensory areas and motion-sensitive temporal cortex, while during active simulation of other' mental state increased synchronization in parieto-temporal components of AON, somatosensory cortex and components of dorsal and ventral fronto-parietal attention networks (warm colors, Figure 4). We also analyzed the data with ISC to confirm that ISPS produces similar outcomes, and found that ISPS was more sensitive in the frontal areas of the brain (white outline, Figure 4). Eye movements were strongly synchronized across participants throughout the experiment. However, synchronization of eye movements was not associated with intersubject synchronization of brain activity in any region.

Synchronization in intrinsic networks during simulation contrasted with passive viewing, resulted in stronger mean ISPS in auditory, dorsal attention, sensorimotor, and visual networks, but not in default-mode or in executive control networks. Moreover, during simulation compared to passive viewing, SBPS analysis revealed increase in large-scale dynamic connectivity of left-hemispheric components of AON, suggesting that sharing others' action plans synchronizes individuals' own brain systems supporting sensation and motor planning (Figure 5).

Neither ISPS nor SBPS connectivity differed between simulating of losing versus winning boxers. However, regional effects estimated with GLM revealed stronger responses during simulating losing versus winning boxers in the right anterior insula, rolandic somatosensory cortex, temporoparietal junction, and bilateral fusiform gyri, whereas the opposite contrast revealed no significant clusters.

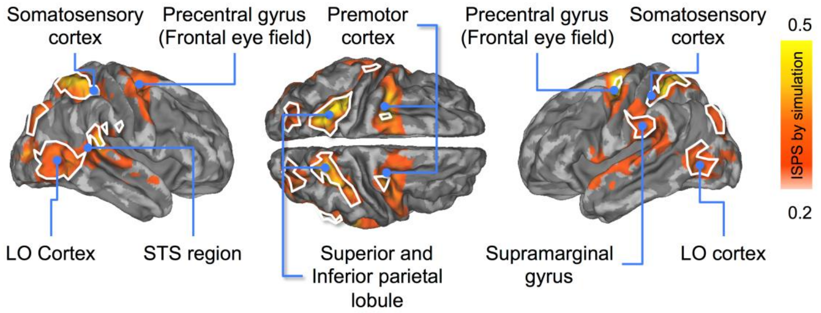

Figure 4. Brain regions showing statistically significantly stronger ISPS during simulation (averaged across simulate winner and simulate loser) than passive viewing (red to yellow). White borders show regions with overlapping ISPS and ISC. The data were thresholded at $p < 0.05$ (FDR corrected).

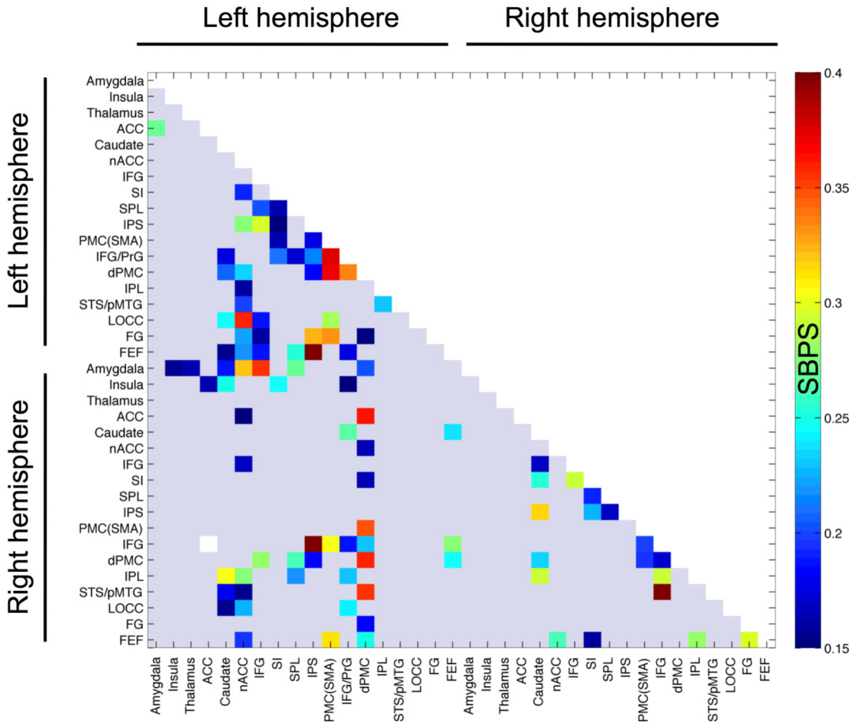

Figure 5. Connectivity matrix for brain regions showing stronger instantaneous SBPS during simulation than passive viewing. The data are thresholded at $p < 0.05$ (FDR corrected).

Finally, when compared against the passive viewing condition, both explicit simulation conditions (simulate loser and simulate winner) resulted in widespread activation in the emotion-related circuits (including thalamus, anterior insula, amygdala) in superior and posterior parietal cortices as well as in bilateral precentral gyri.

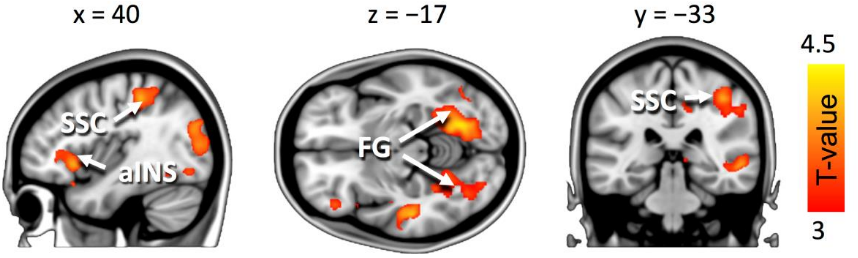

Figure 6. Brain regions showing stronger BOLD responses during simulation of a losing than a winning boxer. The data are thresholded at p< 0.5 (FDR corrected). Color bar denotes the T-Statistic range.

4.1.4 Conclusions

Our findings reveal that when individuals are engaged in simulation of another person's actions and feelings, the neural activity in their attentional and action-observation brain networks becomes synchronized. These findings suggest that active mental simulation of other's motor actions and emotions provides observers with shared somatomotor framework, possibly allowing one to map mental and bodily states into one's own sensorimotor system and support mutual understanding.

4.2 Study 2: Brain-to-brain hyperclassification reveals action-specific motor mapping of observed actions in humans.

4.2.1 Aims of the study

Here we tested whether action observation and execution share neural signatures in the same brain regions across different individuals. While it has been established that mirroring systems can subserve both action execution and observation, it remains unresolved whether brains of interacting individuals share action-specific neural codes. We hypothesized that action-specific neural signatures are shared between individuals and observing executing actions. To test this hypothesis, we trained a pattern classifier to recognize executed actions from neural activity of an "actor" subject, and then successfully validated its performance on neural data collected from independent "observer" subjects viewing the actions. Successful cross-subject, cross-modal classification would provide support for existence of shared, action specific neural signatures of actions in interacting individuals that might promote action understanding via actions-specific motor simulation.

