JYVÄSKYLÄ STUDIES IN EDUCATION, PSYCHOLOGY AND SOCIAL RESEARCH
314

Tiina Parviainen

Cortical Correlates of Language Perception

Neuromagnetic Studies in Adults and Children

JYVÄSKYLÄN YLIOPISTO

JYVÄSKYLÄ STUDIES IN EDUCATION, PSYCHOLOGY AND SOCIAL RESEARCH 314

Tiina Parviainen

Cortical Correlates of Language Perception

Neuromagnetic Studies in Adults and Children

Esitetään Jyväskylän yliopiston yhteiskuntatieteellisen tiedekunnan suostumuksella
julkisesti tarkastettavaksi yliopiston Villa Ranan Blomstedtin salissa
lokakuun 15. päivänä 2007 kello 12.

Academic dissertation to be publicly discussed, by permission of
the Faculty of Social Sciences of the University of Jyväskylä,
in the Building Villa Rana, Blomstedt Hall,, on October 15, 2007 at 12 o'clock noon.

UNIVERSITY OF JYVÄSKYLÄ

JYVÄSKYLÄ 2007

Cortical Correlates of Language Perception

Neuromagnetic Studies in Adults and Children

JYVÄSKYLÄ STUDIES IN EDUCATION, PSYCHOLOGY AND SOCIAL RESEARCH 314

Tiina Parviainen

Cortical Correlates of Language Perception

Neuromagnetic Studies in Adults and Children

UNIVERSITY OF JYVÄSKYLÄ

JYVÄSKYLÄ 2007

Editors
Tapani Korhonen
Department of Psychology, University of Jyväskylä
Irene Ylönen, Marja-Leena Tynkkynen
Publishing Unit, University Library of Jyväskylä

Cover Picture by Tiina Parviainen
Brain Image Courtesy of Mika Seppä

URN:ISBN:9789513930844
ISBN 978-951-39-3084-4 (PDF)

ISBN 978-951-39-2943-5 (nid.)
ISSN 0075-4625

Jyväskylä University Printing House, Jyväskylä 2007

ABSTRACT

Parviainen, Tiina
Cortical correlates of language perception – neuromagnetic studies in adults and children
Jyväskylä, University of Jyväskylä, 2007, 129 p.
(Jyväskylä Studies in Education, Psychology, and Social Research,
ISSN 0075-4625; 314)
ISBN 978-951-39-3084-4 (PDF), 978-951-39-2943-5 (nid.)
Yhteenveto: Kielen käsittely aivoissa – neuromagneettisia tutkimuksia aikuisilla ja lapsilla
Diss.

The end product of language perception, accessing meaning, is a result of complex computation in the human brain and presumably reflects analysis at, and transformation between, various levels of representation. In this thesis, MEG was used to characterize those representations at the neural level in adults and children. The special acoustic nature of speech was reflected in auditory cortical activation at 100 ms after sound presentation. In dyslexia, cortical organization of auditory processing, in general, was disrupted in this same time window (Study I). Meaning-based analysis of speech started at around 250 ms and was induced also by meaningless utterances, particularly when acoustic-phonetic or contextual cues predicted continuation as a word (Study IV). For complete spoken words, influence of sound form (phonology) appeared in neural activation within 250 ms, followed by neural signatures of semantic processing (Study V). Cortical activation to speech and print was similar in children and adults as regards location. However, activation sensitive to linguistic information was delayed and prolonged in children as compared with adults. Importantly, it was correlated with behavioral skills, indicating interdependence between maturing neural processes and developing linguistic skills (Studies II and III). In adults, conversion from letter to sound, an essential process in reading, engaged the superior temporal cortex. Activation increased with letter-string length, particularly with non-words (Study VI). This thesis provides new insights into the question of how mature and developing cortical circuits support the challenging but apparently effortless task of language perception and comprehension.

Keywords: Speech perception, speech comprehension, reading, neuroimaging, magnetoencephalography, N100, N400

Author’s address
Tiina Parviainen
Brain Research Unit
Low Temperature Laboratory
Helsinki University of Technology, Finland

P.O.Box 2200
02015 TKK, Finland
E-mail: tiina@neuro.hut.fi

Supervisor
Academy Professor Riitta Salmelin
Brain Research Unit
Low Temperature Laboratory
Helsinki University of Technology, Finland

Reviewers
Docent, Professeur Associée
Elisabet Service
Department of Psychology
University of Helsinki, Finland
Département de psychologie
Université de Montréal, Canada

Professor David Poeppel
Department of Linguistics
Department of Biology
University of Maryland, Washington, USA

Opponent
Professor David Poeppel
Department of Linguistics
Department of Biology
University of Maryland, Washington, USA

ACKNOWLEDGEMENTS

This work was carried out in the Brain Research Unit of the Low Temperature Laboratory within Helsinki University of Technology. I would like to thank all the people who made it possible for me to work in this inspiring environment. I'm grateful to the head of the laboratory, Prof. Mikko Paalanen, for providing the research facilities and for his support throughout my work. I also had the possibility to meet the former head, Academician Olli Lounasmaa, who had a major impact in creating this interdisciplinary unit with its high scientific ambitions. I am very grateful to the head of the Brain Research Unit, Prof. Riitta Hari, for her friendly support and interest to my work and for providing an open-minded and creative environment for research.

I am deeply indebted to my supervisor, Prof. Riitta Salmelin, who has guided me into the world of MEG with highest expertise and detail. She has had the most important impact on my work in LTL with admirable enthusiasm and systematic research approach. I would like to express my warmest gratitude to Dr. Päivi Helenius, who has patiently and kindly advised me with all the questions in scientific work. Her thorough and productive contribution has been of invaluable importance for this thesis.

I am deeply grateful to my former supervisor Prof. Heikki Lyytinen at the Department of Psychology in the University of Jyväskylä, for a crucial contribution in my first steps into brain research during my undergraduate studies. His encouragement and support has been important throughout my PhD work.

My interest in the field of neuroscience really started during my internship in the Neurological Department, Jyväskylä Central Hospital. I wish to warmly thank Ms. Ritva Hänninen, Ms. Kaija Poutanen and Mr. Pekka Kuikka, for introducing me to the mysterious and fascinating functions of the human brain.

I sincerely thank Prof. David Poeppel and Doc. Elisabet Service, for their valuable comments and suggestions on the manuscript of this thesis. I also would like to warmly thank Dr. Hanna Renvall, Mr. Topi Tanskanen and Mr. Lauri Parkkonen for useful comments and Dr. Jane Erskine for correcting my English. I am grateful to Dr. Ritva Paetau and Prof. Heikki Lyytinen, who formed my follow-up group, for insightful discussions during the thesis work.

I wish to express my gratitude to all my co-authors, Dr. Milene Bonte, Dr. Päivi Helenius, Ms. Kaisa Hytönen, Ms. Marianne Inkinen, Prof. Pekka Niemi, Dr. Elisa Poskiparta, Ms. Johanna Vartiainen and Prof. Taeko Wydell for inspiring collaboration. It has been a pleasure to work with all of you.

The most important impact both for the general atmosphere and for my personal well-being in the laboratory has been provided by the fellow students at the LTL. I am especially grateful to my long-time room-mate Timo Saarinen for providing a clear-sighted perspective and a pleasant company for everyday work. I also want to sincerely thank Topi Tanskanen, Hanna Renvall, Lauri Parkkonen and Jan Kujala for always being there when needed – be it a

neuroscientific, technical, statistical, psychological, philosophical, or personal issue. Our discussions have given me valuable insights into my work and, when needed, fully detached me from brain research. I sincerely thank Johanna Vartiainen for her contagious positive attitude. Big thanks to the whole social group! The value of getting to know you is way above this bunch of papers.

I wish to thank all the past and present colleagues in the Brain Research Unit for the supportive and expert environment in the laboratory. I sincerely thank Maarit Aro, Sari Avikainen, Gina Caetano, Katri Cornelissen, Nina Forss, Nobuya Fujiki, Liisa Helle, Linda Henriksson, Jaana Hiltunen, Yevhen Hlushchuk, Annika Hulten, Matti Hämäläinen, Antti Jalava, Ole Jensen, Veikko Jousmäki, Juha Järveläinen, Jaakko Järvinen, Marika Kaksonen, Ken-Ichi Kaneko, Marita Kattelus, Erika Kirveskari, Hannu Laaksonen, Satu Lamminmäki, Sari Levänen, Martin Lehécka, Mia Liljeström, Sasu Liuhanen, Sanna Malinen, Seppo Mattila, Jyrki Mäkelä, Jussi Numminen, Miika Pihlaja, Marjatta Pohja, Antti Puurula, Tommi Raij, Tuukka Raij, Ville Renvall, Miiamaaria Saarela, Stephan Salenius, Ronny Schreiber, Martin Schürmann, Mika Seppä, Teija Silen, Cristina Simões-Franklin, Jaana Simola, Sini Sipponen, Päivi Sivonen, Linda Stenbacka, Antti Tarkiainen, Samu Taulu, Kimmo Uutela, Simo Vanni, Nuutti Vartiainen and Minna Vihla. I also wish to thank Flamine Alary, Sandra Smeets and all the other visitors who have contributed to the atmosphere of the LTL.

I am grateful to Mr Helge Kainulainen, Doc. Peter Berglund, Ms. Teija Halme, Ms. Marja Holmström, Ms. Pirjo Kinanen, Ms. Tuire Koivisto, Ms. Satu Pakarinen, Ms. Liisi Pasanen and Ms. Leena Meilahti for being patient with me and always helping me with practical issues. I owe big thanks also to Ms. Raija Mehto at University of Jyväskylä for all her help in my PhD studies, especially within the final stage. I am especially grateful to Ms Mia Illmann for her help in the MEG-measurements and to Mr. Samuli Hakala, Mr. Jan Kujala, Dr. Mika Seppä, and Dr. Antti Tarkiainen for their help in solving numerous technical problems.

I would like to thank for the European Union 5th framework program, Finnish Cultural Foundation, Ella and Georg Ehrnrooth Foundation, Sigrid Juselius Foundation and Academy of Finland for the financial support of my work.

This work would have not been possible without the contribution of the subjects recruited from outside the laboratory. I warmly thank all the adults and children taking part in my studies.

I wish to warmly thank all of my friends for still being my friend although I never answer the phone! A special thanks for Donagh Coleman for the inspiring discussions on the issues between brain and reality.

I will always be grateful to my parents Riitta and Jouni Vuorinen, as well as my brothers Jussi, Mikko and Ilkka and sister Hanna-Maija for supporting me in every step of my life. Together with all of the in-laws and the younger generation they give a complete and most enjoyable escape from scientific work. A big hug to Tuire for invaluable help within the final stage of this work.

Finally, I thank my dear husband Jukka, for his love and understanding during all these years. He has given me invaluable support throughout my studies but most importantly he helped me to set the correct balance between research and real life. Most efficient in this latter issue is undoubtedly our sweet energetic daughter Vilja, whose enormous curiosity and delightful attitude towards the world has re-opened my eyes to the amazing things that lie also beyond brain research.

Helsinki, September 2007 Tiina Parviainen

FIGURES

TABLES

CONTENTS

LIST OF PUBLICATIONS

I Parviainen T, Helenius P, Salmelin R (2005) Cortical differentiation of speech and non-speech sounds at 100 ms: implications for dyslexia. *Cerebral Cortex 15: 1054–1063.*

II Parviainen T, Helenius P, Poskiparta E, Niemi P, Salmelin R (submitted) Speech perception in the child brain: cortical timing and its relevance to literacy acquisition.

III Parviainen T, Helenius P, Poskiparta E, Niemi P, Salmelin R (2006) Cortical sequence of word perception in beginning readers. *Journal of Neuroscience 26: 6052–6061.*

IV Bonte M, Parviainen T, Hytönen K, Salmelin R (2006) Time course of top-down and bottom-up influences on syllable processing in the auditory cortex. *Cerebral Cortex 16: 115–23.*

V Uusvuori J, Parviainen T, Inkinen M, Salmelin R (in press) Spatiotemporal interaction between phonology and semantics during spoken word perception. *Cerebral Cortex (doi:10.1093/cercor/bhm076)*

VI Wydell TN, Vuorinen T, Helenius P, Salmelin R (2003) Neural correlates of letter-string length and lexicality during reading in a regular orthography. *Journal of Cognitive Neuroscience, 15: 1052–1061.*

ABBREVIATIONS

ABR	Auditory brainstem response
AEP	Auditory evoked potential
AEF	Auditory evoked field
ANOVA	Analysis of variance
AP	Action potential
CV	Consonant vowel
ECD	Equivalent current dipole
EEG	Electroencephalography
ERP	Event related potential
fMRI	Functional magnetic resonance imaging
HG	Heschl's gyrus
Hz	Hertz
ISI	Interstimulus interval
LGN	Lateral geniculate nucleus
LS	Letter-string
MEG	Magnetoencephalography
MGN	Medial geniculate nucleus
MMN	Mismatch negativity
nAm	nanoamperemeter
PET	Positron emission tomography
PAC	Primary auditory cortex
PT	Planum Temporale
RAN	Rapid Automatized Naming test
RAS	Rapid Alternating Stimulus Naming test
SD	Standard deviation
SEM	Standard error of the mean
STS	Superior temporal sulcus
SQUID	Superconducting quantum interference device
VF	Visual feature
WISC-R	Wechsler Intelligence Scale for Children – Revised

1 INTRODUCTION

The versatile essence of language, representing one of the most characteristic features of the human species, is conveyed in the (auditory or visual) physical signal via the perceptual system. The effortless faculty of language comprehension makes the actual perception rather opaque for us: the elaborate task in which our perceptual system is engaged is not apparent when we, for example, listen to a touching story or read the latest headlines in a newspaper. The fundamental goal of extracting meaning is, however, indebted to the underlying functions of speech perception and reading. These functions provide fascinating examples of the complex operations carried out by the human brain. What are the structures and processes that enable language perception? How do they develop? What are the properties of the physical signal that are of interest to our brain?

Both theoretical considerations and a growing body of neuroimaging literature set the context of a stage-like organization of language perception, where increasingly-complex information is based on initially general processes of the physical input signal. From an information processing perspective, this is plausible, as the physical stream of sounds or string of visual features holds no linguistically-specific property per se. Moreover, the input signal of language is taken in via the same sensory channels as all the other environmental information processed by the brain and thus is likely to be represented in a rather general form at the earliest stages of neural signal processing, at least sub-cortically. It remains an open question with regard to when and where the language specific neural signaling emerges (Study I).

Commonalities across different species in the neural substrates and even types of sounds used for communication have led to speculations of an evolutionarily based and thus innate system for processing communication sounds. However, some mechanisms of speech perception are shown to be uniquely represented in humans. Evolutionarily, reading is a new skill and in the case of written language, postnatal development plays a critical role in forming neural structures specialized for language perception. Reading acquisition is tightly linked to processing of speech sounds; awareness of sub-lexical sound categories develops during childhood and is a prerequisite for learning literacy skills. Thus, whether there are prenatally specialized systems for some aspects of language perception or not, the critical features of language perception are likely to develop post-natally with major influence from environmental input. The way that a child's brain processes linguistic signals in comparison to a mature perceptual apparatus has not been established (Studies II–III).

Processing of physical features of the language input forms the gateway to meaning-based analysis. Spoken words are a continuously changing stream of sounds from which meaning is extracted when sufficient information has been gathered. In reading, the physical string of letters (symbols) can be examined in stationary form and is processed in more chunk-like visual images. The nature of the initial signal processing is thus fundamentally different for auditory and visual language although in both cases, the on-line pre-lexical processing must interact with lexical-semantic processes in some form. The interface between physical/perceptual processing and lexical/semantic processing in the brain is poorly understood (Studies IV–VI).

The issues above represent the field of cognitive neuroscience, where phenomena of the mind are correlated with physical attributes and functions of the brain. Functional imaging, carried out using functional magnetic resonance imaging (fMRI) or positron emission tomography (PET), provides a way to correlate events in perception/cognition with the functional state of the brain, via changes in the blood-flow and oxygenation measures in different cortical areas. Increasingly detailed maps of activations related to different cognitive tasks have been generated. However, the nature of signal in these measurements, hemodynamic changes does not allow direct tracking of the time-varying neural phenomena underlying different functions. The transformation from acoustic or visual signal to meaning takes only a fraction of a second and the complex computation of which our brain is capable is ultimately based on timing of neural signaling. Using electrophysiological imaging methods, magnetoencephalography (MEG) and electroencephalography (EEG), the timing of activation in neural populations can be followed with high accuracy. Source modeling techniques can be used to localize the activated brain areas. MEG has turned out to be a particularly powerful tool for characterizing complex activation sequences in the brain.

In the following, relevant background information for the experimental work is outlined in Chapter 2. I first introduce the basic principles of brain organization and function that determine the possible ways in which language signal processing can be implemented in the brain (Chapter 2.1). Basic principles of the auditory (Chapter 2.2) and visual (Chapter 2.3) systems of the brain then follow, with special emphasis on language perception, supplemented by theoretical considerations on speech perception and reading. Finally, I will consider neural and behavioral aspects of language development in children (Chapter 2.4). Chapters 3, 4 and 5 introduce the aims, methods and main results of the experiments. Chapter 6 considers the findings of this thesis from a more general perspective.

2 BACKGROUND

2.1 Human brain organization

2.1.1 Structure

The structure of the human brain reflects evolution of the nervous system in its organization: phylogenetically older regions are located below the newer brain structures (Figure 1a). The central nervous system can be divided into different sub-regions, perhaps most clearly in terms of evolutionary history – a similar division can be seen in other mammals. The phylogenetically newest and outermost region consists of different structures of forebrain; neocortex, basal ganglia, limbic system and olfactory bulb (in mammalian brain constituting telencephalon). Phylogenetically older structures of brain stem (diencephalon and mesencephalon of mammalian brain) lie underneath the forebrain. Some sources include the diencephalon as part of the forebrain and others as part of the brain stem. Located most centrally in the diencephalon, the nuclei of thalamus mediate all sensory information (except olfactory) from sensory organs to the cortex and also serve as a relay station for cortico-cortical connections. The specific nuclei of the thalamus project to specific cortical areas: for example, the lateral geniculate body sends axons to the primary visual cortex and the medial geniculate body sends axons to the primary auditory cortex. Two important structures in the midbrain (mesencephalon), the superior and inferior colliculi (forming the structure of the tectum), represent the previous stage of processing in the sensory pathway; they receive projections from the retina of the eye and cochlea of the ear, respectively. The pons and cerebellum are part of the metencephalon and the most distant part of the brain stem structures is the medulla (myelencephalon). The oldest form of nervous system comprised only the spinal cord.

In humans, the cortex (neocortex) comprises 80 % of the adult brain tissue. The 2500 cm^2 surface area of the cortex is highly convoluted and forms fissures, sulci and gyri so that the huge area of cortical surface fits within the skull. More than two thirds of the cortical surface is buried in the sulci. The grey matter consists mainly of dendrites and cell bodies and the myelinated axons underneath form the white matter. Axons are often grouped into bundles referred to as 'tracts' in the central nervous system.

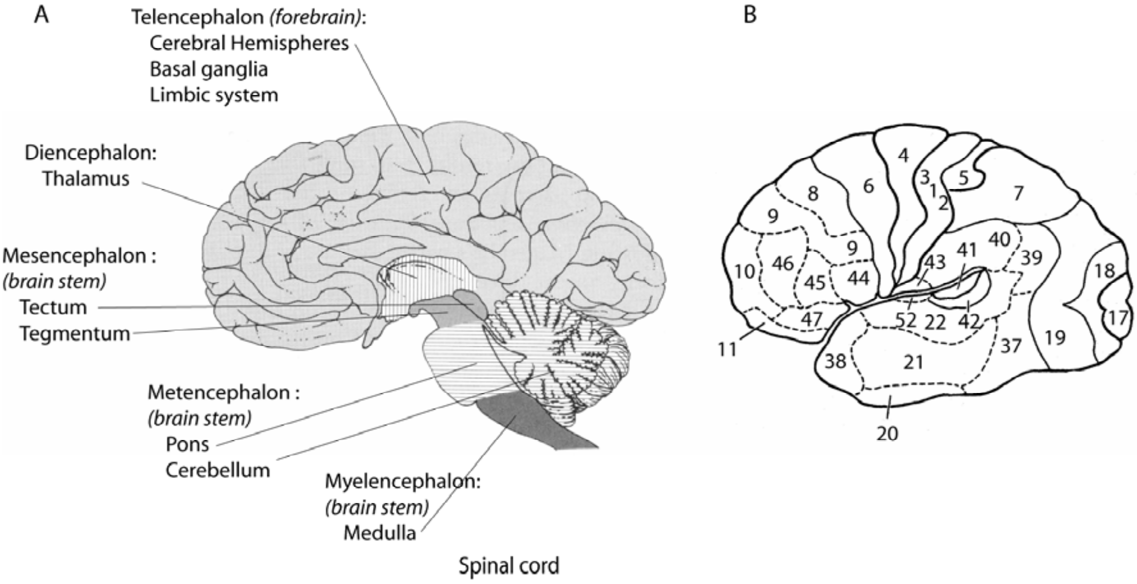


FIGURE 1 (A) Structure of the human brain with phylogenetic (and functional) divisions of the nervous system. The main parts in each division are indicated. Modified from Kolb and Whishaw (1996). (B) Brodmann's areas of the cortex (Elliot, 1969). Areas 41 and 42 represent roughly the primary auditory cortex and area 17 represents primary visual cortex.

There are two main principles in the anatomical organization of the neurons in the cerebral cortex: in the vertical direction, the cortical layer is organized into distinct layers (Figure 2a and b) and in the horizontal direction, the cortex can be divided into anatomically and functionally separable maps (Figure 1b). The 1.5 to 3.0 mm thick cortical layer is structured in (4–)6 layers of cells, each of which has its specific cell type and function in the circuitry of neurons. The cell-to-cell connections are organized mainly vertically, perpendicular to the layers of the cortex. The vertical connections seem to be organized in units (macrocolumns, minicolumns) that process incoming information coherently: The concept of functional columns as a basis of cortical organization was first formulated by Mountcastle (Mountcastle, 1957). A minicolumn, consisting of 80–100 neurons, is the smallest functional unit in the cortex and contains all the essential neuronal elements (Buxhoeveden and Casanova, 2002). Macrocolumns are formed by about 60–80 minicolumns with short-range horizontal connections (Mountcastle, 1997). Cortical columns are postulated to represent the template by which neurons, pathways and local circuitry is organized in the cortex; yet many of the principles of columnar organization are still not fully established (Jones, 2000).

