MULTIMODAL IMAGING OF LANGUAGE PERCEPTION

Doctoral Dissertation

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School of Science and Technology
Low Temperature Laboratory
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ABSTRACT OF DOCTORAL DISSERTATION

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Abstract

This Thesis draws together several lines of research by examining language perception in the same individuals using three neuroimaging methods: magnetoencephalography (MEG), functional magnetic resonance imaging (fMRI), and electroencephalography (EEG).

The MEG experiments conducted in this Thesis demonstrated that neural processing of written and spoken words converges to the superior temporal cortex following initial modality-specific analysis. In both reading and speech perception, the superior temporal cortex is involved in processing word meaning at ~250-450 ms in the left hemisphere and after ~450 ms bilaterally. The data thus support a view of a largely shared semantic system in auditory and visual language perception, in line with the assumption that reading acquisition makes use of the neural systems originally developed for speech perception during evolution and in individual language development.

The MEG experiments on reading morphologically complex words showed that the left superior temporal activation was enhanced for the morphologically complex words at ~200-700 ms. The results suggest that the majority of inflected words in the highly inflected Finnish language are represented in a decomposed form and that the decomposition process requires additional neural resources. Only very high-frequency inflected words may acquire full-form representations.

The MEG results on parafoveal preview in reading indicated that neural processing of written words in the left hemisphere is affected by a preview of words in the right visual field. The underlying neural mechanism may facilitate reading of connected text in natural conditions.

In a direct comparison, MEG and fMRI showed diverging activation patterns in a reading task although the same individuals were performing the same task. Based on the similarity of the EEG responses recorded simultaneously with both MEG and fMRI, the participants were performing the task similarly during the two recordings. The divergent MEG and fMRI results cannot be attributed to differences in the experimental procedures or language since these factors were controlled. Rather, they are likely to reflect actual dissimilarities in the way neural activity in a high-level cognitive task is picked up by MEG evoked responses and fMRI signals.

Keywords	Neuroimaging, MEG, fMRI, EEG, reading, speech perception	

x The dissertation can be read at http://lib.tkk.fi/Diss/2010/isbn9789526031422/

Tiivistelmä

Väitöskirjassa tutkittiin kielen käsittelyä aivoissa toiminnallisilla aivokuvantamismenetelmillä: aivomagneettikäyrällä (magnetoenkefalografia, MEG), toiminnallisella magneettikuvauksella (fMRI) ja aivosähkökäyrällä (EEG).

Työssä verrattiin puheen käsittelyn ja lukemisen aivomekanismeja. MEG-mittaukset osoittivat, että puheen havaitseminen ja sanojen lukeminen aktivoivat ensin aivoista erillisiä kuulo- ja näköaivokuoren alueita, mutta tämän jälkeen kuultuja ja luettuja sanoja käsitellään samoilla alueilla. Sekä kuullut että luetut sanat aktivoivat vasemmassa ohimolohkossa ylemmän ohimopoimun (superior temporal gyrus, STG) alueen noin 250-450 millisekuntia (ms) sanan alun jälkeen. Tässä aikaikkunassa STG-alue osallistuu sanan merkityksen käsittelyyn sekä puhetta kuunneltaessa että luettaessa. Tämän jälkeen merkityksen käsittely jatkuu molemmissa aivopuoliskoissa STG-alueella. Tulokset viittaavat siihen, että aivoissa sanojen merkityksille on yhteinen edustus, jota käytetään sekä puheen havaitsemisessa että lukemisessa. Tulokset tukevat oletusta, jonka mukaan luetun sanan käsittely aivoissa hyödyntää puheen käsittelyyn evoluutiossa ja yksilönkehityksessä muodostuneita aivomekanismeja.

Työssä tutkittiin myös taivutettujen sanojen lukemista. MEG-vasteet vasemmalla STG-alueella olivat voimakkaammat luettaessa taivutettuja sanoja kuin perusmuodossa olevia sanoja noin 200-700 ms sanan alun jälkeen. Tulokset viittaavat siihen, että suurin osa suomen kielen sanoista on aivoissa edustettuna sanojen osina, joiden käsittely aivoissa vaatii ylimääräistä työtä, ja vain erittäin tavallisille taivutusmuodoille on kokosanaedustumat.

Lukemisen MEG-mittauksissa havaittiin, että sanojen näkeminen näkökentän oikeassa reunassa muuttaa aivovasteita seuraavaan tarkan näön alueella nähtävään sanaan. Tämän ilmiön taustalla olevat mekanismit todennäköisesti helpottavat jatkuvan tekstin lukemista.

Väitöskirjassa verrattiin sähköiseen aivotoimintaan (MEG, EEG) ja verenvirtaukseen (fMRI) perustuvia kuvantamismenetelmiä lukemistehtävässä. Havaitsimme, että MEG ja fMRI antavat osin eri kuvan lukemiseen osallistuvien aivoalueiden toiminnasta vaikka samat henkilöt tekevät samaa tehtävää ja yhtä aikaa mitatut EEG-vasteet ovat samanlaiset MEG:n ja fMRI:n aikana. Koska kieli ja koeasetelma olivat samat MEG- ja fMRI-mittauksissa, havaitut erot eivät voi johtua näistä tekijöistä. Tulokset viittaavat todellisiin eroihin MEG:llä mitattujen herätevasteiden ja fMRI:n herkkyydessä havaita aktivoituneita aivoalueita kognitiivisessa tehtävässä.

Academic dissertation

Multimodal imaging of language perception

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Contents

List of publications

This Thesis consists of an overview and the following five publications:

I   **Uusvuori J,** Parviainen T, Inkinen M, and Salmelin R. 2008. Spatiotemporal interaction between sound form and meaning during spoken word perception. Cerebral Cortex, 18, 456–466.

II   **Vartiainen J,** Parviainen T, and Salmelin R. 2009. Spatiotemporal convergence of semantic processing in reading and speech perception. Journal of Neuroscience, 29, 9271–9280.

III   **Vartiainen J,** Liljeström M, Koskinen M, Renvall H, and Salmelin R. 2010. MEG and fMRI reveal different activation patterns in reading. TKK Report, TKK-KYL-022.

IV   **Vartiainen J,** Aggujaro S, Lehtonen M, Hultén A, Laine M, and Salmelin R. 2009. Neural dynamics of reading morphologically complex words. Neuroimage, 47, 2064–2072.

V   Pernet C, **Uusvuori J,** and Salmelin R. 2007. Parafoveal-on-foveal and foveal word priming are different processes: Behavioral and neurophysiological evidence. Neuroimage, 38, 321–330.

Author's contribution

All five Publications are a result of team work. For Publications I–IV, I was the responsible author and had the main responsibility for the data analysis. For Publication I, I analyzed the MEG data measured earlier by the coauthors. For Publication II, I participated in planning the experiment and prepared the stimuli, conducted the MEG measurements, and analyzed the data. For Publication III, I, with the help of the coauthors, planned the experiment, prepared the stimuli, conducted the MEG-EEG and fMRI-EEG measurements, and analyzed the data. For Publication IV, I participated in planning the experiment, and I conducted the MEG measurements and analyzed the data together with the coauthors. For Publication V, I assisted in the planning, MEG measurements, data analysis, and writing.

Abbreviations

ANOVA	Analysis of Variance
BEM	Boundary Element Model
BOLD	Blood-Oxygen-Level-Dependent
fMRI	functional MRI
ECD	Equivalent Current Dipole
EEG	Electroencephalography
EOG	Electro-oculography
FDR	False Discovery Rate
FWE	Family-Wise Error
MEG	Magnetoencephalography
MCE	Minimum Current Estimate
MNE	Minimum Norm Estimate
MRI	Magnetic Resonance Imaging, anatomical Magnetic Resonance Image
NMR	Nuclear Magnetic Resonance
PET	Positron Emission Tomography
SQUID	Superconducting Quantum Interference Device

Preface

This work was carried out in the Brain Research Unit of the Low Temperature Laboratory at the Helsinki University of Technology. (At the beginning of the year 2010 the name of the university was changed to Aalto.) The Thesis was financially supported by the Finnish Graduate School of Neuroscience and Finnish Cultural Foundation.

First, I would like to thank the director of the laboratory, Prof. Mikko Paalanen, for hiring me in 2001, and him together with the director of Brain Research Unit, Prof. Riitta Hari, for providing the excellent research facilities. I would also like to thank the supervising professor Risto Ilmoniemi and the two preliminary examiners, Prof. Daniel Brandeis and Doc. Jyrki Mäkelä, for their valuable comments on the Thesis. Thank you also for members of my FGSN follow-up group, Dr. Ritva Paetau and Prof. Matti Laine, for interest in my work and encouraging comments during the way.

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The co-authors of the publications also worked hard. Therefore, I wish to thank Dr. Tiina Parviainen, M.Sc. Mia Liljeström, M.Ps. Annika Hultén, Dr. Minna Lehtonen, Prof. Matti Laine, Dr. Silvia Aggujaro, Dr. Cyril Pernet, Dr. Hanna Renvall, Dr. Miika Koskinen, and M.Sc. Marianne Inkinen for contribution to the publications and for interesting discussion about the experiments. I have also got advice and practical help from many other lab members numerous times. Jari Kainulainen, Henna Roikola, Marita Kattelus, Toni Auranen, and Mia Ilman have helped me in measurements and Jan Kujala, Lauri Parkkonen, Antti Jalava, Mika Seppä, Pirjo Muukkonen, Petteri Räisänen and Ronny Schreiber in many other, typically computer-related, ways.

What has made the working in the lab so pleasant and supported the progress of the Thesis is the active social life of the laboratory. I have really enjoyed the discussions, coffee breaks, sauna evenings, journeys, parties, and so on with you Mia, Annika, Tiina, Lotta, Hannu, Miiu, Jan, Antti, Timo, Linda, Topi, Lauri, Hanna, Päivi, Sanna, Leena, Silvia, Paolo, Irene, Gina, Pavan, Cathy, and all others. Special thanks for Tiina, Mia, and the English course members Annika and Hannu for memorable moments and for my present and previous roommates Mia, Antti, Timo, Henna, Jan, Gina, and Päivi in Nano-talo and both wings of Siberia for sharing the good and bad days (and the coffee).

And finally, I wish to thank my parents Mervi and Raimo for reminding me of the other forms of life and for emotional and also financial support. Last, I want to thank my husband Juha for his support and love since the Thesis would not have been published without them. Thank you also for interesting discussions, sometimes even remotely related to the Thesis, and for broad views.

Espoo, April 2010

Johanna Vartiainen

1. Introduction

This Thesis aimed at clarifying the neural basis of reading and speech perception. Reading is a skill that we learn after mastering spoken language. However, it is not known to what extent reading utilizes neural mechanisms developed for speech perception. In the brain, processing of written words starts with modality-specific analysis of visual features and graphemes (letter shapes, *e.g.*, *ph* or *f*) and analysis of spoken words with analysis of acoustic signals and phonetic features (*e.g.*, voicing in *b* and *p*). These are assumed to be followed by retrieval of sound form (phonology) and meaning (semantics) of the words. These later processing stages may be shared by written and spoken language.

Reading and speech perception have been intensively studied with brain imaging methods during the past 20 years. Typical neuroimaging experiments aim at detecting neural activation in response to stimuli or tasks. Hemodynamic methods such as functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) measure changes in blood flow with millimeter resolution but their time resolution is typically on the order of a second. In contrast, electromagnetic methods like magnetoencephalography (MEG) and electroencephalography (EEG) provide millisecond-level temporal information. MEG additionally allows localization of the neural currents with reasonable spatial resolution.

Previous neuroimaging experiments have indicated considerable overlap between analysis of sound form and meaning of written and spoken words, both in timing and location. However, the regions involved and their functional roles suggested by hemodynamic and electromagnetic imaging methods have not been fully concordant. For example, fMRI studies have consistently associated activation in the left frontal cortex with both spoken and written word comprehension (*e.g.*, Booth *et al.*, 2002; Chee *et al.*, 1999) whereas with MEG frontal activations are detected in language production (*e.g.*, Hulten *et al.*, 2009; Liljeström *et al.*, 2009) but in silent reading and speech perception they are typically less salient (*e.g.*, Halgren *et al.*, 2002; Helenius *et al.*, 1998; Helenius *et al.*, 2002; Mäkelä *et al.*, 2001; Pylkkänen *et al.*, 2006; Simos *et al.*, 1997). Most studies to date have focused on either semantic or phonological processing and either spoken or written words, and comparison of these processes in the same brain is lacking. The first goal of the Thesis was to characterize the possible spatial and temporal overlap between neural processing of sound form and meaning for spoken and written words. We compared neural correlates of reading and speech perception in the same individuals using MEG and a novel word-list paradigm.

Next, we focused on the systematic differences detected between hemodynamic and electromagnetic imaging results in reading. The second goal of the Thesis was to investigate whether MEG and fMRI yield a similar activation pattern when the paradigm, language, and participants are the same. Previous, separate MEG and fMRI experiments have indicated involvement of partly different cortical regions in reading, although the results are fairly consistent within each imaging modality (*e.g.*, Jobard *et al.*, 2003; Salmelin, 2007).

The origins of the diverging results remain unknown. One source of discrepancy is that the fMRI and MEG studies of reading have mostly been conducted using different experimental paradigms, tasks, and languages, in different participants. However, since fMRI and MEG measure different aspects of brain function (hemodynamics vs. synchronized activation of neurons), they may well

reveal non-identical activation patterns in some tasks or brain regions although the underlying neural activation would be the same. For both interpretation of the published studies and the future meaningful use of the imaging methods, it is important to clarify whether the differences result from variation in experimental procedures or from the different nature of the measured MEG and fMRI signals. In Study III, we addressed this question by characterizing the similarities and differences of the MEG and fMRI activations in a complex cognitive task that should be more likely to show any actual divergence of MEG and fMRI activations than simple perceptual tasks.

The third goal of the Thesis was to extend investigation of reading to more natural conditions. The neural correlates of reading are typically studied with word stimuli presented foveally, at the center of the field of view. However, when reading connected text, neighboring words are simultaneously visible, although less accurately, in the peripheral vision. Little is known of how this parafoveal preview of words affects reading. We studied the relationship between parafoveal and foveal reading using MEG. We also investigated with MEG how neural processing of complex word forms, such as *book + s,* differs from processing of simple word forms, such as *book*. This question is particularly interesting in the Finnish language in which complex word forms are frequently used.

1.1 Speech perception

Understanding speech is remarkably easy for us. Yet, it remains unclear how our brains convert the information carried by the sound waves into a comprehensible message and appropriate behavior. At the cerebral cortex, the acoustic information is converted into word meaning. This process is complicated by the variability of the acoustic signal corresponding to each word. Variation arises, *e.g.*, from the differences in speed of speech and size of the speech production organs between speakers. Further variation results from the dependency of the acoustic signal of a speech sound on the previous and subsequent sounds (coarticulation). It is not well known which features of the acoustic signal enable speech recognition and whether the neural mechanisms involved are specialized to speech or make use of the general auditory processing system.

As an alternative, the motor theory of speech perception proposes that speech perception relies on the motor representations used in speech production (Liberman *et al.*, 1967). The role of the motor system in speech perception remains a source of debate. It has been suggested that motor representations are not necessary for speech perception (*e.g.*, Hickok, 2009) but that information about articulatory and motor features of speech sounds is accessed during speech perception (*e.g.*, Pulvermüller *et al.*, 2006).

The process of spoken word recognition and comprehension presumably involves several levels of representation. It has been suggested that the acoustic signal is mapped into phones which refer to segments of speech sounds with distinct physical/perceptual features and, thereafter, the phones are mapped into phonemes which refer to the smallest segments of language that can change the meaning of the utterance (*e.g.*, phones [k] and [kʰ] both correspond to phoneme /k/). Finally, the meaning of the word is accessed. It has been proposed that the words are stored in a so-called mental lexicon consisting of representations of word meanings and other information related to each word (*e.g.*, Levelt *et al.*, 1999). The levels of representation implemented in the brain are not well known: The acoustic signal may be mapped directly onto lexical-semantic level, or pass via intervening analysis at the phoneme level (Marslen-Wilson and Warren, 1994; Morais and Kolinsky, 1994; Scott and Wise, 2004). Although the question of the representational levels

involved (acoustic-phonetic only or phonological as well) remains unresolved, analysis of sound form of a spoken word must precede lexical-semantic processing.