4.2.2 Materials and methods

We adopted pseudo-hyper-scanning paradigm, where we asked two healthy right-handed volunteers ("Actors") to perform four types of hand actions, which were videotaped while the actors were scanned with fMRI. The actions included two object-directed actions (power grip of a soft spiky ball and precision grip of a plastic pen) and two non-object directed actions (soft slap on the table; and a pointing gesture). In the second stage of experiment, fifteen independent volunteers ("Observers") watched the videotaped actions (Figure 7). In a control experiment, one actor performed the hand actions with eyes closed, and five additional observers viewed the resulting videos. Both actor and observer subjects performed two functional localizer tasks: a motor squeeze and action observation localizer. These data were used to create individual localizer ROIs. For each individual, two ROIs were generated: main effect of action execution from action execution localizer, and action observation versus rest observation contrast from action observation localizer. In hyperclassfication analyses, intersection of subject-wise localizer ROIs was generated. We also generated a meta-analytic ROI consisting of regions systematically activated during action execution and/or observation in previous fMRI studies using Neurosynth.org database.

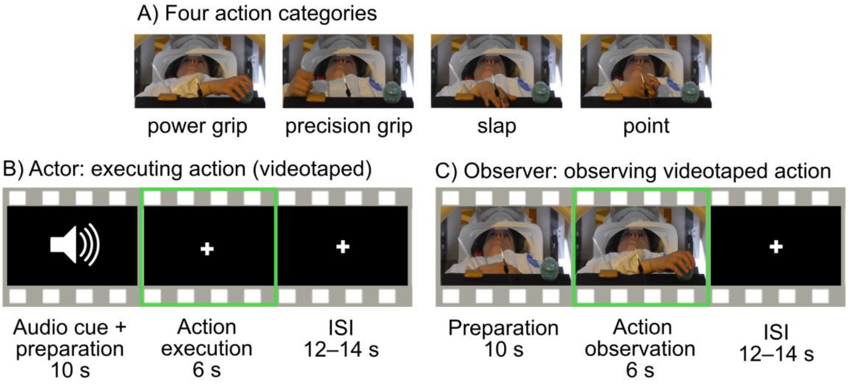

Figure 7. Experimental design and sample trials of action execution and observation. A) The actor performed four different actions (power grip, precision grip, slap and pointing) in the scanner. An actor in the control experiment kept her eyes closed and could not see her own hand actions. B) Trial structure for the actor subjects. C) Trial structure for the observer subjects. Green outline shows the trial portions used for classification.

We assumed that the information represented in brain signals in observers corresponds to the information in actor's brain, but it may be aligned differently. To account for differences in functional localization of action generation and observation across individuals, we used Bayesian canonical correlation analysis (BCCA; Virtanen et al., 2012; Klami et al., 2013) to realign observer's brain data to actor's brain data space. We next performed conventional within-subject classification, where both the training and testing data sets came from each subject. In between-subject classification the training data came from actor, and test data from corresponding observers. Hyperclassification used actor data for training, and functionally realigned observer's data for testing. Classification in all three approaches was accomplished with Bayesian logistic regression.

We characterized the effect of functional realignment by estimating intersubject correlations (ISC) between the brains of actors and observers before and after realignment, assuming that successful realignment would increase ISC in brain regions where shared information between actors and observers increased. Functional realignment for this analysis was done in similar cross-validated fashion as for classification analyzes. Additional searchlight classification analysis was used to compare voxelwise change in predictive accuracy before and after the functional realignment.

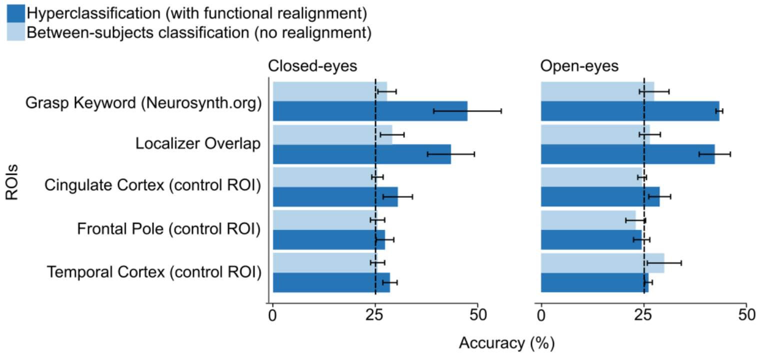

Figure 8. Means and 95% confidence intervals for hyperclassification and between-subject classification accuracy of seen actions in different regions of interest (ROIs). Dashed line indicates the chance level.

4.2.3 Results

Conventional within-subject classification results showed significantly above chance accuracies for both localizer and meta-analytic ROIs (66% and 70% respectively). Hyperclassification accuracy for localizer overlap and meta-analytic ROIs was significantly above chance level (44% and 47% respectively), and also significantly higher than between-subject classification without functional realignment (Figure 8, right). After functional realignment, mean hyperclassification accuracy of a model trained on the closed-eyes actor and tested on five observers significantly exceeded chance level in both meta-analytic and action-execution and action-observation localizer overlap ROIs (43% for meta-analytic and 42% for localizer; Figure 8, left).

Finally, intersubject correlation across actor–observer pairs before and after the realignment highlighted the regions where similarity between the actor and the observers increased due to hyperalignment. Significant increases were observed in bilateral lateral occipital cortex (LOC), supplementary motor area (SMA), and more profoundly in left superior parietal lobe (SPL) and premotor cortex. KNN searchlight classifier in the meta-analytic ROI revealed that hyperalignment increased classification accuracy statistically significantly in all regions within the ROI, with premotor cortex, right pSTS, bilateral SPL, bilateral inferior frontal gyrus and LOC showing more than 5 percentage points increase (Figure 9).

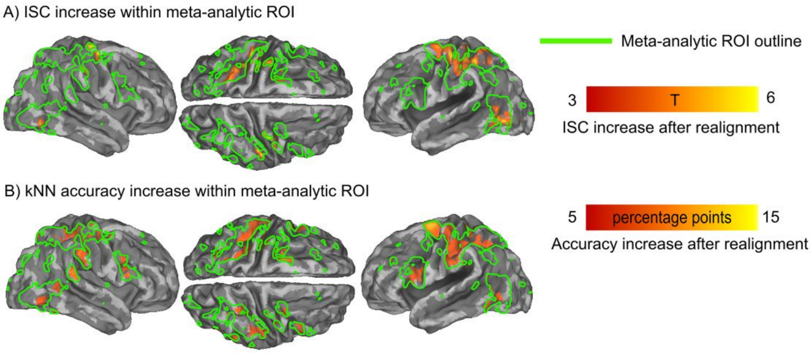

Figure 9. A) Cortical regions showing significant increase of intersubject correlation (ISC) between actors and observers after functional realignment. Colorbar denotes the difference in ISC, indicated with T-statistic. Green outline indicates the regions included in meta-analytic ROI. B) Cortical regions showing significant increase in searchlight kNN classification accuracy after functional realignment thresholded with increase of accuracy of more than 5 percentage points. Colorbar denotes the difference of kNN accuracy. Green outline as in A).

4.2.4 Conclusions

Action observation and execution are tightly linked in the brain and share action-specific neural codes, yet these codes are anatomically misaligned across different individuals and are only discernible following functional realignment. Consequently, functional realignment is required to reveal the neural codes shared by the actor and the observer that may provide basis for inference of another person's motor goals and intentions. In agreement with previous findings, we found that both action execution and observation are supported by activity in an extensive brain network beyond the core mirroring systems (Evangeliou et al., 2009; Molenberghs et al., 2012): hyperclassification following functional realignment allows successful differentiation between observed actions using activation patterns within a distributed network of bilateral LOC, SMG, SPL and precentral and postcentral cortices. Such mapping of seen actions into one's own motor system might also promote mutual understanding, as it provides the observers with a somatosensory / sensorimotor framework that is shared with the actor (Rizzolatti and Sinigaglia, 2010; Kilner, 2011).