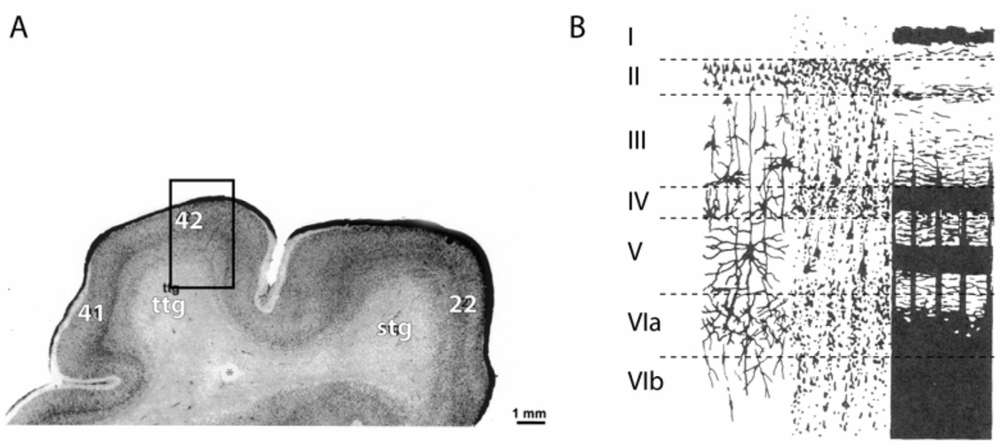


FIGURE 2 Morphology and cellular structure of the cortex. (A) Microphotograph of the topography of the temporal lobe. The cellular layers are visible perpendicular to the cortical surface (square) and the Brodmann areas 41, 42 and 22 are depicted. ttg = transverse temporal gyrus, stg = superior temporal gyrus. Modified from Moore and Guan (2001). (B) The structure of cortical layers as revealed by Golgi staining, Nissl staining and Weigert myelin staining. I: Molecular layer, II: External granular layer, III: External pyramidal layer, IV: Internal granular layer, V: Internal pyramidal layer, VI: Multiform layer

The brain surface can be divided into maps based on different principles: on projections that the neurons have with the sensory systems, on the cellular architecture of which they are built (Brodmann, 1909) (Figure 1b), or on the functions that the neurons seem to be controlling (e.g. the functional maps of the somatosensory and motor areas by Penfield (Penfield and Rasmussen, 1950). The maps based on projections and cellular architecture are naturally interrelated and also seem to roughly (but not absolutely) define the functional maps. The primary sensory areas are most easily defined. They receive projections from sensory organs of audition, vision and somatosensation and thus represent the physical dimensions of the environment in a behaviorally relevant manner in the cortex (e.g. frequencies of sounds, topography of the visual world and the location of sensation in the skin). The primary projection areas are surrounded by, and send axons to, a number of secondary projection areas, or unimodal association areas. In these regions, the neurons no longer respond according to the simple physical features of the stimulus but their activation represents functionally different properties of the sensory experience. For example, the visual cortex is divided into regions V1–V5, each of which has a specific function in the (hierarchy of) visual information processing (e.g. color vision, motion vision). The sensory pathways continue further to higher-level association areas, or multimodal association areas that compile information coming along different sensory pathways and participate in more complex cognitive functions related, for example, to language and memory. For the higher-level functions, it is more difficult to define distinct areas that are devoted to specific behaviors.

The structure and function of the cortical pathways for different sensory information is only beginning to be revealed with the help of functional imaging of the living brain. Recent studies on both the anatomy and physiology of perceptual processing in primary and non-primary sensory areas provide increasing evidence for parallel and distributed information processing (instead of strictly hierarchical) across the perceptual pathway(s) from the earliest stages of cortical processing. More detailed description of the auditory and visual pathways will be given in chapters 2.2.1 and 2.3.1.

2.1.2 Signaling

The sensory organs transform the physical (or chemical) signals of the environment to neural signals that are further processed in the nervous system, giving rise to visual, auditory, somatosensory, olfactory and taste perceptions. After the initial sense-specific signal transformation, the basic principle of signal transmission is the same across different neural pathways, from peripheral sensory systems to the cortical higher-level processing centers. The building blocks of the sensory systems – neurons conveying electric signal – are basically the same, even across different species. Thus, it is not the quality of the signal but rather the origin and destination of the signal pathway that determines the information content of sensation. The initial stages of sensory signaling in the peripheral nervous system are fairly well understood, but the neural functions at the other end of the pathway, constituting perception, are less well established. The following introduction to neural signaling is mainly based on Nicholls et al. (1992) and Purves et al. (2000).

The structure of the neuron was described by Ramón y Cajal in the 19th century. Briefly, a neuron is composed of 3 functionally separable parts; dendrites branch to their surroundings and receive the signal from other neurons in the pathway and carry the electrical impulses to the cell body (soma) and an axon extends to the following neuron in the pathway to convey the signal further (see Figure 3). Functionally crucial parts for signal transfer are synapses, the contact units between two neurons. Synapses are present all around the neuron but are most abundant between the axon of the presynaptic neuron and the dendritic spines of postsynaptic neurons. A synapse consists of the presynaptic and postsynaptic terminals separated by the synaptic cleft (Figure 3).

An important prerequisite for signal transmission within a synapse is a difference in ionic composition between extra- and intra-cellular fluids that are separated by a relatively impermeable cell membrane. During resting state, a ~70 mV potential difference across the membrane is created by 1) selective permeability of the membrane to K+ ions and 2) the use of ion pumps that increase the K+ concentration inside the cell and Na+ outside the cell causing concentration gradient for both ions. As a consequence, K+ ions run down to their concentration gradient until the electrochemical equilibrium is reached i.e. until the balance between the concentration gradient driving K+ out from the cell and electric gradient driving K+ into the cell is established. Other than K+, permeable channels are typically inactive during the resting state.

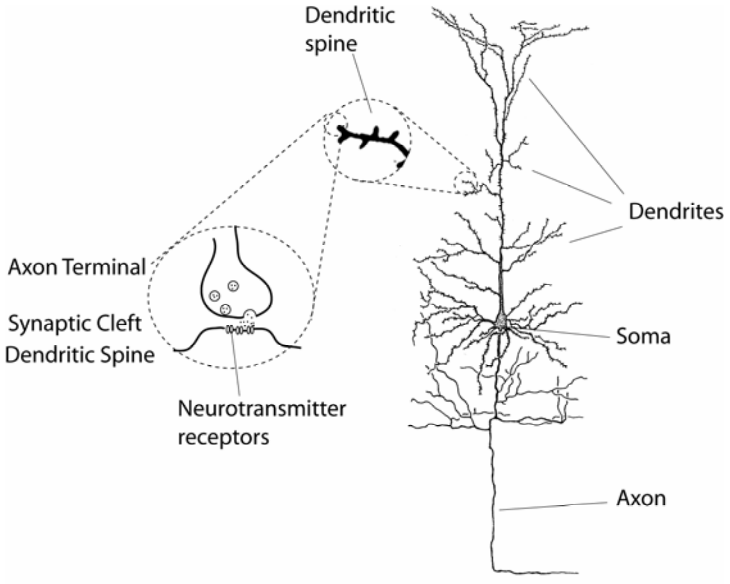


FIGURE 3 Schematic illustration of the structure of a neuron and a synapse. The neuron receives input from other neurons via synapses in the form of postsynaptic potentials (PSP's). When PSP's sum up they may cause an action potential that will propagate over the entire axon to the next synapse in the pathway.

There are two types of electric signals that the nervous system utilizes: localized potentials and action potentials. Localized potentials are evoked either by physical stimulation (receptor potentials in the sensory receptors) or by chemical changes in the ionic concentration in the synapse (post-synaptic potentials between neurons). An electric signal (current) in the presynaptic terminal causes release of chemicals (neurotransmitters) to the synaptic cleft that attach to the postsynaptic membrane. Consequently, opening of the channel enables inward or outward flux of ion currents causing either increase or decrease of the resting potential. Postsynaptic potentials attenuate over a short length of nerve fiber (1–2 mm), but they last tens of milliseconds and when several potentials spatially and/or temporally converge, they sum up and may cause an action potential. A single neuron integrates information from presynaptic neurons and the local potentials are called excitatory when they tend to give rise to nerve impulses and inhibitory when they tend to counteract impulse execution. When the transmembrane voltage is increased to about -50mV the activation of voltage-dependent channels quickly increases the permeability of Na+ ions (and more slowly the permeability of K+ ions). This action potential, after initiation, propagates over the entire axon in millisecond time-scale and again causes the release of neurotransmitter to the synapse with the next neuron in the pathway. Normally, an action potential is thus required to transfer information along a neuronal pathway. Unlike local potentials, the action potential conveys information in a binary manner – the neuron can either fire or not.

From an information processing point of view, there are two highly relevant issues in the functional organization of the nervous system. First, the structural basis of complex neural computation is in the network of individual inhibitory and excitatory synapses (neurons). The connections between neurons are the basis for the information processing i.e. calculation in the neural network and thus the number of synapses in the pathway reflects also the possible level of information processing/refinement.

Second, the functional organization of the nervous system cannot be described without referring to the timing of events. At the level of an individual neuron, the temporal summation across input from presynaptic neurons (postsynaptic currents) and the temporal code of action potentials (e.g. frequency of ap's) carried on to the next neuron occurs within millisecond to tens of milliseconds time-scales. Moreover, e.g. the transformation from acoustic waveform of a speech signal to a conceptual representation takes only a fraction of a second. For this to happen, there has to be an enormous amount of computation and it is intuitive that neural events must happen fast and with precise timing for the normal functioning of the brain. As the cell membrane is not a perfect insulator, there is leakage of ions during action potential propagation; the number of ions is not sufficient to cause fast signal propagation along normal axons. Faster signal transduction within a nerve fiber is enabled by a myelin sheath that covers the axon membrane and restricts the membrane current flow to the nodes of Ranvier that interrupt the high-resistance internodal region. This enables multifold increase in the conduction velocity of the action potential.

In the present thesis, magnetoencephalography was used to measure neural activation during perception of auditory and visual linguistic information. MEG reflects synchronous activation of thousands of neurons and it is thought to reflect mainly the postsynaptic potentials in the apical dendrites of pyramidal neurons.

2.2 Auditory perception

2.2.1 Structure of the auditory system

In the auditory system (described, e.g., in Popper and Fay, 1992) (Figure 4) the acoustic signal, i.e. changes in the air pressure, are transformed to electric signals. The outer ear structures (pinna and ear canal) transform and filter the acoustic signal to the middle ear where the auditory ossicles function as an impedance transformer between vibration in air and fluid. The vibration is transferred to the fluid-filled inner ear and to the basilar membrane, the elasticity and mass of which change along the length of the membrane. Consequently, the travelling wave resonates maximally in different locations of the basilar membrane for different frequencies. The mechanical movement is transferred to the hair cells, the sensory organs that are located between the basilar membrane and another, tectorial membrane, in the organ of Corti. Vibration of the hair cells further generates an electric receptor potential and excitation of the peripheral terminals of cochlear afferent neurons. This excitation initiates the neural impulse in the auditory nerve. The tonotopic organization of the basilar membrane was first described in 1960's by von Bekesy (von Bekesy, 1960). It is preserved throughout the sub-cortical auditory pathway to the cortex: Each auditory nerve fiber innervates a particular section of the basilar membrane, carrying information about a specific frequency range in the acoustic signal. For periodic sounds with frequency below about 4000 Hz, a neuron (or group of neurons) can code the frequency directly by firing at the sound frequency. Peripheral fibers function as bandpass filters that mediate the spectral analysis of the cochlea to higher levels of the nervous system. Each auditory nerve fiber has a characteristic frequency to which it responds at the lowest intensity and a tuning curve which describes the decreasing sensitivity at higher and lower frequencies.

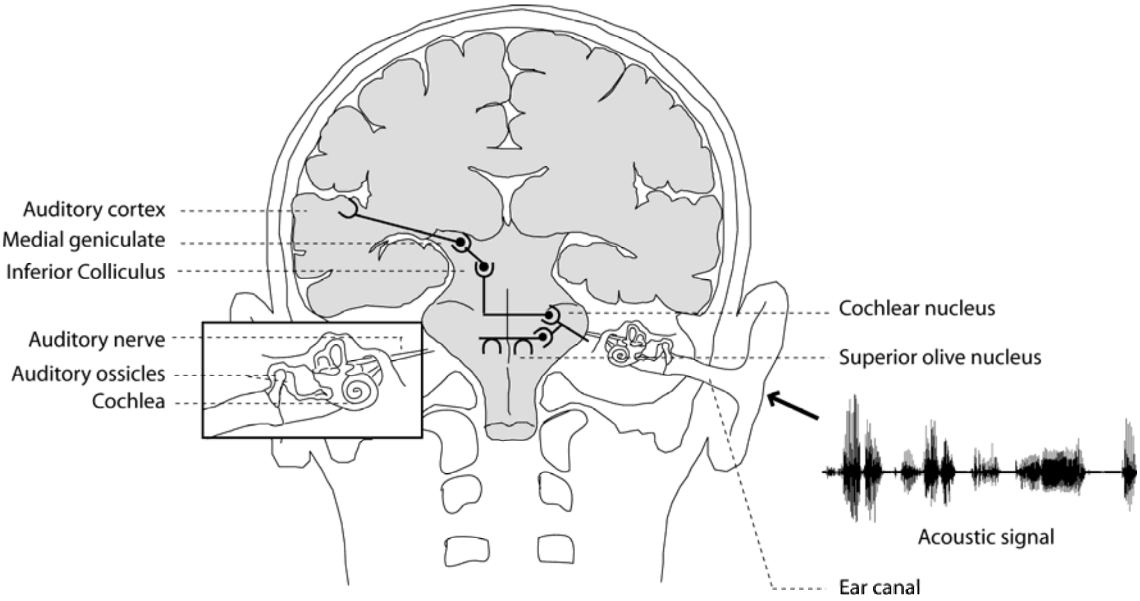


FIGURE 4 Schematic illustration of the auditory pathway. Modified from Wever (1949).

The main auditory pathway is illustrated in Figure 4. The four synapses (synaptic stations) separating the hair cells and the auditory cortex conduct rather complex computation of the auditory signal sub-cortically within both parallel and serial connections. The auditory nerve fibers from the cochlea end in the dorsal and ventral cochlear nuclei in the brain stem (medulla). The pathway proceeds to the contralateral inferior colliculus (midbrain) and bilaterally to the superior olivary nuclei from which there is bilateral input to the inferior colliculus. In the olivary nucleus, the information from the two cochlear nuclei converges for the first time, enabling processes related to sound localization. In the inferior colliculus, multiple ascending pathways converge, integrating almost all ascending acoustic information from the lower brain stem centers. The fibers ascend to the medial geniculate nucleus (MGN) of the thalamus and finally to the auditory cortex. The sub-cortical auditory pathways provide, rather accurately, the original signal from sensory input and also conduct integrative computation via inter/intranuclear circuitry at each relay station enabled by parallel processing.

The higher stations of the central auditory processing pathway include the MGN of the thalamus and auditory cortices. The primary auditory cortices (PAC) are located in the superior temporal gyri, buried in the Sylvian fissure on the surface of the temporal lobes (see figure 5). Studies on non-human primates have provided detailed information on the subdivision of the cortical auditory areas. These can be separated by the pattern of tonotopic organization, cellular/laminar architecture and connectivity with thalamus (Hackett et al., 1998; Merzenich and Brugge, 1973; Pandya and Sanides, 1973; Rauschecker et al., 1997). Alongside hierarchical processing, auditory information is processed in a highly parallel fashion, even from the earliest stages of cortical processing. In the macaque, the core area of the auditory cortex consists of two or three separate areas that express a specific primary-like cellular architecture (Pandya, 1995) and show tonotopic organization (Rauschecker et al., 1997) with rather sharp frequency tuning. The core areas have distinct thalamic connections with the ventral division of the medial geniculate nucleus and represent the first level of cortical auditory processing.

Each core area is heavily connected with adjacent areas that represent the second level of auditory processing and are referred to as the ‘auditory belt’. Seven to eight separate areas have been described surrounding the primary cortex (Kaas and Hackett, 2000). In addition to the input from the core, belt areas also have distinct connections with the ventral geniculate nucleus of the thalamus. Belt areas are separated from the core region by their different cellular and laminar architecture. Moreover, the neurons of the belt area show broader frequency tuning than neurons in the core and they respond better to narrow bands of noise than to pure tones and to, for example, spectrally and temporally complex stimuli such as vocalizations (Rauschecker et al., 1995). The parabelt-region surrounds the belt areas laterally (Hackett et al., 1998) and receives input mainly from the belt-areas although it also has distinct thalamic connections. There is no direct input from the core areas to the parabelt, indicating some level of hierarchy in the processing across the cortical auditory areas. The posterior parabelt further connects with the temporoparietal junction and with the dorsolateral prefrontal cortex (suggested to represent spatial information processing) and the anterior parabelt region connects with the anterior temporal and ventrolateral frontal lobe (suggested to represent non-spatial auditory information processing) (Kaas and Hackett, 2000; Romanski et al., 1999).

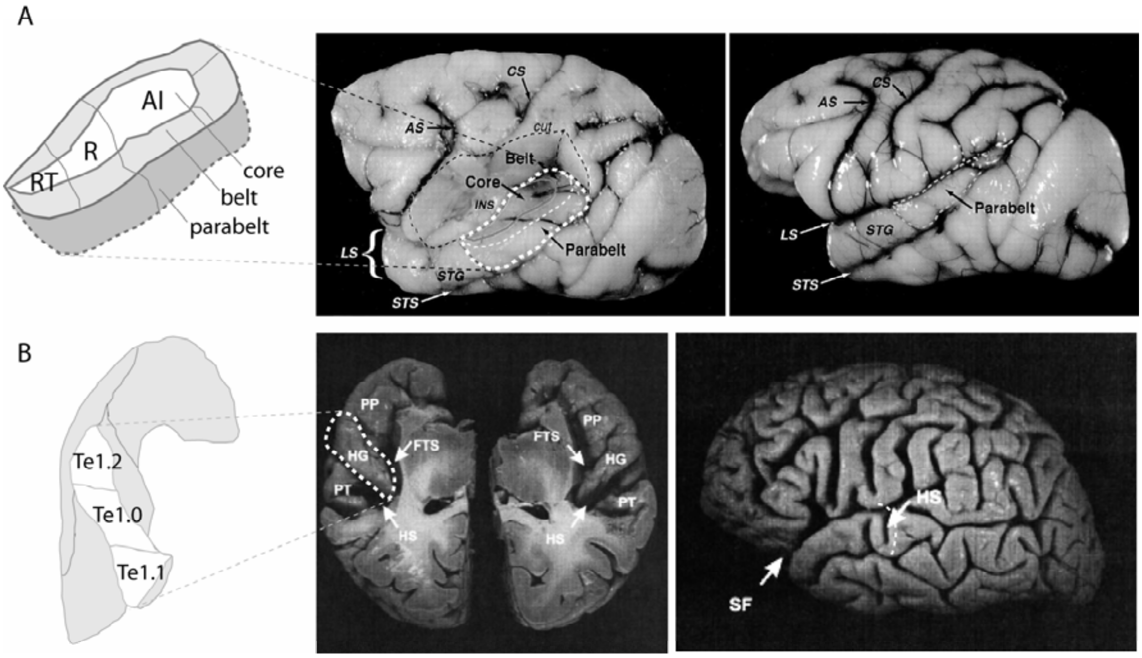


FIGURE 5 (A) The cortical auditory areas in macaque. In the lateral view (right) only the parabelt region is visible. The parietal cortex is removed to uncover the core and belt regions (middle). Schematic illustration of the subdivision of core, belt and parabelt regions is shown in the left. AI = auditory area I, R= rostral area, RT = rostrotemporal area. Modified from Kaas and Hackett (2000). (B) The cortical auditory areas in human. The parietal and frontal opercula are removed to uncover the superior temporal plane (middle). Schematic illustration of the cytoarchitectonic division of primary auditory cortex is shown in the left. The secondary auditory areas planum temporale (PT) and planum polare (PP) surround the primary auditory area posteriorly and anteriorly. SF= Sylvian fissure, HG = Heschl's gyrus, HS = Heschl's sulcus, FTS = first transverse temporal sulcus. Modified from Morosan et al. (2001).

Comparable auditory cortical fields with different functional properties have also been suggested in the human brain (Galaburda and Sanides, 1980; Morosan et al., 2001; von Economo and Koskinas, 1925) (see Figure 5). Closely resembling other primates, primary-like cellular architecture in the human brain is found in the medial 2/3 of the transverse gyrus of Heschl (Broadman area 41), sometimes spreading anteriorly/posteriorly to the nearby sulcus and surrounding gyri (especially when more than one Heschl's gyrus is present) (Hackett et al., 2001; Rademacher et al., 2001). A well-developed inner granular layer (layer 4) is characteristic to primary sensory areas. Also in humans, the primary-like region has been suggested to include separate areas (Galaburda and Sanides, 1980; Morosan et al., 2001; von Economo and Koskinas, 1925) showing subtle differences in laminar/cellular organization. Morosan and co-workers (2001) identified three sub-regions in the primary auditory cortex along Heschl's gyrus (see Figure 5). The primary-like cortex Te1 was divided to Te1.0, which showed the highest degree of granularization, Te1.2 laterally and Te1.1 medially. Inter-individual variability in the localization of the primary-like cortex has been shown by multiple studies (e.g. Hackett et al., 2001; Morosan et al., 2001; Rademacher et al., 2001). Functional imaging has proposed tonotopic organization of the auditory cortex, using magnetoencephalography (Hari et al., 1984; Pantev et al., 1989; Romani et al., 1982) and functional magnetic resonance imaging (Bilecen et al., 1998; Formisano et al., 2003; Talavage et al., 2000).

The most lateral portion of Heschl's gyrus is thought to represent part of the secondary auditory area (Morosan et al., 2001; Wallace et al., 2002) and possibly the belt region of the human auditory cortex. There are no macro-anatomical features coinciding accurately with the cytoarchitectonically-defined primary auditory area, although roughly, the anterior border between the PAC and an anterior area of the planum polare (PP) is defined by the first transverse temporal sulcus (FTS) (sulcus transverses primus) and the posterior border between the PAC and a posterior area of planum temporale (PT) is defined by Heschl's sulcus (HS) (Hall et al., 2003). The planum polare anteriorly and the planum temporale posteriorly represent the non-primary or secondary auditory areas of the human auditory cortex. The correspondence between human and primate belt areas has not been established (Hall et al., 2003). Recently, functional imaging studies have shown that broadband sounds evoke wider activation in these non-primary auditory areas posterior to the primary auditory cortex (Hall et al., 2002; Wessinger et al., 2001), suggesting functional correspondence to the belt areas identified in non-human primates (Rauschecker et al., 1995).

2.2.2 Functional properties of the auditory system

The properties of the input signal are thought to be represented in different, complementary and parallel codes in the neurons which operate in various combinations to provide the spectral and temporal information from which a normal listener operates in everyday situations (Eggermont, 2001; Sachs, 1984). For example, frequency information can be coded as a place of maximal firing in the basilar membrane and further in the ascending auditory pathway, or as a rate of discharge in the neurons (place vs. rate coding of frequency). According to present understanding, none of the different codes alone is able to transmit all the different types of information buried in the acoustic waveform of sounds with varying magnitude and different spectral and temporal characteristics.

The neural representation of complex sounds, as described in terms of discharge activation, is fairly well known at the level of the auditory nerve and cochlear nucleus (e.g. Delgutte, 1984; Sachs, 1984 for speech sounds), but at the cortical level, the complex sound analysis is less clear. The physical features of the stimulus (e.g. periodicity, temporal structure and frequency spectrum) are already encoded in the sub-cortical auditory pathway (Griffiths et al., 2004; Langner, 1992; Nelken, 2004) but also modulate activation at the cortical level where the processing is likely be represented based on more perceptual attributes (such as pitch in contrast to frequency spectrum) (Bendor and Wang, 2005; Zatorre and Belin, 2001). The higher stations in the auditory system of non-human primates are less accurately tuned to respond to pure tones but instead respond to combinations of tones, for example sweeping upward or downward in frequency, to binaural but not monaural sounds, and to other complex auditory stimuli (Rauschecker et al., 1995; Rauschecker et al., 1997). A recently-presented view on auditory processing, based on single cell recordings in non-human primates, proposes that the primary auditory cortex is involved in "object-based" processing in contrast to "feature-based" processing that takes place sub-cortically (Nelken, 2004). In accordance with this view, responses from primary auditory neurons seem to reflect less redundant (and possibly more abstract) information than sub-cortical neurons (Chechik et al., 2006). It is, however, not known whether these response properties can be generalized to human auditory processing.

The functional properties of the primary and non-primary auditory cortex in humans have been studied in neuroimaging experiments. These have identified increasing sensitivity to complex features, such as increase in harmonic complexity, modulations in frequency and amplitude (Giraud et al., 2000; Hall et al., 2002) or in pitch and melody (Patterson et al., 2002), in areas anterior and posterior to primary auditory cortex. However, the way in which different features of complex sound processing are combined to form a single percept of a speech sound remains to be clarified.

As described in chapter 2.1.2, the timing of neural activation is a central property of the neural code underlying computations and representations of perceptual events. The timing of auditory (and neural) signal processing can be followed from the cochlea to the auditory cortex using electrocochleography that measures the potentials from the cochlea and the eighth cranial nerve (Eggermont, 1974), and electroencephalography and magnetoencephalography that measure the electric or magnetic field produced by neural currents in the brain stem and forebrain (Hari, 1990; Picton et al., 1974). Auditory-evoked potentials (AEPs) and auditory-evoked fields (AEFs) are a subclass of event-related potentials/fields (ERPs/ERFs) that are neural responses time-locked to some "event", either sensory stimulus or mental event. An auditory evoked response is obtained by averaging a large number of single responses (typically 80–100) to auditory events. The resulting mean waveform reflects the time-course of underlying neural activation. Recurrent synchronous activation of neuronal populations is reflected as peaks (or 'components') in the evoked response waveform.