In the influential Cohort model (Marslen-Wilson and Welsh, 1978) the analysis of a spoken word is divided into three processing stages: lexical access, lexical selection, and post-lexical integration. At the lexical access stage, representations of words whose first phoneme(s) match the acoustic input are automatically activated. At the lexical selection stage, the number of activated word representations is reduced to one candidate word that best fits the further input and the context. At the post-lexical integration stage, the selected candidate word is combined with this context. Interactive models such as TRACE (McClelland and Elman, 1986) or Logogen (Morton, 1969) allow the context to affect processing at any stage.

Theoretical models do not provide direct predictions of how these processes could be implemented in the brain. Behavioral reaction time experiments have provided estimates for the timing of the neural processing, such that spoken words can be identified based on the first 330 ms of input when heard in isolation and based on the first 200 ms within sentence context (isolation point; Grosjean, 1980). Behavioral data also indicate that spoken words can be recognized within ~500 ms or less (*e.g.*, Tyler *et al.*, 2002).

Neural correlates of speech perception

Analysis of spoken words begins in the ears where the sound waves traveling in the air are first converted to pressure waves traveling in the cochlear fluid. The pressure waves bend the hair cells of the organ of Corti that mediates the frequency encoded signal to the primary auditory neurons. The acoustic signal proceeds along the auditory and vestibulo-cochlear nerve to the brainstem nuclei, and finally to the thalamus. Considerable amount of processing occurs before the signal reaches the primary auditory areas in the bilateral superior temporal cortex. The primary auditory cortex is tonotopically organized and projects to the surrounding regions in the superior temporal gyrus where further acoustic processing occurs (Rauschecker and Tian, 2003). Thereafter, processing of spoken words continues in the temporal association cortices (Hickok and Poeppel, 2004; Scott and Wise, 2004). Figure 1 gives an overview of the cortical regions suggested to be involved in speech perception and reading.

Based on hemodynamic neuroimaging experiments, it has been suggested that two anatomically and functionally distinct processing pathways originating in the primary auditory cortex are involved in speech perception (Hickok and Poeppel, 2004; Scott and Wise, 2004). The anterior stream running anterior and lateral from the primary auditory cortex to the anterior superior temporal sulcus (Scott and Wise, 2004) or to the posterior inferior temporal lobe (Hickok and Poeppel, 2004) is suggested to be involved in mapping of sound onto meaning. The posterior stream running from the primary auditory cortex to the junction of the posterior superior temporal gyrus and inferior parietal cortex, and finally to the frontal cortex, is suggested to be involved in a mapping of speech sound onto articulatory-based representations. Hemodynamic studies associate analysis at the level of sound-based representations with widespread activation of the superior and middle temporal gyri and superior temporal sulcus bilaterally (Hickok and Poeppel, 2004) whereas the left inferior frontal gyrus has been implicated in explicit phonological processing (Bookheimer, 2002). Semantic processing of spoken words has been found to engage the left inferior frontal gyrus (Chee *et al.*, 1999), left anterior temporal cortex (Spitsyna *et al.*, 2006), left posterior temporal cortex (Booth *et al.*, 2002; Spitsyna *et al.*, 2006), and middle superior temporal cortex in the left (Howard *et al.*,

1992; Kotz *et al.*, 2002; Rissman *et al.*, 2003) and right (Kotz *et al.*, 2002) hemisphere. However, due to the slow reactivity of the hemodynamic responses, fMRI and PET cannot follow the timing of activation and track the sequence of activation via these cortical regions.
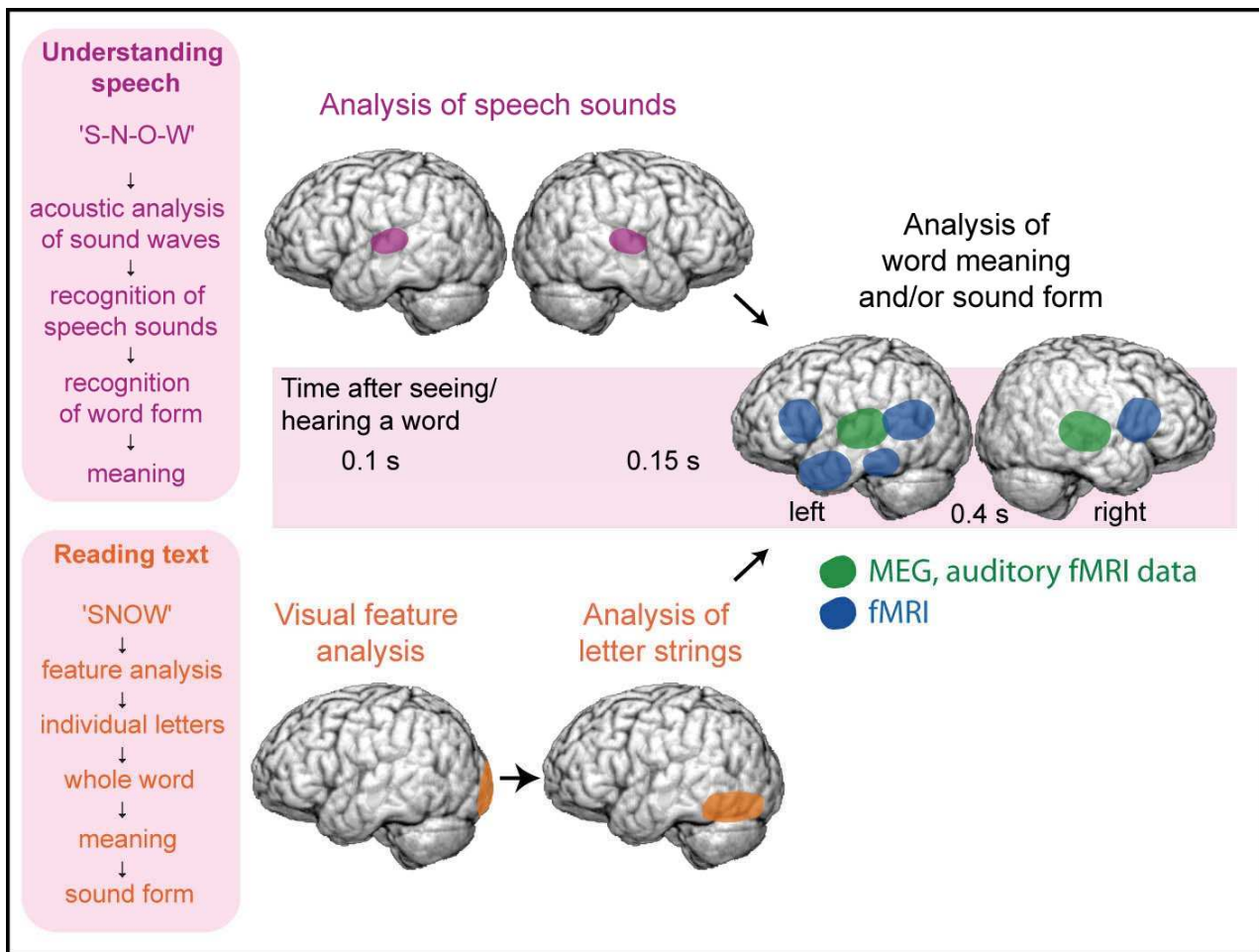
Figure 1: *Overview of the neural correlates of language perception and the assumed processing stages. Brain regions that have been systematically suggested to be involved in language perception by hemodynamic experiments (e.g., Cohen et al., 2002; Hickok and Poeppel, 2004; Jobard et al., 2003; Scott and Wise, 2004; Spitsyna et al., 2006; Vigneau et al., 2006; Vinckier et al., 2007) and MEG experiments (e.g., Cornelissen et al., 2003; Helenius et al., 1998; Salmelin, 2007; Salmelin et al., 1996; Simos et al., 1997; Tarkiainen et al., 1999). Hemodynamic methods and MEG have associated partly different cortical regions, e.g., with semantic analysis of words.*

The spatiotemporal activation sequence of speech perception, as detected by MEG, starts with bilateral activation of the planum temporale, immediately posterior to the primary auditory cortex, and of the close-by regions at ~100 ms after the word onset (Lütkenhöner and Steinsträter, 1998). This N100m response is not detected only in response to words but it is evoked by any sound onset, offset, or a change in the sound (Hari, 1990). However, the N100m response differs between simple speech and acoustically matched nonspeech sounds (Tiitinen *et al.*, 1999; Vihla and Salmelin, 2003) specifically in the left hemisphere (Parviainen *et al.*, 2005), indicating that neural processing is sensitive to the acoustic-phonetic features of speech already in this time-window.

At ~150–200 ms after the word onset, the MEG activation is reduced. An experimental oddball paradigm in which infrequent deviant stimuli interrupt a sequence of frequent standard stimuli has been used to focus on this time window. The deviant stimuli evoke a mismatch field (MMF) which is the MEG counterpart of the mismatch negativity (MMN) that was originally described using EEG (Näätänen *et al.*, 1978; Sams *et al.*, 1985). Experiments employing the oddball paradigm have demonstrated that the supratemporal auditory cortex is sensitive to the phonological structure of speech sounds by ~150 ms after stimulus onset (Näätänen *et al.*, 1997; Phillips *et al.*, 2000; Vihla *et al.*, 2000).

At 200-800 ms after the spoken word onset, a sustained activation usually referred to as the N400m is consistently detected in the middle part of the superior temporal cortex (Biermann-Ruben *et al.*, 2005; Bonte *et al.*, 2006; Helenius *et al.*, 2002; Kujala *et al.*, 2004). Activation in this time window may additionally extend to frontal and anterior temporal areas (Marinkovic *et al.*, 2003). The N400m (N400 in EEG literature) response is affected by semantic manipulation and, therefore, thought to reflect semantic analysis. When participants listen to sentences that end with a semantically congruent or incongruent word, the N400/m is attenuated to the semantically congruent final words and is significantly stronger to the incongruent final words (*e.g.*, Connolly and Phillips, 1994; Hagoort and Brown, 2000; Helenius *et al.*, 2002). This semantic priming effect occurs similarly for word pairs (*e.g.*, Perrin and Garcia-Larrea, 2003; Radeau *et al.*, 1998).

Phonological manipulation also influences neural activation in the N400/m time window. EEG experiments using sentences with final words that are semantically congruent but phonologically unexpected have suggested presence of a separate response at 200–350 ms that would reflect analysis of phonological congruity, seemingly independent of any semantic processing (phonological mismatch negativity, PMN, or N200; Connolly and Phillips, 1994; D'Arcy *et al.*, 2004; Kujala *et al.*, 2004; van den Brink *et al.*, 2001). In word-pair experiments, reduced responses are detected in response to words that are preceded by phonologically related prime words, although the effects are weaker and more variable than for semantic priming (Dumay *et al.*, 2001; Perrin and Garcia-Larrea, 2003; Praamstra *et al.*, 1994; Praamstra and Stegeman, 1993; Radeau *et al.*, 1998). Furthermore, also simple, non-speech sounds elicit a sustained response lasting as long as the stimulus presentation (Pantev and Lütkenhöner, 2000). Therefore, acoustic analysis of speech sounds may be reflected to some extent in the N400m time window as well.

Taken together, the existing experimental evidence from the hemodynamic and electrophysiological studies suggests that semantic and phonological analysis of spoken words may be reflected in temporally and spatially overlapping cortical activation. In particular, activation in the superior temporal cortex appears to be sensitive to both semantic and phonological manipulations of spoken words. However, the interplay between phonological and semantic processing remains unclear since the sentence paradigm typically used does not allow studying semantic and phonological effects separately, and the semantic and phonological word-pair experiments have been conducted in different individuals. Study I aimed at clarifying the time windows and regions involved in processing the meaning and sound form of a spoken word. In Study I, a new word-list paradigm was developed for studying processing of meaning and sound form separately.

1.2 Reading

Reading involves transformation of the information carried by a visual image of the text into the word meanings and also patterns of speech, especially when reading aloud. Since writing is a relatively new invention in human history and reading is a learned skill, the brain mechanisms for reading are likely to build on existing visual object recognition and speech perception systems. Processing of a written word starts with an analysis of visual features. The low-level visual processing common to all visual stimuli is assumed to be followed by recognition of graphemes (letter shapes) and word forms. The visual word recognition system is able to recognize words invariantly of changes in position, case, and font and, at the same time, it is sensitive to small differences between letters and letter order (Dehaene *et al.*, 2005). Open bigram coding of written words has been suggested to account for the detection of letter position and order (Grainger and Whitney, 2004). In this computational model, words are coded by ordered letter pairs that can be separated by a few letters.

Recognition of visual word forms is assumed to be followed by retrieval of semantic and phonological information from a word lexicon and integration of this information to the semantic context (Coltheart *et al.*, 2001). The dual-route model of reading (Coltheart *et al.*, 1993) suggests that for familiar words the meaning of the word is accessed directly based on the visual word form. In parallel, the sound form of the word may be retrieved letter-by-letter, a process that facilitates overt reading via grapheme-to-phoneme conversion, and the analysis may then proceed to semantic associations. This route seems particularly useful in transparent languages, such as Finnish, with a strong, direct correspondence between letters and sounds. Connectionist models of reading (Harm and Seidenberg, 2004; Seidenberg and McClelland, 1989) suggest that word meaning is activated cooperatively via direct and phonologically mediated routes.

Behavioral and eye-movement experiments have provided estimates for timing of the written word recognition. Behavioral data indicate that written words can be recognized within ~500 ms or less (Balota *et al.*, 2004). Eye-movement data have shown that the duration of the eye fixation period varies with word frequency and regularity that are considered as information that is available only after lexical access has started. Therefore, it has been suggested that lexical access should have proceeded to some extent when the next eye-movement is initiated at ~150 ms after the fixation onset (Sereno and Rayner, 2003).

Neural correlates of reading

At the neural level, analysis of written words begins in the eyes where the retinal cells process the visual input. From the retina, the main visual pathway proceeds via the optic nerve, optic chiasm, and optic tract to the thalamic lateral geniculate nucleus (LGN). Neurons in the LGN project to the primary visual cortex in the occipital lobe via the optic radiations. The spatial organization of the visual image is preserved in the primary visual cortex that projects to higher-level visual regions in the occipital cortex.

Two major pathways originate from the primary visual cortex: the dorsal stream running to the posterior parietal cortex and the ventral stream running to the inferior temporal cortex. The dorsal stream (where/how pathway) is associated with processing of visual motion and location whereas the ventral stream (what pathway) is involved in visual object recognition (Mishkin *et al.*, 1983),

also in reading. A hierarchical system of neurons sensitive to progressively larger fragments of words has been proposed in the left occipito-temporal cortex (Dehaene *et al.*, 2005). Further processing of written words has been suggested to occur in temporal and frontal regions, primarily in the left hemisphere (Jobard *et al.*, 2003; Salmelin, 2007), see Figure 1.

Hemodynamic experiments (see Jobard *et al.*, 2003; Vigneau *et al.*, 2006 for meta-analyses) have associated phonological processing of written words with left-hemisphere structures, such as the superior temporal cortex, supramarginal gyrus, and inferior frontal cortex. The regions most consistently implicated in semantic processing of written words are the left basal temporal area, posterior middle temporal gyrus, and inferior frontal gyrus.

When measured with MEG, the spatiotemporal sequence of reading starts with bilateral activation of posteromedial extrastriate cortex at ~100 ms after the word onset. This activation is sensitive to the amount of visual detail in the image and, presumably, reflects basic visual feature analysis (Tarkiainen *et al.*, 1999). Several occipital regions are involved within the first ~140 ms. However, when the focus is on the processing stages following the early visual analysis, it is usually sufficient to consider a representative subset of the early occipital activations. After the low-level visual analysis, activation proceeds to the occipito-temporal regions. All types of letter strings elicit MEG activation particularly in the left inferior occipito-temporal cortex at ~150 ms (letter-string response; Cornelissen *et al.*, 2003; Salmelin *et al.*, 1996; Tarkiainen *et al.*, 1999). At ~200–800 ms, written words evoke a sustained MEG activation in the left and, in some individuals, also in the right superior temporal cortex (N400/N400m response; *e.g.*, Helenius *et al.*, 1998; Pylkkänen *et al.*, 2006; Simos *et al.*, 1997). This N400m activation is sensitive to lexical-semantic (*e.g.*, Helenius *et al.*, 1998; Pylkkänen *et al.*, 2006; Simos *et al.*, 1997), phonological (Wydell *et al.*, 2003) and syntactic (Service *et al.*, 2007) manipulation of written words.