4.3 Study 3: Speaker-listener emotional contagion synchronizes brain activity across individuals

4.3.1 Aims of the study

Study III investigated whether emotional contagion via speech enhances synchronization of brain activity between the speaker and the listener. We hypothesized that emotional valence and arousal conveyed by the speech semantics would enhance speaker-listener neural coupling in limbic and somatosensory circuits, as well as speech-related brain regions. To test this hypothesis, we implemented pseudo-hyperscanning experimental paradigm, where one individual told emotional stories, and another individual listened to these stories and empathized with speaker.

4.3.2 Materials and methods

In the first fMRI phase, two healthy right-handed female volunteers ("speakers") narrated a set of thirty-five 1-minute, pleasant, neutral, and unpleasant emotional stories. The stories were based on pre-selected topics (*Pleasant:* I was lying on a blanket underneath a tree with my lover. We were kissing passionately, and I felt I was so much in love with him. *Neutral:* I was spending an afternoon at home. There was nothing particular to do, so I went to the kitchen. I opened the fridge and started wondering what I should eat for dinner. *Unpleasant:* I was sitting with my mother on her hospital bed. She fell into a coma during an unsuccessful operation. She could no longer talk to me, and I knew she would never recover).

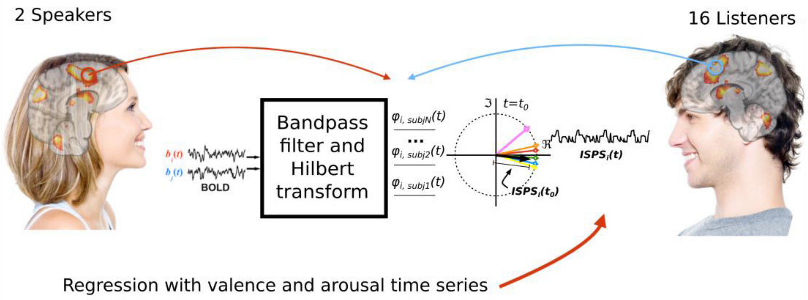

Figure 10. Overview of the experimental design and data analysis. Two individuals told 35 stories while being scanned in fMRI, and 16 listeners heard those stories while also being scanned in fMRI. ISPS was used to estimate intersubject similarity of brain signals between speakers and listeners.

The speaker subjects were asked to prepare a short story on each topic based on their autobiographical events before the fMRI experiment. The stories were recorded with a MRI-compatible microphone, cleaned from noise and presented to the sixteen healthy right-handed female listeners. After the scanning, speakers and listeners were presented with the recorded stories, and asked to rate continuously how pleasant versus unpleasant (valence) and aroused versus calm (arousal) they felt while listening to the stories. These data were originally collected at 5 Hz but resampled to 0.59 Hz (1 / TR) and rescaled to range from 0 (displeasure / low arousal) to 1 (pleasure / high arousal).

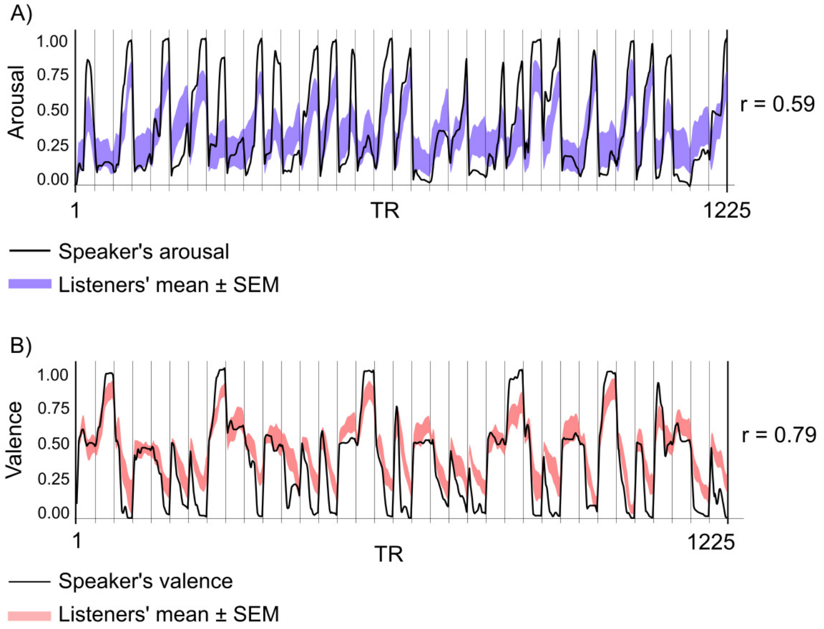

Figure 11. Self-reported valence and arousal time series of speaker and listener subjects. Solid black line indicates speaker's behavioural ratings, and shaded area indicates SEM, derived from listener's data.

We first analyzed the effects of valence and arousal on BOLD responses with GLM implemented in SPM12. A two-stage random effects model was used. For each participant, we used the GLM to assess regional effects of the valence and arousal parameters on BOLD indices of activation. Data were modeled separately for speaker and listener subjects, using the corresponding valence and arousal time series as regressors. Individual contrast images were generated for main effects of story as well as for valence and arousal. Next, a second level (random effects) analysis was applied to these contrast images in a new GLM.

ISPS (Figure 2) was used to quantify similarity of the time series of BOLD signals for the speaker and the listeners (Figure 10). Because we were interested in speaker-listener synchronization, only speaker-listener pairwise ISPS time series were used in the analyses. We first calculated mean speaker-listener ISPS to reveal brain regions where the listener's and speaker's neural activity was synchronous regardless of their emotions. Only data acquired during speaking / listening to speech were used in the analysis. To estimate how emotions modulate speaker-listener ISPS, we next regressed the voxelwise speaker-listener ISPS time series with valence and arousal time series. Mean valence and arousal time series were z-transformed and convolved with a gamma function ($\theta = 1$, $k = 6$) to account for the hemodynamic lag. We next calculated voxelwise Pearson's correlation coefficient between speaker-listener ISPS and valence and arousal time series. This analysis was used to reveal brain regions where reported similarity in feelings was associated with neural synchronization.

Finally, to test whether similarity of speaker-listener emotional states would be associated with similarity of brain states, we used representational similarity analysis (RSA). In addition to the voxel-wise neural speaker-listener ISPS time series, we also computed ISPS for speaker-listener self-reported arousal and valence time series to index similarity of emotional feelings between speaker-listener pairs. Using analysis similar in spirit to RSA (Kriegeskorte et al., 2008), we then compared the voxel-wise neural ISPS time series with ISPS time series of valence and arousal. These results indicated where the brain activity became similar, when emotional feelings became similar between speakers and listeners.

4.3.3 Results

The narratives successfully elicited strong and time-variable emotional reactions, correlated strongly between speaker-listener pairs (Figure 11).

Regional effects analysis revealed overlapping brain activity in visual, auditory and inferior parietal cortices as well as midline structures during storytelling and listening. Valence and arousal of the speech modulated brain activity in overlapping regions for speakers and listeners. Specifically, overlapping activation modulated by arousal was found in visual cortex, SMA, premotor cortex, right TPJ, thalamus and temporal cortex. When modulated by valence, overlapping brain regions included bilateral temporal poles and precuneus. Irrespective of emotional content of the narratives, brain activity between speakers and listeners was synchronous in left inferior frontal gyrus (IFG), bilateral insula, left temporal pole, bilateral superior auditory cortex, bilateral AG/SMG, left V2, V3 and V4, precuneus, posterior and anterior cingulate cortex, and medial prefrontal cortex (Figure 12).