Auditory evoked responses include receptor potentials, the compound action potential of the auditory nerve (AP, wave I), various auditory brain-stem responses (ABRs, waves II–VII), and the early and late cortical responses (middle latency responses or MLRs and cortical AEPs/AEFs) (Kraus and McGee, 1992). Due to their different response properties and distance from measurement sensors, sub-cortical and cortical auditory responses are not all captured using the same parameters. Cochlear responses are evoked without a delay and the auditory nerve is activated within 2 ms of signal onset (wave I). From wave II onwards, the ABRs, peaking within 15 ms after signal onset, reflect neural activation of several separate auditory brainstem structures. The later in the hierarchy of auditory processing, the less stable the response latencies and properties become. The early signals from the auditory nerve and auditory brain stem are widely studied using clicks and they are fairly stable and independent of sleep stage, arousal and anesthesia, unlike MLR and cortical late AEP (Picton et al., 1981). Due to their high reliability, the latency of ABR wave components (waves I–V) is used to diagnose various neural disorders and the development of the auditory system (Kraus and McGee, 1992).

The middle latency responses are evoked between 10 and 60 ms, the earliest of which are at least partly generated sub-cortically (Deiber et al., 1988; Kileny et al., 1987; Kraus and McGee, 1992). Responses evoked at around 18 ms (Na), 25–30 ms (Pa) and around 50 ms (Pb, P50/P50m or P1) are likely to originate from the auditory cortex, most probably Heschls' gyrus, thus reflecting the first stages of cortical auditory processing (cf. chapter 2.2.1). Involvement of the auditory cortex at these latencies has been suggested both in MEG experiments (Mäkelä et al., 1994; Scherg et al., 1989) and in research based on cortical lesions and EEG (Kileny et al., 1987; Kraus et al., 1982; Vaughan and Ritter, 1970). These components are identified using both EEG and MEG.

The most prominent of the later cortical auditory responses is evoked at around 100 ms after stimulus onset (N100, N100m). Neurons in at least three distinct cortical regions have been suggested to contribute to the N100 response (Näätänen and Picton, 1987) but the strongest contribution, especially for magnetic N100m, originates in the superior temporal cortex. Intracranial measurements indicate a source posterior to the primary auditory cortex as the origin of the signal (Liegeois-Chauvel et al., 1991); the N100m response is thus likely to reflect activation of non-primary auditory areas, possibly in the human auditory belt region. The N100m response is localized more anteriorly in the right hemisphere (Elberling et al., 1982; Kaukoranta et al., 1987), in agreement with the anatomical asymmetry reported for the planum temporale (Galaburda et al., 1978; Geschwind and Levitsky, 1968). Activation within this time-window is also stronger and earlier for stimulation from the contralateral ear (when presented monaurally) (Elberling et al., 1982; Mäkelä et al., 1993; Pantev et al., 1986), reflecting the stronger contribution of the contralateral input in the auditory pathway. The N100m response is sensitive to repetition of sounds and increasing the ISI increases the response until about an ISI of 8–16 s in adults (Hari et al., 1982; Hari et al., 1987). This behavior has been interpreted to reflect inhibitory processes (McEvoy et al., 1997; Sable et al., 2004) or the 'refractory period' of underlying neural generators, i.e. that the population response of neurons is not fully recovered from the previous event (Budd et al., 1998; Ritter et al., 1968).

Other late auditory evoked potentials include the P2 or P200 and N2 or N200. Auditory evoked components can be described in terms of how much they reflect the physical stimulus characteristics vs. attentional and task-related functions; this distinction has been defined as 'exogenous' (or obligatory) vs. 'endogenous' influence (Sutton et al., 1967). While ABRs reflect rather directly the physical features of the stimuli, later auditory responses are characteristically increasingly influenced by perceptual attributes and task. Later auditory evoked responses that are highly influenced by stimulus manipulations, mainly studied using linguistic stimuli, include the P300, N400, P600 and mismatch negativity (MMN). For many of the AEPs/AEFs, the distinction between exogenous vs. endogenous influence is not absolute but a question of degree (Kraus and McGee, 1992). A more detailed description of the late auditory evoked response components related to speech perception will follow in the next section.

2.2.3 Speech perception

2.2.3.1 Theoretical considerations

The speech signal, as any other sound, is a series of pressure changes in the air between the sound source and the listener. This ‘voicing waveform’ in speech (see Figure 4) is produced by the vocal organs. The air is pushed from the lungs to flow via the glottis, a small cleft between the vocal folds that vibrate and cause quasi-periodic pulses to the signal. This signal is further filtered in the vocal tract or nasal tract. Continuous speech is a stream of sounds where this ‘quasi-harmonic’ signal (corresponding roughly to vowels) is interrupted by transient less harmonic periods such as broad band noise or silence (corresponding roughly to consonants). The speech signal can be described in the time-domain or the frequency domain. The mass and tension of the vocal folds and the length of the vocal tract mostly determine the dominant frequency of the sound produced by the vocal folds. This fundamental frequency (F0) varies from around 100 Hz for an adult male speaker to around 300 Hz for a child speaker.

The field of phonetics describes the acoustic (physical) details of speech sounds whereas phonology is concerned with the way speech sounds are structured in (each) language. The most basic functional units of language, distinctive features, describe the abstract and invariant properties of speech sounds. Phonemes, representing the smallest units that can alter the meaning of a word, can be described as a bundle of these features. Phonemes can be divided into vowels and consonants that are normally described separately due to the difference in both manner of production and perceptual features. Vowels are always voiced, i.e. they include periodic structure by vocal fold vibration (except e.g. when whispering). Vowels can be classified by the place of articulation (front-back, high-low) and by the shape of the mouth in this location (open-closed). These properties of the articulators cause different resonance characteristics for different vowels and, consequently, distribution of peaks in the frequency composition (spectrum). The peaks (or formants, F) carry relevant acoustic information for speech perception. The formant with lowest frequency is called F1, the second lowest F2 and so forth. The F1/F2 relation, in principle, distinctively separates all the vowels of the world’s languages. This is however complicated due to the acoustic variation in natural speech (Hillenbrand et al., 1995)(see below). Consonants can be described based on manner of articulation (e.g. plosives that are produced by complete stoppage of air flow) and place of articulation (e.g. dentals, articulated with tongue touching upper teeth) or combinations of these two dimensions. In addition, consonants can be voiced (vocal folds vibrate) or voiceless (no vocal fold vibration). For example, /t/ is a voiceless dental plosive.

In the time domain, the speech signal involves changes at different time-scales. Changes at the level of phonetics occur within tens of milliseconds, for example when the frequency composition changes (in a consonant-vowel, CV-syllable) or the complete stoppage of airflow through the vocal folds is followed by a sudden release (beginning of a CV). Changes of hundreds of milliseconds underlie the perception of syllables and changes of seconds are associated with stress in a word or a sentence.

Due to speaker gender, speed of speaking and co-articulation, among other things, the acoustic waveform of the same speech sound can substantially differ and there is no one-to-one relationship between acoustic elements and linguistic units. Acoustically (and phonetically) differing utterances of the same phoneme are called allophones. The mapping between a continuous acoustic signal and discrete linguistic elements appears complex and there is no straightforward explanation of how and based on what features, speech is perceived (Miller and Eimas, 1995). Neither is the fundamental difference between speech and non-speech sound processing known in the brain.

There are different theoretical perspectives on the problem of how variable acoustic correlates of speech sounds can be perceived as invariant linguistic segments (Diehl et al., 2004). The motor theory of speech perception (Liberman et al., 1967) and direct realism suggest that the perceptual invariance arises from the way speech sounds are articulated. The targets of perception are the actual gestural patterns (Fowler, 1994) or motor 'plans' that are consequently used to control muscle contraction during articulation (Liberman, 1996; Liberman et al., 1967; Liberman and Mattingly, 1985). Alternative accounts view the fundamental perceptual units as purely auditory in nature without linking them to articulatory gestures (Stevens, 1980). Multiple experimental findings, such as perceptual categorization of speech sounds based on articulatory features, seemed to support the motor theory of speech perception early on but were shown not to be specific to speech sounds (Miller et al., 1976; Pisoni, 1977) or even to humans (Kuhl and Miller, 1975; Kuhl and Miller, 1978). Nevertheless, the fast and effortless encoding of speech with an average rate of 20–30 phonemes/second (Liberman et al., 1967) (in contrast to 1.5 non-speech sounds/second, Warren et al., 1969) suggests that there is some specialized system for perceiving phonetic information (cf. Harley, 2001).

As described earlier, the special nature of speech is not entailed in the speech signal itself. Moreover, the speech signal is received through a common auditory system, evolved to process all acoustic information. Thus, the linguistic information is not physically encoded anywhere but must arise from the processing and transformations along the neural pathway. From an information processing point of view, it seems reasonable to model speech perception as proceeding in several stages/levels of processing with computational transformations in between (Cutting and Pisoni, 1978). This would enable the apparent reduction in the number of information carrying elements and modification of information from the acoustic waveform to semantic identity. The first transformation, from the continuous acoustic signal to neural signal already takes place in the cochlea. The further linguistic description is likely to be reflected in the neural signal at later stages.

The fundamental goal in language perception is to extract the meaning of the utterance (semantics), which, in everyday life, seems fast and effortless. Traditionally, the study of speech perception, aimed at understanding how acoustic properties are mapped onto invariant linguistic units such as features, phonemes or syllables, has been separate from the study of spoken word recognition, aimed at understanding the process of comprehension of the linguistic message. Naturally, there is no real boundary between these processes, and their neural implementation might well be interwoven. The nature of the interface between the physical signal and higher level linguistic functions is unclear and there are different theoretical perspectives on how the acoustic signal is mapped to the lexical items (Jusczyk and Luce, 2002; Miller and Eimas, 1995).

Before access to lexical entries (i.e. access to all the linguistic information related to a concept), the incoming speech stream must be segmented into words or morphemes. Context has an effect, both at the level of segmenting sounds in the speech stream and in segmenting words. In continuous speech, individual speech sounds also provide information on the next sound in the stream which facilitates perception of spoken words (Marslen-Wilson and Warren, 1994). This assimilation of adjacent sounds is a result of the co-articulated production of speech: articulatory movements are not controlled phoneme-by-phoneme but in larger units. Thus, previous and subsequent segments are reflected in vocal tract configuration and, consequently, in the acoustic speech signal. Context also facilitates the perception of words: words are identified almost twice as quickly in context than in isolation (Lieberman, 1963). However, there is no consensus on whether the higher-level linguistic context affects pre-lexical processing of the input signal (as suggested by interactive models, e.g. McClelland and Elman, 1986) or whether the effects arise later, after the initial perceptual mapping (modular/feed-forward accounts, Fodor, 1983; Norris et al., 2000). For example, there is some evidence for lexical influence on phoneme level processing (Samuel, 1990; Samuel, 1996; Samuel, 1997), but the question remains controversial (e.g. Massaro and Cohen, 1991). In other words, beyond priming between elements at the same level of linguistic representation, it is not clear whether there are top-down influences on the bottom-up processing of the acoustic signal.

A related question in speech perception is the nature of the pre-lexical code. It is not clear whether phonemes are involved in processing prior to the identification of a word (Klatt, 1979; Marslen-Wilson and Tyler, 1980; McClelland and Elman, 1986). It has been proposed that lexical information is accessed directly based on phonetic features in the acoustic signal (Marslen-Wilson and Warren, 1994). Indeed, the information on single phonemes might be necessary only within the context of written language. Developmentally, larger units, such as syllables, are more easily available for the perceiver than individual phonemes (Treiman and Zukowski, 1996). Morais & Kolinsky (1994) suggest that there are both conscious and unconscious phoneme representations, the former are present in the acquisition of literacy and the latter in spoken word recognition.

Theoretically-based computational models are used to explain behavioral phenomena and to suggest underlying cognitive operations in spoken word recognition (reviewed in Harley, 2001). Word recognition is thought to start with sensory input that, in some form of representation, contacts with the lexicon. The accumulation of sensory information leads to recognition of the word at the so-called 'uniqueness point' (the point at which there is no other word that could match the collected information). Word recognition enables lexical access, i.e. access to all stored information about the word and integration of word meaning to a higher level sentence representation can follow. Although the general scheme is commonly accepted, theoretical accounts differ, for example, in the way they include context information in the model. The Cohort Model (Marslen-Wilson, 1989; Marslen-Wilson, 1987) emphasizes the role of bottom-up processes and suggests direct access to lexical entries on the basis of an acoustic analysis of the incoming speech signal. In more interactive models (e.g. TRACE), the main emphasis is on the interaction between levels of information. The input signal is processed in units at three levels – phonological features, phonemes and words – which can work 'simultaneously' to activate possible concepts. Mutual connections and competition between units influence the strength of activation based on which the recognition occurs. A neighborhood activation model (NAM) presented in Luce and Pisoni (1998) describes auditory word recognition through a computational model that takes into account the number of similar words in the 'neighborhood', the degree of phonetic similarity among words and the frequency of their occurrence in the language. According to NAM, greater competition among words that are phonologically similar results in slower word recognition.

2.2.3.2 Neural basis of speech perception

The first findings linking speech perception and specific brain regions date back to the 19th century and Carl Wernicke who, based on lesion studies, associated the left hemisphere temporal cortex with receptive language (Wernicke, 1874). Non-invasive neuroimaging has made it possible to study the intact human brain and, during the past two decades, the neuroanatomical and functional organization of speech perception has been intensively investigated. A common framework, arising from theoretical accounts (see previous chapter) and neurophysiological studies on speech perception (e.g. Phillips, 2001) indicates multiple stages in the processing of speech (Hickok and Poeppel, 2007; Poeppel and Hickok, 2004). Congruent with this framework, the hierarchical subdivision of the auditory cortex shown in non-human primates (Rauschecker et al., 1997), has also been indicated in the human auditory cortex (Morosan et al., 2001; Rauschecker, 1998) with apparent significance also for the neural implementation of speech perception. The functional subdivision of the auditory cortex does not necessitate strict hierarchy; on the contrary, substantial parallelism of processing is suggested based on both the anatomical organization of auditory functions (see chapter 2.2.1) and some theoretical accounts and behavioral phenomena in speech perception (see chapter 2.2.3.1). However, it seems likely that the information reflected in the neural code changes along the perceptual pathway and becomes less redundant.

Hemodynamic neuroimaging studies propose that multiple areas in the non-primary auditory cortex in the superior temporal region are sensitive to different aspects of the sound that are also relevant for the early processing of the speech signal. However, there seems to be no clear consensus between studies on what the brain structures devoted to speech specific perception are, or whether such structures even exist. Studies that specifically contrasted acoustic vs. phonetic analysis have shown speech sensitive activation in regions of the left superior and middle temporal gyri (STG and MTG) (Benson et al., 2001; Binder et al., 2000; Vouloumanos et al., 2001) and superior temporal sulcus (STS) (Benson et al., 2006). However, comparable regions in the lateral supratemporal plane and STS have showed increased activation also for harmonic tones and frequency-modulated tones (in contrast to single stationary tones) (Hall et al., 2002), and the caudal lateral belt posterior to the primary auditory cortex appears sensitive to changes in spectral motion (Thivard et al., 2000). More anterior regions (anterior STS) have shown sensitivity to intelligible speech (Scott et al., 2000).

The heterogeneous area of the planum temporale (PT) in the posterior portion of the superior temporal gyrus has gained special attention in terms of its being related to language lateralization due to its left-dominant asymmetry in humans (Galaburda et al., 1978; Geschwind and Levitsky, 1968). Some neuroimaging studies have linked the area of the PT to speech perception (Benson et al., 2001; Vouloumanos et al., 2001; Zatorre et al., 1992), but other studies suggest the PT as important for more general auditory processing (Belin et al., 2000; Binder et al., 2000; Binder et al., 1996). The anatomical lateralization has also proven to be more complicated than originally described (Eckert and Leonard, 2000; Rumsey et al., 1997a) and not directly related to language lateralization to the left hemisphere (Dorsaint-Pierre et al., 2006).

The difficulty in finding a speech-specific area in the brain has led to speculation that speech perception emerges from distributed resources that are shared by both verbal and non-verbal auditory processing (Price et al., 2005). This view is in accordance with the fact that there are no unique acoustic features in speech, but rather the unique combination of features separates it from non-speech sounds. Thus, it is no surprise that the neural correlates for speech would appear to consist of integrated activation of different areas that are, supposedly, processing these different aspects of speech sounds.

The further mapping between acoustic/phonetic representations and conceptual/semantic representations has been suggested to involve the posterior parts of the middle temporal gyrus (MTG) and inferior temporal gyrus (ITG) (Hickok and Poeppel, 2004), overlapping with the traditional Wernicke's area. Brain regions associated with lexical information processing have additionally been shown in areas anterior to the primary auditory cortex in the superior temporal gyrus (Davis and Johnsrude, 2003). Language comprehension has also been suggested to involve hetero-modal regions in the posterior temporal cortex and in the anterior temporal pole in both auditory and visual tasks (Marinkovic et al., 2003; Spitsyna et al., 2006).

Neurophysiological studies on non-human primates suggest that the primary auditory cortex initiates a posterior stream for processing information aimed at the localization of sound ('where') and an anterior stream aimed at recognition of the content in the sound ('what') (Kaas and Hackett, 1999; Rauschecker, 1998; Rauschecker and Tian, 2000), comparable to findings for visual signal processing (Ungerleider and Mishkin, 1982). A similar organization has been suggested based on hemodynamic human brain imaging studies with special emphasis on speech perception, although with less clearly established functional specialization of areas. The areas running antero-laterally to the core auditory region (ventral stream) are suggested to be involved in speech perception targeted at accessing lexical and semantic information (Hickok and Poeppel, 2000; Hickok and Poeppel, 2004; Scott and Johnsrude, 2003) and/or for general object identification in the sound stream (Zatorre et al., 2004). Posterior areas (dorsal stream) have been proposed to process the spatial aspects of sounds; articulatory movements/ representations of speech sounds (Hickok and Poeppel, 2004) or, as suggested by Belin and Zatorre (2000), the spectral motion in the acoustic signal. Recently, the dorsal stream was proposed as important for sensory (auditory)–motor integration in speech processing (Hickok and Poeppel, 2007).

Imaging studies provide an increasingly detailed mapping of different cognitive processes within the cortical auditory system (Price et al. 2005; Scott and Johnsrude, 2003). However, localization of functions (or the functional identities of different regions) and especially the temporal characteristics and sequence of activation between brain areas, is largely lacking (Griffiths et al., 2004). Given the framework of ordered levels and transformations in the processing of the speech signal, as well as the temporal nature of the speech signal itself, the timing of events is of fundamental importance. Due to the inertia of the blood flow, it is not possible to follow the timing of neural activation in the time-scale relevant for perceptual processes using hemodynamic neuroimaging methods. Recent evidence from electrophysiological brain imaging highlighted the importance of timing, particularly changes at the level of a syllable, for accessing meaning from a stream of speech signal (Luo and Poeppel, 2007). These authors showed that the phase pattern of neural oscillatory activity arising from the auditory cortex tracks the acoustics of natural spoken sentences so that it reliably discriminated between different sentences. The oscillatory activity occurred at 4–8 Hz, corresponding with ~200 ms temporal window that was suggested to segment the incoming speech signal. Electrophysiological brain imaging methods (MEG and EEG) have provided an approximate timeline for speech perception (and spoken word recognition) in the human brain (Phillips, 2001; Salmelin, 2007). The time-course of neural activation is evident in temporary synchronous neural activations reflected as subsequent peaks in the averaged MEG- or EEG-response.

Although the sub-cortical structures have already markedly processed the incoming sound, the relevant processes for speech perception are likely to take place cortically. The neural signal reaches the cortex within 20 ms after auditory stimulation. At around 100 ms, the non-primary auditory areas are activated, as indicated by the N100m response, generated mainly in the planum temporale (Liegeois-Chauvel et al., 1991; Lütkenhöner and Steinsträter, 1998). The N100m response is evoked by any change in the auditory environment (Hari, 1990). Its role in speech perception remains undetermined (Eulitz et al., 1995; Gootjes et al., 1999; Kuriki and Murase, 1989; Obleser et al., 2004a; Obleser et al., 2004b; Poeppel et al., 1996; Tiitinen et al., 1999).

From about 150 ms onwards the neural activation has shown sensitivity to phonological information. In so-called oddball paradigms, frequent (standard) auditory stimuli are interspersed with infrequent (deviant) stimuli. The difference between the responses to deviant and standard stimuli is referred to as the mismatch response, or mismatch negativity (MMN) in EEG literature and magnetic mismatch field (MMF) in MEG literature (Alho, 1995; Hari et al., 1984; Näätänen, 1992). The mismatch response typically reaches the maximum at ~150 ms after stimulus onset. It is seen as a reflection of auditory sensory memory at the neuronal level. MMN/MMF behaves differently for speech and non-speech stimuli (Aulanko et al., 1993; Phillips et al., 2000; Shtyrov et al., 2000; Vihla et al., 2000). Moreover, MMN responses to phoneme contrasts in the native language are stronger than those to non-native contrasts (Näätänen et al., 1997). Phonetic representation of the speech sound must, therefore, be available in this time window to enable memory traces based on phonetic (or phonological) labels. In their MEG study, Phillips et al (2000) uniquely showed that by 150 ms, the auditory cortex has access to phonological categories beyond acoustic-phonetic analysis. They used CV stimuli in which a many-to-one ratio (standard versus deviant) was present only at the phonological level, while their acoustic-phonetic features varied along a continuum.

From this latency onwards, the activation reflects higher-level linguistic processing such as lexical and semantic analysis when complete words or sentences are used as stimuli (Connolly and Phillips, 1994; Hagoort and Brown, 2000b; Helenius et al., 2002b). Starting around 200 ms, a broad, long-lasting response referred to as the N400/m shows modulation by semantic congruence of words in the sentence to preceding context (see Kutas and Hillyard, 1980 for the original ERP study of reading). The neural activation within this time-window is likely to reflect distributed activation, but the center of activation as revealed by source modeling techniques, is located in the superior temporal gyrus, in the vicinity of the auditory cortex (Helenius et al., 2002b; Kujala et al., 2004). Phonological manipulations have also been shown to influence the N400 response (Dumay et al., 2001; Perrin and Garcia-Larrea, 2003; Praamstra et al., 1994; Praamstra and Stegeman, 1993; Radeau et al., 1998) although the reports have been more variable than for semantic processing. In addition, phonologically unexpected (incongruent) words have been shown to evoke a separate response peaking between 200 and 300 ms (phonological mismatch negativity or phonological mapping negativity, PMN) (Connolly and Phillips, 1994; D'Arcy et al., 2004; Kujala et al., 2004) and suggested to reflect pre-lexical mapping between phonemic expectation and acoustic input. Later responses have been associated e.g. with syntactic processes and integration of the word to larger contexts (Hagoort and Brown, 2000a).

The present thesis contains three studies that investigated some open issues in the cortical processing of speech in adults. Study I focused on pre-lexical processing of acoustic speech signal. Identification of speech-sensitive activation has proven to be difficult, yet there is evidence from neurophysiological studies that phonetic features are encoded by ~150 ms to enable memory traces based on phonetic labels (MMN response). We examined whether the sensitivity to speech signal has already emerged by the prominent transient activation arising from the non-primary auditory cortex at about 100 ms after sound onset. This study therefore investigated the perception of speech at the level of acoustic-phonetic processing. Accessing meaning from the stream of sounds requires further transformation from the sound-based analysis to meaning-based analysis of the speech signal. The principles of processing at the interface between pre-lexical and lexical-semantic analysis of speech input, especially at the cortical level, remains to be clarified. In study IV, we approached this question by tracking the neural responses to meaningless syllables when acoustic-phonetic (bottom-up) and linguistic (top-down) information encouraged meaning-based analysis. In study V, we further investigated the cortical timing of spoken word recognition. The possible interaction between the analysis at phonological and semantic level in recognizing spoken words has not been established, either theoretically or at the neural level (see above). We examined this issue by studying the influence of expectation, either for sound form (phonology) or meaning, on the neural processing of a spoken word.