Thus, similarly as for spoken words, the hemodynamic and electrophysiological data suggest that semantic and phonological analysis of written words may be reflected in temporally and spatially overlapping cortical activation. The first aim of Study II was to clarify the interplay of semantic and phonological processing in reading using the word-list paradigm developed in Study I.

1.3 Comparison of reading and speech perception

Since the information about written and spoken words arrives into the brain via different sensory modalities, the initial processing stages in reading and speech perception involve the separate visual and auditory processing pathways. However, the later neural processing stages, such as analysis of meaning and sound form of the word, could be shared by written and spoken language. Although reading is likely to make use of many of the linguistic processes and neural computations originally developed for speech processing, the different characteristics of the speech signal and written text could have resulted in penetrating differences in the neural processing of written and spoken words. For example, unlike written text, speech unfolds over time. Models of language processing often assume that retrieval of word meaning from a semantic system and integration of this information with the context is common for spoken and written words whereas the role of the analysis of sound form may differ between the two modalities (*e.g.*, Patterson and Shewell, 1987; Seidenberg and McClelland, 1989).

In neuroimaging experiments, hemodynamic methods have shown overlap of activation for spoken and written words in the left inferior frontal and temporal cortex, and areas in and near the left supramarginal and angular gyrus (see, *e.g.*, Cabeza and Nyberg, 2000; Demonet *et al.*, 2005 for reviews). The MEG studies that provide information of timing of cortical activation as well, suggest that analysis of written and spoken words starts in modality-specific regions and converges to overlapping areas in the temporal and prefrontal cortex, primarily in the left hemisphere, after ~250 ms (Marinkovic *et al.*, 2003). The specific functional roles of these spatially and temporally overlapping activation patterns have remained largely unresolved since most studies that have investigated functional processing stages have focused on either the visual or auditory input modality but not both.

Those few fMRI and PET studies that have directly compared semantic processing of visual and auditory words in the same individuals have found overlapping activation for the written and spoken words in the left (Booth *et al.*, 2002; Chee *et al.*, 1999) and right (Booth *et al.*, 2002) inferior frontal gyrus, bilateral anterior prefrontal cortex, left premotor region and anterior supplementary motor area (Chee *et al.*, 1999), left anterior temporal cortex (lateral temporal pole and anterior fusiform gyrus; Spitsyna *et al.*, 2006) and left posterior temporal cortex (Booth *et al.*, 2002; Spitsyna *et al.*, 2006).

MEG experiments have consistently associated activation of the middle superior temporal cortex at ~200–800 ms after the word onset with lexical-semantic processing of both written (Halgren *et al.*, 2002; Helenius *et al.*, 1998; Pylkkänen *et al.*, 2006; Simos *et al.*, 1997) and spoken (Helenius *et al.*, 2002; Mäkelä *et al.*, 2001) words. In EEG experiments, sensitivity to semantic manipulations has been detected in approximately the same time window for both written (~330–500 ms) and spoken words (~250–600 ms) (Holcomb and Neville, 1990). Phonological processing also tends to influence neural activation in the N400/N400m time window and in the general area of superior temporal cortex both in the visual (*e.g.*, Helenius *et al.*, 1998; Rugg, 1984; Wydell *et al.*, 2003) and auditory modality (*e.g.*, Connolly and Phillips, 1994; Helenius *et al.*, 2002; Praamstra and Stegeman, 1993). Thus, the N400 time window appears to reflect a level of representation that is shared by the written and spoken language.

Taken together, the existing neuroimaging data implies considerable overlap between analysis of sound form and meaning of spoken and written words in timing and location. However, most studies to date have focused on either semantic or phonological processing and either spoken or written words. The second aim of Study II was to characterize the differences and similarities of cortical dynamics of reading and speech perception when measured in the same individuals, using the same paradigm.

1.4 Language perception: MEG vs. fMRI

Speech perception and reading have been investigated using both electrophysiological and hemodynamic neuroimaging methods. In speech perception, different imaging approaches have provided mostly converging evidence. MEG and fMRI experiments on reading, in contrast, have indicated involvement of partly differing cortical regions, although a systematic pattern of activation has emerged within each imaging modality (Jobard *et al.*, 2003; Salmelin, 2007; Vigneau *et al.*, 2006). In fMRI, activation to visually presented letter-strings is detected in the same general region in the left occipito-temporal cortex as in MEG, but the fMRI activation is stronger to real

words than to consonant strings (visual word form area, VWFA; Cohen *et al.*, 2002; Vinckier *et al.*, 2007) in an area slightly anterior to the MEG letter-string response region (Tarkiainen *et al.*, 2002). Furthermore, fMRI has consistently associated frontal regions, especially the left inferior frontal gyrus, with high-level linguistic analysis, such as semantic, phonological, and morphological processing of written words (see, *e.g.*, a meta-analysis by Jobard *et al.*, 2003; Yokoyama *et al.*, 2006). In MEG, frontal activations are detected in other cognitive tasks, *e.g.*, in speech production (Hulten *et al.*, 2009; Liljeström *et al.*, 2009), but in reading they are typically less salient. In fMRI experiments, activation in the left superior temporal cortex has been associated with phonological processing whereas the temporal regions most consistently implicated in semantic processing of written words are the left posterior middle temporal gyrus and left basal temporal area (Jobard *et al.*, 2003).

The reasons for these diverging results have remained unknown. One source of discrepancy is that the fMRI and MEG studies of reading have mostly been conducted using different experimental paradigms, languages, and populations. Nevertheless, MEG and fMRI also probe neural activation via different measures (synchronous electrical activation of neurons vs. hemodynamic responses) and, therefore, it is possible that the diverging results reflect actual differences in the sensitivities of these methods. In direct comparisons, fairly good spatial convergence of MEG evoked responses and fMRI signals has been observed in low-level sensory and motor processing (*e.g.*, Moradi *et al.*, 2003; Sharon *et al.*, 2007; Stippich *et al.*, 1998). Fewer studies have compared MEG evoked responses and fMRI signals in complex cognitive tasks (Billingsley-Marshall *et al.*, 2007; Croize *et al.*, 2004; Liljeström *et al.*, 2009) although these tasks are more likely to show any potential divergence of the MEG and fMRI sensitivities. Reading, in particular, is a well suited task for an MEG-fMRI comparison since it is a high-level cognitive task that has been extensively investigated and characterized with both MEG and fMRI.

Study III was designed to characterize the similarities and differences between the MEG and fMRI results on reading when experimental paradigm, language, and the participants are the same. We investigated whether the diverging results obtained in earlier, separate MEG and fMRI experiments reflect actual differences in the sensitivities of these methods or differences in the experimental procedures.

1.5 Reading in a more natural setting: morphologically complex words

In normal language use, words appear in several forms: nouns in singular and plural forms and in different cases, verbs in different tenses, etc. Morphology refers to the study of these word forms, while a morpheme is the smallest unit of language carrying meaning. Words that are composed of several morphemes, such as *car + s* or *play + er,* are referred to as morphologically complex words.

Despite years of investigation, it remains an open question how morphologically complex words are represented and accessed in the brain. Early theoretical models suggested that they would either be stored as a whole in the mental lexicon (*e.g.*, having a separate lexical entry for *cars*) or represented and accessed via their constituent morphemes (*e.g.*, decomposing the input into *car* and *–s*, the representations of which are then recombined to arrive at the meaning of the complex word form) (Butterworth, 1983; Taft and Foster, 1975). More recent models on morphological processing combine features from both models (Caramazza *et al.*, 1988; Giraudo and Grainger, 2000, 2001; Schreuder and Baayen, 1995).

Finnish is a highly inflectional language where previous behavioral studies have yielded a robust inflectional processing cost, *i.e.*, the recognition of the inflected words is slower and more error-prone than the recognition of monomorphemic words (Hyönä *et al.*, 1995; Laine *et al.*, 1995; Laine *et al.*, 1999; Niemi *et al.*, 1994). This processing cost could stem from decomposition of inflected words into stem and suffix and/or from subsequent recombination to arrive at the semantic-syntactic interpretation of the word form. The behavioral effect is modulated by the frequency of the word form so that it may vanish in the (very) high frequency range (Laine *et al.*, 1995; Lehtonen and Laine, 2003; Soveri *et al.*, 2007), suggesting that massive exposure to an inflected form may result in a full-form representation for that form.

Neural correlates of morphological processing have been investigated using hemodynamic methods and in these experiments, effects of morphological structure have typically been reported in activation of the left inferior frontal gyrus, interpreted to reflect analysis of grammatical features, and the left temporal regions, thought to denote access to the semantic representations of the stem and affix (Beretta *et al.*, 2003; Bozic *et al.*, 2007; Devlin *et al.*, 2004; Jaeger *et al.*, 1996; Sach *et al.*, 2004; Sahin *et al.*, 2006; Tyler *et al.*, 2004; Vannest *et al.*, 2005; Yokoyama *et al.*, 2006). EEG recordings have indicated effects of morphology at ~250–700 ms after the word onset (Dominguez *et al.*, 2004; Lehtonen *et al.*, 2007; Leinonen *et al.*, 2009; Münte *et al.*, 1999; Penke *et al.*, 1997; Rodriguez-Fornells *et al.*, 2001; Weyerts *et al.*, 1996; Weyerts *et al.*, 1997). MEG studies have revealed activation sensitive to English morphology at ~350 ms over the left temporal cortex (Fiorentino and Poeppel, 2007; Pylkkänen *et al.*, 2004; Stockall and Marantz, 2006). Diverging from this more common pattern, a recent MEG study (Zweig and Pylkkänen, 2009) investigating the processing of derived vs. monomorphemic English words, found an early effect of morphological complexity at 170 ms after the stimulus presentation, primarily in the right hemisphere.

The neuroimaging experiments on morphological processing have mainly focused on past tense inflection of regular and irregular verbs, typically using a verb generation task and the English language, although some experiments have also considered derived or inflected nouns and other languages. Study IV aimed to shed light on the neural correlates of the inflectional processing cost using MEG. The aim was to investigate at which stage in the sequence of neural processing the effects of morphological complexity emerge and whether such effects are influenced by word frequency.

1.6 Reading in a more natural setting: parafoveal vision

Human visual acuity is sharpest in the fovea, a pit in the surface of the retina. When reading, we make small and fast eye movements (saccades) approximately every 250 ms to move the fovea in such way that the region of the sharpest vision lands on the text approximately every 7–9 letters. Visual information is gathered during the ~250 ms periods when the eyes remain fixated on one location. The fovea is surrounded by a parafoveal region with lower resolution. In natural reading when fixating on a word, information about the subsequent text is available in the parafoveal vision. This parafoveal preview contributes to fluent reading of connected text since fixation times increase to ~300 ms in the absence of parafoveal information (Blanchard *et al.*, 1989).

The parafoveal preview has been investigated using behavioral reaction time measurements and eye-movement recordings (*e.g.*, Blanchard *et al.*, 1989). However, the neural correlates of reading have mostly been studied with foveally presented stimuli and, thus, the effect of the parafoveal

preview on brain responses to foveally presented words is not known. At the neural level, foveally and parafoveally presented visual stimuli initially activate different parts of the visual cortex (Stenbacka and Vanni, 2007). For parafoveal stimuli presented in the left or right visual field, the visual input initially activates the contralateral hemisphere. Foveally presented input, however, extend to both the left and right visual field and, therefore, visual pathways projecting to both hemispheres are involved. Thereafter, the neural processing of the parafoveal and foveal word stimuli may or may not share common mechanisms. Study V investigated how the parafoveal preview of words affects foveal reading in the brain.

2. Methods

2.1 Magnetoencephalography (MEG)

Magnetoencephalography (MEG) is a non-invasive method for recording neural currents. MEG measures the weak magnetic fields associated with the electrical activity of neurons. It allows tracking of the neural activation at high temporal accuracy with (sub)millisecond resolution and with a reasonable spatial accuracy, from a few millimeters to a centimeter. The following summary on MEG and electrical activity of neurons is mainly based on texts by Hämäläinen *et al.* (1993), Niedermeyer *et al.* (2005), and Purves *et al.* (2004).

Electrical activity of neurons

A sensory stimulus activates receptor cells that transmit the information to the brain in the form of action potentials propagating along neurons. At rest, concentration gradients of ions, such as Na^+, K^+ and Cl^-, exist across the cell membrane of a neuron. The propagation of an action potential is based on the permeability changes of the cell membrane for mainly Na^+ and K^+ ions through voltage-gated protein channels.

Information spreads from one neuron to another predominantly via chemical synapses. An action potential in the presynaptic cell causes intake of Ca^{2+} to the axon terminal, and release of neurotransmitter vesicles to the synaptic cleft. The transmitter molecules bind to their receptors on the postsynaptic cell membrane. There are a large variety of neurotransmitters and their receptors, and the resulting effects on the postsynaptic cell depend on the type of the receptor.

When the permeability of the postsynaptic membrane changes, the cell will either depolarize or hyperpolarize. If the binding of the neurotransmitter to the receptors leads to opening of Ca^{2+}-channels, the cell will depolarize resulting in an excitatory postsynaptic potential (EPSP). Multiple EPSPs are required to produce an action potential. If the binding of the neurotransmitter results in opening of other ion channels, for example Cl^--channels, the result is hyperpolarization and an inhibitory postsynaptic potential (IPSP). The inhibitory and excitatory postsynaptic potentials sum up at the axon hillock. If the potential change reaches the threshold, voltage-gated Na^+-channels open and a new action potential is generated.

Magnetic fields detectable with MEG

The major source of the MEG signal is suggested to be the post-synaptic currents flowing in the apical dendrites of pyramidal cells towards the cell soma (Hämäläinen *et al.*, 1993; Murakami and Okada, 2006; Okada *et al.*, 1997). It has been approximated that ~50 000 pyramidal neurons must be simultaneously active to produce a detectable signal outside the head, and even then, the magnetic flux density produced by the neuronal currents is weak, typically in the range of 50–500 fT. These small fields can be measured using superconducting quantum interference devices (SQUIDs).

Since summation of currents is required, MEG mainly detects magnetic fields generated by post-synaptic currents. The post-synaptic current may be approximated with a current dipole and an action potential by a current quadrupole. In an infinite homogeneous conductor, the dipolar field decreases more slowly ($1/r^2$) with distance than the quadrupolar field ($1/r^3$). The post-synaptic currents also last longer (tens of ms) than action potentials (1 ms) and, therefore, the spatial and temporal summation of post-synaptic currents is more likely than summation of action potentials. The current flow in the pyramidal cells generates a magnetic field large enough to be detected since the pyramidal cells' apical dendrites often run parallel which enables the summation of the currents. Thus, MEG signal reflects mainly the input to and processing within a cortical region.

Because of the essentially spherical geometry of the head, fully radial currents produce almost no magnetic field outside of the head. Therefore, MEG detects mainly magnetic fields produced by tangential components of currents. Since the apical dendrites of the pyramidal cells are mainly oriented perpendicular to the surface of the cortex, MEG is most sensitive to activation in the fissural cortex. Fortunately, the major part of the cortical surface is located in fissures, and the magnetic field produced by most currents arising in the cortex can therefore be detected with MEG. Among the different brain regions, the localization accuracy of MEG is best for currents in the superficial, cortical regions (~2–4 mm) and worst for currents in the anterior frontal lobe and deep brain structures (~1–2 cm) (Tarkiainen *et al.*, 2003).

MEG device

The data reported in this Thesis were collected with an Elekta Neuromag VectorView whole-head MEG device (Elekta Oy, Helsinki, Finland). It measures the magnetic flux density with 306 SQUIDs in a helmet array. The SQUIDs are located at the bottom of a helmet-shaped insulated container filled with liquid helium. During the measurement, the participant is seated on a chair, with his head covered by the helmet and is presented with auditory, visual, or other stimuli while the electrical activity of the brain is measured.