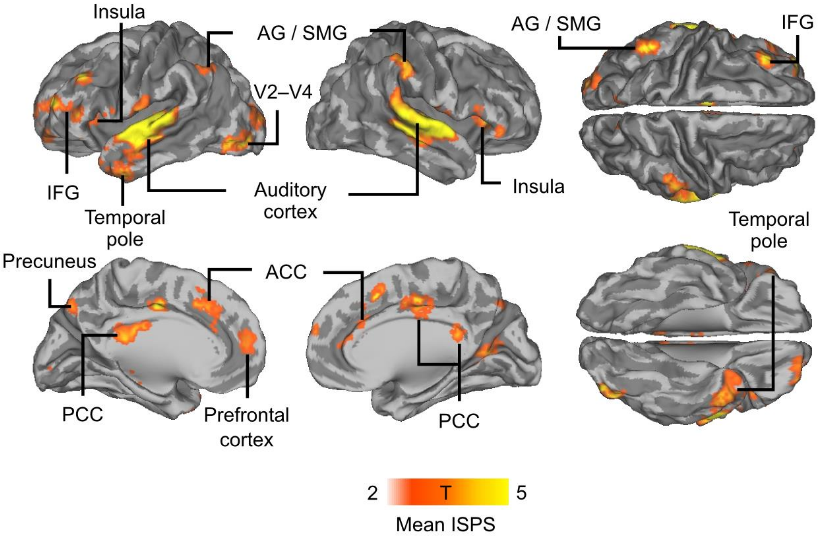

Figure 12. Mean speaker-listener synchronization throughout the experiment.

Valence and arousal dimensions of emotions were associated with spatially distinct patterns of increased speaker-listener neural synchrony (Figure 13). Arousal was positively associated with speaker-listener neural coupling in premotor cortex, left primary somatosensory cortex (SI), left middle frontal gyrus (MFG) left SPL, right pSTS and STG, left STG and Heschl's gyrus, precuneus and SMA. Negative associations were observed in bilateral temporal pole, right AG, thalamus and lingual gyrus. Valence was positively associated with speaker-listener neural coupling in bilateral amygdala and hippocampus, lingual gyrus, precuneus, temporo-parietal cortex, right AG, left temporal pole and right IFG / frontal pole. Negative associations were observed in premotor cortex, left Heschl's gyrus, right pSTS, left SPL and bilateral frontal pole.

The RSA results revealed that similarity of emotional states was associated with similarity of neural states, that is, when emotional feelings are aligned across two individuals, their brain activity also becomes synchronized in spatially selective manner (Figure 14). Similarity of arousal ratings was associated with increased neural similarity in visual and somatosensory cortex, bilateral fusiform cortex and right amygdala / hippocampus. Similarity of valence was, in turn, associated with increased neural similarity in ACC, left superior parietal lobule (SPL) and precuneus, premotor cortex, bilateral AG/SMG, right temporal pole, right MTG and right amygdala.

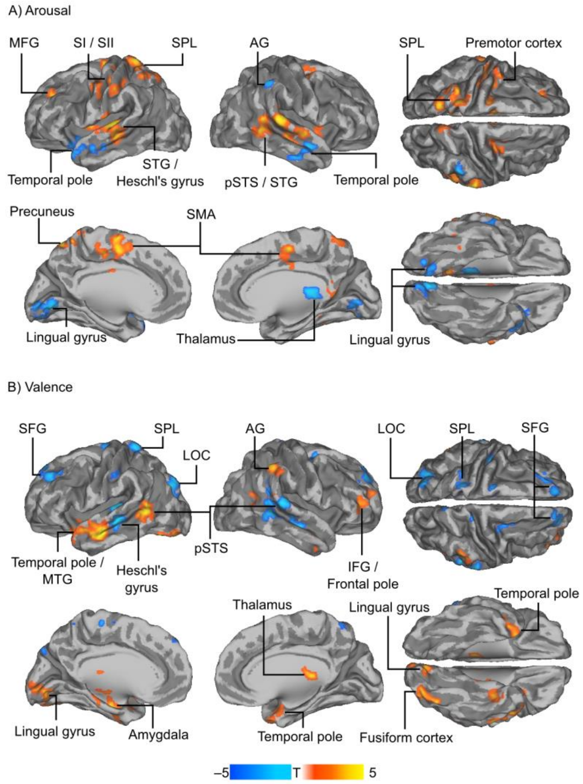

Figure 13. Enhanced speaker-listener neural coupling as a function of valence and arousal. Section A indicated regions, where neural coupling was enhanced as a function of arousal, and section B indicated regions, where neural coupling was enhanced as a function of valence.

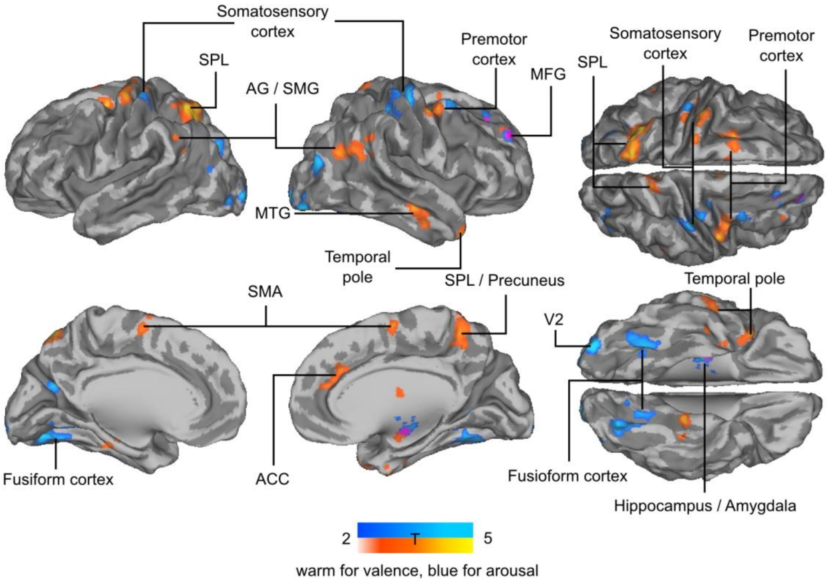

Figure 14. RSA between emotional valence, arousal and brain activity (ISPS) between speakers and listeners. Warm colour indicates increase in neural coupling between speakers and listeners associated with increase in similarity of valence ratings, and cold colour indicates increase in neural coupling associated with increase in similarity of arousal ratings.

4.3.4 Conclusions

This study highlighted how speaker-listener synchronization in the brain's somatomotor, sensory and emotional circuits was associated with the emotional semantics of the speech. When hearing emotional speech, the listener automatically mimics the emotional state of the speaker in their own brain. A potential role for such synchronization of specific brain regions when emotional feelings are similar could be to support more accurate inference and prediction of feelings of others. Such emotional contagion potentially allows listeners to replicate in part the mental and possibly somatovisceral state of the speaker, providing a framework that supports understanding of the feelings of the other person. Previous studies have showed synchronization of brain activation between individuals exposed to similar emotional content (Nummenmaa et al., 2014a). Our results extend these findings including emotional semantics of speech in addressing brain-to-brain coupling between individuals involved in spoken interaction.