2.3 Visual perception

2.3.1 Structure of the visual system

The basic principles of the functioning of eye and vision were proposed by Helmholtz in the 19th century (Helmholtz, 1867). Four synapses separate the photoreceptors of the eye and visual cortex but rather complicated analysis is already conducted in the eye before the information is sent further to the thalamus and cortex. The primary or striatal visual pathway carries information on different aspects of vision in parallel. From area V2 onwards in the visual cortex, multiple processing streams elaborate the signal further.

The visual pathway (illustrated in Figure 6) begins at the retina; light (electromagnetic radiation) reaches the receptors of the visual system, rods and cones, after passing through the cornea and lens. Rods and cones differ both functionally and in their anatomical distribution. Rods, distributed widely in the retina, provide high sensitivity under dim light at the expense of spatial accuracy whereas cones, the density of which peaks in the centre of the retina (fovea), provide high spatial resolution under better lighting conditions.

The next processing stage in the retina consists of three specific cell-types: bipolar, horizontal and amacrine cells. Bipolar cells connect 1–45 receptors in a specific manner and together with horizontal and amacrine cells form a complex network for early processing and integration of visual information. The integration of information from multiple photoreceptors enables, for example, the perception of relative contrasts rather than absolute luminance. In the area of the center of the gaze (fovea) one-to-one connections between cones and bipolar cells make particularly accurate vision possible.

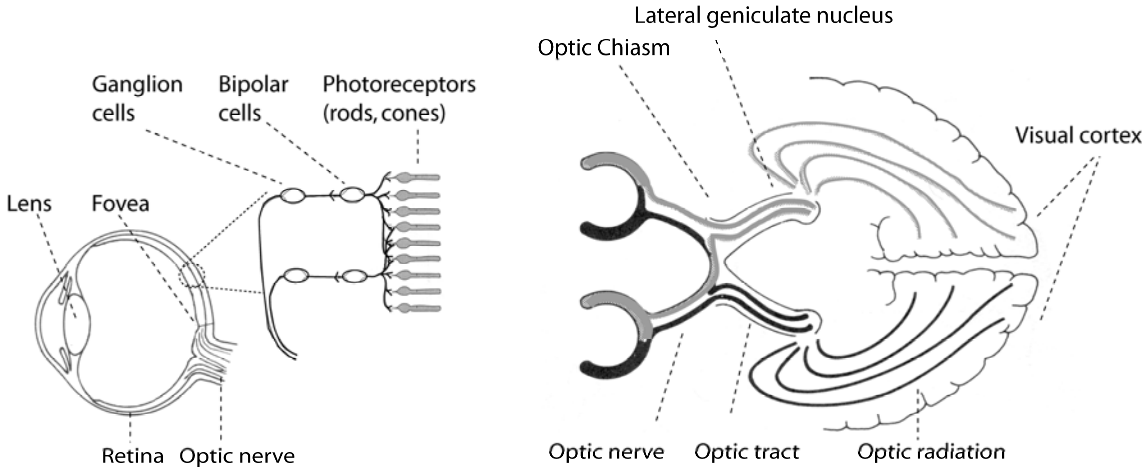


FIGURE 6 Schematic illustrations of retina (left) and the visual pathway (right). Modified from Kolb and Whishaw (1996).

Bipolar cells connect the photoreceptors to ganglion cells which form the output of retinal information processing. The optic nerve (and optic tract) transmits the neural signal to the lateral geniculate nucleus (LGN) in the thalamus via the optic chiasm. In the optic chiasm the axons arriving from each visual field (left/right) are further delivered to the contralateral side (right/left) so that the left visual field is represented in the right LGN and the right visual field in the left LGN. Moreover, information from the two eyes is kept distinct in separate layers of neurons in the LGN.

The information from the lateral geniculate nucleus is further transferred along the optic radiations to the primary visual cortex that is located in the occipital lobe, along the calcarine sulcus. Similarly to the tonotopic organization in the auditory system, the spatial organization of the visual fields (topography) are maintained in the visual pathway so that in the primary visual cortex, the central part of the visual field is represented at the back of the brain and the peripheral part is represented toward the middle of the brain. Thus, at each level of the visual system, the neurons are responsive to a specific region of the visual field, their receptive field.

In the visual pathway, there are separate processing streams that are sensitive to different aspects of vision, originating at the ganglion cells in the retina (Kaplan and Shapley, 1986) and continuing all the way to the visual cortex. The ganglion cells can be identified as large (magno, M) and small (parvo, P) cells that differ in their physiological properties and connectivity. M-cells are sensitive to rapid changes and to small differences in contrast (they function in dim light) whereas P-cells are sensitive to wavelength and have high spatial resolution (they require rather bright light). The magno-parvo division is preserved in the lateral geniculate nucleus of the thalamus in separate layers, overlapping with the anatomical separation between the two eyes.

In humans, at least ten separate representations of the visual field have been identified (Sereno et al., 1995). The primary visual cortex projects to a number of extrastriate visual areas that are organized topographically and seem to be specialized for different aspects of visual processing. After initial heterogeneous processing in V1 and V2, the information processing proceeds in segregated streams; the pathway via the color sensitive area V4 to inferior parts of the temporal lobe (ventral stream) seem to be related to object recognition, and the pathway via the motion sensitive area MT to the parietal lobe (dorsal stream) is associated with spatial awareness and guidance of actions (Figure 7). The parallel streams of processing in the cerebral cortex have been identified with anatomical and electrophysiological studies (Goodale and Milner, 1992; Ungerleider and Mishkin, 1982) as well as functional imaging studies with humans (Haxby et al., 1991; Ungerleider and Haxby, 1994). Although there is a clear continuum from the sub-cortical parvo- and mango-systems, the processing streams in the cortical level seem not to simply continue the sub-cortical streams, but their relationship is more complicated (Maunsell, 1992). The relevant visual processing stream as regards the present thesis is the ventral visual stream, responsible for object recognition.

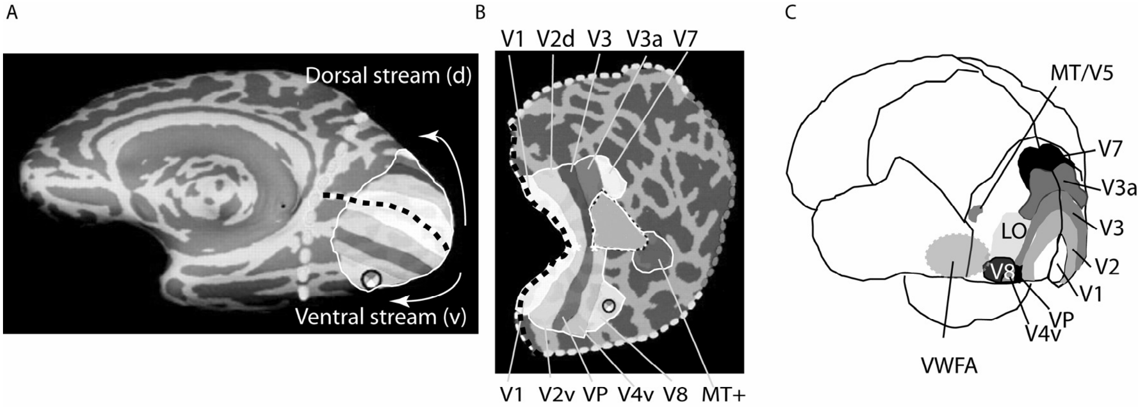


FIGURE 7 Visual areas (V1, V2, V3, V4, V5/MT, V7, V8, VP) represented in inflated cortex (A) and in two-dimensional flattened cortex (B). The cortical surface is unfolded to reveal the areas buried in the sulci, and the inflated cortex is cut along the calcarine sulcus (dashed black line) and posterior to Sylvian fissure (dashed white line). The dorsal and ventral divisions of each area are indicated. Modified from Tootell and Hadjikhani (2001). (C) Visual areas represented in schematic brain. The location of presumed visual word form area (VWFA) is roughly delimited in occipital-temporal area (after Cohen et al., 2002). Modified from Logothetis (1999).

2.3.2 Functional properties of the visual system

As is evident from the preceding summary of the anatomy of the visual pathway, rather complicated analysis of visual information takes place even in the retina. The seminal work by Hubel and Wiesel on the cat (Hubel and Wiesel, 1962) showed that the cells in the primary visual cortex are organized in columns that are sensitive to different orientations. Moreover, in the primary visual cortex, the information from separate eyes is still preserved in specific ocular dominance columns, (Hubel and Wiesel, 1962) but by output to region V2 the representation from the two eyes are combined (Horton and Hedley-Whyte, 1984). Representation of visual information in the primary visual cortex thus seems to be organized in overlaying spatial arrays that convey information from different aspects of vision: the topography of the visual field, visual information from the two eyes, the visual information from the magno vs. parvocellular pathways (low vs. high resolution) and finally the orientation specific columns. Visual information in the extrastriate visual cortex seems to be represented in distinct regions reflecting sensitivity to different features of the visual world. Although the non-primary visual areas are better characterized than the non-primary auditory areas (see figure 7), the identity and functioning of the visual areas beyond V1 and V2 are still under continuing research.

Single cell recordings in non-human primates provide information on the timing of activation in the visual pathway (Schmolesky et al., 1998). Responses evoked by the onset of a flashing stimulus in the macaque visual system were detected in the lateral geniculate nucleus of the thalamus on average at 33 ms in the magnocellular layer (with very little variance) and between 31 and 76 ms in the parvocellular layer. Responses of visual cortex neurons were measured on average at 66 ms (± 10 ms) for V1 neurons and at 82 ms (± 21 ms) for V2 neurons. Absolute timing varies substantially depending on the experimental paradigm and stimuli. Also in humans, the timing of activation in the different cortical visual areas depends on the stimuli used; the earliest cortical responses are evoked at around 60–80 ms, followed by activation around 100 ms and around 140 ms (e.g. Tobimatsu and Celesia, 2006). In addition to the hierarchical feed-forward processing of visual information, recurrent (re-entrant) processing via feedback connections from higher to lower level visual areas has been indicated both in monkeys (Hupe et al., 1998) and humans (Pascual-Leone and Walsh, 2001). This type of processing has been suggested to be especially important for attentive vision and visual awareness (Lamme and Roelfsema, 2000).

Here, we will concentrate on the visual responses related to object recognition and generated mainly in the ventral stream. The responses within the first 100 ms from stimulus onset have been suggested to originate from the striate cortex (Aine et al., 1995; Hashimoto et al., 1999; Nakamura et al., 1997; Seki et al., 1996; Vanni et al., 2004) and they show sensitivity to changes in, for instance, luminance and contrast. Accordingly, different classes of objects (such as houses, words and faces) with equally large luminance contrasts show no difference in the early occipital cortex activation at around 100 ms (Allison et al., 1994).

At around 150–200 ms, activation is sensitive to object identity and relatively insensitive to low-level features, as shown both by intracranial ERP recordings (Allison et al., 1999) and MEG studies (Liu et al., 2002; Tanskanen et al., 2005; Tarkiainen et al., 2002). Responses in this time-window originate from the extrastriate areas in the occipital lobe and further in the ventral stream in the temporal lobe. Face-sensitive responses have been localized to the fusiform gyri in direct neurophysiological recordings (Allison et al., 1994; Allison et al., 1999), MEG studies (Halgren et al., 2000; Tanskanen et al., 2005) and fMRI studies (Haxby et al., 1999; Kanwisher et al., 1997; Puce et al., 1996). Accordingly, an area in the middle fusiform gyrus has been dubbed as the Fusiform Face Area (FFA), although the representations of faces and objects in the ventral temporal cortex have also been shown to overlap (Haxby et al., 2001; Ishai et al., 2005; Ishai et al., 1999). In summary, after the initial non-specific visual processing in the primary visual areas, object recognition seems to be enabled by partly specialized areas in the occipital and temporal lobes, with neuronal groups that favor certain biologically/socially meaningful signals, such as faces.

2.3.3 Reading

2.3.3.1 Theoretical considerations

Although both auditory and visual senses mediate linguistic information, there are fundamental differences between these systems as regards language. While speech perception (and comprehension) represents primary language functions and develops rather automatically, reading is seen as a secondary language function which is built on primary spoken language processes. The spoken and written words also differ as signals – spoken words are transient and composed of a continuously changing signal, whereas written words can be inspected for longer and are composed of ready-'segmented' stationary units, letters. Owing to the 'derivative' nature of written language, these visual symbols embody a connection to auditory language, i.e. speech sounds that were set-up according to the alphabetic principle during reading acquisition. The periodic movement of eyes provides the dynamic signal for reading-related neural networks.

The visual input in reading is taken in during periodic eye-movements consisting of jumps (saccades) of about 25–60 ms, and still periods (fixations) of 200–250 ms during which information of about 15 characters to the right and 3–4 characters to the left is taken in (McConkie and Rayner, 1976; Rayner et al., 1980). The most sensitive part of the visual field, the fovea, captures only about 7 central characters of average-size text, based on which most of the meaning is extracted.

Similarly, with regard to spoken word recognition, there are numerous models depicting reading as a cognitive process where the physical features of the sensory input are converted into meaning-based representation. The first level of visual word recognition is thought to be shared with other object recognition processes and the associated neural activation to respond to basic perceptual features such as lines, angles and contours. These features are combined to form letters and letter-combinations (grapheme units). Unlike for continuous speech, written text provides clear markers for word boundaries. The resulting string of letters is further used to match with word forms in the lexicon. After lexical access (cf. spoken word recognition) all the information related to the given word is 'activated'. Traditionally, the fundamental goal of accessing meaning has been described as a process where the visual word form contacts the permanent representation of 'meanings', the lexicon. Alternative accounts see word identification as emerging from patterns of activation without the need for permanent representations of words (symbolic vs. emergent accounts of word identification, Perfetti, 1999).

The cognitive models of word recognition and reading can also be categorized in terms of whether they see 'phonological mediation', i.e. activation of the associated speech sounds, as a necessary or an optional function in the process of reading. The dual route models (as the most influential among multiple-route models) assume two parallel routes in word recognition (Coltheart et al., 1993; Coltheart and Rastle, 1994). The direct (or addressed) route provides contact to a word representation directly from the graphic input and is thought to be faster and especially useful for irregular words, i.e. words for which the regular grapheme-phoneme coding rules do not result in correct pronunciation. In the 'mediated' (or assembled) route, the graphemes are converted into phonemes before the lexicon can be accessed. This route is thought to be used for regularly written words and especially when words without a corresponding item in the lexicon (non-words) are read.

An alternative way of modeling word recognition and reading is provided by connectionist (emergent) models in which word recognition emerges from the distributed pattern of activations across, for instance, a graphic input layer and a phonological output layer (via a hidden layer) (Plaut et al., 1996; Seidenberg and McClelland, 1989) (cf. connectionist models in spoken word recognition). In these accounts, phonology is automatically activated as part of the network. Connectionist models emphasize the role of feedback information (e.g. from a phonological layer to a graphic layer) that alters the weights of the connections between input–output pairs. Both of these models have been successfully used to explain some behavioral data related to word recognition and reading.

2.3.3.2 The neural basis of visual word recognition and reading

Intracranially-implanted electrodes in epileptic patients have been used to explore functional properties and the timing of striate and extrastriate neural activation in response to diverse visual stimuli (Allison et al., 1994), including words (Nobre et al., 1994). The timing of neural activation during visual word perception has also been investigated non-invasively with EEG (e.g. Nobre and McCarthy, 1994) and timing and localization with MEG (Marinkovic et al., 2003; Salmelin et al., 1996; Tarkiainen et al., 1999). The spatial distribution of activation during letter-string perception and reading has further been investigated with fMRI (reviewed e.g. in Cohen et al., 2002; Fiez and Petersen, 1998). There is fairly good agreement with regard to the overall spatiotemporal sequence of activation during reading among different methodologies and studies.

Early visual activation that shows sensitivity to visual complexity (and non-sensitivity to linguistic content) has been localized to the bilateral occipital gyri in visual areas V1–V3 (Allison et al., 1994; Grill-Spector et al., 1998; Malach et al., 1995). The neural populations within these regions are activated around 100 ms after stimulus presentation (Salmelin et al., 1996; Tarkiainen et al., 1999). Multiple studies have shown the sensitivity of extrastriate areas to visual words, letters or letter-strings, localized typically to the fusiform gyrus in the inferior temporal area (occipitotemporal junction, on the occipitotemporal sulcus, see figure 7) (McCandliss et al., 2003; Paulesu et al., 2000; Petersen et al., 1990; Polk et al., 2002; Puce et al., 1996; Pugh et al., 1996). Based on MEG and EEG studies, the letter-string sensitive activation reaches maximum within 150–200 ms after stimulus onset (Nobre et al., 1994; Salmelin et al., 1996; Tarkiainen et al., 1999). It is not clear whether the activation reported in the fMRI studies corresponds exactly to the letter-string specific response detected in MEG studies, which typically shows a somewhat more posterior localization (Tarkiainen et al., 2002). Moreover, direct electrophysiological recordings from striate and extrastriate cortex reveal a mosaic of discrete regions in the inferior extrastriate cortex that are sensitive to faces, words, numbers and colors (Allison et al., 1994; Nobre et al., 1994).

The existence of a specific "word-form area" in the middle portion of the left fusiform gyrus has been suggested by recent reviews of visual word recognition (Cohen et al., 2000; McCandliss et al., 2003), although the exact location and role of this region in visual word perception has been discussed (Cohen and Dehaene, 2004; Price and Devlin, 2003; Price and Devlin, 2004). Cohen suggested a possible gradient from more posterior occipitotemporal areas sensitive to any letter-string to more anterior areas in inferior temporal cortex sensitive specifically to real words (Cohen et al., 2000; Cohen et al., 2002).

The two types of models of reading appoint a different role for phonological processing in the course of visual word recognition. While dual-route models suggest a separate pathway (and possibly different anatomical distribution of activation) for the reading of irregular words vs. regular words and non-words, connectionist models suggest a single route and presumably the same anatomical distribution of activation for processing of all types of words. There is however no clear consensus on whether neuroimaging results support either of these models (Fiez and Petersen, 1998). Some views support the connectionist account based on distributed processes between brain areas (Catani et al., 2005) and others support the dual-route accounts showing specialized regions for processing words via a phonological route and via direct access from pre-lexical word forms (Jobard et al., 2003). The timing of phonological effects in visual word processing has not been carefully examined but priming paradigms propose that there might be an overlap between semantic and phonological processing in time (Rugg, 1984; Rugg and Barrett, 1987). Increased activation within the left inferior frontal cortex for non-words and low-frequency words (Fiez and Petersen, 1998; Hagoort et al., 1999; Indefrey et al., 1997; Price et al., 1996) has been interpreted to reflect sub-lexical phonological processing involved in visual word recognition. Additional areas e.g. in the left inferior temporal and supramarginal gyri have also been associated with sub-lexical phonological processing (Paulesu et al., 1993; Price et al., 1996).

The timing of semantically sensitive activation via visual input (e.g. Helenius et al., 1998; Kutas and Hillyard, 1980) matches closely that detected for auditory input (Connolly and Phillips, 1994; Hagoort and Brown, 2000b; Helenius et al., 2002b). Moreover, activation reflecting semantic processing in the visual and auditory domain is localized in similar areas in the left temporal cortex (Cabeza and Nyberg, 2000; Marinkovic et al., 2003). Studies on neural processing of modality independent meaning are, however, scarce (Booth et al., 2002; Chee et al., 1999; Spitsyna et al., 2006).

The present thesis examines visual word perception/reading in adults (Study VI) and in children (Study III, which will be described in the next section). Behavioral studies show that short letter-strings are read faster than long letter-strings, but also words are read faster than non-words. Both dual-route and connectionist models of reading have sought to account for these findings. In study VI, we examined the cortical correlates of these behaviorally and theoretically predicted length and lexicality effects.

2.4 Development of language perception

2.4.1 Language development and speech perception

The primary functions of language, speaking, signing and language comprehension, develop without conscious learning and are at least partly built on innate capacities. In contrast, secondary abilities, such as reading and writing, require conscious effort and learning (teaching). There are thus cultural vs. biological influences in these two types of language functions. The type and amount of information that is available innately, in the initial state of language learning remains a matter of dispute among different theoretical perspectives (nature vs. nurture in language development: Chomsky, 2002; Piattelli-Palmarini, 1994).

The challenge faced by human infants is not apparent for adults, for whom the use of sound sequences to convey meaning in many different forms is effortless and natural. However, the problematic nature of automatic speech recognition and, for example, the difficulty of even segmenting foreign language into separate words, shows that speech perception is a much more complex task than first appears. To become a fluent listener, children must overcome several challenges (reviewed in Juszyk, 1997). First, they have to be able to cope with the physical variability in the speech signal and learn the acoustic differences conveying meaningful distinctions, i.e. phoneme boundaries in their native language. Moreover, for lexical access, words must be segmented from the speech stream and, consequently, sound patterns must be stored for later retrieval of associated meanings. For the fundamental requirement of communication, the speech details must be perceived sufficiently fluently and automatically for children to be able to pay attention to the semantic organization of the whole utterance.

In spite of these major challenges, speech perception capacities develop rapidly during the first years of life. At birth, infants are sensitive to all acoustic differences that are used to signal phonetic distinctions. This sensitivity to acoustic properties is not linear but, both in adults and children, displays better separation of sounds that belong to different phonological categories than of sounds that belong to the same category (Eimas et al., 1971; Liberman et al., 1967; Liberman et al., 1961). The tendency to perceive sounds on an acoustic continuum as falling into two distinct categories is not unique to humans (Kuhl and Miller, 1975; Kuhl and Miller, 1978). Indeed, it has been suggested that languages use natural perceptual boundaries that are innate and shared with other mammals (Kuhl, 2004). What seems to be unique to humans is the way the speech input is used to organize the perceptual capacities during development (Kuhl, 2004).

The universal perceptual capacity at birth seems to be lost or, more precisely, the perceptual properties are reorganized so that by the age of 6–8 months there is a decline in the infants’ capacity to discriminate non-native sound contrasts (Werker and Tees, 1984; Werker and Tees, 1999). This change has been suggested to result from neural commitment to patterns of language input: Infants (or their auditory system) are able to learn the statistical distribution of sound patterns in their native language (Kuhl et al., 1992; Maye et al., 2002). Kuhl suggested that the statistical distribution of elements of speech input are utilized by the infant perceptual system so that perceptual boundaries develop at phonologically meaningful points in the acoustic continuum (perceptual magnet effect, Kuhl, 1991).

By the end of the first year of life, the acoustic/phonetic and phonological properties of the native language have mostly been learned, together with the ways these sounds can be used to construct words (phonotactic rules) (Juszyk et al., 1994). The sensitivity to statistical distribution of sound sequences at the word level serves as a potential basis for later learning of semantics (Saffran, 2001; Saffran et al., 1996). Processes at various levels of linguistic organization interact during development; e.g. speech perception skills, achieved in infancy, predict the level of higher level linguistic skills such as word and phrase understanding (Silven et al., 2003; Tsao et al., 2004). By the age of 36 months, children are able to understand sentence level information with rather complex structure, although higher linguistic functions, such as syntactic comprehension, continue to develop still in adolescence (Harley, 2001).

Furthermore, the general auditory processing skills continue to develop during childhood and adolescence. Both simple pure-tone detection and more complex auditory processing, such as spectral and temporal resolution or spectral pattern discrimination, are poorer in pre-school and school-aged children than in adults (Allen and Wightman, 1992; Allen et al., 1989; Schneider et al., 1989; Wightman et al., 1989). These auditory skills, especially spectral pattern discrimination, are utilized also in speech perception. Interestingly, Wightman and Allen showed large inter-individual differences in school-aged children's performance in a spectral pattern recognition task; some children performed at the adult level in some of the trials whereas others were still performing at chance level (Wightman et al., 1989). It is, however, not clear how much these differences reflect so-called 'central processes', such as memory and attention.