The SQUID magnetometers are the only practical devices sensitive enough to detect the magnetic fields of the brain. A dc SQUID is a superconducting ring including two Josephson junctions (Silver and Zimmerman, 1967). A Josephson junction is a thin insulator gap between two superconducting parts through which Cooper pairs of electrons tunnel (Josephson, 1962). With a SQUID, one may measure the magnetic flux through the SQUID loop since the voltage over the Josephson junction is a periodic function of the magnetic flux. When the bias current fed to the SQUID and the current induced by the magnetic flux together exceed a critical current, a voltage appears across the Josephson junction. The sensitivity of the SQUID is based on the fact that, around zero, the voltage is approximately a linear function of the magnetic flux. The SQUID is operated at the zero point using feedback electronics, and it thus serves as a highly sensitive

magnetic-flux-to-voltage transformer. As voltage can be measured very accurately, a SQUID allows reliable recording of changes of magnetic field.

The signal is brought to the SQUID via a flux transformer. In the VectorView MEG system, there are two planar gradiometers and a magnetometer at each measurement location. A planar gradiometer contains a figure-of-eight pickup coil, with the two loops wound in opposite directions. The two orthogonally oriented planar gradiometers measure the gradient of the magnetic flux density, $\partial B_z / \partial x$ and $\partial B_z / \partial y$, where B_z is the component of the magnetic flux density perpendicular to the surface of the helmet. A planar gradiometer detects the maximum signal directly above a source area, where the magnetic field varies most rapidly with location. It is most sensitive to close-by current sources since the field generated by a distant source is essentially the same in the two oppositely wound loops of the pickup coil, thus resulting in a zero total current. Magnetometers have a single loop in the pick-up coil. They are more sensitive to fields generated by currents in deep brain structures than the gradiometers but also more sensitive to noise.

Noise in the MEG signal

The magnetic field produced by the brain (~50–500 fT) is orders of magnitude weaker than the field produced by, *e.g.*, eye movements, blinking, heart, and muscles (~10 000 fT). Other sources of noise in an MEG measurement are geomagnetic fluctuations (~300 µT), electrical devices and any moving magnetic material. Due to the weak signal and high noise level, the measurements must be conducted in a magnetically shielded room. The electronic noise may also be partly removed by using high- and low-pass filters and by averaging the signals over several stimuli of the same type.

The forward problem

The forward problem in MEG denotes calculation of the magnetic field $\mathbf{B}(\mathbf{r})$ produced outside the head by known current sources in the brain. The current generated by neuronal activity can be divided to the primary current $\mathbf{J}^{\mathrm{P}}$ flowing inside or in the vicinity of neurons and the passive volume current $\mathbf{J}^{\mathrm{V}}$ distributed over the whole brain

$$\mathbf{J}^{\mathrm{V}} = \sigma \mathbf{E}, \tag{1}$$

where σ is the conductivity of the medium and $\mathbf{E}$ is the electric field. Both the primary and the volume current create a magnetic field that can be calculated starting from the Maxwell equations. The frequency spectrum for neuromagnetic signals in the MEG is typically below 1 kHz. Consequently, the frequencies are low enough to justify the quasi-static approximation, and the Maxwell equations take the form

$$\nabla \cdot \mathbf{E} = \frac{\rho}{\varepsilon}, \tag{2}$$

$$\nabla \times \mathbf{E} = -\frac{\partial \mathbf{B}}{\partial t} \approx 0, \tag{3}$$

$$\nabla \cdot \mathbf{B} = 0, \tag{4}$$

$$\nabla \times \mathbf{B} = \mu \left(\mathbf{J} + \varepsilon \frac{\partial \mathbf{E}}{\partial t} \right) \approx \mu \mathbf{J}, \tag{5}$$

where ρ is the total charge density, ε is the permittivity of the medium, **B** is the magnetic flux density, **J** is the current density, and μ is the permeability of the medium. The permeability of the brain can be approximated with the permeability of vacuum μ_0.

The magnetic flux density can be calculated from the Ampère-Laplace law

$$\mathbf{B}(\mathbf{r}) = \frac{\mu_0}{4\pi} \int \mathbf{J}(\mathbf{r}') \times \frac{(\mathbf{r} - \mathbf{r}')}{|\mathbf{r} - \mathbf{r}'|^3} d^3 r', \qquad (6)$$

where **J** is the total current density. The human head (brain, skull, and scalp) can be closely approximated as a spherically symmetric conductor. In this special case, the magnetic flux density **B** outside the conductor can be obtained without explicit reference to volume currents (Hämäläinen *et al.*, 1993). The radial component of the flux density, $B_r = \mathbf{B}(\mathbf{r}) \cdot \mathbf{e}_r$, can be calculated as

$$B_r(\mathbf{r}) = \frac{\mu_0}{4\pi} \int \frac{\mathbf{J}^P(\mathbf{r}') \times (\mathbf{r} - \mathbf{r}')}{|\mathbf{r} - \mathbf{r}'|^3} \cdot \mathbf{e}_r dv'. \qquad (7)$$

From this equation it can be seen that B_r vanishes for radially oriented primary currents. Since $\nabla \times \mathbf{B} = 0$ outside the conductor, **B** can be determined from the magnetic scalar potential U

$$\mathbf{B} = -\mu_0 \nabla U. \qquad (8)$$

Since also $\nabla \cdot \mathbf{B} = 0$, the scalar potential U can be determined if its normal derivative on the surface of the conductor is known

$$U(\mathbf{r}) = \frac{1}{\mu_0} \int_{t=1}^{\infty} B_r(t\mathbf{r}) dt. \qquad (9)$$

B outside of a spherically symmetrical conductor can therefore be calculated without knowing the conductivity profile. If the conductor is of an arbitrary shape, **B** must be computed numerically.

The inverse problem

The location and strength of the current sources generating the magnetic field can be estimated from the field pattern measured with MEG. However, theoretically, this inverse problem has no unique solution: an infinite number of source distributions inside the conductor can, in principle, produce identical magnetic field patterns outside of the conductor. Thus, additional constraints are needed to select the appropriate solution. In the case of MEG, such constraints are set by brain anatomy and physiology.

Equivalent Current Dipoles

Focal sources can be modeled by equivalent current dipoles (ECDs) that represent the location, strength, and orientation of the underlying electric current. ECD models attempt to explain the measured field with a set of dipolar source currents. To find the optimal ECD parameters, the field patterns predicted by the model and the measured data are matched in the least-squares sense. In our approach, we first localize ECDs at the time instants when the measured field patterns are most dipolar and distinct from each other. The location and orientation of these ECDs are then fixed, and the amplitudes are allowed to vary over the time interval of interest to find the time behavior that optimally explains the measured data given the selected ECDs. Localization of activation is most

accurate for small activated regions. If an extended activation (several centimeters in diameter) is modeled using a single ECD, the estimation of the source depth and strength may be less accurate. In this Thesis, ECD analysis was applied in all MEG experiments as the primary source localization technique.

Distributed source modeling

As an alternative for ECD analysis, distributed source modeling techniques can be used to localize the current sources in the brain. Distributed models do not make assumptions about the source structure but, instead, require that the overall source current distribution minimizes the norm of the source current strengths. The current distribution is often approximated by a set of hundreds or thousands of dipolar sources. We used minimum current estimates (MCEs) and minimum norm estimates (MNEs) as complementary source localization methods, mainly for visualization of the MEG results. Minimum Current Estimate (Uutela *et al.*, 1999) is an implementation of the minimum L1-norm estimate (Matsuura and Okabe, 1995). The measured signals are accounted for by a distribution of electric current that has the minimum total amplitude. Minimum Norm Estimate (Hämäläinen, Martinos Center for Biomedical Imaging, Massachusetts General Hospital, MA) is an implementation of the minimum L2-norm estimate where the measured signals are accounted for by a distribution of electric current that has the minimum overall power.

Although these methods provide a spatially distributed model of the activation sequence, they do not provide direct information about the extent or shape of an active cortical region. At present, statistical comparison of MCE or MNE maps is not feasible, as robust tools for random-effects analysis of the spatially highly correlated MEG data are still lacking. Instead, a region of interest analysis, comparable to the ECD analysis, can be conducted on the distributed maps. In the MNE analysis, we computed cortically constrained, noise-normalized MNEs (dynamical Statistical Parametric Maps, dSPMs) that provide an estimate of the signal-to-noise ratio for each potential source location (Dale *et al.*, 2000).

Model of the volume conductor

For computation of the forward problem, the electrical conductivity geometry of the head must be taken into account. There are two common types of models: spherically symmetric models and more realistic models that estimate the shape of the head more precisely. In the ECD analysis, a spherically symmetric model is adequate in most cases, as the noise typically present in real brain signals masks the errors due to the imperfections of the conductor model (Tarkiainen *et al.*, 2003). Realistic head models are typically used with the distributed source modeling techniques. In this Thesis, in the ECD analysis, the cranial volume was approximated by a homogeneous conducting sphere that was fitted to the inner curvature of the skull based on the individual anatomical magnetic resonance image (MRI). In the MCE and MNE analysis, an individual single-compartment boundary element model (BEM) was used.

Evoked responses vs. rhythmic activity of the brain

The MEG responses to individual stimuli are too weak compared to noise to allow source localization or comparison of responses between stimulus types. The most common approach for MEG (and EEG) data analysis is to present a large number of stimuli of each type (~100 stimuli/category) to the participant and average the signals with respect to the onset of the stimulus. The aim of averaging is to cancel out random noise and brain signals that are unrelated to the

stimulus presentation.   The features of the brain signal that are time- and phase-locked to the stimulus and occur similarly from trial to trial, for a certain stimulus category, are detected in the resulting averaged evoked responses. Here we used this approach and analyzed evoked responses in MEG and EEG.

An alternative approach is to determine the time-frequency profile of the MEG/EEG signals and analyze changes in the cortical rhythms in response to stimuli. Rhythmic brain activity was discovered in the early EEG recordings (Berger, 1929) and oscillations in some frequency bands were found to have physiological correlates. For example, alpha rhythm (8–12 Hz) is detected in the EEG and MEG recordings in the posterior brain regions when the subject's eyes are closed. The functional significance of the rhythmic activity of the brain is currently unknown. Based on intracranial recordings in animals, it has been hypothesized that neuronal oscillations mediate selection of relevant sensory inputs (Fries *et al.*, 2002; Schroeder and Lakatos, 2009) and binding of distributed neuronal activity (Singer, 1999). Furthermore, phase re-setting and synchronization of the ongoing oscillations has been suggested to contribute to generation of the evoked responses, especially in late time windows (Schroeder and Lakatos, 2009), although the evoked responses have been suggested to be mainly generated independently of the ongoing oscillations (Shah *et al.*, 2004; Mäkinen *et al.*, 2005). When measured outside of the head, rhythmic activity is typically detected in certain brain regions only (*e.g.*, in the visual, somatosensory, and motor cortex). In particular, the gamma oscillations (typically frequencies above ~30 Hz) that have been suggested to have an important role in cognitive functions (Fries *et al.*, 2007) have been detected in MEG recordings primarily with certain visual tasks, in the occipital cortex (Hoogenboom *et al.*, 2006).

2.2 Magnetic resonance imaging (MRI)

Magnetic resonance imaging, MRI, is a method that provides structural images of the brain and other organs with high spatial resolution (~1 mm in the present work). It is based on the behavior of hydrogen nuclei of the human tissues in the magnetic field. The following summary on MRI and fMRI is mainly based on texts by Ballentine (1998), Huettel *et al.* (2004), and Logothetis (2008).

MRI scanners

An MRI scanner consists of a superconducting electromagnet that creates a strong static magnetic field, gradient coils that enable spatial coding of the signal, shim coils that correct the inhomogeneities of the static field, and a transmitter/receiver system that excites the nuclei and measures the MRI signal. The data in this Thesis was collected on a 3 tesla Signa EXCITE MRI scanner (GE Healthcare, Chalfont St Giles, UK). During MRI and fMRI recordings of the brain, the participant lies on a bed within the scanner, with the head inside the transmitter/receiver coil and a mirror system for visual stimulus presentation in front of the eyes.

Nuclear magnetic resonance

Nuclei with spin (internal angular momentum) in the magnetic field can be described using quantum mechanics. Particles with nonzero spin have a magnetic moment

$$\boldsymbol{\mu} = \gamma\mathbf{S}, \tag{10}$$

where γ is the gyromagnetic ratio and $\mathbf{S}$ is the spin operator. The possible energy states of a particle with spin in a magnetic field $\mathbf{B}$ and the energy E_i associated with them are the eigenvectors and the eigenvalues of the Hamiltonian operator

$$H = -\mathbf{\mu} \cdot \mathbf{B} = -\gamma \mathbf{B} \cdot \mathbf{S}. \tag{11}$$

For a particle with spin ½, such as a proton, the spin operator is

$$\mathbf{S} = \frac{1}{2}\hbar\mathbf{\sigma}, \tag{12}$$

where $\mathbf{\sigma} = (\sigma_x, \sigma_y, \sigma_z) = \begin{pmatrix} 0 & 1 \\ 1 & 0 \end{pmatrix}, \begin{pmatrix} 0 & -i \\ i & 0 \end{pmatrix}, \begin{pmatrix} 1 & 0 \\ 0 & -1 \end{pmatrix}$ are the Pauli spin operators. When a particle with spin ½ is in an external magnetic field $\mathbf{B}_z$ along the z-axis with magnitude B_0, H becomes

$$H = -\tfrac{1}{2}\gamma\hbar B_0 \sigma_z \tag{13}$$

and the time evolution of the state is given by the Schrödinger equation

$$\left|\psi(t)\right\rangle = a_1 \exp(\frac{i\omega_0 t}{2})\left|+\right\rangle + a_2 \exp(\frac{-i\omega_0 t}{2})\left|-\right\rangle, \tag{14}$$

where $\left|+\right\rangle$ and $\left|-\right\rangle$ are the eigenvectors of σ_z, aligned parallel and anti-parallel with the applied magnetic field, $\omega_0 = \gamma B_0 = (E_2 - E_1)/\hbar$ and the constants a_1 and a_2 are determined by the initial conditions. Equation (14) indicates that the field $\mathbf{B}_z$ does not change the occupations of the spin states but rotates the phase difference of the components. For example, if $a_1 = a_2 = \sqrt{0.5}$, the average magnetic moment is

$$\left\langle \mu_x \right\rangle = \frac{1}{2}\hbar\gamma\cos(\omega_0 t), \left\langle \mu_y \right\rangle = \frac{1}{2}\hbar\gamma\sin(\omega_0 t) \tag{15}$$

indicating that the magnetic moment is precessing at the rate ω_0 around the axis of the static magnetic field.

When a time-dependent field is applied, transitions between the energy levels become possible. In particular, if a rotating field in the transverse xy plane with angular frequency ω is applied, the transition probability reaches its maximum when $\omega = -\omega_0 = -\gamma B_0$. This is called the resonance condition and the frequency ω_0 the Larmor frequency. At resonance, the average magnetic moment precesses around the rotating field in the xy plane. By applying the transverse field for a suitable period of time, one can rotate the magnetic moment through any desired angle from the z-axis.

In a large ensemble of spin ½ particles, the average initial conditions are determined by the temperature T, and the relative proportion of the two spin states is

$$\frac{P_p}{P_a} = \exp(\frac{E_2 - E_1}{k_B T}), \tag{16}$$

where P_p and P_a are the probabilities of a nucleus being in the parallel and antiparallel state and k_B is Boltzmann's constant. Since the energy difference $E_2 - E_1$ increases with the field strength, the

probability of a nucleus being in the parallel state and the net magnetic moment of the ensemble also increase with the field strength.

Magnetic resonance imaging of human tissues

Magnetic resonance imaging of human tissues utilizes the magnetic properties of hydrogen nuclei that are abundant in water and fat. The hydrogen nucleus is a single proton that has spin ½. When placed in a magnetic field, the hydrogen nuclei in the human tissues together form a net magnetization that is aligned with the static magnetic field created by the magnet of the MRI device. The net magnetization is tilted by applying a radio frequency pulse at the Larmor frequency, *i.e.*, a rotating magnetic field transverse to the static field. The applied time-dependent field enables transitions to the higher energy level and synchronizes the spin phases. With time, the spins release the absorbed energy into the surrounding tissue, thus realigning the net magnetization gradually with the static magnetic field. The resulting decaying electromagnetic field in the transverse plane is measured with a receiver coil, and it forms the basis of the nuclear magnetic resonance (NMR) signal.