4.4 Study 4: Fronto-parietal network supports context-dependent speech comprehension.

4.4.1 Aims of the study

In the final study we aimed at revealing the brain mechanisms that support speech comprehension based on prior knowledge (i.e. contextual understanding). Knowing the context of a narrative facilitates its comprehension (Bransford and Johnson, 1972), but the brain basis supporting contextual understanding of text or speech has remained unresolved (for review see Martin-Loeches et al., 2008). While there is evidence for fronto-temporal and parietal regions contribution to linguistic processing (Binder et al., 2009; Price, 2012), the actual cortical network supporting contextual understanding remains unspecified. Moreover, prior studies addressing contextual effects on comprehension have used highly impoverished linguistic stimuli, thus not representing the complex auditory communication used in everyday life (St George et al., 1999; Martín-Loeches et al., 2008). We also extended the previous research on contextual effects and coherence of text and context (Maguire et al., 1999, Martín-Loeches et al., 2008 and St George et al., 1999) by addressing both regional responses and functional connectivity of the brain′s language network during naturalistic context-dependent speech processing. We hypothesized that listening to ambiguous narratives with a semantically mismatching context would increase semantic selection demands due to lacking contextual cues, which would be reflected in increased activation in Broca’s area. In addition, we hypothesized that Broca’s area would function as the central “hub” for the fronto-temporo-parietal brain network for context-dependent speech processing.

4.4.2 Materials and methods

During fMRI, twenty right-handed healthy volunteers listened to 20 52-72-s ambiguous narratives. Narratives described complex action sequences (such as fishing) in general terms that were ambiguous without any specific context-clarifying cues, similarly as in the original Bransford and Johnosn (1972) study. For example, here is an excerpt of the narrative describing process of painting the walls: “It is quite clear, that the process should be done with either great accuracy or a good skill. Then there will be no problem with finding a way of cleaning all the things. An additional trouble might be the temperature and general climate. Choosing a proper time for it might allow one to avoid a lot of potential problems.” Prior to listening to each narrative, participants were given a contextual cue regarding the upcoming passage (Figure 15). The cue was either matching (i.e. giving a correct context to the passage) or conflicting (i.e. giving an incorrect context to the passage). Participants listened to the narratives in a fixed, pseudo-random order while being scanned.

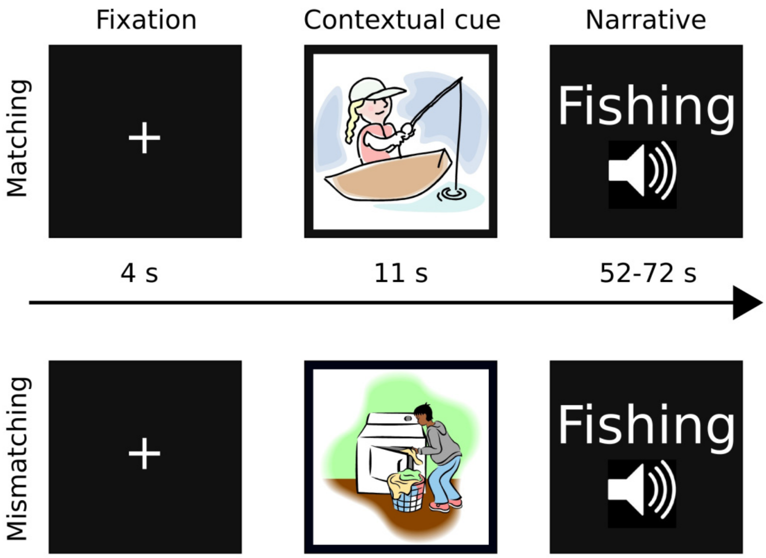

Figure 15. Sample trials with matching (top) and mismatching (bottom) contextual cues. Narratives described complex action sequences such as fishing in general terms that were ambiguous without the contextual cues. Before each narrative, participants saw a contextually matching or mismatching visual cue.

The picture-narrative congruency was counterbalanced so that every participant received exactly the same auditory stimulation, yet the picture context for each narrative was different across the two groups. Comprehension of narratives was rated after the experiment on the scale from 1 to 4, and recall of the narratives was measured after the experiment as a ratio of recalled idea units to maximum idea units recalled for each trial.

Regional effects were analyzed in GLM. Two boxcar regressors – matching context trials and mismatching context trials – were used to model subject's fMRI voxel time series. The regressors included only time points when narrative was presented. We also quantified the temporal similarity of brain activity across subjects during mismatching and matching cue conditions using intersubject correlation (ISC) analysis. ISC was calculated separately for each of the 20 narratives for the two counterbalancings, including all time points when the story was told, resulting in a total of 40 ISC group maps. ISC values across conditions were linearly regressed with the average behavioral comprehensibility ratings. Functional connectivity was estimated using PPI implemented in SPM8. Spheres of 5-mm radius were drawn around the mean stereotactic location of Broca's area (MNI coordinates: −44, 23, 15), as well as posterior and anterior parts of the Broca's region (pars opercularis; MNI: −50, 14, 16 and pars triangularis; MNI: −46, 30, 6). These coordinates were taken from the middlemost voxel in corresponding region in Harvard-Oxford FSL atlas.

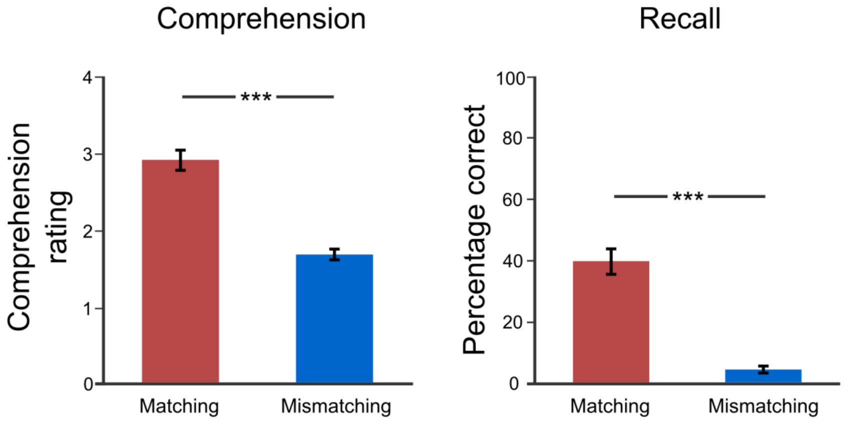

Figure 16. Means and standard errors of means for comprehension (left) and recall (right) ratings.

4.4.3 Results

Matching contextual cues improved the comprehension and subsequent recall of the narratives (Figure 16). GLM analysis revealed significantly stronger task-evoked BOLD responses when listening to narratives preceded by contextually mismatching compared to matching pictures in the cluster that covered left BA 44 and BA 45, as well as a portion of the left dorsal and ventral premotor cortex (Figure 17). No significant differences were observed in this analysis or in the opposite contrast (matching versus mismatching).

Functional connectivity analysis using PPI extended these findings to show how these areas are interacting with other brain structures during context-dependent speech processing. Increased narrative comprehension and recall were paralleled by enhanced functional connectivity between Broca's area and bilateral inferior parietal cortex, anterior and posterior cingulate cortices, and left anterior superior frontal gyrus (Figure 18). Importantly, in spite of its enhanced connectivity in the matching condition, hemodynamic activity in Broca's area was stronger in conflicting condition. Regressing ISC against comprehension ratings revealed stronger ISC for lower comprehension ratings in anterior part of Broca's area, left lobule VIIIa of the cerebellum and left middle temporal gyrus.