2.4.2 Learning to read

In most literate environments, children are surrounded by printed material from a very early age, making them aware of text as a special visual category long before they actually learn to read. However, many behavioral studies indicate a significant role of spoken word processing skills in learning to read (Adams, 1990). The development of reading skills requires the child to become aware of the auditory form and structure of the word. Instead of meaning, the child must be able to pay attention to sub-word-level units of spoken language such as syllables, syllable onsets, syllable rimes and, most importantly, phonemes, in order to learn that speech can be turned into print with certain rules. Although infants learn to use the phonological categories of their natural language very early during postnatal development, they do not become fully aware of the constituents of spoken words, ability referred to as phonological awareness, before the early school years. The awareness of speech sounds, phoneme awareness, is very intimately related to learning the alphabetic principle – the connection between letters and phonemes.

Many studies have shown that tasks measuring phonological awareness in preliterate children are good predictors of later reading skills (Bradley and Bryant, 1983; Muter et al., 1998). Moreover, reading itself is known to facilitate phonological awareness (e.g. Wimmer et al., 1991). Thus, there is a bi-directional influence between phonological awareness and reading (Bertelson et al., 1985). This holds also for poor reading: poor phonological skills predict difficulties in reading and vice versa; illiterate adults perform poorly on phonological awareness tasks (Castro-Caldas et al., 1998; Morais et al., 1986).

Phonological awareness is thought to arise at 5 to 6 years of age through rich experience in oral language (Adams, 1990). This is normally followed by active tutoring that develops understanding of the alphabetic principle. According to Ehri (Ehri, 1992) after starting to learn the letter names and pronunciation, children can access parts of words; normally the first and final letters are recognized more easily as they visually stick out from the word (partial alphabetic phase). When children learn all the corresponding letter-speech sound (grapheme-phoneme) associations – given they possess the required working memory skills – they are in a position to start reading any words by sounding them out, letter by letter (full alphabetic phase). Gradually, children also learn to recognize larger scale units in the written word such as syllables and whole words and can read via the direct route (dual-route based accounts). Although some studies suggest a phase of reading based on larger visual units before the letter-sound correspondence develops (pre-alphabetic phase), it is now generally agreed that phonological recoding provides the most critical aspect in learning to read (Share, 1995), especially in the early phases of reading acquisition (Poskiparta et al., 1999; Sprenger-Charolles et al., 2003). The ability to transform an unfamiliar letter string from printed to spoken form, referred to as 'self-teaching mechanisms' makes independent build-up of an orthographic lexicon possible (Share, 2004).

Some theoretical accounts emphasize stage-like progression in learning to read where grapheme-to-phoneme coding precedes the direct orthographic reading (dual route based accounts, e.g. Frith, 1985; Morton, 1989), which then dominates adult reading. Other models emphasize the role of phonological recoding during the entire course of reading development (Ehri, 1998; Perfetti, 1992; Share, 1995). These approaches come close to the connectionist models, according to which both adult reading and developing reading skills build on functional connections between phonological, orthographic and semantic representations and development of reading skills occurs via construction and strengthening of these connections (Plaut et al., 1996).

The emphasis of direct grapheme-to-phoneme coding in developing reading skills presumably differs between different writing systems (Goswami et al., 2003; Seymour et al., 2003; Share, 2004). In Finnish, there is practically a one-to-one relationship between phonemes and letters and, thus, the writing system represents the most regular end among world languages (Leinonen et al., 2001; Niemi et al., 1994). This makes the grapheme-to-phoneme coding the most optimal way in which to sound out the words when learning to read. In countries with regular orthography, most children acquire phonological recoding and word-reading skills rapidly, by the end of the first grade (Holopainen et al., 2001; Seymour et al., 2003).

2.4.3 Neuroanatomical development during childhood

Although the human brain development starts during the early weeks of gestation in utero, humans are born with a rather immature brain that develops in interaction with the environment during postnatal development. The refinement of the neuronal circuitry by relevant sensory experience is essential for the normal development of the nervous system. However, the genetically controlled establishment of neural pathways and circuits provides a necessary scaffold and determines the range of possible changes for the influence of sensory signals (Pascual-Leone et al., 2005). The level of impact the environment has on the construction of neural circuits is a question of continuing research. Examples of experience-dependent brain plasticity in deaf children with cochlear implants (Gordon et al., 2003; Ponton and Eggermont, 2001) and as a result of sensory deprivation in humans (Neville and Bavelier, 2002) and in animals (Chang and Merzenich, 2003; Wiesel, 1982) indicate significant influence of the environment that is especially emphasized during maturation.

Post mortem studies give the most detailed picture of cellular level changes in the developing brain (Huttenlocher, 1979; Huttenlocher and Dabholkar, 1997). Only small samples of participants are available for these studies and nowadays anatomical and diffusion tensor (DT) MR imaging have provided important information on the development of grey and white matter.

During the first two decades of human life, parallel processes contribute to the formation of the mature brain. By the time of birth, the neurons have migrated to their target regions in the cerebral cortex – the gross anatomical structures of the brain stem and forebrain are present. The sub-cortical structures are more or less adult-like at birth but the cerebral cortex is very immature in its inter/intra regional connections (Yakovlev and Lecours, 1967). A central feature of brain development is an initial overproduction followed by gradual selective elimination of neural elements; neurons, synapses and axons. Two major processes taking place during postnatal development are the formation of connections and myelination, both of which continue throughout childhood and even adolescence, thus coinciding with the period of active cognitive development (Casey et al., 2005).

Axonal outgrowth, which starts before the neuron has finished migrating, is guided by chemical signals secreted at the target tissue. The regression of axons later in development is affected by activity-dependent mechanisms so that functioning (active) connections will survive (see e.g. Price et al., 2006 for a review). The final stage in setting up connections, synaptogenesis, begins as soon as axons reach postsynaptic cells. In humans, the maximum in synaptic density is reached between 2 and 6 years, at different times in different regions of the brain. Although in other primates (e.g. monkeys), synaptogenesis seems to proceed in parallel throughout the cortex and limbic system (Rakic et al., 1986), post mortem studies of human brains suggest that synaptogenesis in humans proceeds hierarchically from sensory and motor areas to higher-level association areas and so forth (Huttenlocher and Dabholkar, 1997). In each region, the increase in synaptic density is followed by a gradual decline in the number of synapses by means of activity-dependent pruning. The changes in synaptic density measures include elimination of some axonal input (synapses), increased number of synaptic boutouns in surviving axons and elaboration of dendritic arbor. This is the most important phase of development as regards environmental influence.

Although the basic principles of how connections are formed in developing synapses are to some extent understood, the exact mechanisms of how the spatiotemporal patterns of afferent neuronal activity determine the changes in, for example, synaptic strength, have not been revealed in detail (Yao and Dan, 2005). Moreover, relatively little is known about the system-level development of the circuitry of the human brain (Rash and Grove, 2006). Generally speaking, as stated by the well-known Hebbian rule for synaptic learning (Hebb, 1949), when an axon of cell A consistently participates in causing action potentials in cell B, the efficiency of cell A as firing cell B increases.

Recent accounts suggest mutual influence of both genetically-programmed cues and signaling from the environment in the development of neural networks (Sur and Rubenstein, 2005): The early establishment of cortical areas and layers seems to develop largely under genetic control but important refinement of the neural circuitry takes place later via activation of afferent thalamic axons. The latter are especially interesting from the point of view of cognitive development during childhood, for example developing literacy skills.

Myelination of axons provides multifold increase in the conduction velocity of the action potential, and is thus likely to have an influence also on cognitive functions. Similar to synaptogenesis/synaptic pruning, myelination of axons seems to proceed in a hierarchical manner, indicated by post mortem investigations (Benes et al., 1994; Brody et al., 1987; Verhaart, 1950; Yakovlev and Lecours, 1967). The pons and cerebellar peduncles are myelinated by birth and the fiber tracts in the sensory and motor systems of the cerebral cortex are adult-like by the end of 2 years. However, the myelination continues throughout the first decade of life for e.g. nonspecific thalamic connections, and even longer for cortical intra-hemispheric and inter-hemispheric connections (Benes et al., 1994; Yakovlev and Lecours, 1967).

The cellular level phenomena are indirectly reflected in the neuroimaging data measured with magnetic resonance imaging. The general phenomena observed in numerous developmental MRI studies are the initial increase and gradual decrease in gray matter volume/thickness by age and more linear increase in white matter volume (Giedd et al., 1999; Huppi et al., 1998; Jernigan et al., 1991). The changes in thickness and volume of cortical gray and white matter roughly coincide with the cellular level changes (changes in neuronal and synaptic densities, myelination). The normal adult appearance of brain structure is reached by 2–3 years, during which time brain growth (volume) is most rapid. A more gradual development follows, during which white matter expands and gray matter becomes thinner (reviewed e.g. in Toga et al., 2006). The changes in gray matter thickness do not directly reflect changes in neuronal/synaptic number but most likely comprise the combined effect of myelination and synaptic pruning, as well as glial and vascular changes. More subtle changes in white matter configuration and 'maturity' can be studied with diffusion tensor imaging (DTI), which enables the visualization of fiber tracts and provides information on the microstructure of white matter (Klingberg et al., 2000; Paus et al., 2001).

Regional differences in the development of gray matter are evident in MRI studies in similar fashion, as shown at the cellular level (Giedd et al., 1999; Jernigan et al., 1991; Sowell et al., 1999; Sowell et al., 2004). The loss of gray matter is first observed in the primary sensori-motor cortices, followed by parietal-to-frontal progression of development (Gogtay et al., 2004; Sowell et al., 2004). The posterior temporal cortex seems to show a particularly prolonged maturational trajectory although the temporal lobes, in general, mature early (Gogtay et al., 2004). Also, white matter develops in a region-specific fashion (Barkovich and Kjos, 1988; Bird et al., 1989; Giedd et al., 1999; Paus et al., 2001; Pfefferbaum et al., 1994; Reiss et al., 1996). Interestingly, white matter comprising fiber tracts for fine motor movements (corticospinal tract) and motor-perceptual speech processing (corticocortical pathway connecting left frontal and temporal speech regions) show protracted development (Paus et al., 1999).

To summarize, there are clear macro-anatomical changes during development that indirectly reflect cellular level changes and seem to continue well into adolescence and even adulthood. Although the most extensive changes in the brain take place during the first years of life (concordant with behavioral/cognitive development), it is noteworthy that a great deal of the changes reflecting formation of neuronal circuitry takes place late in postnatal development, at the time children are behaviorally acquiring more and more complex skills. It is apparent that the changes at the level of the brain are tightly linked to the changes observed in the psychological development of the children. Indeed, given the increasing influence of afferent input in the formation of functional neural networks, it is not trivial to distinguish between changes occurring due to 'biological maturation' and 'psychological development' as they are necessarily interwoven. Direct studies correlating behavioral skills and different measures of brain development are still rare (Moore, 2002; Sowell et al., 2004).

2.4.4 Functional maturation of the auditory and visual systems

The functional maturation of the brain has been most extensively studied with EEG, although recently, fMRI has also been used in developmental brain imaging. Most of the studies on children are cross-sectional, i.e. different participants are used in different age-groups. Longitudinal studies would be necessary to more reliably show the effect of maturation. Here, we focus on studies of auditory and visual evoked potentials.

The development of auditory brain-stem potentials (ABRs) is quite reliably known and the detection of the I–V waves within 15 ms of cochlear stimulation are widely-used in diagnosis of developmental hearing disorders. These early potentials are generated in the auditory nerve and sub-cortical structures and show mature latencies at about 2 years of age (Starr and Amlie, 1981), in agreement with structural maturation of the brain stem. The development of later components generated in sub-cortical and cortical structures between 20 and 400 ms is much less well known and reflects complex changes in the underlying neural generators, as well as slower developmental trajectories (Eggermont, 1988; Ponton et al., 2002; Ponton et al., 2000).

In infants and children, the cortical auditory evoked response differs considerably from that in adults. In adults, the typical sequence of responses consists of P1 at 50 ms, N1 at 100 ms, P2 at around 200 ms, sometimes followed by a small N2 deflection of opposite polarity (see chapter 2.2.2). In newborns and young infants, the auditory evoked potential is composed of a large positive-going deflection at around 200 ms followed by a large negative-going deflection between 300 and 550 ms (Kurtzberg et al., 1984; Rotteveel et al., 1986). This biphasic waveform changes during development and the more transient and earlier components appear gradually in the response. The P1 component has been reliably shown in children by early school-years (Albrecht et al., 2000; Ponton et al., 2002; Sharma et al., 1997) and the most prominent response in adults, a transient negative-going response (N100/N1), emerges by 9 years of age (Ceponiene et al., 2002; Cunningham et al., 2000; Kraus et al., 1993). At long inter-stimulus intervals N100/N1 may also be detected in younger children (Ceponiene et al., 2002; Paetau et al., 1995; Rojas et al., 1998; Takeshita et al., 2002). Both P1 and N1/N100 components first emerge at somewhat longer latencies than in adults, but the latencies decrease with age until adolescence and even adulthood (Albrecht et al., 2000; Cunningham et al., 2000; Johnstone et al., 1996; Kraus et al., 1993; Ponton et al., 2000; Sharma et al., 1997; Takeshita et al., 2002; Tonnquist-Uhlen et al., 1995).

The most prominent and consistently reported response throughout childhood is a prolonged activation detected after 200 ms, referred to as the N250 response (Albrecht et al., 2000; Paul et al., 2006; Ponton et al., 2000; Sharma et al., 1997). By maturation, the transient negative-going response (emerging N1) seem to increase in strength while the later prolonged negative-going activation (N250) decreases in amplitude and is only occasionally recorded in adults (Cunningham et al., 2000; Takeshita et al., 2002). The adult type of activation sequence is attained by late adolescence (Wunderlich et al., 2006). With strongly changing response morphology, it is not straightforward to identify components of the auditory responses that correspond to each other across different age groups. While the development of the P1 response to its adult form seems rather clear, the correspondence between the immature (prolonged) N250 and the adult responses with a prominent N1 and smaller (or non-existent) N2 is not clear.

Auditory evoked response development is thus accompanied by a general decrease in latency – or transition of emphasis to earlier waveform components. The variable developmental rates for different components have been suggested to reflect parallel development of different underlying neural systems (Ponton et al., 2002). The functional sensitivities of different components has been investigated in only a few experiments (Ceponiene et al., 2005).

Visual evoked potentials (VEP) have been used to investigate the development of vision in infants and children. The early cortical processing (in primary visual areas) is typically studied with simple visual stimuli such as gratings, bars and checks. Dynamic visual stimuli (pattern reversal) evoke a different type of response from non-recurring stimuli (pattern onset/offset). In adults, a typical sequence of visual evoked responses to pattern onset consists of three main components at around 65–80 ms (C1), 90–110 ms (C2, or P1) and 130–150 ms (C3) (Odom et al., 2004; Tobimatsu and Celesia, 2006). The latency of evoked responses decreases with age (Brecelj, 2003; Brecelj et al., 2002) and also the component structure has been shown to change during development (Madrid and Crognale, 2000). Some studies show mature P1 responses already at one year of age (Crognale, 2002; Moskowitz and Sokol, 1983) but others suggest P1 latency to decrease until adolescence or adulthood (Allison et al., 1984; Brecelj et al., 2002).

As was evident for the auditory system, it is also not straightforward to find corresponding components in adults and children in the visual domain. Category specific activation in children has been studied using faces (de Haan et al., 2003; Taylor et al., 2004). Face-sensitive responses have been detected also in infants but in a very different time-window to that of older children or adults (de Haan et al., 2003). Similar to the early positive component (P1), a face sensitive component, detected at around 170 ms (N170) in adults, shows a gradual decrease in latency with age (from 4 year olds to adults) and the steepest rate of change in latency occurs before 10 years (Taylor et al., 2004).

Reading is evolutionarily a new skill and no brain area can be assumed to be involved in written word perception at birth. Studies of reading and word recognition in adults have lead to theoretical speculations on the development of the visual word form area as an outcome of exposure to printed material (McCandliss et al., 2003). However, this has not been directly tested in neuroimaging experiments. Processing of visual language, as measured with fMRI, was shown to involve partly different regions of the brain in adults and children (Schlaggar et al., 2002). During equalized task performance, children aged between 7 and 10 years engaged less the frontal regions and more the extrastriate regions than adults. Moreover, Turkeltaub and co-workers

(Turkeltaub et al., 2003) suggested increased involvement of left-hemisphere middle temporal and inferior frontal areas with better reading skills. According to this fMRI study, the principal area recruited by young children during reading was the posterior superior temporal sulcus that showed sensitivity to words over false fonts in children (similarly as for adults).

Few studies have investigated the timing of category-specific activation for letter-strings and words in children. In a recent EEG study (Maurer et al., 2006), evoked responses to words and symbol strings were compared between preliterate kindergarten children and adults. The timing of activation was delayed in children as compared with adults. Moreover, the responses between words and symbol strings were less clearly separated in children than in adults. Also MEG has been used to investigate brain activation during printed word recognition in children (Simos et al., 2001). The sequence of activation in the children (8–15 years) started from bilateral occipital areas at around 140 ms and proceeded via basal temporal areas at 230 ms to left (330 ms) and right (430 ms) temporal areas. All of these activation stages were delayed in children as compared with adults. Lack of non-linguistic control stimuli precluded the possibility to examine early activation sensitive to letter-strings over other visual symbols. The main focus in developmental EEG studies using linguistic stimuli has been in the higher-level effects in reading, such as semantic (Coch and Holcomb, 2003; Holcomb et al., 1992) and phonological (Grossi et al., 2001) processing.

The present thesis includes two studies of language perception conducted with 7- to 8-year-old children. Earlier studies have shown prominent maturational changes in the general response morphology of auditory and visual evoked responses. However, the time-behavior of the underlying neural sources is poorly understood and, in particular, the functional significance of these effects has not been established. Literacy acquisition is known to be accompanied by increased auditory speech processing skills. In study II, we examined whether children, at the age of intensive reading development, show similar sensitivity to speech as adults. Crucially, we tested for correlation between their behavioral performance in phonological and reading tasks and cortical activation to speech sounds. It has been hypothesized that the exposure to printed material during childhood induces tuning in the extrastriate visual cortex to letters and words. In adults, neural responses from the occipitotemporal cortex reflect sensitivity to visual words (letter-strings). In study III, we characterized the spatiotemporal sequence of word perception in children to examine whether similar sensitivity can be detected in beginning readers.

2.4.5 Atypical reading development: dyslexia

Developmental dyslexia or specific reading disability is a brain-based developmental disorder in which reading ability is much lower than expected on the grounds of other cognitive abilities (Diagnostic and Statistical Manual of Mental Disorders, 4th edition, 1994). In practice, dyslexia is typically diagnosed in the early school years when actual reading skills lag behind the expected reading skills based on age and IQ (Dykman and Ackerman, 1992; Fletcher et al., 1992; Shaywitz et al., 1992). Depending on the research method, 10–15 % of the population has been estimated to be affected by this disorder (Shaywitz et al., 1992; Stein and Walsh, 1997).

Linkage studies of families with many affected members have been used to identify genes involved in dyslexia and there are several chromosomes (at least in chromosomes 6 and 15) that seem to be involved in the symptom (Grigorenko, 2001). Based on a study of Finnish familial dyslexics, Taipale and co-workers proposed the first candidate gene for dyslexia (Taipale et al., 2003). There is, however, a complex interaction between genetic factors and environmental factors that determine the final outcome of reading ability.

Reading problems in dyslexia are manifested as difficulties in acquiring basic reading sub-skills, such as word identification and phonological (letter-sound) decoding, resulting in slow and error-prone reading. Many dyslexic individuals still experience reading difficulties in adulthood (Leinonen et al., 2001; Scarborough, 1984). It is commonly agreed that the underlying deficits in dyslexia are associated with impaired phonological skills (Bradley and Bryant, 1978; Bradley and Bryant, 1979; Fletcher et al., 1994; Shankweiler et al., 1995; Shaywitz et al., 1998; Stanovich and Siegel, 1988). Phonological ability is, however, not a homogeneous body of capacity but is constructed of a relatively heterogeneous set of different components (Lyytinen, 1997; Wagner and Torgesen, 1987). Wagner and Torgesen defined phonological skills as consisting of awareness of the sound structure of the spoken language (phonological awareness), coding and temporarily memorizing sound-based representations (phonological coding), and rapid access to phonological information during production.

There are varying views concerning the nature of the core deficit (or deficits) underlying dyslexia. The idea of a specific language related impairment dates back to the early 1980's (Snowling, 1981) and is still strongly supported by behavioral and imaging findings (Vellutino et al., 2004). However, an underlying deficit in basic auditory processing, not specific to speech sounds, has also gained support from experimental findings. This hypothesis claims that the ability to process the versatile properties of sounds is somehow impaired in dyslexia. According to Tallal (Tallal, 1980; Tallal et al., 1993), difficulties in speech perception of children with specific language learning impairment or with dyslexia arise from the inability to process brief acoustic changes, i.e. temporal features of auditory information. Consequently, language- and reading-impaired children are unable to establish stable and invariant phonemic representations. This could affect reading acquisition due to difficulties in accurately perceiving speech and the sub-word segments of words. A counter-argument to Tallal's hypothesis states that the difficulties in identification of temporal changes stem from a deficit in discriminative capacity, not in temporal processing of acoustic phenomena in general (Mody et al., 1997). According to Mody and co-workers (Mody et al., 1997) dyslexia stems from a domain-specific deficit in discriminating or segmenting different sounds in language.

Impairments of other sensory modalities have also been suggested. Before the hypothesis of a language-based deficit in dyslexia emerged, reading problems were thought to stem from visual deficits in processing letters and words (Orton, 1925). The current version of the visual deficit hypothesis proposes lower-level visual dysfunctions as underlying dyslexia. According to the magnocellular theory of dyslexia (Stein and Walsh, 1997), disruption in the magnocellular system causes difficulties in processing rapidly changing information, e.g. visual motion (Eden et al., 1996), a problem which generalizes also to auditory and tactile modalities. Although low-level visual deficits have been reported in dyslexic participants (Eden et al., 1994; Lovegrove et al., 1980), their causal role in reading disability is unclear (Ramus et al., 2003). Dyslexia has also been hypothesized to be related to dysfunctions in visuospatial attention (Hari et al., 2001). Because of the multiple symptoms found in dyslexia at the behavioral level, some authors have suggested that dyslexia would be better explained as different sub-syndromes with distinctive core deficits than as one homogeneous syndrome (Manis et al., 1996; Ridder et al., 1997).

During the past decades, both structural and functional brain imaging have been widely used to explore the neural processes affected in dyslexia, but the general conclusion remains fragmentary. Early post mortem studies suggested unexpected symmetry of the area of planum temporale when the area is normally larger in the left than right hemisphere (Galaburda, 1993; Galaburda et al., 1985). These early post mortem investigations have been critically evaluated and subsequent anatomical MRI studies have shown both atypical symmetry (Hynd et al., 1990; Larsen et al., 1990; Leonard et al., 1993) and normal asymmetry (Schultz et al., 1994) of the planum temporale in dyslexia. Recently, the structural integrity of white matter in the temporoparietal area in the left hemisphere was shown to correlate with reading skills in both dyslexic and control readers (Klingberg et al., 2000).

In neurophysiological studies of dyslexic participants, the spatiotemporal sequence during reading has indicated intact early visual processing in occipital visual areas at around 100 ms, but lacking or diminished activation in the left occipitotemporal area that shows letter-string specific activation at around 150 ms after stimulus onset in fluent readers (Helenius et al., 1999b; Salmelin et al., 1996). In the following stages of visual word processing activation was delayed – the N400 response reflecting semantic information processing occurred significantly later in dyslexic participants than in controls (Helenius et al., 1999a). The lack or diminished activation of posterior temporal/ occipitotemporal region in dyslexia has been corroborated in fMRI/PET studies (Brunswick et al., 1999; Rumsey et al., 1997b; Shaywitz et al., 1998). Interestingly, hemodynamic response in this occipitotemporal area was found to be positively correlated with non-word reading skills in dyslexic children (Shaywitz et al., 2002); moreover, activation in the left occipitotemporal and superior temporal areas increased after phonological training (Shaywitz et al., 2004; Shaywitz et al., 2002). Taken together, unusually weak activation in the posterior language-related areas seems to be the most consistent finding in dyslexia at the neural level.