The NMR signal decays with time at a tissue-specific rate depending on the energy absorption properties of the surrounding tissue. This enables discrimination of tissues using MRI. The realignment of the net magnetization with the static magnetic field consists of two processes: exponential recovery of the longitudinal magnetization with time constant T1 (~100–1000 ms, T1/spin-lattice relaxation) and exponential decay of the transverse magnetization with time constant T2 (~10–100 ms, T2/spin-spin relaxation). The former is related to the release of energy to the surrounding nuclei and the latter to the loss of phase coherence of the spins due to field inhomogeneities caused by spin-spin interactions. Inhomogeneities in the main magnetic field cause further dephasing of the spins (~ms, T2* relaxation) that is utilized in functional MRI.

The magnetic resonance image is created by recording the strength of the NMR signal from each measurement location (voxel) in the brain. The strength of the NMR signal depends on the local density of nuclei, tissue type, magnetic field inhomogeneity, and other factors. A suitable sequence of radiofrequency pulses can be used to emphasize the factors of interest. The spatial coding of the signal is achieved by establishing a location-dependent magnetic field. First, a slice selection gradient field is applied simultaneously with a radiofrequency pulse. Only the nuclei in one slice within the imaging volume precessing with the frequency of the radiofrequency pulse will be excited. Next, two additional gradient fields are applied to encode the spatial locations in the selected slice. These frequency and phase encoding gradients result in different frequency and phase of precession at each measurement location within the selected slice.

2.3 Functional magnetic resonance imaging (fMRI)

Blood-oxygen-level-dependent functional magnetic resonance imaging (BOLD fMRI) is a method for studying hemodynamic responses of the brain. It allows localization of the changes in the cerebral blood oxygenation with mm resolution (~3 mm in the present work). Due to the slow reactivity of the hemodynamic response, the time resolution of fMRI is typically on the order of about one second.

BOLD fMRI is based on the magnetic properties of the deoxygenated blood. The hemoglobin proteins in the red blood cells include four iron-containing heme groups that bind oxygen transported from the lungs to the tissues. Deoxygenated hemoglobin (deoxy-Hb) has paramagnetic properties, and therefore, it causes local inhomogeneity in the magnetic field, resulting in decrease of the T2* relaxation time and attenuation of the NMR signal. Oxygenated blood, water, and most macromolecules in the tissues are diamagnetic and affect the magnetic field only minimally. The BOLD signal changes reflect changes in the deoxy-Hb concentration that are affected by cerebral blood flow, volume, and oxygen extraction rate (Ogawa *et al.*, 1993). The signal increases typically observed in BOLD fMRI experiments are due to increased flow of oxygenated blood into the given brain region. A typical hemodynamic response to a brief stimulus begins with a delay of 2–3 s, reaches the maximum at ~6 s and then declines back to the baseline.

Cerebral microvasculature and neural events underlying the hemodynamic response

Brain tissue is dependent on the supply of oxygen and glucose via blood flow and receives blood via a complex network of branching arteries. Small arterioles penetrate the cortex perpendicular to the surface of the cortex and give rise to the capillary bed where the oxygen exchange occurs. The capillaries drain to small venules that combine to form intracortical veins extending to the cortical surface.

Local changes in the cerebral blood flow have been associated with synaptic and electrical neural activation (Iadecola *et al.*, 1997) but the mechanisms that trigger the hemodynamic response are not fully understood. Hemodynamic responses have been suggested to reflect increased metabolic demands of the active neurons (*e.g.*, Heeger and Ress, 2002). It was first hypothesized that the increased delivery of oxygenated blood to the active brain region compensates the increased oxygen demand of the metabolically active neurons. However, PET experiments demonstrated that the cerebral glucose uptake and blood flow are uncoupled from the metabolic rate of oxygen. It was shown that visual stimulation is accompanied with a local increase in cerebral blood flow and glucose uptake but with only a slight increase in oxygen metabolism in the human visual cortex (Fox *et al.*, 1988). Several models (Buxton and Frank, 1997; Buxton *et al.*, 1998; Magistretti and Pellerin, 1999; Malonek and Grinvald, 1996) have been put forward to explain the relations between blood flow, oxygen consumption, and glucose metabolism in the brain, but at present the issue remains unresolved.

It has been argued that the BOLD responses should be interpreted as reflecting neural signaling within a brain region instead of increased energy utilization since the energy demands of the brain tissue do not directly determine the blood flow changes (Attwell and Iadecola, 2002). Cortical microcirculation is controlled by several mechanisms that are not well understood. The local blood flow increases associated with neural activation have been suggested to be mediated, for example, by neurotransmitter glutamate that increases synaptic release of local vasoactive factors, such as nitric oxide and adenosine. Additional control mechanisms independent of local neuronal activation have been suggested as well. Diffuse modulatory neurotransmitter systems (*e.g.*, dopamine, noradrenalin, and serotonin systems) consist of brain stem nuclei and spreading afferents projecting to various cortical regions. These neuromodulatory signals affect large masses of neurons, and they have been suggested to affect blood flow of wide cortical areas by constricting the microvessels.

The control mechanisms and the architecture of the cerebral microvasculature restrict how well the spatial distribution of the hemodynamic changes can reflect the spatial distribution of the neural

activation. Experiments in rats have shown that during sensory stimulation, arterioles dilate and blood flow increases in the immediate vicinity of the electrophysiological activation but, to a smaller extent, also 2–3 mm upstream from the neural activation (Iadecola *et al.*, 1997). Signal changes can also be observed downstream from the neural activation. An activated cortical area of 100 mm^2 has been estimated to generate an undiluted change in the blood oxygenation ~4 mm beyond the edge of the activated region (draining vein contamination; Turner, 2002).

BOLD signal and electrophysiological activation of neurons

The relationship of the BOLD signal and electrophysiological activation of neurons has been studied using intracranial recordings, mainly in other species than humans. Invasive microelectrode measurements can reveal action potentials of single neurons and of neural populations within ~50–350 µm from the electrode tip (multiunit activity), reflecting the output of the neurons. The same electrodes can be used to measure local field potentials that reflect local cortical processing and input to a neural population within 0.5–3 mm from the electrode tip. Recordings in monkeys and cats have indicated coupling of local field potential spectral power and BOLD responses in the primary visual cortex, in simple perceptual tasks (Goense and Logothetis, 2008; Logothetis, 2008; Niessing *et al.*, 2005). Recently, similar findings have been obtained in humans, in the temporal cortex using an associate learning paradigm (Ojemann *et al.*, 2010). However, the coupling of the local field potential power and BOLD signal in the monkey visual cortex is context dependent and it vanishes during perceptual suppression (Maier *et al.*, 2008). Separate intracranial studies in monkeys and fMRI studies in humans also point to diverging effects of visual attention on the electrophysiological and hemodynamic measures (Blake and Logothetis, 2002). In particular, BOLD responses can be recorded in the absence of action potentials (*e.g.*, Goense and Logothetis, 2008). Furthermore, in a recent optical imaging study, hemodynamic responses were detected in the absence of electrical neural activation, suggesting an anticipatory hemodynamic mechanism (Sirotin and Das, 2009).

The dissociation of the BOLD response and intracranial electrophysiological measures, especially action potentials, has been suggested to reflect neuromodulatory signals that are more readily measurable in fMRI than in electrophysiological recordings (Logothetis, 2008; Logothetis and Wandell, 2004). Since the diffuse modulatory neurotransmitter systems affect large masses of neurons and blood flow in wide cortical regions, they may contribute significantly to the BOLD signal. It has been suggested that the BOLD signal is primarily affected by the excitation-inhibition balance in cortical subsystems at the level of cortical columns, and this balance may be affected more by the neuromodulatory signals than by the driving input (Logothetis, 2008).

The relationship between the BOLD signal and electrophysiological activation has been investigated also using non-invasive methods, EEG and MEG, in humans. However, the comparison of BOLD signals with EEG and MEG has focused mainly on low-level sensory and motor processing. MEG evoked responses and fMRI BOLD signals have been directly compared in the primary sensory and motor cortices and typically found to show fairly good spatial convergence (*e.g.*, Moradi *et al.*, 2003; Sharon *et al.*, 2007; Stippich *et al.*, 1998) although some spatial (Korvenoja *et al.*, 2006) and functional differences have been observed (Tuunanen *et al.*, 2003). Only a few studies have focused on more complex cognitive tasks (Billingsley-Marshall *et al.*, 2007; Croize *et al.*, 2004; Furey *et al.*, 2006; Liljeström *et al.*, 2009), and they have found some divergence between the evoked responses and BOLD signals.

It has been suggested that changes in cortical rhythms measured by MEG and EEG would correspond better with hemodynamic signals than the evoked responses (Foucher *et al.*, 2003). However, comparisons have again mainly focused on low-level sensory processing, most often on visual processing in the primary visual cortex, and a complex pattern of results has emerged. Different frequency bands or the relative power between high and low frequencies have been found to correlate either negatively or positively with the BOLD signal (Brookes *et al.*, 2005; Lachaux *et al.*, 2007; Rosa *et al.*, 2010; Singh *et al.*, 2002; Winterer *et al.*, 2007; Zumer *et al.*, 2010). Furthermore, this coupling seems region-dependent (Ekström *et al.*, 2009; Martuzzi *et al.*, 2009).

Taken together, changes in the BOLD signal result from a series of physiological effects that are not well understood. Further experiments are needed to clarify the relation of the hemodynamic responses to the neural electrical activation and to the extracranial electrophysiological measures.

Statistical significance of the fMRI results

BOLD signals are typically analyzed within the general linear model (GLM) framework. Stimulus timing is first convolved with a hemodynamic response function that represents the assumed or measured BOLD response to a very short stimulus. The resulting regressors for the different stimulus categories, possibly other variables, and an error regressor are included in the GLM to evaluate which regressor best explains the measured data in each voxel in the brain. A parameter estimate describing the goodness of fit is obtained for each regressor and voxel. The estimates are compared across the different stimulus categories using statistical testing. Due to the large number of voxels (~100 000), a massive multiple comparisons problem is encountered and needs to be corrected for using, *e.g.*, Family-Wise Error (FWE) or False Discovery Rate (FDR) correction.

2.4 Electroencephalography (EEG)

Electroencephalography, EEG, is a technique that is used in research and clinics to measure the time course of the neural activation at a millisecond scale. EEG measures electric potential associated with the electrical activity of neurons at various locations on the scalp with respect to a reference electrode.

The EEG signal is generated by the same primary currents as the MEG signal (Hämäläinen *et al.*, 1993). Similarly as for the MEG inverse problem, the underlying current distribution can be estimated from the measured electric potential distribution. However, the electric potential V, unlike the magnetic field **B**, is strongly affected by the conductivity profile. The skull and other conducting tissues between the neural currents and the EEG electrodes cause distortion of electric potential, and therefore, source localization in EEG is less accurate than in MEG. Deep and radial current sources contribute significantly to the electric potential as well. The calculation of the current sources from EEG requires a multicompartment model with conductivities and shapes of the brain, skull, and other tissues. In this Thesis, EEG was used in Study III to further validate the MEG-fMRI comparison by verifying that the participants' electrical brain responses were similar during the MEG and fMRI recordings. For this purpose, we conducted sensor-level analysis on the EEG data; localization of the currents from EEG was not necessary.

Electric potential is measured with electrodes placed on the scalp. In this Thesis, EEG was collected with caps containing 28–64 EEG electrodes. The electric potential at each electrode is contrasted to

the potential at a reference site. Optimally, the reference electrode would be placed in a location where it does not detect voltage changes due to neural electrical activation but captures the noise that is similar at the measuring electrodes and at the reference site. In practice, this is not feasible, and the selection of the reference site thus affects the appearance of the individual electrode signals. Several solutions, each with advantages and disadvantages, have been suggested to circumvent this problem. Here, a common reference between Cf and Cz was used during the measurement, and the reference was changed off-line to the average reference (mean of all electrodes; Dien, 1998).

Simultaneous EEG and fMRI measurement

Simultaneous EEG and fMRI measurement is problematic since the strong electromagnetic fields used in the fMRI recordings mask the electrical signal originating from the brain. The EEG equipment also causes a potential safety risk when brought into the MRI environment. The artifacts on the EEG signal induced by the magnet are due to the changing gradient fields during the MR pulse sequence and the movement of magnetic blood with the cardiac rhythm (ballistocardiogram artifact). Recently, methods to overcome the signal analysis problems have been developed and MRI-compatible EEG equipment has become available. In Study III, the gradient artifact was removed by subtracting a high-precision artifact template (Koskinen and Vartiainen, 2009). The ballistocardiogram artifact was not removed since it was considered to have only a minor effect on the averaged evoked EEG responses.

3. Experiments

Study I: Cortical processing of meaning and sound form of spoken words

Study I aimed at determining the time windows and regions involved in processing the meaning and sound form of a spoken word. Previous studies of auditory language perception have suggested that semantic and phonological analysis of spoken words may be reflected in temporally and spatially overlapping cortical activation. However, the neural correlates of semantic and phonological processing and, in particular, the possible interplay between them has remained elusive.

To investigate the neural representation of semantic and phonological processing systematically, they need to be manipulated independently. We used a priming approach that has been widely employed in behavioral and neuroimaging experiments. In general, priming refers to the influence of the prior presentation of a stimulus (the prime) on the processing of a subsequent stimulus (the target). In typical semantic priming experiments, the target word is preceded by a prime word that has related meaning (*e.g.*, Nobre and McCarthy, 1994). EEG and MEG studies have also used sentences that end with the expected word or a semantically inappropriate one (Connolly *et al.*, 1995; Helenius *et al.*, 1998; Kutas and Hillyard, 1980). In a sentence, a strong expectation of a particular final word can be built but the disadvantage is that the sentence always creates expectation of both the meaning and the sound form of the word.

In Study I, a novel priming paradigm that enables investigation of semantic and phonological priming separately was developed. In order to build a stronger semantic expectation of the target word than in a word pair, while avoiding contamination by expectation of sound form present in sentence tasks, we used lists of four words, see Figure 2. The first three words of the list were

semantically related, and the final word either agreed with that context or was semantically unrelated. The areas and time-windows that show suppression of activation over the course of the first three words and increase of activation to a semantically unrelated list-final word may be interpreted as reflecting sensitivity to semantic information. The semantic content of the word must be available in the time window in which the suppression/increase occurs.
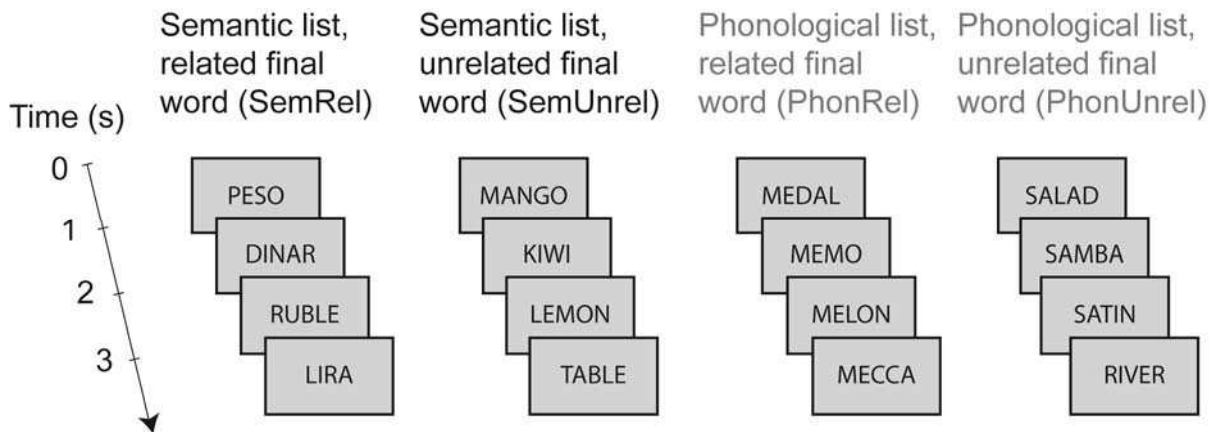

Figure 2. *Stimuli of Studies I–II. Examples of the four types of word lists (actual stimuli were in Finnish). The same word lists were presented aurally in Study I and visually in Study II.*

Semantic processing was contrasted with phonological analysis. In typical phonological priming experiments the prime and the target share phonemes (*e.g.*, Rugg and Barrett, 1987). Our study included phonological lists in which the words had the same initial phonemes but were not related semantically. If suppression/increase is specific to semantic processing, it should not appear for the phonological lists.