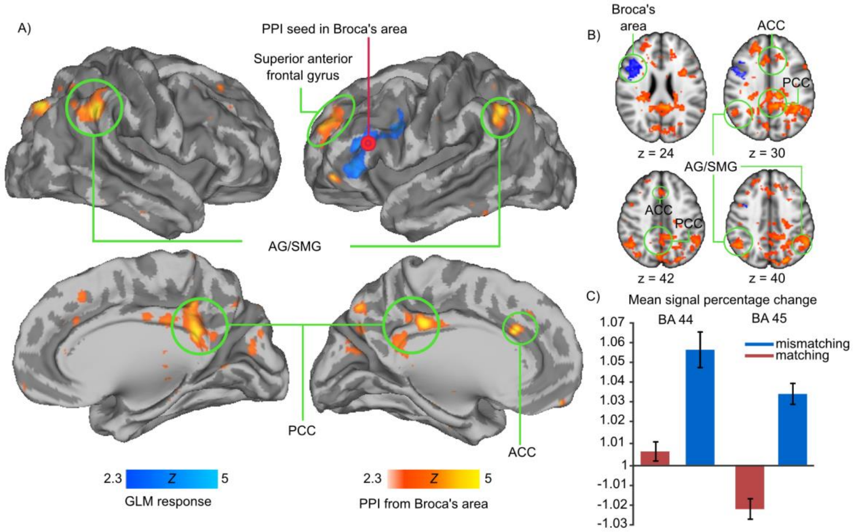

Figure 17. (A) and (B) Brain regions showing increased activity (cold colour) for narratives presented in mismatching versus matching context, and enhanced functional connectivity (hot colour) for narratives presented in matching versus mismatching context. Seed region in Broca's area for connectivity analysis is denoted by the red circle in the volume renders. Data are thresholded at Z>2.3, and FDR corrected (p<0.05) at the cluster level. (C) Mean signal percentage change plot shows averages for BA 44 and BA 45 seeds. Error bars show standard error of the mean.

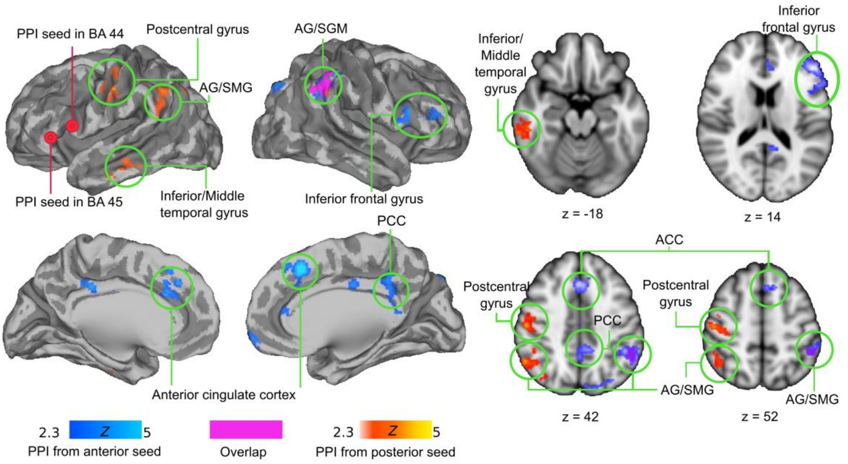

Figure 18. Brain regions showing significant functional connectivity with posterior (hot colour) and anterior (cold colour) Broca's area (seeds indicated by orange and blue circles respectively) during matching versus mismatching trials. Overlap is indicated in purple. Connectivity from both seeds increases only in the right inferior parietal cortex (AG/SMG, indicated by purple). Data are thresholded at Z>2.3, and FDR corrected (p<0.05) at the cluster level.

4.4.4 Conclusions

This study highlights that Broca's area and its connections with the inferior parietal and cingulate cortices play a critical role in context-dependent narrative comprehension. Listening to narrative disambiguated with appropriate context facilitates access to and selection of relevant semantic information and further integration of words and sentences into a coherent narrative. We propose that at the neural level, such contextual understanding is supported by enhanced connectivity of posterior and anterior portions of Broca's area with fronto-parietal network of brain regions. Speculatively, we suggest that within this network a recurrent linguistic process involves inferior parietal cortex which participates in access to semantic representation (Price, 2012) of incoming information which is further selected and unified into larger units in Broca's area (Hagoort, 2005; Moss et al., 2005) on the basis of available context and later matched and updated to a new representation in inferior parietal cortex (Humphries et al., 2007; Binder et al., 2009), while the dACC monitors for consistency of narrative in relation to context (Paus, 2001; Hagoort, 2005).

5. Discussion

5.1 Possible mechanism for matching intersubjective experiences

Altogether these studies show that when two individuals' mental states become more similar, their brain activity becomes more synchronous. This effect was observed across multiple domains spanning from action observation to emotional contagion and speech processing.

In the first study we discovered that active simulation of observed person's mental states was associated with enhanced neural synchrony in brain network supporting action execution and observation across multiple observers. It is crucial to understand the interlocutor's goals and intentions during social interaction, and mapping of the mental and bodily states of others' onto our own sensorimotor system may enable us to understand their actions via direct simulation mechanisms, also called direct matching (Rizzolatti and Sinigaglia, 2010). Such direct matching may support social interaction by providing a somatomotor framework for understanding others' actions.

The study II extended the findings of study I to two-person interaction by showing that motor neural codes of actor are automatically mapped to observer's brain as corresponding action-related neural signatures. When individuals actively simulate the mental state of observed actors, their attentional and action-observation brain networks synchronize. Previous research showed matching neural signatures between action execution and observation within single individuals (Kilner et al., 2009; Gazzola & Keysers, 2009; for review see Heyes, 2010; Molenberghs et al., 2012). Our study II for the first time has showed how these neural signatures are mapped between two individuals, actors and observers. During motor interaction, neural signatures between executed and observed actions are likely shared in the brains of interlocutors.

In the third study we investigated how emotional feelings synchronize attention, limbic and somatosensory networks across interacting individuals and revealed that emotional interaction was accompanied by spatially selective synchronization of brains of listener and speaker. Such neural synchronization was also associated with stronger and more similar emotional feelings in speakers and listeners. Previous research has shown that emotional brain activity becomes synchronized across the individuals exposed to similar emotional stimuli (Nummenmaa et al., 2012; Nummenmaa et al., 2014a). The study III extends these findings to speaker-listener interaction context and confirms the hypothesis that emotional contagion is associated with both increased similarity in emotions and neural activity of interacting individuals.

Finally, study IV revealed that relevant contextual information enhances speech comprehension, due to increased functional connectivity between Broca's area and regions involved in semantic access and error monitoring. The up-to-date mental representation of the semantic information is crucial for communication with our peers (Wlotko and Federmeier, 2012). Knowing the context of a conversation thus is key ingredient for mutual understanding during social communication, and the findings of study IV revealed how contextual understanding is supported in the brain during listening to a narrative.

It was suggested that mutual understanding during social interaction is achieved by employing similar neural computations in similar regions and temporal scales across the interlocutors (Stolk et al., 2016). Neural processes coupled between the two individuals constrain and shape their behavior in interactive environment, and allow more complex joint modes of behavior than would have been possible for each isolated individual (Hasson et al., 2012). Our studies support the general notion that neural coupling between human brains supports social interaction. Specifically, selective synchronization of brain activity across the interacting individuals may reflect simulation of the interlocutor's perceived mental, somatic, and motor state in one's own brain. Such simulation allows direct matching mechanism to infer the feelings, goals and intentions of other, as well as predictions on how the interaction will develop. When we interact with others, we actively simulate their mental states in our own minds. In speech comprehension, action understanding and emotional contagion, perception of motor actions such as hand and facial movements allows individual to simulate the behavior of interlocutor and infer the possible feelings, goals and intentions, as well as anticipate the consequences of observed behavior. Neural coupling between interacting individuals may hint at an overarching functional pattern that allows mapping own experience to experience of other individuals (Gallese, 2003; Oosterhof et al., 2013) and under these circumstances support direct inference of others' mental states.