Functional imaging has also been used to investigate the processing of spoken language in dyslexic participants. Activation to semantic violation (the N400 response) from the temporal cortex was shown to be similarly delayed for spoken words as earlier described for written words (Helenius et al., 2002b). Thus, the neural correlates of semantic processing seem to be delayed in both modalities. Also the sub-lexical stages of spoken word perception seem to be atypical in dyslexia, reflected in neural activation at around 150 ms in an MMN paradigm with synthetic speech sounds (Schulte-Korne et al., 2001). Some studies have also shown an atypical N100 response in dyslexia (Brunswick and Rippon, 1994; Helenius et al., 2002b). It is however not clear whether this response reflects processing based on linguistic information in the speech signal or processing of purely auditory information. In line with the general auditory deficits in dyslexia, abnormal activation in dyslexic participants have been indicated in response to various types of auditory stimuli (Baldeweg et al., 1999; Kujala et al., 2003; Kujala et al., 2000; McAnally and Stein, 1996; Renvall and Hari, 2002; Temple et al., 2000). Although some of these studies suggest that the dysfunction is specifically in processing rapidly changing auditory information (e.g. Nagarajan et al., 1999), this is not always the case (Ramus et al., 2003). In accordance with behavioral findings, functional imaging studies show deviant neural processing associated with a variety of auditory functions, most reliably when requiring phonological processing.

In the present thesis, study I focused on the question of whether the speech processing deficits in dyslexia stem from an underlying dysfunction in general auditory processing. We investigated the prominent neural response arising from the left planum temporale at around 100 ms and its possible differences in dyslexic and typically-reading participants when they process speech and non-speech sounds.

3 AIMS OF THE STUDY

This thesis describes studies designed to investigate the time course of auditory and visual language perception in mature and immature human brain, specifically at the early, pre-lexical level to find out how and when auditory and visual units of language are perceived in the brain.

The specific aims were

1. To investigate the sensitivity of cortical activation to the acoustic signal of speech in adults with normal language development and with developmental dyslexia (Study I)

2. To characterize the spatiotemporal sequence of cortical auditory processing in general and timing of speech sensitive activation in particular, in children learning to read (Study II)

3. In the same children, to investigate sensitivity of cortical activation to printed words and examine the correlation of the neural measures with auditory and visual linguistic skills (Study III)

4. To investigate cortical correlates of higher-level stages of speech perception in adults: First, the effect of acoustic-phonetic cues (bottom-up influences) and linguistic context (top-down influences) on the cortical processing of naturally spoken syllables; second, cortical processing of sound form (phonology) and meaning (semantics) of naturally spoken words (Studies IV–V)

5. To characterize the cortical effects of physical features (letter-string length) and linguistic features (lexicality, i.e. words vs. non-words) in written word perception in adults (Study VI)

4 MATERIALS AND METHODS

4.1 Participants

Altogether 29 typically-reading adults (aged 20–39 years, 15 females), 10 adults with developmental dyslexia (aged 20–39 years, 5 females) and 19 children with typical language development (aged 7 years and 2 months – 8 years, 10 females) were studied (Table 1).

TABLE 1 The number and age of subjects participating Studies I–VI

	Number of Participants (females + males)	Age (years)
Study I (Dyslexic Ss)	5 + 5 (5 + 5)	23–39 (20–39)
Study II & III	10 + 9*	7.2–8.0
Study IV	5 + 5	23–29
Study V	5 + 5	20–29
Study VI	4 + 4	22–32

* One male subjects was excluded from study III due to poor eyesight

The dyslexic participants were selected on the basis of self-reported early history of reading problems. They had all been tested for dyslexia by a psychologist, a speech therapist or a special education teacher and/or had received special tutoring for reading difficulties during their school years. Based on an interview, individuals who reported other developmental disorders were excluded.

The children were recruited from three Finnish schools. They attended the first grade of the elementary school and had normal language development. All children participating in the experiments had an average level of reading skills (or above) as screened in the classroom using the Comprehension of Statements test (TL3: A and B versions) of the standardized Elementary School Reading Test battery [ALLU (Lindeman, 1998)] that has been constructed to evaluate the reading status of 7- to 13-year-old Finnish-speaking children. This test consists of three practice and 52 testing trials, each composed of one statement (sentence). The children are asked to read the sentences and decide whether they are true or not (e.g. "Adults eat books") with a time limit of 5 minutes. The number of correct answers is calculated. All the children participated in both the auditory and visual experiments (Studies II–III) except for one male subject who, due to poor eyesight, did not take part in the visual experiment.

The MEG data on children were compared with data collected from adults using essentially the same paradigm. In the auditory experiment, the adult data for comparison were taken from Study I and in the visual experiment, from a previous study on letter-string perception in adults (Tarkiainen et al., 1999), with 12 adult participants (21–42 years, four females).

All participants were right-handed, had normal (or corrected to normal) vision and no history of neurological abnormalities. All participants were native Finnish speakers.

4.2 Behavioral testing

4.2.1 Dyslexic adults

The dyslexic participants were tested for general linguistic and non-linguistic abilities using a subset of the standardized Finnish version of the Wechsler Adult Intelligence Scale – Revised (WAIS-R) and Wechsler Memory Scale – Revised (WMS-R) tests (Vocabulary, Comprehension, Similarities, Block Design, Digit Span, Visual Span) (Wechsler, 1981; Wechsler, 1987). The reading and naming speed of dyslexic participants was also measured. Reduced reading speed (Leinonen et al., 2001) and naming speed (Wolf and Obregon, 1992) have been found to be reliable markers for dyslexia. In the Oral Reading test, participants were asked to read aloud a narrative printed on a sheet of paper. Reading speed was measured as words per minute. In the Rapid Automatized Naming test (RAN: Denckla and Rudel, 1976) and in the Rapid Alternating Stimulus naming test (RAS: Wolf, 1986) participants were asked to name a 5 x 10 matrix of colors, numbers and letters and the naming speed was measured. The results of these tests were compared against norm data of 38 (Oral Reading, RAS) and 15 (RAN) typically-reading participants.

In addition, the following auditorily-presented phonological tests were administered. In the Phoneme Deletion test (Leinonen et al., 2001) 16 words with 4–10 phonemes and with 2–4 syllables were presented via headphones. Participants were asked to pronounce each stimulus without the second phoneme (e.g. /studio/ → /sudio/, /kaupunki/ → /kupunki/). The number of correct responses was calculated. In the Syllable Reversal test (Leinonen et al., 2001), 10 words and 10 non-words with 5–9 phonemes and with 3–4 syllables were presented via headphones and participants were asked to change the order of the last two syllables and to say the new pseudo word aloud (e.g. /aurinko/ → /aukorin/, /rospiemi/ → /rosmipie/). The number of correct responses was calculated. Due to the one-to-one correspondence between phonemes and letters in the Finnish language these phonological tasks can be performed both by relying on phonological working memory and/or manipulating a visualized letter-string. For Phoneme Deletion and Syllable Reversal tests, the vocal reaction times to the stimuli were measured from a microphone signal. In the Spelling test (Leinonen et al., 2001), the participants were asked to spell to dictation 10 non-words and 10 words, each with 6–14 letters and comprising 2–7 syllables. The number of errors was calculated. These phonological tests were also administered to seven of the control participants participating in this study.

All the dyslexic participants had normal intelligence, as measured by the general linguistic and non-linguistic cognitive tests (WAIS-R, WMS-R). The dyslexic participants were significantly slower than typically-reading controls in the Oral Reading test [mean (SD) in dyslexic participants: 105 (31) words and in controls: 164 (28) words, $t(46) = 5.8$, $P<0.001$] and Rapid Naming tests [RAS: mean (SD) in dyslexic participants: 33 (5.8) seconds and in controls: 24 (4.8) seconds, $t(46) = 5.9$, $P<0.001$; RAN: mean (SD) in dyslexic participants 29 (3.7) seconds and in controls 24 (5.0) seconds, $t(23) = 2.5$, $P<0.05$]. In the phonological tests the dyslexic participants were significantly slower and more error-prone than controls. The reaction times of the dyslexic individuals were longer than those of the controls in the auditorily-presented Phoneme Deletion test [difference on average 3.7 s, $t(15)=-4.6$, $P<0.001$] and Syllable Reversal test [difference on average 5.4 s, $t(15) =-4.8$, $P<0.001$]. Dyslexic participants also made significantly more errors in the Phoneme Deletion [$t(15) = 2.5$, $P < 0.05$], Syllable Reversal [$t(15) = 2.3$, $P < 0.05$] and Spelling tests [$t(15) =-2.9$, $P < 0.05$] than did control participants.

4.2.2 Children

The reading skills of each child were evaluated using four tests, including the Comprehension of Statements test described above (chapter 4.1). Two more tests from the Elementary School Reading Test battery (Lindeman, 1998) were administered. The Word Recognition test (TL2: A version) and the Sentence Comprehension test (TL4: A version) consist of 4/3 (TL2/TL4, words/sentences) practice trials and 80/20 testing trials. Each trial is composed of a picture that matches one of four written words/sentences. The task is to identify as many correct picture word/sentence pairs as possible in 5/2 min. The total score was the number correct of 80/20 trials. In the Story Reading task, the child was given a narrative 55-word story printed on paper and asked to read it aloud in the way he/she usually does in a reading situation (Kajamies, 2003). The experimenter recorded the time the child spent on the story and the number of incorrectly read words.

In addition to reading skills, we tested phonological awareness, rapid naming, and phonological memory for each child. The test of phonological awareness consisted of four subtests, each having 10 items (Poskiparta, 1994) (for psychometric properties, see Silvén, 2004). In Syllable Deletion, the examiner said aloud a word and asked the child to pronounce the word without a given syllable. The remaining part also formed a word. The deleted syllables were at the end, at the beginning, or in the middle of the original word. In Phoneme Blending, two- to four-letter words were presented phoneme-by-phoneme, and the child was asked to say aloud the resulting word. In Single Phoneme Isolation, the child was asked to say aloud the first phoneme/letter of the word. In Phoneme Deletion, the child was asked to delete the initial phoneme and to say aloud the remaining part, which formed a word. In the Single Phoneme Isolation test, all children identified all initial phonemes correctly (10 of 10) and, therefore, this measure was not included in further analyze. Rapid naming tests were used to measure the efficiency of phonological information retrieval from the long-term store. We used two tasks from the Finnish version of the rapid serial naming test (Ahonen et al., 1999), which is based on the Rapid Automatized Naming test by Denckla and Rudel (Denckla and Rudel, 1976). In the rapid naming of colors/letters, the child named as fast and correctly as possible a series of colored squares/letters, 50 items of each. The naming speed was measured as the time it took in seconds to complete each task, and the rate variables were computed as total task duration/50.

Phonological memory/auditory short-term memory was tested using Digit Span and general linguistic and non-linguistic abilities using the Similarities and Block Design items of the Wechsler Intelligence Scale for Children – Revised (WISC-R) (Wechsler, 1974). The tests were administered 7–10 months after school start.

All children had normal (or better) general cognitive skills (WISC-R: Wechsler, 1984). The overall reading level was within or above the age-normal range [ALLU; mean score of word and sentence recognition and sentence comprehension (Lindeman, 1998)]. Nevertheless, the speed of reading a passage of narrative text aloud (Kajamies, 2003) varied substantially between individuals, from 0.5 to 6.6 s/word. A compound measure of phonological awareness was obtained as an average across three tests: Syllable Deletion, Phoneme Blending, and Phoneme Deletion (Poskiparta, 1994); the participants' performance in these tasks varied from 7 to 10, 6 to 10, and 5 to 10 (max of 10), respectively. The naming speed of colors varied from 0.8 to 1.8 s/item and that of letters from 0.5 to 1.0 s/item (Ahonen et al., 1999); the results of both tests fell within normal limits.

4.3 Magnetoencephalography

4.3.1 Instrumentation and signal genesis

The following introduction is mainly based on Hari (1990; 1993) and Hämäläinen (1993). Magnetoencephalography (MEG) is based on the recording of weak magnetic fields that are produced by the electric currents in the brain (see chapter 2.1.2). Magnetic fields from the human brain were first measured in 1968 by Cohen (Cohen, 1968). Introduction of high-sensitivity detectors employing Superconducting Quantum Interference Devices (SQUIDs) in the late 1960's (Zimmerman et al., 1970), and later development of multichannel MEG systems enabled studies of neural phenomena related to sensory functions of the human brain. The development of the sensor arrays to cover the entire head as well as improvements in the signal analysis methods has further increased the power and suitability of MEG to the study of complex cognitive functions with multiple neuronal populations activated simultaneously.

The changes in the measured magnetic field reflect postsynaptic activity of neurons. The currents flowing in the apical dendrites of pyramidal cells are the primary source of the signal seen by MEG and EEG. When postsynaptic currents flow synchronously in thousands of cells oriented in parallel, the net current is large enough to give rise to a measurable magnetic field outside of the skull. The net current in a small patch of cortex can be represented as a current dipole whose position, direction and magnitude can be estimated from the MEG measurements. According to the right-hand rule, the magnetic field lines circulate around the axis of the current.

A superconducting flux transformer, consisting of a pickup coil and a signal coil, couples the measured magnetic field into the SQUID. The geometry of the pickup coil determines the sensitivity pattern to source currents and interference fields. The Vectorview system (Elekta Neuromag Oy, Helsinki, Finland) used in this thesis comprises 102 triple sensor elements, each having one magnetometer and two planar gradiometers (see Figure 8). Magnetometers, with a single pickup loop, exhibit two maxima, negative and positive, symmetrically on the sides of a dipolar source current. Planar gradiometers, consisting of two oppositely wound loops in the same plane (a figure-of-eight loop), detect the maximum signal directly above a current source where the magnetic field changes most rapidly. Moreover, a homogenous magnetic field from a far-away source couples equally to both of the opposing coils, and is thus cancelled out, which greatly reduces the influence of distant artifact sources on planar gradiometer signals.

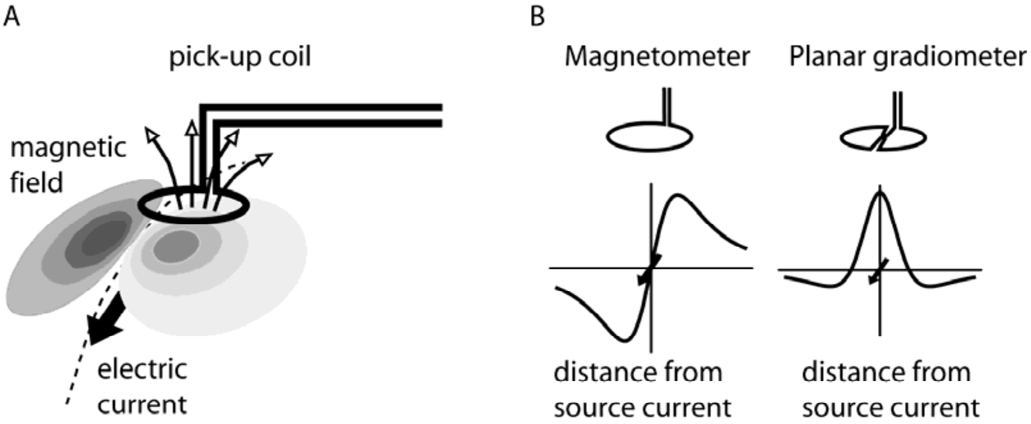


FIGURE 8 (A) Schematic illustration of the coupling of the magnetic field due to an electric current into the pickup coil. (B) The sensitivity profiles of a magnetometer and a planar gradiometer to the magnetic field produced by a current source. The curve illustrates the measured signal (y-axis) as a function of lateral distance from the source current (x-axis).

The strength of the currents that can be detected outside of the head is typically on the order of tens of nanoamperemeters (nAm). The parameters of an equivalent current dipole representing the activity in a small patch of cortex, i.e., the strength and location of the current flow can be estimated from the measured magnetic field. The electric potential on the scalp and the magnetic field outside of the head can be computed if the source parameters and the conductivities and geometries of the surrounding tissues are known (forward problem). However, determining the source current distribution in the brain based on the measured magnetic field (or electric potential distribution on the scalp) is not unambiguous (inverse problem) – several current configurations can give rise to the same field pattern. Thus, certain prior assumptions or constraints must be used when localizing the currents in the brain. In this thesis, the neural sources of electric currents are modeled as equivalent current dipoles that approximate the current flow in a small region of cortex.

4.3.2 Stimulation

In studies I–II and IV–V the auditory stimuli were delivered to the participant through plastic tubes and earpieces, using monaural stimulation to the right ear in Studies I–II and binaural stimulation in studies IV–V. Stimulus presentation was controlled by the Presentation program (Neurobehavioral Systems Inc., San Francisco, CA) running on a PC. In studies III and VI the visual stimuli were delivered via PC and data projector to a screen placed at a distance of 1 m in front of the subject.

4.3.3 Measurement

Magnetic signals were recorded using a helmet-shaped 306-sensor whole head neuromagnetometer (Vectorview; Electa Neuromag OY, Helsinki, Finland). During the measurement, the participants were sitting in a magnetically shielded room with their head leaning on the back of the measurement helmet. For children (Studies II–III) there was always an adult with the child in the measurement room.

The MEG signals were bandpass filtered at 0.03–200 Hz and sampled at 600 Hz. The horizontal and vertical electro-oculograms (EOGs) were recorded for on-line rejection of epochs contaminated by blinks or saccades (Studies I–IV, VI). Due to a long averaging window in study V, the artifacts caused by blinks and saccades were removed off-line: data were averaged with respect to eye movements, then a principal component analysis (PCA) was performed on this average and the component that contained the artifacts due to eye movements was removed from the data.

Some additional sources of artifact were detected, especially in studies with a long averaging window. In study II, the potential artifact signal produced by heartbeat was removed by off-line averaging the data with respect to heart signal that was clearly detectable in the raw MEG signal along the rim of the helmet. In addition, in studies II and V, the data were visually inspected to exclude epochs contaminated by major artifacts. On average, 100 artifact-free epochs per participant were gathered for each stimulus category. For children and in the studies using a long averaging window, a minimum of 60 artifact-free epochs were required (II,III, V).

The position of the participant's head within the MEG helmet was determined at the beginning of each measurement session by briefly energizing four head position indicator coils attached to the participant's head. The location of the coils was determined with respect to three anatomical landmarks (pre-auricular points and nasion) using a three-dimensional digitizer (Polhemus, Colchester, VT). The same landmarks were identified on the anatomical MR images thus allowing alignment of the MEG and MRI coordinate systems. The MRIs were recorded at the Department of Radiology, Helsinki University Central Hospital, with a 1.5 T Siemens Magnetom ™ device.

4.3.4 Data analysis

To obtain an initial overview of the data, the sensors of the measurement helmet were divided into 7–10 areas and the mean signal over the channels within each area was calculated (Studies II, IV, V). The vector sums of each gradiometer pair were first computed by squaring the MEG signals, summing them together, and calculating the square root of this sum. Areal mean signals (AMS) were computed by averaging these vector sums for each area of interest, individually for each participant. Finally, the areal mean signals were averaged across participants. Because of the way the sensor-level areal mean signals are calculated (square root of sum of squared signals) they do not contain information about the orientation of the current sources and they always have a positive value (>0).

The activated cortical areas were modeled as equivalent current dipoles (ECD), which represent the mean location, direction and strength of the current flowing in a given cortical patch (Hämäläinen et al., 1993). To determine the ECDs, the magnetic field patterns were first visually inspected to identify local dipolar fields. The time point when there was minimal contamination by other active source areas was chosen to estimate the ECDs. Based on the signal distribution across the sensors covering dipolar field patterns, the ECDs were calculated using a least-squares search. The ECDs were incorporated into a multi-dipole model in which the locations and orientations of the ECDs were fixed but their strengths were allowed to vary in time to best explain the signals recorded by all sensors over the entire analysis interval. The signal distribution in the individual sensors predicted by the multi-dipole model was compared against the signal distribution of the original measured data to evaluate the goodness of the model. The number of ECDs needed to explain the measured signal varied between studies and individuals, from 2 to 12 sources.

In the source analysis of the data, the conductivity profile of the brain was modeled with a sphere. The parameters of the sphere were determined by fitting a sphere into the curvature of the skull in the individual MR images. When an MR image was not available, an average sphere model of the group of interest (average over females, males or children previously studied in our laboratory) was used. Small variations in the parameters of the sphere model do not significantly affect source localization (Tarkiainen et al., 2003).

Sources of interest were selected for further analysis. Sources that showed similar behavior in terms of localization and general timing (e.g. N100m/N400m sources) could be further analyzed statistically to examine the effect of stimulus manipulations in a given cortical region across participants. The time-course of ECDs (source waveforms) represent the strength and timing of activation in the source area. For transient responses, the strength and timing of activation was estimated by measuring the maximum amplitude and the time point at which the waveform reached this peak value (peak amplitude, peak latency). For more sustained activation we measured the mean amplitude over a fixed time-window or, alternatively, determined the time points at which the waveform reached half of the maximum amplitude in the ascending and descending slopes and measured the mean amplitude and duration between these time points.

A repeated-measures analysis of variance (ANOVA) was used to evaluate systematic effects in strength and timing of cortical activation to the different stimulus types. The differences in the activation strength and timing between groups (adults vs. children in studies II & III and controls vs. dyslexics in study I) were calculated by including a between-participants factor 'subject group' in the analysis (Studies I and II) or by conducting an independent samples t-test (Study III). The correlation between cortical measures and behavioral performance was computed using Pearson's correlation coefficients (Study I), or Spearman's rank correlations (Studies II, III), when the behavioral measures were not normally distributed.

In studies III and VI, the time course of activation in each source of each subject was tested for difference in source strength between conditions of interest to isolate source areas with similar functional dependence on the stimuli. The difference was required to exceed 1.96/2.58 times the standard deviation (SD) in the pre-stimulus interval (200 ms before stimulus onset), corresponding to a significance level of $p<0.05$/ $p< 0.01$ (Study III/Study VI).

5 EXPERIMENTS

5.1 Cortical timing of speech sensitive analysis in normally reading and reading-impaired adults (Study I)

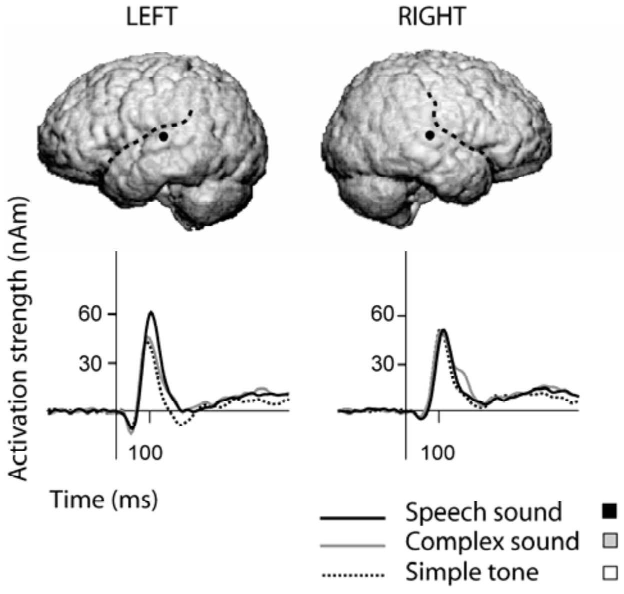
In Study I we examined the neural processes reflecting the early steps in processing of speech signal in 10 typically reading and 10 dyslexic adults. Earlier findings indicate cortical sensitivity to phonological categories by 150 ms, as reflected in the MMN response, but results concerning the preceding N100 have been more variable. For assessing the sensitivity of the N100m response to the difference between speech and non-speech, we used stimuli that were acoustically carefully matched but were unambiguously perceived as speech or non-speech. Dyslexia has been associated with deficient skills in manipulating speech sounds (phonological processing), possibly stemming from a lower level auditory dysfunction. We also investigated whether dyslexic participants show abnormalities in the N100m response for one or for both of the sound types.