In Study I, we measured MEG evoked responses while 10 participants were listening to the four types of word lists. Prominent, bilateral activation of the superior temporal cortex was detected in all participants and, as suggested by previous neuroimaging data, this activation was sensitive to both meaning and sound form of spoken words. However, the role of each hemisphere varied over time: The left superior temporal activation was sensitive to phonological priming at ~100 ms, followed by sensitivity to semantic priming from ~250 ms onwards, see Figure 3. From ~450 ms onwards, semantic effects were present bilaterally, accompanied by a subtle late effect of sound form in the right hemisphere.

The results of Study I thus suggest that the middle part of the left superior temporal cortex is involved in processing the sound form of spoken words from ~100 ms onwards and in processing the meaning of spoken words from ~250 ms onwards. Thereafter, analysis continues in the bilateral superior temporal cortex at ~450–800 ms. This detailed spatiotemporal characterization of analysis of sound form and meaning in speech perception provides the fine structure that may underlie the activation patterns obtained using temporally or spatially less sensitive neuroimaging methods.

Study II: Cortical processing of meaning and sound form of written vs. spoken words

Study II aimed at characterizing the differences and similarities of cortical dynamics of reading and speech perception. Retrieval of word meaning from the semantic system and its integration with context are often assumed to be shared by spoken and written words, and neuroimaging experiments have indicated overlapping activation in reading and speech perception. Nevertheless, a direct comparison of the cortical activation sequences of visual and auditory word comprehension in the same brain has still been lacking. In Study II, we compared neural correlates of lexical-semantic and phonological processing for written and spoken words in the same individuals using MEG. The MEG data measured during the reading task in Study II was compared with the auditory data measured in Study I in the same paradigm and participants.
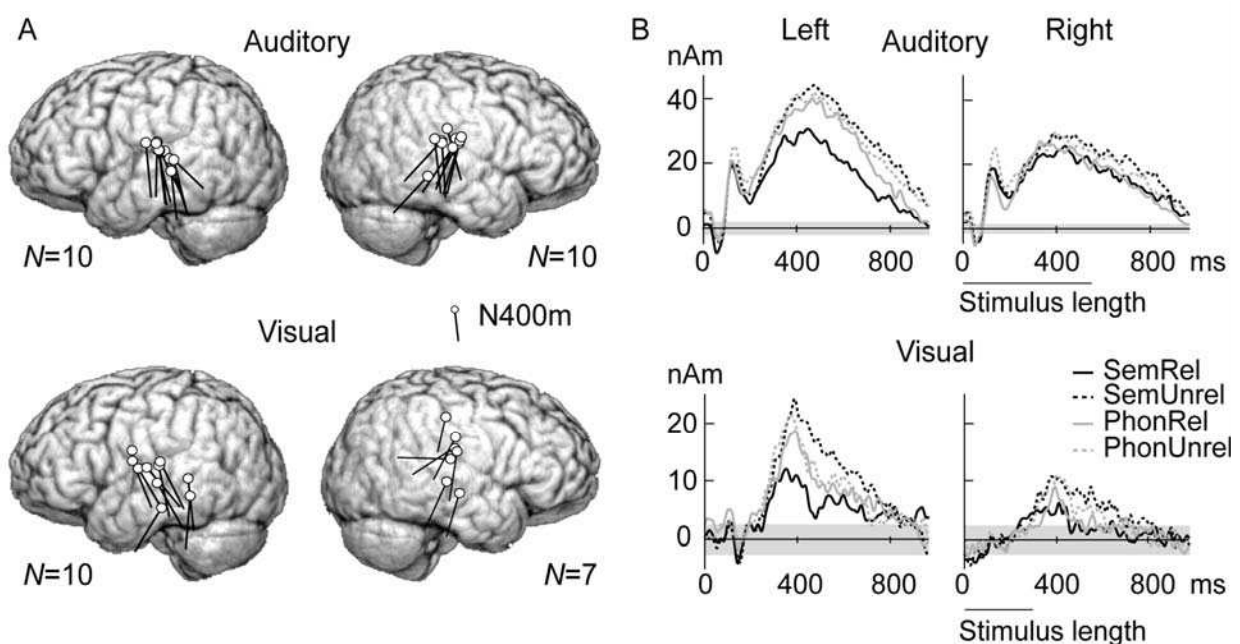

Figure 3. *Main results of Studies I–II. A Superior temporal activation in response to the spoken (top row) and written (bottom row) word lists. The white circles indicate the individual N400m source locations, as revealed by the ECD analysis. B Source waveforms that represent the time-course of activation in the left and right superior temporal cortex. Responses are depicted to the list-final word, showing the semantic and phonological priming effects (SemUnrel > SemRel, PhonUnrel > PhonRel). The gray horizontal bar indicates the noise level (±2 SD of the signal level during the 200-ms period immediately preceding the list onset).*

The main result of Study II was the spatiotemporal convergence of semantic processing in reading and speech perception. We found that the middle part of the left superior temporal cortex is involved in semantic processing of both written and spoken words from ~300 ms onwards, see Figure 3. Effect of sound form was detected in the superior temporal cortex as well, and it preceded the semantic effect in speech perception (at ~100 ms) but not in reading (at ~300 ms).

Semantic priming effects for written and spoken words, when measured in the same individuals in the two input modalities, were similar in function, timing, general location and lateralization. This

result is consistent with previous EEG and MEG data from separate auditory (*e.g.*, Connolly and Phillips, 1994; Helenius *et al.*, 2002) and visual (*e.g.*, Helenius *et al.*, 1998; Kutas and Hillyard, 1980) experiments. The data point to shared neural representation of word meaning between the two modalities that has been suggested by word processing models (*e.g.*, Patterson and Shewell, 1987; Seidenberg and McClelland, 1989).

Activation associated with semantic processing was found in the superior temporal cortex in agreement with previous MEG studies (*e.g.*, Helenius *et al.*, 1998; Mäkelä *et al.*, 2001; Pylkkänen *et al.*, 2006; Simos *et al.*, 1997), but in contrast with hemodynamic data that typically show overlap between modalities in semantic tasks in the frontal cortex, particularly in the left inferior frontal gyrus (Booth *et al.*, 2002; Chee *et al.*, 1999). Study III focused on this and other differences detected between the MEG and hemodynamic results in reading.

Study III: Reading as revealed by MEG and fMRI

MEG and fMRI have provided partly differing views of reading. In Study III we investigated whether they yield a similar activation pattern when the paradigm, language, and participants are the same. We measured MEG and fMRI while 15 participants were performing a reading task. The paradigm was constructed by merging previous MEG and fMRI reading paradigms that have elicited responses to letter-strings in the left occipito-temporal cortex (Cornelissen *et al.*, 2003; Tarkiainen *et al.*, 1999; Cohen *et al.*, 2000; Cohen *et al.*, 2003) and it was optimized in pilot experiments to yield good signal-to-noise ratio in both MEG and fMRI. The subjects were shown mini-blocks of 7 Finnish words, pseudowords, consonant strings, symbol strings, and words embedded in noise, see Figure 4 A. The task was to attend to the stimuli and to press a button whenever an immediate repetition of a stimulus occurs. EEG was measured simultaneously with MEG and fMRI to evaluate whether the participants performed the task similarly in both recordings. We compared results obtained using analysis approaches that are typically employed in reading experiments: evoked responses were analyzed in MEG and EEG, and BOLD responses in fMRI.

The main result of Study III was the divergent activation pattern revealed by MEG and fMRI in reading. Functional and spatial differences between MEG and fMRI emerged in several cortical regions although the simultaneously measured EEG responses indicated that the participants were performing the task similarly during the two recordings.

In the left occipito-temporal cortex, MEG and fMRI showed clearly diverging functionality, see Figure 4 B. In line with previous MEG data, the MEG responses in this region at ~150 ms were stronger to letter strings than to symbol strings (letter-string responses; Cornelissen *et al.*, 2003; Tarkiainen *et al.*, 1999). In contrast, fMRI BOLD responses in the same location were stronger to symbol strings than to letter strings, in line with previous fMRI data (Brem *et al.*, 2009). fMRI showed no differences between words and consonant strings in the LOTC, in agreement with earlier fMRI studies that have employed similar type of reading tasks (Cohen *et al.*, 2003; Tagamets *et al.*, 2000).

In the frontal and temporal cortex, Study III revealed the typical pattern of activation with prominent fMRI activation in the left inferior frontal gyrus and prominent MEG activation in the left superior temporal gyrus in response to linguistic stimuli (see Figure 5; Jobard *et al.*, 2003;

Salmelin, 2007). The weak frontal activation detected in MEG did not differentiate between stimulus types, unlike the fMRI activation in the left inferior frontal gyrus. In the superior temporal gyrus, MEG responses were enhanced to words and pseudowords as compared with consonant strings whereas fMRI activation in the same location was detected when contrasting letter strings to symbols and noisy words.
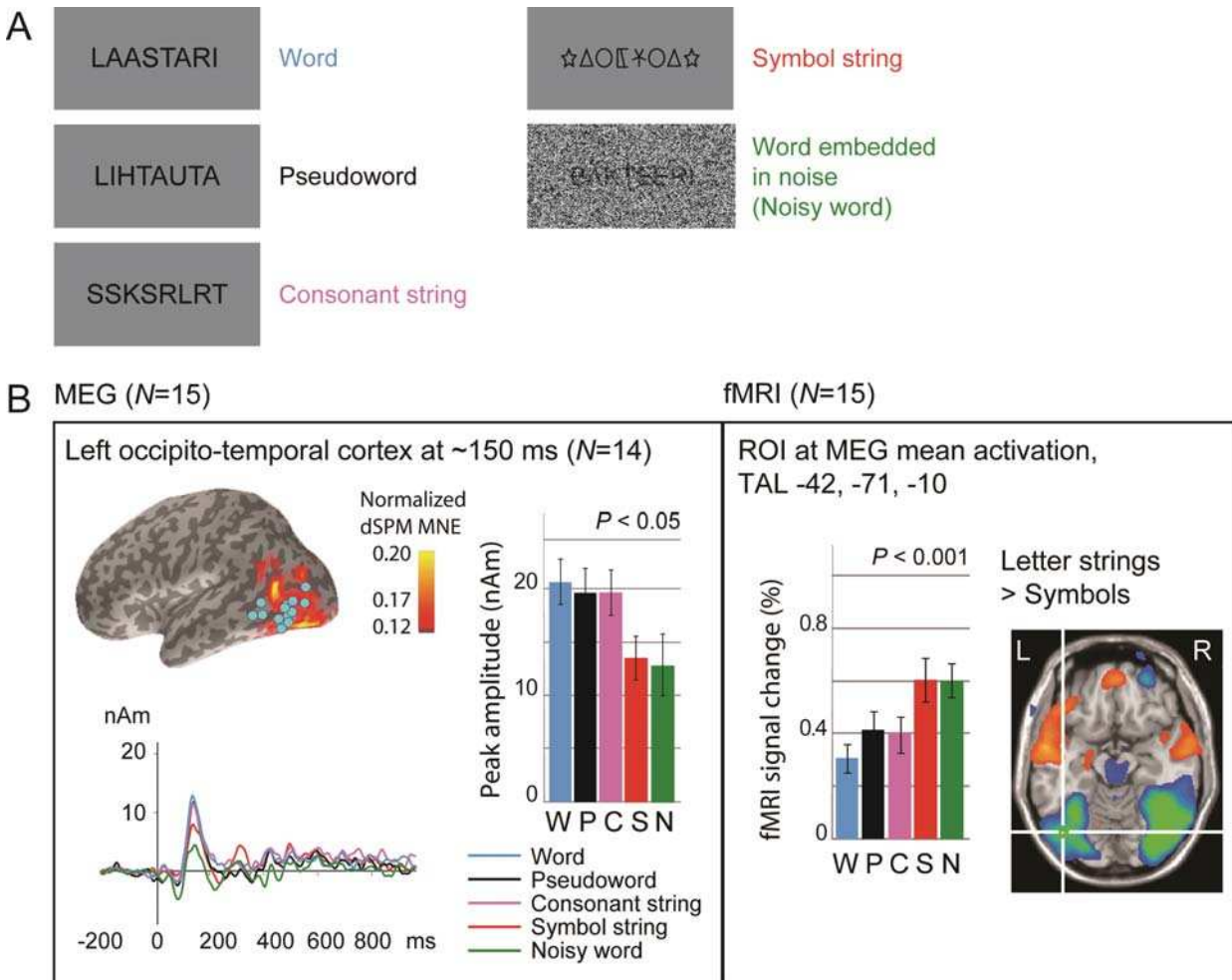

Figure 4. *Stimuli and main results of Study III. A Stimuli. B Example of the diverging MEG and fMRI results: MEG and fMRI activations of the same individuals in the left occipito-temporal cortex.*

The results demonstrate differences between fMRI and MEG that cannot be attributed to variation in the experimental procedures or subjects' performance since these factors were controlled. In particular, the enhanced left inferior frontal activation to words was absent in MEG but was detected in fMRI despite the one-back task that does not require explicit semantic processing of the stimuli. Therefore, the lack of systematic frontal MEG activation in silent reading (*e.g.*, in Studies II and III) cannot be explained solely by the implicit semantic tasks typically used in the MEG reading experiments. The MEG and fMRI data of Study III were in agreement with earlier MEG and fMRI findings, respectively. Study III thus verified the differences suggested by evaluation of previous MEG and fMRI studies.
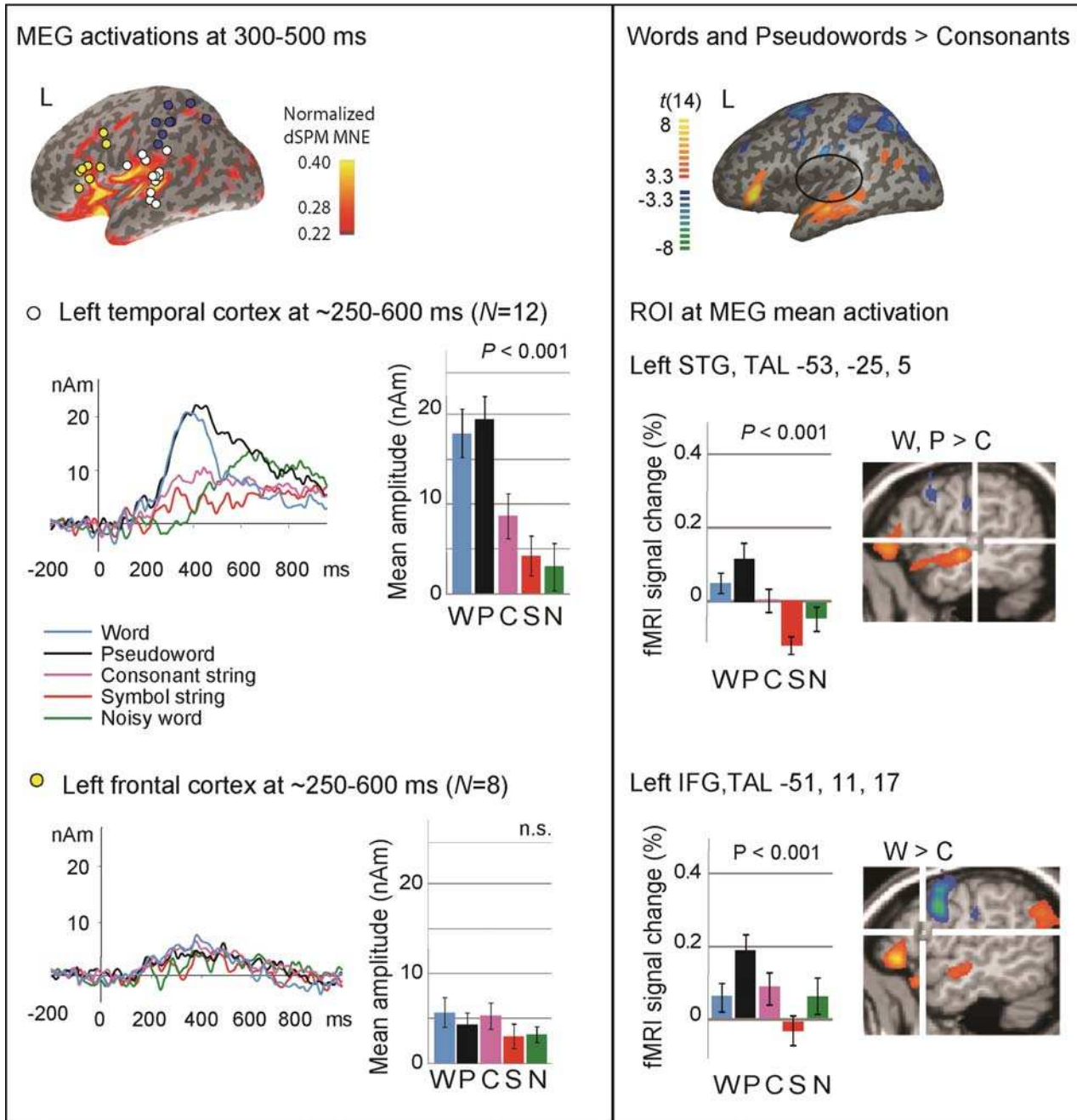
Figure 5. *Main results of Study III. Examples of the diverging MEG and fMRI results: MEG and fMRI activations of the same individuals in the left temporal and frontal cortex. The black ellipse on the fMRI contrast image indicates the approximate location of the left temporal MEG activation.*

Several possible causes for the diverging MEG and fMRI results exist and should be explored in future studies. For example, fMRI activations appear to be more sensitive to attentional modulation and task demands than the MEG evoked responses. In the left occipito-temporal cortex, in particular, the stimulus effects on MEG evoked responses seem to be fairly insensitive to the task demands (Cornelissen *et al.*, 2003; Salmelin *et al.*, 1996; Tarkiainen *et al.*, 1999) whereas hemodynamic effects in this region seem to be task-dependent (Cohen *et al.*, 2003; Furey *et al.*, 2006; Starrfelt and Gerlach, 2007; Vinckier *et al.*, 2007). Due to the slow generation of the

hemodynamic response (several seconds), the fMRI signal integrates activation from a long time interval and may therefore emphasize long-lasting activations that may mask brief but synchronous MEG activations seen in early time windows (Furey *et al.*, 2006; Im and Lee, 2006).