5.2 Analogous mechanisms supporting social interaction across action, language and emotions

Multiple lines of evidence suggest that neural substrates for action perception, language, and emotions may indeed be shared. For example, core speech processing region in Broca's area also contributes to action planning, observation, understanding and imitation, and serves as a part of mirroring system in humans (for review see Nishitani et al., 2005). Pulvermüller (2005) has shown that perception and understanding of action words activates not only linguistic, but also the action control and execution brain areas. Hearing a word is associated with activation of the related articulatory motor program, and in a similar fashion to mirroring, it seems that action word understanding triggers an automatic thought of the related action. In their fMRI study, Hauk et al., (2004) showed overlapping activation of somatotopic brain areas during observation of finger, tongue and foot movements, and silent reading of action words related to face, arm and leg. Together, these studies suggest that motor system contributes to language processing, and vice versa.

Action and language are also tightly linked with emotions. Ferry et al., (2013) revealed that action observation in emotional context was associated with stronger neural response in motor frontal cortex, temporal and occipital cortices in contrast to observation of the same action in neutral context. Another study found that motor evoked potentials induced with TMS are larger during observation of pleasant and unpleasant versus neutral images (Hajcak et al., 2007). In line with evolutionary research showing relevance of emotional stimuli for survival, Grecucci et al., (2011) has shown that imitative behavior is enhanced by negative stimuli. Moreover, Broca's area activity becomes more synchronized across individuals during highly arousing events (Nummenmaa et al., 2014a). These studies suggest that emotions may modulate activity in brain regions involved in action understanding. Such modulation is highly relevant for survival – observation of negative emotion in other individual (e.g. fear or disgust) hints us towards potentially dangerous entities and suggests relevant action or behavior. All in all, our findings suggest that understanding and prediction of other's thoughts, actions and feelings is supported by similar mechanisms involving sharing neural information between brains of interacting individuals.

5.3 Role of temporoparietal junction in social communication

Our studies revealed that social interaction and perception recruit a widely distributed set of brain areas. To visualize the commonalities of the brain responses supporting action, speech, and emotion, we summarized the regional activation profiles from the studies included in this thesis. This summary shows that some regions have more task-specific responses (ACC, PCC, SI / SII, Insula, Temporal poles), whereas strikingly consistent activation patterns are found across the four studies in bilateral AG / SMG extending to pSTS (Figure 19). The parietal segment of this region is often referred to as temporoparietal junction (TPJ; Binder et al., 2009). This pSTS / TPJ region is likely contributing to social communication process. Multiple studies show that pSTS is important hub for social neural processes (Lahnakoski et al., 2012a) and is crucial for encoding others' intentions (Nummenmaa and Calder, 2009). Monkey studies show that inactivation of pSTS in macaques suppresses social gaze following (Roy et al., 2012). Role of SMG in social communication is also supported by a study showing that overcoming egocentrically biased empathetic judgments was associated with activation of rSMG, and suppression of activity in this region by rTMS caused increase in egocentric bias (Silani et al., 2013). Another study with brain-damaged patients has shown the necessity of left TPJ, including SMG, for reasoning about beliefs of others (Samson et al., 2004).

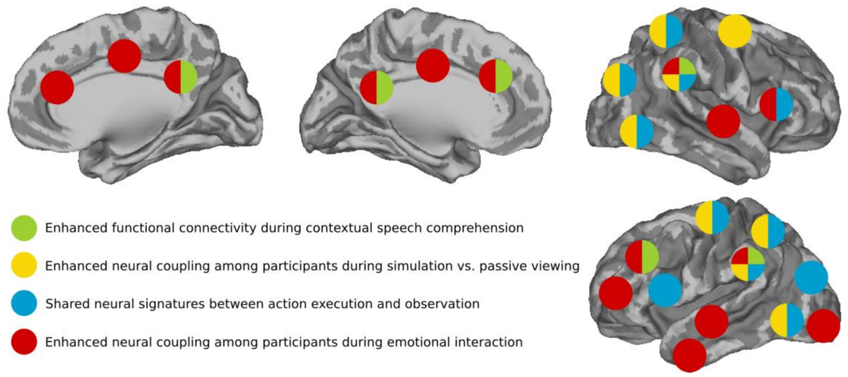

Figure 19. Brain regions involved in studies reported in this thesis. Black circles indicate clusters from results of individual studies. Green circles indicate regions showing enhanced functional connectivity with Broca's area during contextual speech comprehension (Study IV). Red circles indicate enhanced neural coupling between speakers and listeners in emotional communication (Study III). Yellow circles indicate enhanced neural coupling between individuals empathizing with observed boxers vs. neutral observers (Study I). Blue circles indicate regions where neural signatures of actions were shared among actors and observers (Study II).

TPJ plays a significant role in reasoning about other's beliefs, emotions, goals and intentions (for review see Saxe, 2006; Seghier, 2013) but also in perspective taking (Ruby and Decety, 2003), empathy (Jackson et al., 2005), and ToM (Lawrence et al., 2006). Uddin et al. (2006) have shown that rTMS applied to rIPL suppressed distinction between self and other in perceptual task involving discrimination of one's own face and other familiar faces. There is also accumulating evidence from neuroimaging and lesion studies showing that rTPJ is crucial region for distinguishing signals from self-produced actions and signals from environment (for review see Decety and Lamm, 2007).

If shared representations of speech, action or emotion play a role in social perception, it would require some way of distinguishing between self and other (Lawrence et al., 2006). Decety and Lamm (2007) suggested that the TPJ activity during social cognition may be based on lower-level mechanism that generates, tests and corrects internal predictions about external events, which is also in line with our findings in study IV, where we show increase in functional connectivity with TPJ associated with efficient parsing of a narrative. Prediction of how our peers will behave, what emotions they will feel - is at the core of social behavior (Dunbar and Shultz, 2007). Social communication requires understanding speech, intentions and feelings of others and when inferred behavior could be explained by multiple competing options – TPJ may support selection of appropriate program.

Together, the pSTS / TPJ are involved in a wide range of social interactive behaviors, and may serve as a source of information for successful parsing of socially relevant information in the environment, such as gaze, emotions, beliefs and intentions of others.

6. Highlights and future directions

6.1 Statistical modeling of shared neural codes

Multiple studies addressing similarity of neural activity patterns between action execution and observation have not found shared action-specific signatures between motor and seen actions (Dinstein et al. 2008; Etzel et al. 2008; Oosterhof et al. 2010). In our approach we took additional steps to model execution and observation-specific information, and separate it from the information shared between modalities (Virtanen et al. 2012; Klami et al. 2013). This information allowed us to functionally realign the neural data of actors and observers and reveal that the action-related neural codes are indeed shared. Prior work has shown that such "hyperalignment" approaches allow realigning functional activity patterns between multiple individuals if they are initially misaligned due to differences in neuroanatomy and functional specialization of cortical patches (Haxby et al. 2011). However, this analytic approach proved to be challenging to interpret, since intuitive model visualization means were absent. As George Box (1976) said, all models are wrong, but some models are useful. Complex models require simple and intuitive results to be communicated; otherwise their explanatory potential is not useful. ROI-based approach adopted in study II allowed to both visualize subject-specific variation in regions involved in action encoding, as well as inspect how well does meta-analytic data map the regions participating in action execution and observation. While this method provided crucial details regarding effect of functional realignment, informative visualization of shared components that contributed to realignment remains an unsolved challenge.