5.1.1 Stimuli

The stimuli were synthetic speech sounds, complex non-speech sounds and simple sine-wave tones, each 150 ms in duration. The speech sounds were Finnish vowels (/a/ and /u/) and consonant-vowel syllables (/pa/ and /ka/). The non-speech sounds were complex sounds combining three sine-wave tone components of exactly the same frequency as the formants of each of the four speech sounds, and simple sine wave tones containing only one formant frequency. The envelopes of speech and non-speech sounds were similar, including 15-ms fade-in and fade-out periods, and a slope fade-in for the CV syllables and their non-speech equivalents. The amplitudes of all sounds were adjusted so that at the end of the sound delivery system they differed by less than 2 dB (SPL). The stimuli were delivered in two sessions monaurally to the right ear. The participants watched a silent film and were instructed to ignore the stimuli.

5.1.2 Results

Figure 9 shows the group mean location of the ECDs that best represented the activated cortical areas in each participant. The dipoles were mostly localized to Heschl's sulcus or posterolateral to it. The mean time course of activation (Figure 9) shows that the activation was mainly accounted for by a strong transient response, peaking at 100 ms (N100m) in both the left and right hemisphere. As illustrated in Figure 10, the strength of the N100m response varied by sound type in the left but not in the right hemisphere. In the left hemisphere the responses were stronger to speech sounds than to complex non-speech sounds and simple tones; the effect of stimulus type was significant for all stimulus categories. This different sensitivity in the two hemispheres for speech vs. non-speech sounds was not affected by switching the stimulated ear.



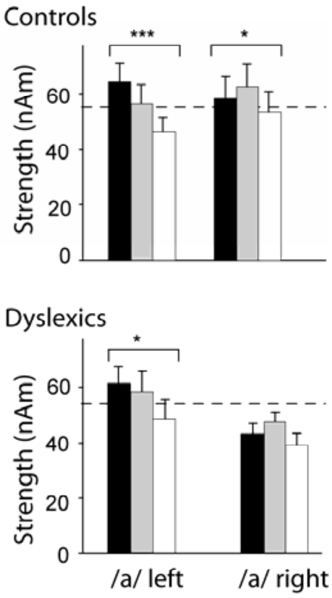


FIGURE 9 (left) The mean N100m response location in the left and right hemisphere, and the mean time behavior of activation for speech sound /pa/ (black line), its complex non-speech equivalent (grey line) and simple tone equivalent (dashed line). The Sylvian fissure is highlighted in the MR image.

FIGURE 10 (right) Mean (± SEM) strength of the N100m activation for the control and dyslexic group. Speech sounds, complex non-speech sounds and simple tones are represented by black, gray and white bars, respectively. The dashed line represents the mean amplitude of activation across all sounds in the left hemisphere of the control participants.

The peak of the response was earliest for the sine-wave tones and was delayed for complex non-speech sounds and, further, for speech sounds, similarly in both hemispheres. Interestingly, the ascending slope of the N100m response for speech sounds was steeper in the left than in the right hemisphere (figure 11).

For non-speech sounds, there was no significant difference in rise-time between hemispheres. Notably, in dyslexic participants, the activation was overall weaker in the right than in the left hemisphere, for all sound types. Moreover, dyslexic participants did not show the typical pattern of an earlier contralateral than ipsilateral response, due to longer left hemisphere latencies in dyslexic than control participants (see Figure 11).

In the control participants, better phonological skills were associated with a shorter ipsi-contra delay in the N100m response latency ($r = -0.8$, $p > 0.05$). In the dyslexic participants, there was a similar trend but no significant correlation ($r = -0.5$, $P = 0.1$). No significant correlations were found between phonological scores and the left versus right N100m strength ratio (left hemisphere N100m responses divided by right hemisphere N100m response).

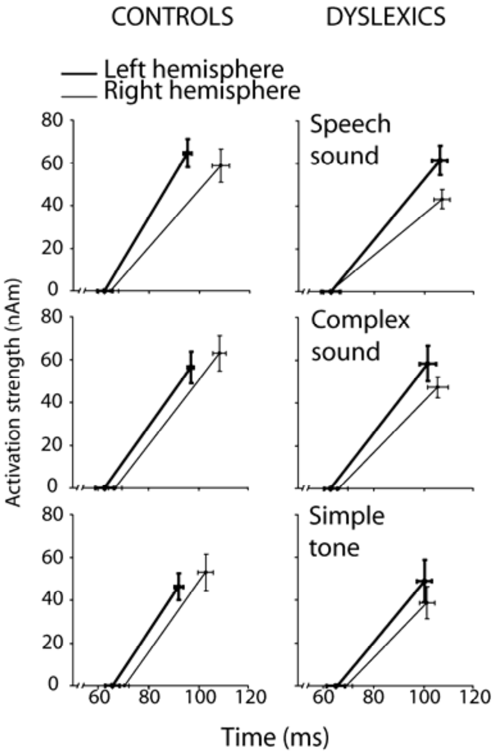


FIGURE 11 Schematic illustration of the build-up of the N100m response (from onset to peak) to speech sound /a/ (top), complex non-speech sound (middle) and simple tone (bottom) in the left (thick lines) and right (thin lines) hemispheres of control (left) and dyslexic participants (right).

5.1.3 Discussion

Study I demonstrated that the activation arising from the left planum temporale and the surrounding auditory cortex at 100 ms after sound onset is sensitive to the difference between acoustically matched speech and non-speech sounds. Neural sensitivity to the phonological categories of the native language, reflected in the MMN response at around 150 ms, is thus preceded by neural processes that are sensitive to the presence of phonetic features. Our findings agree with and extend earlier reports showing stronger amplitude (Gootjes et al., 1999), longer latencies (Eulitz et al., 1995; Tiitinen et al., 1999), or leftward shift of hemispheric balance (Vihla and Salmelin, 2003) for vowels as compared with various types of non-speech sounds. The combined increase of peak latency and strength for speech sounds in the left hemisphere could reflect a larger number of neurons being synchronized over a longer period of time. The increase in peak latency with no accompanying changes in activation strength in the right hemisphere suggests a slower rate of neuronal recruitment or less synchronous firing of neuronal populations for increasing sound complexity. The steeper ascending slope of the N100m response for speech vs. non-speech sounds speaks for a qualitative difference between the analysis of these sound types in the left auditory cortex by 100 ms.

The supratemporal auditory cortex shows preference to complex sounds (Hall et al., 2002), and it has also been suggested to reflect processing at the level of auditory objects instead of single features (Nelken, 2004; Zatorre et al., 2004). Our result of qualitatively different processing of speech vs. non-speech in activation arising from the non-primary auditory cortex at around 100 ms agrees with this idea, perhaps reflecting processing at the level of a "phonetic object". Based on the present results, we are, however, unable to specify the features in the signal that give rise to the increased response for speech. The sensitivity expresses a leftward shift of activation which could be associated with the frequently reported lateralization of language function. To account for the present findings, neural sensitivity to speech does not necessitate an anatomically specialized region for speech, but can be represented in the dynamics across neurons with different properties.

The unusual timing and amplitude effects in dyslexic participants (general reduction of activation in the right hemisphere and simultaneously peaking ipsi/contralateral responses) could reflect separate processes but they can also be readily understood as components of a single process. The activation in the contralateral auditory cortex is thought to modulate the ipsilateral auditory cortex via callosal connections (Mäkelä and Hari, 1992; Oe et al., 2002) and a delay in the left-hemisphere N100m response could reduce the strength of the right-hemisphere N100m. Further, abnormalities in the anatomy of grey and/or white matter structures in the left hemisphere (Galaburda, 1993; Klingberg et al., 2000) might cause the small but significant slowing down of the left-hemisphere response. The present data suggest changes in general auditory processing in dyslexia in the time window when speech information is extracted and the left planum temporale becomes involved in the process.

5.2 Cortical timing of speech-sensitive analysis in children, and its correlation with linguistic skills (Study II)

Study I indicated that, in adults, speech-sensitive activation emerges in the non-primary auditory cortex by 100 ms. Although children acquire speech perception skills early in life, literacy acquisition is accompanied by awareness of speech sounds as constituents of spoken words. The period when children start to show phonological awareness and learn to read thus represents a particularly interesting point in development for tracking neural representation of speech sound perception. In Study II, we investigated the timing of speech-sensitive analysis and the relationship between the neural correlates of speech and non-speech sound analysis and behavioral measures of phonological skills in 7- to 8-year-old children at the stage when they were becoming fluent readers.

5.2.1 Stimuli

A reduced set of stimuli from the adult study was used: speech sounds (/a/, /pa/) and their complex and simple non-speech sound equivalents. The correlation between cortical responses and behavioral scores in reading skills and phonological skills was computed (see chapter 4.2.2).

5.2.2 Results

The time course of activation in children was remarkably extended over time, as compared with the adult pattern, and displayed more inter-individual variability in the underlying spatiotemporal sequence within and between hemispheres. The areal mean analysis showed long-lasting activation in the temporal lobes with local maxima at around 100 ms, 250 ms and 400 ms after stimulus onset. Clear effects of sound type were evident after 250 ms, over both hemispheres. The source analysis revealed two recurrent types of activation sequences underlying this activation (Figure 12).

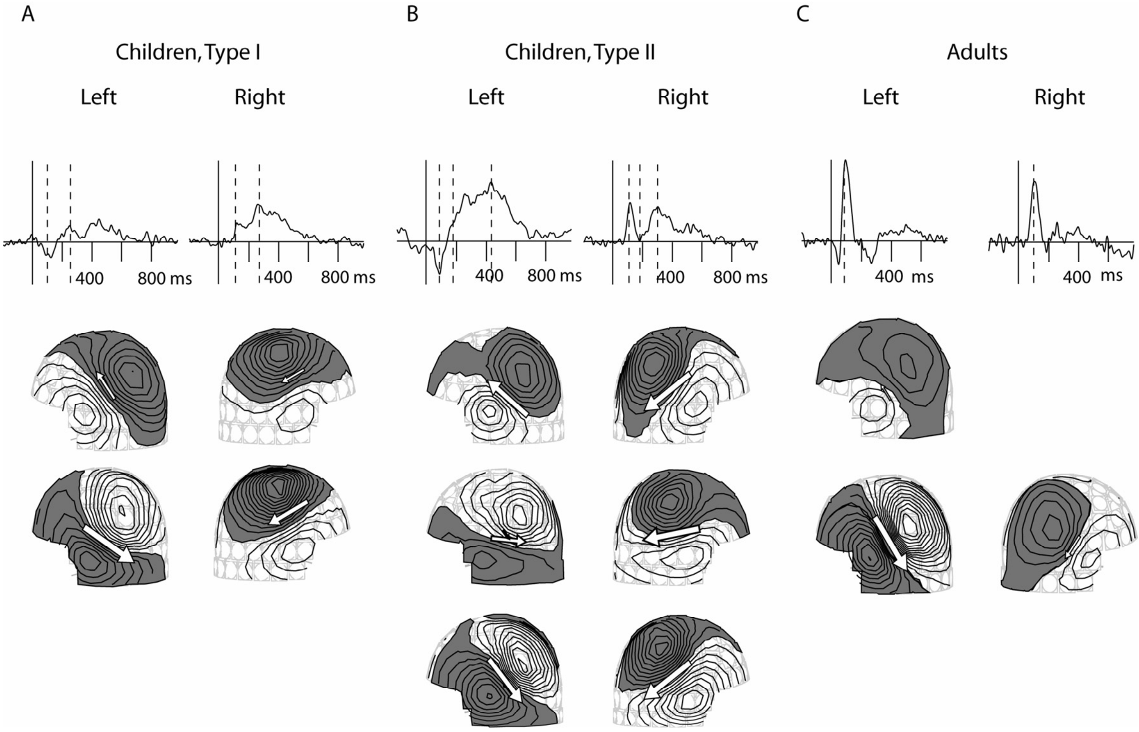
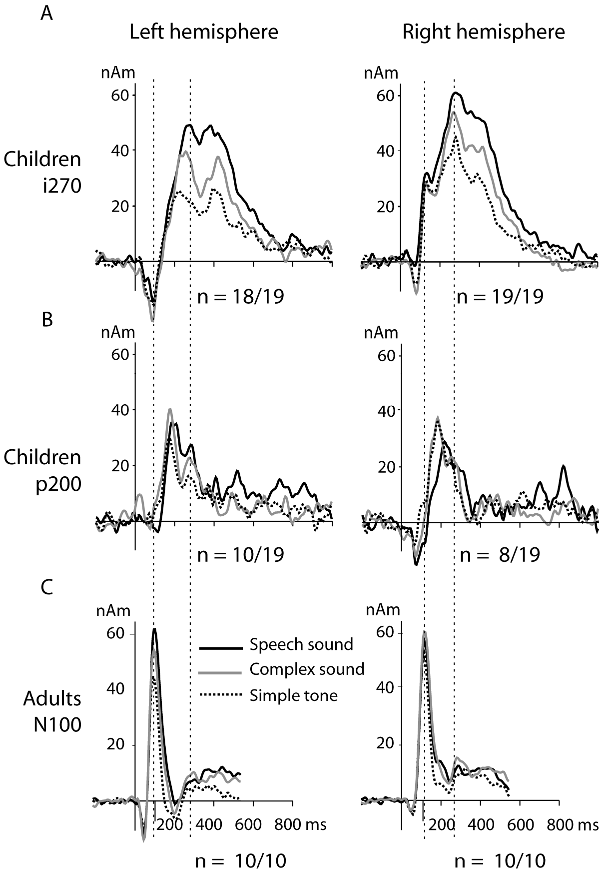


FIGURE 12 MEG signals in selected sensors and typical field patterns in children (A, B) and in adults (C) in the left and right hemispheres. In children, two types of activation sequences emerged, without (TYPE I, A) and with (TYPE II, B) a horizontally oriented source. The equivalent current dipole (ECD) is represented with a white arrow and the dashed line indicates the time point at which each field pattern was extracted.

In the simpler sequence, the current flow was directed superiorly and anteriorly at about 50–150 ms post-stimulus and, thereafter, until about 600 ms in the opposite (inferior-posterior) direction (i270 source), roughly at the same location, resembling a stretched version of the adult P50–N100 complex. The patterns in the two hemispheres, however, differed in the early time window: In the left hemisphere, the current flow directed inferiorly and posteriorly emerged only after 150 ms, but in the right hemisphere, half of the participants showed this type of source even before 150 ms (i100 source) (2/19 participants in the left hemisphere, 11/19 participants in the right hemisphere). In the more complex sequence there was an additional source structure between these two whereby the electric current was directed posteriorly (p200 source) (10/19 participants in the left hemisphere, 8/19 participants in the right hemisphere). The most consistent source type across participants and hemispheres was the late prolonged i270 response (18/19 participants in the left hemisphere, 19/19 participants in the right hemisphere). As illustrated in Figure 13, sensitivity to sound type appeared in this response: Speech evoked stronger and longer-lasting activation than complex and simple non-speech sounds in both the left and right hemisphere. The peak latency was also longer for speech than non-speech sounds.



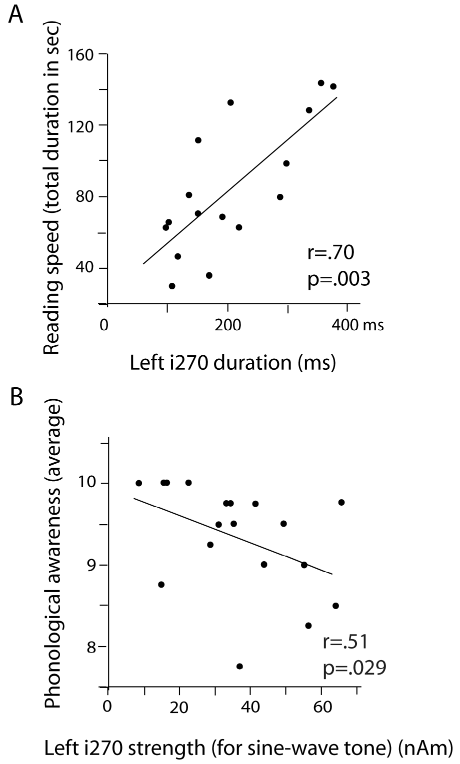


FIGURE 13 (left) The mean time course of activation of the i270 (A) and p200 (B) sources in left and right hemisphere (left and right columns, respectively) in children and the mean time course of activation of the N100m sources in adults (C). The responses to speech sound, complex sound and sine-wave tone are plotted with different line types. The dashed vertical lines indicate the peak amplitude of i270 source in children and of N100m source in adults.

FIGURE 14 (right) Correlation between cortical activation and behavioral scores in children. (A) i270 response duration for complex sound plotted against reading speed. (B) The amplitude for sine-wave tone plotted against phonological awareness.

The timing of the left-hemisphere i270 response was correlated with reading speed and comprehension – shorter latencies and durations of the neural response were accompanied with better reading scores. The strength of the i270 response was correlated with phonological skills – smaller responses were related to better performance in phonological tasks (Figure 14).

5.2.3 Discussion

Study II showed that the responses to all types of sounds displayed delayed and longer-lasting activation in children than in adults, with the most prominent activation peaking at around 270 ms. This finding is in agreement with earlier studies showing that, during development, there is typically a general decrease in response latencies and a shift in the emphasis from the prolonged N250 to the transient N100 type of response (reviewed in Wunderlich et al., 2006). The emerging literacy skills place special emphasis on speech sound perception and phonological skills in children in their early school years. We showed that, in children learning to read, the sensitivity to sound type emerged bilaterally at about 270 ms post stimulus as opposed to the left-lateralized effect in adults at about 100 ms. However, judging by location and direction of current flow, the neural sources of the speech-sensitive effect (and N100m and i270 responses) were remarkably similar in the two age groups.

The further question is, whether functionally comparable processes are delayed and longer-lasting in children than in adults, or whether the two time windows reflect different functions that are weighted differently between children and adults. The differences in timing and component structure might reflect purely maturational aspects of underlying synaptic and cellular organization (Huttenlocher and Dabholkar, 1997): the i270 response in school-aged children and N100 in adults can simply reflect functioning of the neural substrate that is available at a given age. However, the correlation of the i270 response (in the left hemisphere) with reading skills and phonological skills indicate that these changes are not independent from behaviorally meaningful functions and may even reflect modification of the auditory cortex by activity-dependent mechanisms.

In an earlier EEG study (Ceponiene et al., 2005), evoked responses in both adults and 7–10 year old children, showed stronger activation for speech than non-speech sounds at around 200–400 ms. This activation was concluded to reflect sensitivity to "sound content features", and the underlying processes were suggested to be largely matured by the age of 7–10 years. In contrast, our results imply that the neural activation in this time-window in 7- to 8-year-old children may actually reflect processes that are relevant for development and are not present to the same extent in the mature system. This idea is compatible with the interpretation that decreasing ERP latencies (and the weakening of the N250 response) by age reflect reorganization in perceptual processing to establish more effective network structures and increasing automation of information processing (e.g. Albrecht et al., 2000).

Moreover, our results indicate hemispheric differences in the emergence of the transient N1-type activation. In most of our 7- to 8-year-old participants, the N1-type response (current flow directed inferiorly and posteriorly before 150 ms) had already emerged in the right hemisphere but not to the same extent in the left hemisphere which was dominated by P1-type activation (current flow directed anteriorly and superiorly before 150 ms). Developmental delay in the left hemisphere as compared with the right hemisphere has also been suggested by the results of Paetau and co-workers (Paetau et al., 1995) that showed longer P1 latencies in the left than right hemisphere regardless of the stimulated ear.

5.3 Cortical sequence of written word perception in beginning readers (Study III)

In studies I and II, we clarified the timing and sensitivity of neural activation for spoken language. Written language represents a 'secondary level' of linguistic representation and is thought to be partly built on spoken language skills. Accordingly, the sensitivity of the neural activation to written language is likely to be formed by experience during reading acquisition. The cortical sequence for written word perception in adults, as demonstrated in previous studies by Tarkiainen et al. (1999) and Helenius et al. (1999b), involve occipital activation at ~100 ms that is sensitive to general visual features and occipitotemporal activation at ~150 ms that is sensitive specifically to letter strings. At around 400 ms, letter-string sensitive activation is evoked also in the left (and right) temporal cortex. In study III, we investigated the cortical sequence of written word perception in 7- to 8-year-old children who were on the verge of becoming fluent readers.

5.3.1 Stimuli

The stimuli were modified from Tarkiainen et al. (1999) to be suitable for children. The paradigm was designed to distinguish between activation that is sensitive to the amount of visual information and activation that is specifically sensitive to letter strings. The stimuli were 1) four-letter words embedded in three different levels of visual Gaussian noise and 2) symbol strings with no noise (Figure 15). The amount of visual detail was highest in the noisiest patches whereas the visibility of the letter-strings was highest in the noiseless patches. The task was to pay attention to the stimuli and press a button whenever an animal (target trial) was presented on the screen.

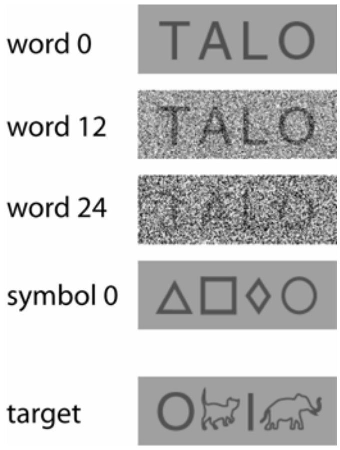


FIGURE 15 (left) The stimuli were four-letter words embedded in three different levels of Gaussian noise (word 0, word 12, and word 24) and symbol strings with no noise (symbol 0). Animal figures presented among symbols were used as targets.

5.3.2 Results

The sources in which the activation was significantly stronger to the noisiest words than to the clearly visible words and symbols were considered to be involved in basic visual feature (VF) analysis. Correspondingly, the sources in which activation was significantly stronger for the clearly visible words than the noisiest words, as well as stronger for the clearly visible words than symbols, were considered to reflect sensitivity to letter-strings (LS). Across all individual participants, the VF sources were found predominantly in the occipital lobes whereas the LS sources were clustered to the left occipitotemporal cortex and to the left and right temporal lobes.

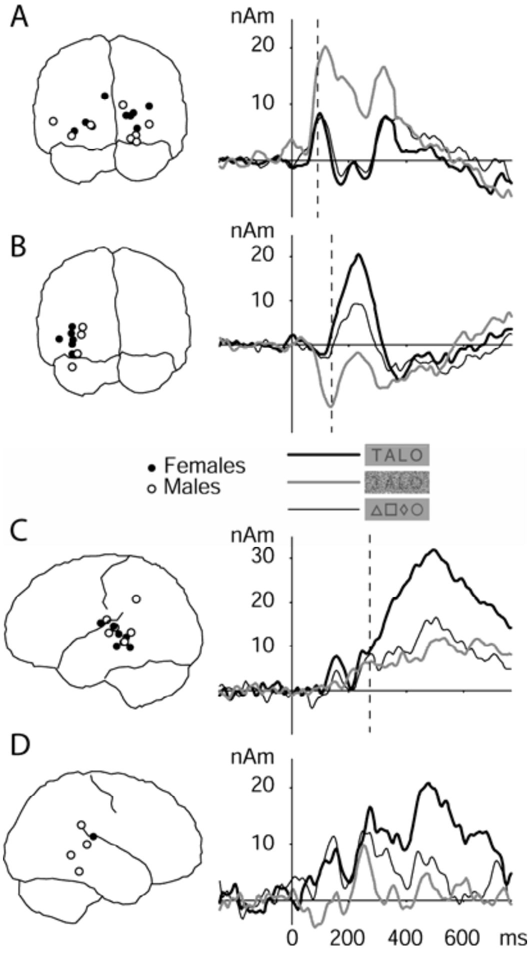
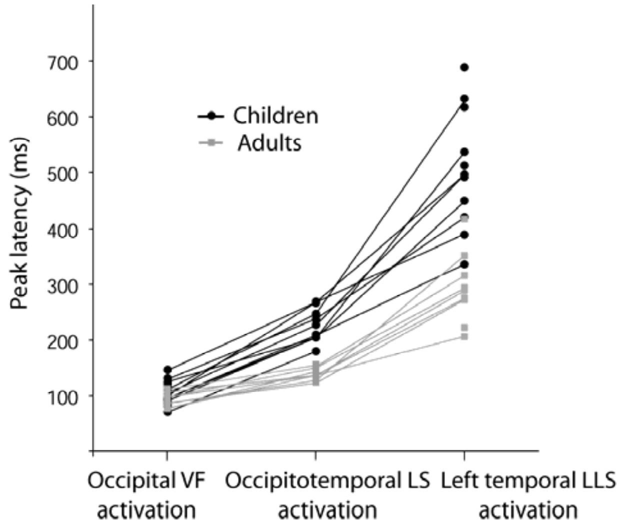


FIGURE 16 (right) The spatial distribution (left column) and mean time course of activation (right column) of the occipital visual feature sources (A), left occipitotemporal letter-string sources (B), and left and right temporal letter-string sources (C,D). Black and white circles represent sources of female and male participants, respectively. The responses to the noisiest words, noiseless words, and symbol strings are plotted with different line types. The mean timing of the corresponding activations in adults (Helenius et al., 1999; Tarkiainen et al., 1999) is marked with a dashed line.