If the fMRI signals are dominated by late, long-lasting neural activation (Cornelissen *et al.*, 2003), they may be more susceptible to top-down modulation than the MEG evoked responses that may emphasize the early bottom-up processing of written words to a higher degree. This could explain the divergence of the MEG and fMRI effects in the left occipito-temporal cortex observed in Study III. In the one-back reading task employed in Study III, the participants may have attended the more demanding stimulus categories (Symbols and Noisy words) more carefully, resulting in an increase of the fMRI activation in the left occipito-temporal cortex. Interestingly, a similar dissociation of electrophysiological and hemodynamic effects in this region was detected in a recent EEG-fMRI reading experiment (Brem *et al.*, 2009).

It is also possible that since MEG detects synchronous activation of neurons, non-synchronous electrical activation, that may well generate considerable metabolic requirements, would remain undetected with MEG but could be reflected in the fMRI BOLD signal. Furthermore, if the neural responses are not accurately time- and phase-locked to the stimulus, they would not show in the MEG evoked responses but could be seen as changes in cortical rhythms or in fMRI. In some specific situations, the orientation or location of the electrical activation may also be such that it produces little electromagnetic field outside of the head (radially oriented or deep sources in MEG). Therefore, utilization of the EEG data in the source localization could, in principle, reveal some additional electrical activation.

In conclusion, the results of Study III suggest that the diverging fMRI and MEG results in reading reflect actual differences in the sensitivities of these methods. Next, having verified that the observed differences are not due to variation in experimental procedures, the investigation can focus on the causes underlying the diverging activation patterns. It will also be important to ask whether one can identify other electromagnetic and hemodynamic markers that would yield more similar results than the evoked responses and the BOLD signals.

Study IV: Morphological processing in reading

In Study IV, we investigated the neural correlates of morphological processing in the morphologically rich Finnish language. It is not well known how morphologically complex words are represented and processed in the brain. Previous behavioral studies in Finnish have indicated a processing cost (more errors and slower recognition times; Hyönä *et al.*, 1995; Laine *et al.*, 1995; Laine *et al.*, 1999; Niemi *et al.*, 1994) for inflected words. Theoretically, this effect could stem either from decomposition of inflected words into a stem and a suffix at input level and/or from subsequent recombination at the semantic-syntactic level to arrive at an interpretation of the word. In order to clarify the neural correlates of these assumed processing stages, we used MEG to reveal the time-course and localization of neural effects of morphological structure and frequency of written words. Ten participants silently read high- and low-frequency Finnish words in inflected and monomorphemic form during the MEG recording, see Figure 6.
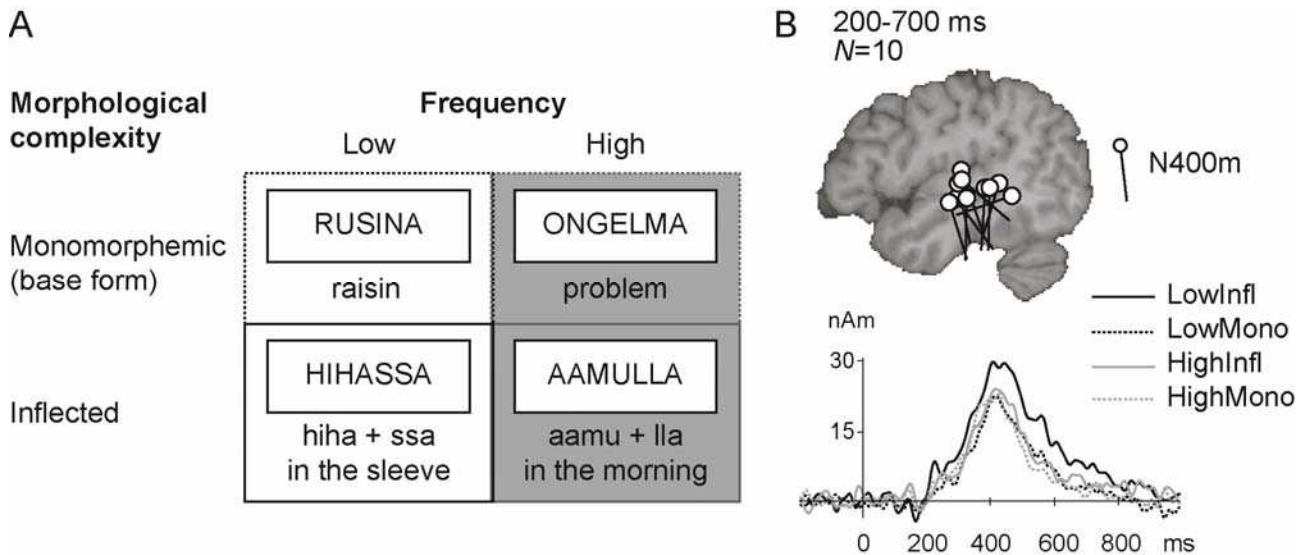
Figure 6. *Stimuli and the main result of Study IV. A Examples of the four types of word stimuli. B Effect of morphological structure and word frequency on the left superior temporal activation.*

The results of Study IV showed that the middle part of the left superior temporal cortex is involved in processing of morphologically complex written words at ~200–700 ms. Previous MEG and EEG studies of reading have associated activation in this region and time window with lexical-semantic analysis (*e.g.*, Helenius *et al.*, 1998; Kutas and Hillyard, 1980; Pylkkänen *et al.*, 2006), morphosyntactic processing (Barber and Carreiras, 2003; Service *et al.*, 2007) and analysis of phonological structure (*e.g.*, Helenius *et al.*, 1998; Rugg, 1984; Wydell *et al.*, 2003). Thus, the present effects of morphology most likely reflect more demanding analysis of morphologically complex than monomorphemic words at the semantic-syntactic or phonological level rather than pre-lexical visual or orthographic processing. Access to the meaning of the parts constituting the complex word separately, as opposed to meaning of the whole word alone, may require additional neural processing. The combination of these meanings into a temporary representation may additionally burden and delay the neural processing. These assumed processing costs may explain the increased and lengthened neural responses to morphologically complex words.

Similarly as for semantic processing in the Studies I–II, MEG data revealed no activation in the frontal cortex that would have been sensitive to morphological complexity. This result is in contradiction with fMRI data on the Finnish language (Lehtonen *et al.*, 2006; Lehtonen *et al.*, 2009) and other languages (*e.g.*, Jaeger *et al.*, 1996; Yokoyama *et al.*, 2006) that have revealed effects of morphology in the left inferior frontal gyrus.

Earlier effects of morphology were not found, supporting the view that the behavioral processing cost for inflected words stems from the semantic-syntactic level rather than from early decomposition. The present data together with previous results (Lehtonen *et al.*, 2007; Lehtonen *et al.*, 2006; Lehtonen *et al.*, 2009; Leinonen *et al.*, 2009), gathered altogether from over fifty individuals using two different reading tasks, provide compelling evidence for a late morphological effect in the temporal cortex and for the lack of early effects in the Finnish language. One possible explanation for the lack of early neural effects of decomposition is that, irrespective of morphological complexity, the system automatically attempts to map orthographic input representations with both the whole input string and its parts (*e.g.*, the monomorphemic word

canvas might not only activate the orthographic representations for canvas but also for can- and –s). The present experimental design would, thus, not yield any clear differences in the corresponding early neural responses between inflected vs. monomorphemic words. The lack of early effects is unlikely to be explained by slightly varying boundary locations between the stem and the affix since the relatively short written words that were used in the Study IV typically fit in a single fixation.

Since the effect of morphology was detected throughout the range of word frequencies employed, the majority of inflected Finnish words appears to be represented in decomposed form and only very high-frequency inflected words may acquire full-form representations.

Study V: Parafoveal preview in reading

In natural reading, several words appear in the visual field simultaneously. Although visual acuity is highest for the word that is being fixated and seen in the foveal vision, information about the neighboring words is available in the less accurate parafoveal vision. Reading times have been found to increase when pre-exposure to the words in the parafoveal vision is not possible (Blanchard *et al.*, 1989), suggesting that the parafoveal preview contributes to fluent reading in natural conditions. Yet, the neural correlates of reading are mostly studied with foveally presented stimuli and little is known of the parafoveal influence on them. Study V investigated how the parafoveal preview of words affects foveal reading.

We used a parafoveal-on-foveal priming paradigm that refers to the presentation of a prime in the parafoveal vision followed by the presentation of a target in the foveal vision. This paradigm simulates natural reading where the prime word seen in the parafoveal vision becomes the target word after a saccade is performed toward the prime. It is often assumed that the neural effects in a priming paradigm result from repeated activation of a common neural representation by the prime and the target. According to this view, a parafoveal priming effect (*e.g.*, attenuation of the neural response) would indicate that the neural representations of the parafoveal prime and the foveal target overlap in the brain region and time-window where the priming effect is detected. In Study V, we measured behavioral and MEG responses in a parafoveal-on-foveal priming paradigm and compared them with foveal-on-foveal priming. In the behavioral experiment, a word or a non-word was first presented either foveally, in the left visual field (LVF), or in the right visual field (RVF). After a delay of 50 or 100 ms, a target word or non-word was presented. The MEG experiment sought to identify the neural correlates of the priming effects detected in the behavioral data, focusing on word targets with a 50 ms delay, see Figure 7.

Both the behavioral and MEG results showed differences between parafoveal-on-foveal priming and foveal-on-foveal priming. Behavioral parafoveal priming effects were detected only for a very short time delay between prime and target (50 ms) whereas foveal priming was not influenced by the delay duration. The persistence of the neural activation may provide an explanation for the strong and long-lasting foveal priming effect and the weaker and short-lasting parafoveal priming effect. It may be hypothesized that, in addition to the bottom-up activation, the foveally presented prime words activate a feedforward-feedback loop maintaining activation. This could result in a strong and sustained priming effect for the subsequently presented foveal target word that activates the same representations. In contrast, the parafoveal prime words may be unable to launch the recurrent loop of activation and elicit only short-lasting bottom-up activation.
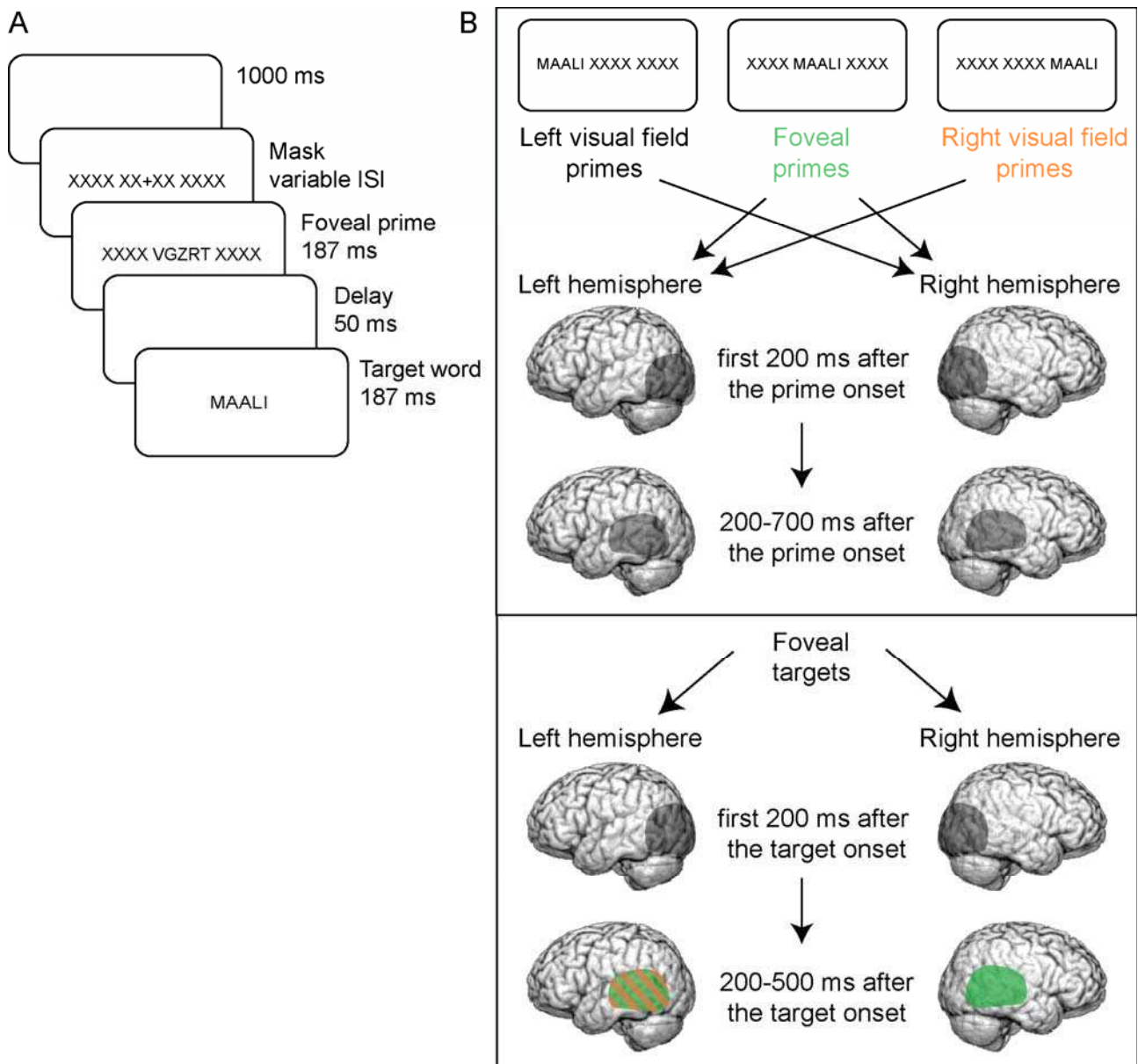
Figure 7. *Stimuli and the main results of Study V. **A** An example of a stimulus trial used in the MEG experiment with an incongruent prime-target pair. **B** Schematic presentation of the cortical regions activated by the prime and target words. The green and orange color indicate the approximate regions and time-window in which the MEG activation was affected by foveal and RVF priming, respectively.*

After the initial visual analysis of the parafoveal and foveal prime words in the right, left, or bilateral occipital cortex, the overall neural sequence of activation was similar for foveal and parafoveal primes followed by foveal target words. However, the priming effects detected at ~160–460 ms after the target onset mainly in the occipito-temporal and superior temporal cortex were bilateral for the foveal primes versus left-lateralized for the parafoveal RVF primes. This result is in line with neuroimaging data that have associated these left-hemisphere regions with abstract representations of words rather than low-level perceptual representations that could be dependent on the location of the word in the visual field (*e.g.*, Dehaene *et al.*, 2005). However, it remains open why the right superior temporal activation in the same time window was sensitive to foveal priming only.