6.2 Advantages of the naturalistic paradigm

Naturalistic stimuli are required to study realistic social behavior with high ecological validity. Previous research has shown that social context and perception of life-like interaction are required to more strongly recruit the attentional, mentalizing and reward networks involved in social interaction (for review see Rice and Redcay, 2015). Studies on multisensory perception and integration revealed that neural responses during, for example, audiovisual stimulation show super-additivity property: the joint response is larger than the summed response for each sense when stimulated individually (Holmes and Spence, 2005). This suggests that naturalistic stimulation, which typically involves multisensory input, may provide results that expand what is known from highly controlled single modality studies. Hence neural activity associated with complex naturalistic stimulation may differ significantly from simplified and highly controlled stimuli (Hasson et al., 2004). Results from studies I and IV reveal the changes in functional connectivity of linguistic brain regions during narrative comprehension and enhanced neural synchronization in attention and action-observation networks for individuals observing naturalistic videos with similar perspective. These findings expand our understanding of human brain functions in realistic interactive situations. Traditional strictly controlled stimulation paradigms reveal how specific brain systems that are involved in social interaction tend to respond to various stimuli. Naturalistic paradigms extend our understanding of these brain systems to realistic complex semantics of interactive situations, and reveal how brain networks interact in natural environment. Together these two approaches are synergistic in the way they reveal how brain parses simple and complex aspects of everyday life, since responses to complex stimuli cannot always be predicted from combinations of responses to simple stimuli.

6.3 Studying true social interaction

The traditional approach in social interaction research is to study a single individual, i.e. sender or receiver of social information (Schillbach et al., 2013). Studies presented here went one step further and measured both individuals and investigated the alignment of their brains and mind states. When one individual communicates thoughts, actions and feelings to another individual, this information may be mapped into the listener's own behavioural repertoire, leading to more similar thoughts and feelings in listener (cf. mirroring; Rizzolatti and Sinigaglia, 2010). Modeling similarity of neural activation during interaction targets this process and allows revealing the regions and their connections that resonate when, for example, individuals empathize with each other. Investigating senders and receivers of social information together provides valuable insights about the neural subserving of social communication, however in the future this approach should be taken yet another step further to allow real interaction and bidirectional information exchange between two individuals.

While simulation of cell firing is important for modelling the fundamental properties of nervous system, as it reveals the building blocks of human brain (D'Angelo et al., 2013), modelling high-level cognitive processing is important for understanding the way real brain in complex environment figures out the needs, wants and feelings of another real brain. Knowing that neural processes can be similar between individuals that feel mutual trust, understand and empathise with each other is important hint towards understanding why do we make certain social and moral choices, how do we treat ones that are like us, and how do we treat ones that are very different. Moreover, we learn how those choices can be affected by disease. Finding groups with deficits that allow pinpointing the failures in normal system is an unmatched validator of a model. For example, Williams syndrome is associated with strong interest towards social interaction and social stimuli, while, in contrast, autism is characterized with diminished interest in socially relevant information (Riby and Hancock, 2008). Salmi et al. (2013) used ISC during naturalistic movie watching to show significantly less neural synchronization in individuals diagnosed with Asperger syndrome, compared to neurotypical individuals. Studying how brains of interacting individuals with these disorders work in naturalistic situations may reveal the consequences of, for example, absence of neural synchronization in interaction.

6.4 Future directions in social interaction research

The present studies strongly suggest that the next step in understanding neural subserving of social interaction should constitute a switch from “spectator science” focusing on single individuals to two-person brain imaging. Most common approach in social cognitive experiments is to position experimental subject into a role of observer of some static or dynamic stimuli and report their feelings related to content of the stimuli (for review see Schillbach et al., 2013; Garcia and Ibáñez, 2014). Such approach essentially reduces the experimental subjects into passive observers that cannot interact with their (social) environment. Multiple studies show fundamental differences in social cognition between situations where individuals are in interaction, or merely observing other individuals (Schillbach et al., 2013). It has been proposed that real-time social interaction would allow individuals to create a shared psychological state that entails both the desire of one individual to interact and recognition of that desire by the other individual (Tomasello et al., 2005) and assumes that agents actively make use of the behaviorally relevant information conveyed by interlocutors (Schillbach et al., 2013).

In study II we show that action-related neural signatures are shared between interacting individuals and may provide means for direct matching mechanism of action understanding. Moreover, in study III we reveal that emotional contagion, or synchronization of emotional feelings between speaker and listener is associated with neural synchronization in multiple brain networks, possibly reflecting the transmission of emotional information between interacting individuals. However, in both cases, the information flow is unidirectional; one individual is “transmitting”, while the other is “receiving” the information. Two-person setting would allow expanding these findings to an even more realistic situation of bidirectional interaction, where feedback loops will emerge between the two interacting individuals (Hari et al., 2015).

Two-person neuroscience with fMRI is still limited by interaction constraints imposed by the experimental environment. Real world interaction in confined scanner, the environment suffers from multiple limitations, and, first of all, from significant constraint of individual's ability to actively participate in experimental situation. One improvement of the situation is suggested by advances in virtual reality technologies, allowing individual not only to view environments otherwise not available in confined scanner space, but also to certain extent experience embodiment, or presence in an avatar (Cohen et al., 2014). Virtual reality provides high degree of ecological validity, supporting naturalistic and contextually rich stimulation scenarios, as well as featuring control over key variables of environment (Bohil et al., 2011). However, it still remains challenging, even with virtual reality technologies, to record brain data from two interacting individuals simultaneously.

7. Conclusions

Mutual perception and understanding of the physical world is associated with enhanced neural coupling across the interlocutors. Sharing information between the brains of interacting individuals, be it similar encoding of actions, similar prior knowledge, or similar dynamics of activation in emotional brain network, could be one of the core principles that support mutual understanding. Shared information may enable us to simulate others' mental and bodily states and help us to understand and view the external world in a similar fashion (Hari and Kujala, 2009; Nummenmaa et al., 2012). Our findings on the shared neural signatures between executed and observed action across multiple individuals directly support such simulation hypothesis of action understanding.

Inference regarding mind state, thoughts, feelings, goals and intentions enables mutual understanding and prediction of behavior of other individual. Realistic social interaction is an active process, and we show that naturalism of stimulation and inclusion of second individual in interactive situations provides novel information regarding functional connectivity of the brain and neural coupling between brains of two individuals. Our results also show multiple brain regions sharing the neural information between individuals involved in social interaction. Among those regions, we found that pSTS / TPJ were involved in every task. The key role of this region in social processes and prediction of external events may extend to social cognition, potentially supporting selection of adequate prediction of other's behavior.

This thesis addressed neural mechanisms that support social communication and allow us to align our own minds with minds of others. We have shown the role of similarity, both in neural activity and in mind states, in supporting social interaction. However, the practical implication of investigating such alignment of individuals during social interaction remains unresolved. Overall, there is a tendency to have stronger connection with individuals that are more similar to us: our interpersonal connections are strengthened when we are alike. While it allows us to more easily establish connection to our peers, it also extends the divide between an individual and others, whom one considers being different (McPherson et al., 2001). The findings presented in this thesis expand our understanding on the role of similarity in social interaction, and unraveling the features that make us similar or different not only on behavioral, but also on neural level, may enable us to bridge these gaps and find ways to avoid conflicts.

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