No neural effects of priming appeared for the LVF primes, suggesting that words seen in the parafoveal vision activate neural representations overlapping with those of foveally presented words only when presented in the RVF. The result may reflect learned preference for the words visible in the right visual field in the Western writing system.

In conclusion, the results indicate that neural processing of written words in the left hemisphere is affected by preview of words in the right visual field. The underlying neural mechanism may facilitate reading of connected text in natural conditions.

4. Discussion and conclusions

The present work draws together several lines of research by examining language perception in the same individuals in the visual and auditory input modality and using MEG, fMRI, and EEG. The two main findings of the Thesis were (i) the convergence of semantic processing in reading and speech perception to the left superior temporal cortex at ~300 ms and (ii) the different activation patterns detected with MEG and fMRI in reading.

Convergence of semantic processing to the superior temporal cortex in reading and speech perception

Our MEG results on the cortical dynamics of written and spoken word perception (Studies I–II) showed that the bilateral superior temporal cortex is a particularly important region in language perception and comprehension. The results indicate that, following initial modality-specific analysis, processing of written and spoken words converges to the left superior temporal cortex. Processing of meaning in the superior temporal cortex occurs similarly (timing, general location, lateralization) for written and spoken words. The data thus support a view of a largely shared semantic system in auditory and visual language perception, in line with the assumption that reading acquisition makes use of the neural systems originally developed for speech perception during evolution and refined in individual language development.

Time-line of reading and speech perception

The present MEG data adds new information to the time-line of language perception in the brain. Figure 8 summarizes the cortical sequence of activation in response to written and spoken words, based on the present data and previous evidence.

Our MEG experiments in Studies I–II focused on the late processing stages (~250 ms onwards) that might be shared by written and spoken language. The MEG responses in the left temporal cortex were sensitive to semantic manipulations of the stimulus words at ~300–450 ms, indicating that information about the word meaning must be available at this time, at the latest. The semantic activation occurred within the time window that has been suggested to still reflect bottom-up access to the memory representations of the words (*e.g.*, Lau *et al.*, 2008); however, other authors have suggested that lexical access occurs earlier (*e.g.*, Hauk *et al.*, 2006). Possibly the existing data could be explained by assuming that at ~300–450 ms access to the word representations has begun but is not completed.
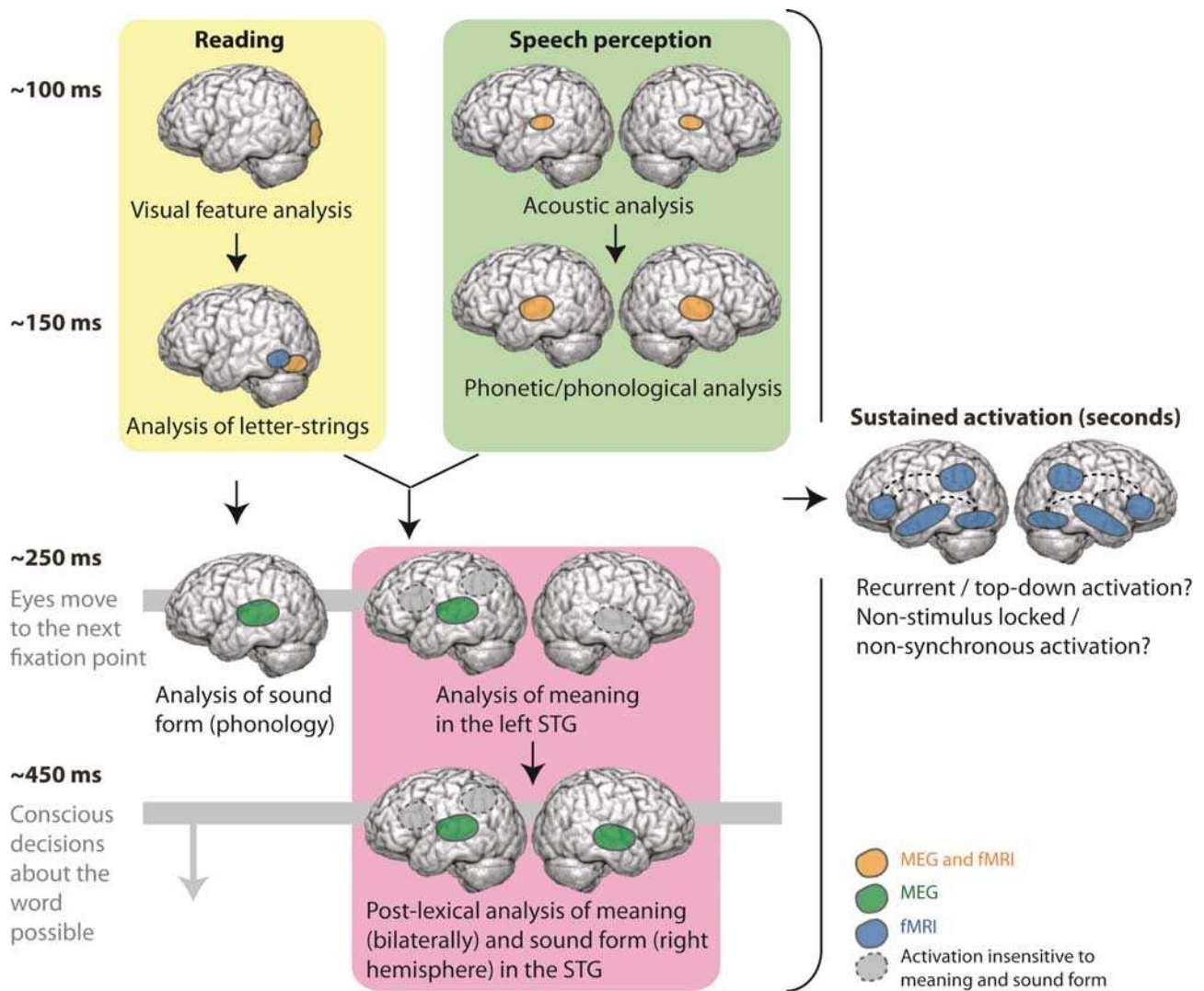
Figure 8: *Overview of the neural correlates of reading and speech perception based on the present findings and previous data (e.g., Hickok and Poeppel, 2004; Salmelin, 2007; Vinckier et al., 2007).*

We detected sensitivity to the sound form of written and spoken words in the superior temporal cortex as well. The results suggest that for spoken words the analysis of sound form begins before analysis of meaning (at ~100 ms) whereas for written words phonological and semantic information become available simultaneously (at ~300 ms). As regards timing, these results are in keeping with models of spoken word processing that suggest analysis of sound form of spoken word at acoustic-phonetic and possibly at phonological level prior to lexical-semantic processing (Patterson and Shewell, 1987) and with models of reading that suggest simultaneous semantic and phonological processing of written words via direct and phonologically mediated routes (dual-route model Coltheart *et al.*, 1993; connectionist model Harm and Seidenberg, 2004).

From ~450 ms onwards, MEG activation to written and spoken words was detected bilaterally in the superior temporal cortex with sensitivity to both meaning (bilaterally) and sound form (in the right hemisphere). This activation is likely to reflect post-lexical integration of all available information in the context created by the preceding words, as behavioral data indicate that both

written and spoken words can be recognized within ~500 ms or less (*e.g.*, Balota *et al.*, 2004; Tyler *et al.*, 2002).

Based on the results of Studies I–II, the enhanced activation to morphologically complex written words observed in Study IV can be understood as increased semantic and/or phonological processing demands for the morphologically complex words. Enhanced activation was detected in the left superior temporal cortex at ~200–700 ms, thus overlapping with the assumed time windows of lexical-semantic access and post-lexical integration. Accordingly both lexical access and post-lexical processing of morphologically complex words appear to require additional neural resources.

MEG data of Study IV together with previous behavioral and neuroimaging data (*e.g.*, Gold and Rastle, 2007) suggest that morphologically complex words are decomposed. It remains unclear why the early decomposition does not typically show in the brain responses. At present, it is not fully understood how the recognition of a written word begins and which representation levels are implemented in the brain. According to the hierarchical model suggested by Dehaene *et al.* (2005) neurons in the posterior-anterior axis of the left occipito-temporal cortex are tuned to increasingly larger fragments of words. Since short words and recurring substrings, such as morphemes, are suggested to be represented in the anterior parts of the left occipito-temporal cortex (Dehaene *et al.*, 2005), activation of this region could show sensitivity to morphological structure of words in neuroimaging experiments. However, words we read cannot be labeled as complex or simple prior to neural processing, and therefore, the earliest stages of written word recognition may well proceed similarly for all letter strings (real words and pseudowords, morphologically complex and simple words). Detailed characterization of the early stages of written word perception could also clarify how the morphologically complex words are decomposed in the brain.

MEG vs. fMRI activations in reading

MEG experiments in Studies I–V all showed activation to written or spoken words in the bilateral superior temporal cortex but showed little or no activation in the frontal cortex. This pattern is in line with previous MEG experiments but diverges from the existing fMRI data that have consistently shown activation sensitive to semantic, phonological, and morphological manipulations in the left inferior frontal cortex. Study III indicates that this diverging activation pattern in MEG vs. fMRI studies of reading appears although the same participants are performing the same task. Study III indicated functional and localization differences in the left occipito-temporal, bilateral temporal and parietal cortex as well, in line with previous, separate MEG and fMRI studies. The divergent results cannot be attributed to differences in the experimental procedures or language since these factors were controlled but rather they appear to reflect different generation mechanisms of the MEG evoked responses vs. fMRI BOLD signals.

At present, the timing and functional significance of the fMRI activation detected in the frontal cortex remain unclear. Based on the present and previous data (Cohen *et al.*, 2003; Furey *et al.*, 2006; Tagamets *et al.*, 2000), it appears that fMRI activation is more susceptible to top-down modulation and task demands than the MEG evoked responses that may emphasize bottom-up processing of written words to a higher degree. One possibility is that some of the fMRI activations reflect sustained top-down modulatory signals, as depicted in Figure 8. However, it seems that bottom-up processing can be emphasized in fMRI by selecting a task that does not allow long processing times and conscious strategies (Vinckier *et al.*, 2007).

The superior temporal gyrus and inferior frontal gyrus that systematically appear activated in MEG and fMRI experiments of reading, respectively, are anatomically connected. In monkeys, the homologue regions are connected via two pathways: the extreme capsule running anterior from the STG and the middle and superior longitudinal fasciculus running posterior from the STG to the temporo-parietal junction and to the inferior frontal gyrus (Petrides and Pandya, 2009). Similar anatomical connections have been suggested to exist in the human brain (Petrides and Pandya, 2009). It seems likely that written and spoken words evoke activation in a wide network of connected brain regions, including the superior temporal and inferior frontal gyri. Possibly, MEG evoked responses and fMRI BOLD signals emphasize different parts of this network due to the different sensitivities of the two methods. In line with this interpretation, frontal regions do appear as nodes in MEG functional connectivity analysis in silent reading (Kujala *et al.*, 2007).

MEG evoked responses and fMRI BOLD signals are typically used as a measure of neural activation when studying cognitive functions like reading and speech perception. The results of Study III point out that when interpreting results obtained with these neuroimaging techniques, it should be kept in mind that each measured quantity can provide only a limited view on the neural processing (*e.g.*, metabolic vs. electrical activity, short- vs. long-lasting activity, processing within a region vs. input to or output from a region) and that the origins of the BOLD signal are not well known. Study III was an essential step towards more accurate interpretation of the neuroimaging results on reading. Next, having established the differences between the commonly used measures of MEG evoked responses and fMRI BOLD signal, it can be asked what exactly do these measures reflect and whether one can identify electromagnetic and hemodynamic markers that would yield more similar results. Optimally, the complementary information obtained with MEG and fMRI could be combined to build a more accurate view of the neural basis of reading and speech perception.

Conclusions

The MEG, fMRI, and EEG data measured in this Thesis suggest that:

(i)   Processing of written and spoken word meaning converges to the left superior temporal cortex at ~300 ms. The data support a view of a largely shared semantic system in auditory and visual language perception, in line with the assumption that reading acquisition makes use of the neural systems originally developed for speech perception.

(ii)   The left superior temporal cortex is involved in processing the sound form of the spoken and written words. For spoken words the analysis of sound form begins before analysis of meaning (at ~100 ms) whereas for written words phonological and semantic information become available simultaneously (at ~300 ms).

(iii)   MEG and fMRI provide complementary measures of neural functionality in reading. MEG evoked responses and fMRI BOLD signals show marked functional and spatial divergence in a reading task and, if considered separately, lead to different interpretations of the neural correlates of reading.

(iv)   The majority of inflected Finnish words are represented in a decomposed form in the brain, and the decomposition process requires additional neural resources at ~200–700 ms, as reflected by an enhanced and prolonged activation of the left superior temporal cortex.

(v)   Neural processing of written words in the left hemisphere is affected by a preview of words in the right visual field. The underlying neural mechanism may facilitate reading of connected text in natural conditions.

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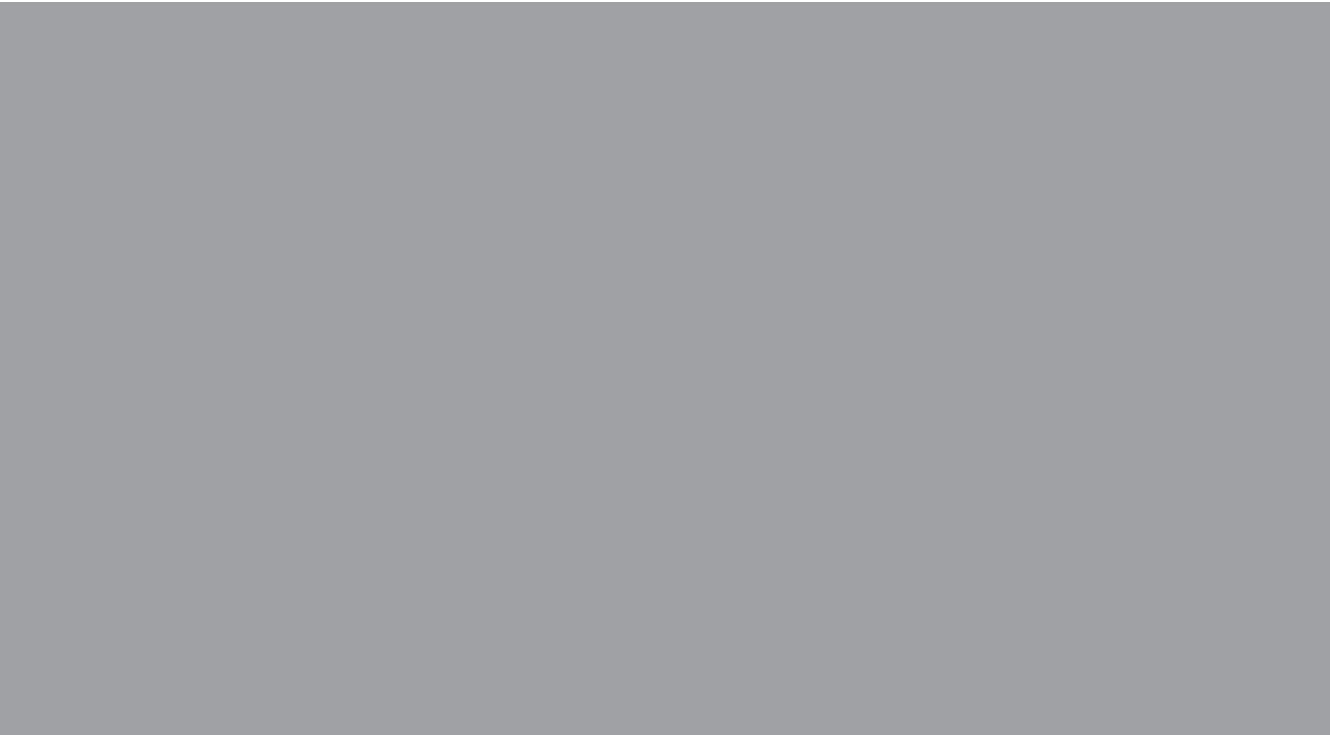
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