Figure 16 depicts the selected VF and LS sources (one per child) across all children and the mean time course of activation of these sources to the noiseless words, noisiest words and symbol strings. At least one VF source was found in 16/18 of participants, and the mean time course of activation in these source areas, averaged across participants, peaked at around 120 ms. LS sources in the occipitotemporal cortex were found in 10/18 participants with maximum amplitude at around 230 ms. LS sources in the left (right) temporal lobe were found in 13/18 (6/18) participants, and the source waveform reflected broad, long-lasting activation peaking around 500 ms. The timing and strength of the early VF and early LS activations were correlated, as were the strength of early LS and late temporal LS activation. Compared with adults, the timing of activation in children was progressively delayed when advancing from occipital (delay 12 ms) to occipitotemporal (84 ms) and further to temporal (227 ms) source areas (Figure 17). Moreover, the inter-individual variability was larger in the LS activation than in the VF activation in children.

The presence of any particular source type was not coupled with specific behavioral skills. However, for those participants who showed occipitotemporal LS activation, its strength was negatively correlated with phonological skills; children with better phonological skills had smaller LS amplitudes (Figure 18).



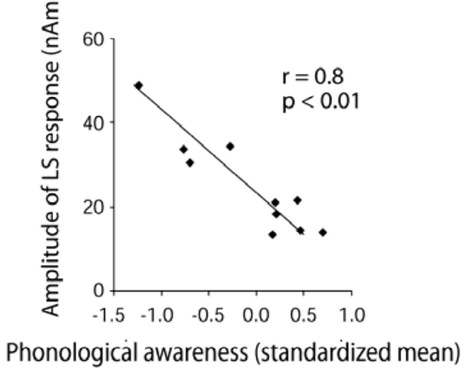


FIGURE 17 (left) Timing of activation in children (black) and in adults (gray). The peak latencies for the occipital VF response, the occipitotemporal LS response, and the left temporal LLS response are depicted for individual participants. The responses of each subject are connected with a line.

FIGURE 18 (right) Amplitude of the occipitotemporal LS response plotted against standardized mean of tests measuring phonological awareness.

5.3.3 Discussion

Study III showed that the overall cortical sequence of activation to visually presented words and symbols is similar in children to that described previously in adults (Tarkiainen et al., 1999): activation was sensitive to non-specific visual features in the occipital cortex and to letter-strings in the occipitotemporal and temporal areas. However, the overall timing of activation was clearly delayed in children. Longer latencies in children than in adults are in line with previous EEG and MEG results (Brecelj, 2003; Grossi et al., 2001; Licht et al., 1988; Simos et al., 2001; Taylor et al., 2004). Interestingly, our study indicated increased delay in response timing in children versus adults when advancing from low-level visual analysis to letter-string–sensitive analysis. This is likely to reflect increasing immaturity of the neuronal generators with increasing latency and functional complexity; neuronal development in humans approximately reflects the sequence from primary sensory cortices to higher-level association areas (Huttenlocher and Dabholkar, 1997). Moreover, correlated activation between these areas indicates that their development is not independent. Differences in cognitive skills (reading fluency) between adults and children could also contribute to this latency difference. It is, however, difficult to tell apart changes caused by maturation versus cognitive development in the developing nervous system as the plastic changes in neural networks are always influenced by environmental input.

Our results imply that the neural circuits for visual word perception in the occipitotemporal cortex of 7- to 8-year-old children are still under maturation; only half of the children demonstrated sensitivity to letter-strings in this region and the activation was delayed from that in adults. In adults, nearly all participants demonstrate letter-string sensitivity in the occipitotemporal cortex (Tarkiainen et al., 1999). This result is compatible with the hypothesis by McCandliss et al (McCandliss et al., 2003) suggesting cortical tuning to visual features of letters during exposure to printed words. The behavioral skills were not directly linked to the presence of letter-string–sensitive occipitotemporal activation. However, when a letter-string sensitive response could be detected in children, its strength correlated with phonological skills. This agrees with the theoretical accounts emphasizing the importance of phonological skills for reading acquisition (e.g. Share, 1995). Some behavioral results show that an adult-like pattern of word recognition, measured with the number of fixations to a word, is reached rapidly after exposure to text; additional reading experience mainly reduces the duration the words have to be fixated (Aghababian and Nazir, 2000). Based on the present MEG data and these behavioral findings, it seems that the general spatiotemporal organization of brain activation and word recognition skills can develop rapidly after exposure to printed material to resemble the patterns seen in adults, but with marked differences, especially in timing.

5.4 Effect of linguistic context and acoustic-phonetic cues on the cortical processing of natural meaningless speech sounds (Study IV)

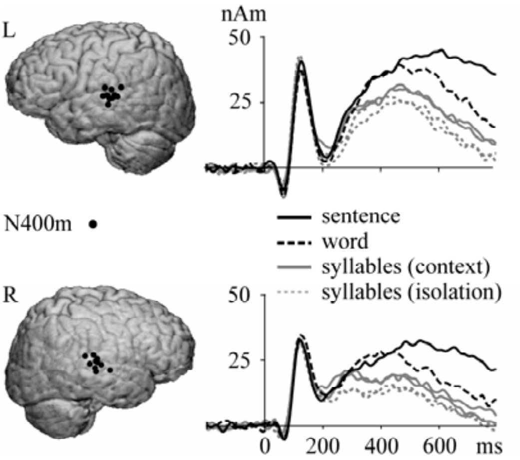
In study I (and II) we concentrated on the early pre-lexical processing of speech. Activation in adults evoked by simple meaningless speech sounds without a particular listening task was limited to the prominent N100m response arising from the superior temporal plane in both hemispheres. The perceptual processes that are engaged when hearing a natural, continuous speech signal are, however, not likely to be captured in the passive listening to simple synthetic speech sounds. In study IV, we examined neural processing at the interface between sound-based and meaning-based analysis of speech by presenting natural meaningless syllables in the experimental context of words and sentences. The participants were 10 typically-reading adults.

5.4.1 Stimuli

The stimuli were meaningless CV syllables, bi-syllabic words and three-word sentences. Each CV syllable was used as an initial syllable in the words and each word was used as an initial word in the sentences. The acoustic signal of sentences, spoken by a male speaker, was recorded and the acoustic signal of words and syllables was cut from the sentences. In addition to the set of CV syllables cut from the sentences, another set of (the same) syllables was pronounced separately by the same speaker. The sound intensity was equated across stimuli. Bottom-up effects on syllable processing were studied by comparing the syllables pronounced separately (syl) versus sentence-initial syllables (sylsent). Top-down effects were investigated by comparing the processing of these syllables in two types of experimental blocks: together with words and sentences and in two blocks where each syllable type was presented in isolation. The participant was asked to repeat the preceding stimulus whenever she/he heard a beep signal.

5.4.2 Results

The typical sequence of activation showed an N100m response bilaterally followed by a more variable source pattern at about 200 ms and then a prominent N400m response again bilaterally. The most prominent response with largest experimental effects was the long-lasting activation at around 400 ms, apparently corresponding to the N400m reported in earlier MEG studies on semantic processing (Helenius et al., 2002b). The N400m response was smallest and of shortest duration for syllables and was increased for words and sentences (Figure 19). When presented mixed with word and sentence stimuli, syllables evoked a stronger N400m response bilaterally than when presented in isolation (Figure 20); in the left hemisphere the N400m response also started earlier and lasted longer. The comparison between syllables pronounced separately versus sentence-initial syllables showed increased neural activity for sylsent during the build-up of the N400m response (i.e. the ascending flank of N400m response) in the left hemisphere (Figure 21). The presence of both bottom-up and top-down factors, i.e. sylsent in mixed blocks, led to the largest, most word-like responses, whereas the absence of both factors i.e. syl in isolation, led to the smallest, least word-like responses.



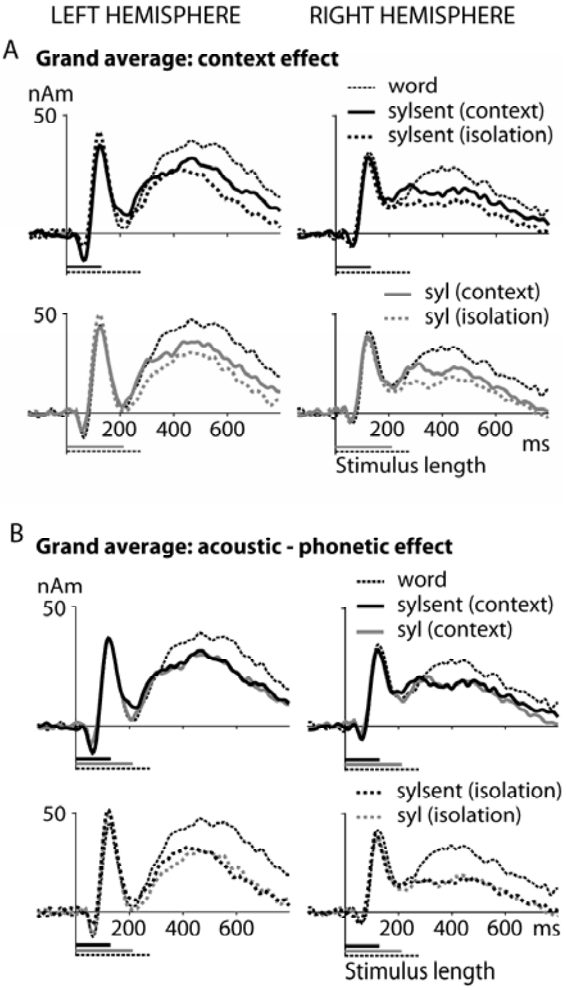


FIGURE 19 (left) Locations and mean time course of the N400m sources. Black dots indicate the individual sources for all 10 participants in the left (L) and right (R) posterior superior temporal areas. Syllables include both syllable types (syl and sylsent, indicated with same line type) presented in the context of word and sentence stimuli and as a separate sequence of syllables.

FIGURE 20 (right) Effects of context and acoustic-phonetic cues on the mean time course of activation in the left and right N400 source areas. (A) Grand average source waveforms of sentence-initial syllables (sylsent) and syllables uttered separately (syl) when presented in the context of words and sentences (context) and in isolation (isolation). (B) Grand average source waveforms of sentence-initial syllables (sylsent) and syllables uttered separately (syl) in context and isolation blocks. The activation elicited by words is included for reference. The horizontal bars below each graph indicate the mean length of the stimuli.

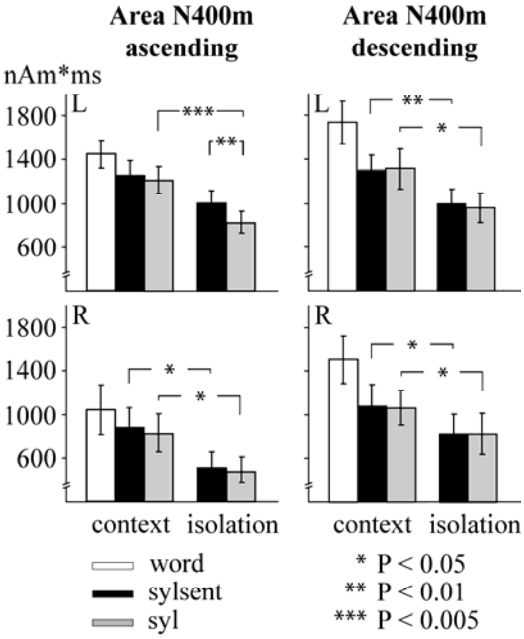


FIGURE 21 Mean area under the ascending and descending parts of the N400m source waveform. The ascending window was defined as the time-window between the latency at which the ascending slope reached 25 % of the maximum activation and the latency at the maximum. Correspondingly, the descending window was defined as the time-window between the latency at the maximum and the latency at which the descending slope had reached 25 % of the maximum activation. Mean area (activation strength multiplied by duration) was determined separately in the left (L) and right (R) hemisphere. Error bars represent standard error of the mean. Asterisks indicate significant differences between conditions (post-hoc comparisons).

5.4.3 Discussion

Study IV shows that natural meaningless syllables can elicit word-like neural activation, namely an N400m-type of response. The responses to syllables showed similar activation as words, especially in the ascending slope of the N400m response. Word-like activation within this time window was enhanced by linguistic context (words, sentences) and acoustic-phonetic cues in the stimuli, such as duration and pitch. Our results show that the mere presence of word and sentence stimuli changes the cortical processing of meaningless syllables. These results indicate that the time window of 200–300 ms is relevant for cognitive processes at the interface between phonological and lexical-semantic analysis, as suggested by Hagoort and Brown (2000b). The preceding activation at 100 ms did not reflect similar enhancement of activation with linguistic context or acoustic-phonetic information. Moreover, as suggested by fMRI studies on pre-lexical phonological processing (Gandour et al., 2004; Jacquemot et al., 2003; Jancke et al., 2002), the enhancement by acoustic-phonetic cues was lateralized to the left hemisphere. The cortical system sub-serving meaning-based analysis of speech seems to exploit predictive bottom-up cues in natural speech (i.e. information in the speech signal that predicts continuation of the syllable into a word) and context-induced expectation (i.e.

expectation for meaningful signal based on presentation together with meaningful signals) to enable efficient speech comprehension.

5.5 Influence of sound form and meaning in the cortical processing of spoken words (Study V)

Study IV indicated that the expectation for linguistic information influences the processing of meaningless speech sounds starting at around 200–300 ms. In study V, we further investigated the effect of context, more precisely, the effect of phonological vs. semantic expectation, on the neural processing of whole spoken words in 10 typically-reading adults. We sought to clarify the time window and hemispheric distribution of neural activation affected by the sound form of a word, on the one hand and the meaning of a word on the other hand.

5.5.1 Stimuli

The stimuli were lists of four spoken nouns. The first three words had either a related meaning or began with the same two phonemes. The final word of the list either matched the framework set by the first three words or differed from it semantically or phonologically. Thus, the list fell into four categories: semantically related, semantically unrelated, phonologically related and phonologically unrelated. The build-up of semantic and phonological information was evaluated by examining the effects over the first three words and the effect of semantic vs. phonological mismatch was evaluated by comparing the list-final words. The participant's task was to press a button when s/he detected a word list in which one word appeared twice.

5.5.2 Results

Source analysis revealed the following sequence of activation: A bilateral N100m response was followed by a more variable field pattern at around 200 ms, most consistently after the first word, and finally by prominent long-lasting activity, peaking at 400–500 ms, corresponding to the N400m response by source location, orientation of current flow (Figure 22a) and time-course of activation. Figure 22 shows the grand average source waveforms to the 1st, 2nd and 3rd words in both semantic and phonological lists (b) and the source waveforms to the semantically/phonetically related/unrelated final words (c).

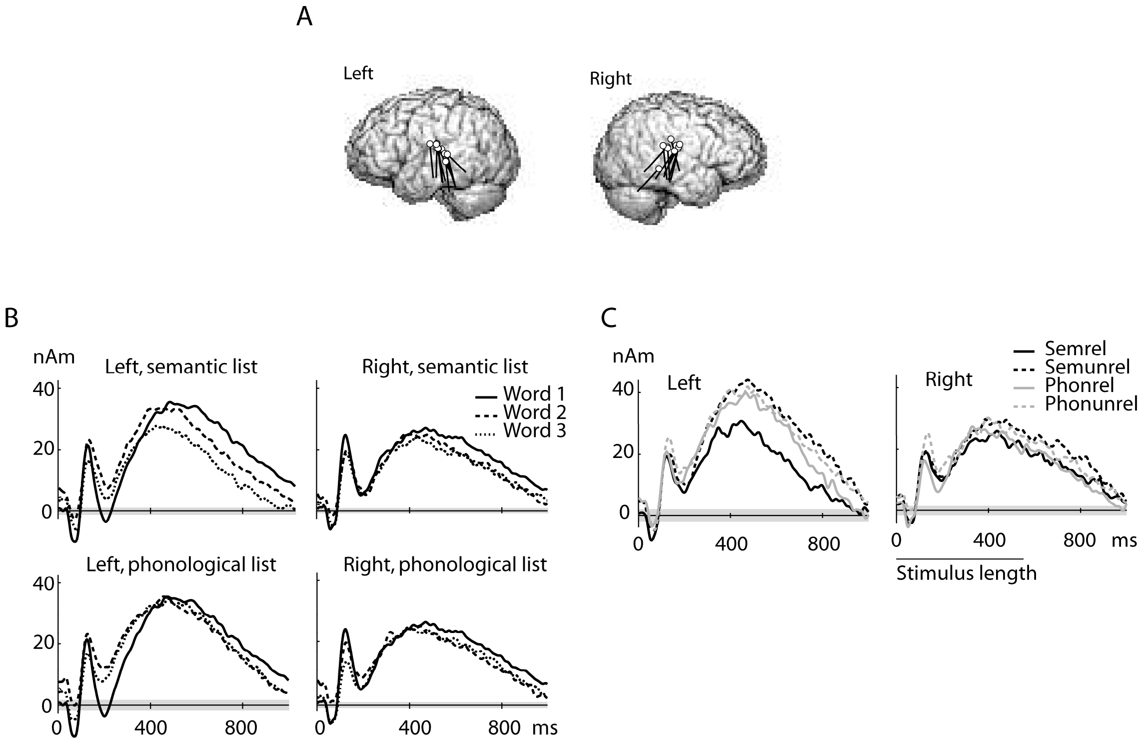


FIGURE 22 (A) Locations of the N400m sources of all 10 participants in the left and right superior temporal cortex. (B) Mean time course of activation for the 1st, 2nd and 3rd words in both semantic and phonological lists in the left and right hemisphere. For the list-initial word, the response is averaged over all word lists and for the second and third words over semantic or phonological lists. (C) Mean time course of activation for the list-final words. All four categories are plotted separately.

Progression along the word list (during the first 3 words) was accompanied by attenuation of the N100m response bilaterally and a shift of the N400m response to 50 ms earlier. Semantic and phonological information attenuated the response differently in the N400m time window: The onset phase of the N400m response was attenuated only by semantic information, and only in the left hemisphere. The offset phase of the N400m response was attenuated by semantic information bilaterally and by phonological information in the right hemisphere. The mismatch (at the fourth word) increased the activation; in the N100m time window for the phonological mismatch and in the N400 time window for the semantic mismatch. Figure 23 shows the summary of effects evoked by build-up of expectation during the first three words and break-down of the expectation in the fourth word.

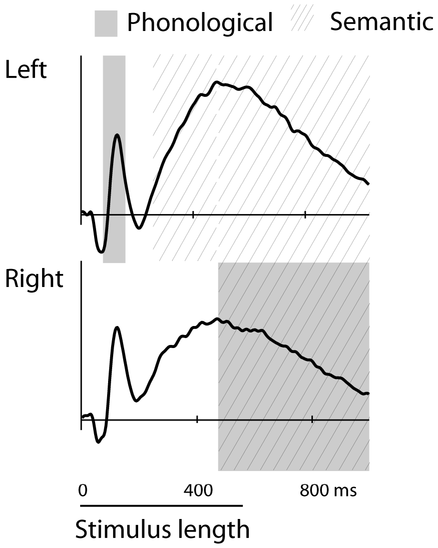


FIGURE 23 Schematic representation of the time windows and hemispheric interplay of phonological and semantic effects, overlaid on the N100m/N400m source waveforms. The gray and striped bars indicate the time windows in which phonological and semantic priming (mismatch) attenuated (increased) the response, respectively.

5.5.3 Discussion

Study V shows that the sound form (acoustic, phonetic and phonological information) and meaning (lexical-semantic information) of a word influence neural processing in different time windows and with different hemispheric distributions. The superior temporal cortex, especially in the left hemisphere, was engaged in processing of the sound form at around 100 ms, in line with earlier findings (Bonte and Blomert, 2004; Gootjes et al., 1999). Starting around 250 ms, the activation reflected sensitivity to meaning, first lateralized to the left hemisphere and later bilaterally.

Behavioral experiments show that a word can be identified by 200–330 ms after onset, depending on context (single words or words in sentence) (Grosjean, 1980). The early effects (at ~100 ms) in our study occur before the presumed time of identification, in line with the interpretation of prelexical level of processing in this early time-window. According to our results, this phase is influenced by the acoustic-phonetic/phonological similarity of the preceding words, i.e. not only on-line perceptual information. Three consecutive phonologically similar words (or word beginnings) followed by a phonologically incongruent word might be sufficient to evoke processes similar to the MMN response on top of the N100m response. Despite the phonological similarity, there was natural acoustic variation in the speech signal caused by articulatory factors in the words of the phonological list. Thus, the observed attenuation and increase in the N100m response presumably reflects processing at the level of phonology. Some earlier studies have indicated a separate response at around 250–300 ms that is suggested to reflect spoken word analysis at the phonological level. This PMN response is elicited when the expectation for a certain (whole) word form is broken by presentation of an (phonologically) unexpected spoken word (Connolly and Phillips 1994; Kujala et al., 2004). The effects in our study, evoked by the break-down of the alliterative series of spoken words, were restricted to the time-window within 200 ms after stimulus onset, possibly reflecting involvement of processes at a different level of speech perception (phonetic/phonological categories vs. whole spoken words).

The build-up phase of the N400m response and the early stage of semantic effects coincide with the estimated timing of word identification. Congruency with preceding semantic context seems to influence neural processing in this time-window. When the meaning of a word did not match the category formed by preceding words, activation was increased starting at ~250 ms. While this can be interpreted to reflect a stage of processing when semantic level has already been accessed, it does not require that a specific word (meaning) has been selected, as expectation was created at the level of semantic category.

5.6 Influence of letter-string length and lexical status on the cortical processing of written words (Study VI)

In study VI we investigated the effect of physical features (short/long words) and linguistic features (words/non-words) and their possible interplay in the neural processing of written words. Behavioral investigations show that both factors influence naming latencies, but the neural dynamics underlying these effects are not known. The participants were 8 typically-reading adults.

5.6.1 Stimuli

The stimuli were 400 letter strings, half of which were high-frequency Finnish words in base form and the other half, pronounceable non-words. All the non-words had the syllabic structure of a legal Finnish word but had no known meaning. The stimuli were further divided into long (eight letters) and short (four letters) strings resulting in four categories with 100 stimuli in each: short words (SW), long words (LW), short non-words (SNW) and long non-words (LNW). The non-words had the syllabic structure of legal Finnish words but had no known meaning. All stimuli were presented in a random sequence, for 400 ms with ISI of 2600 ms. The task for the participant was to read each stimulus silently and when prompted by "?" to read aloud the preceding word.

5.6.2 Results

Both the sensor-level data and the source modeling indicated temporally well-defined peaks before 200 ms and more long-lasting activation after 200 ms. The sources that showed a statistically significant difference in activation strength between the extreme cases, i.e. SW and LNW were selected from among all sources in each individual. These sources formed two distinct clusters: Sources with peak activation within 200 ms after stimulus onset and showing significantly stronger activation to LNW than SW stimuli were clustered around the occipital midline and sources with long-lasting activation after 200 ms and a significantly stronger response to LNW than SW were clustered in the left superior temporal cortex (Figure 24). Figure 24 shows the time course of activation in these source areas, averaged over participants. The occipital activation strength increased as the string length increased, regardless of the lexical status of the stimuli. The duration of the long-lasting temporal activation was significantly longer for eight-letter strings than for four-letter strings, for both words and non-words. However, the length effect for words was attenuated compared with that for non-words.

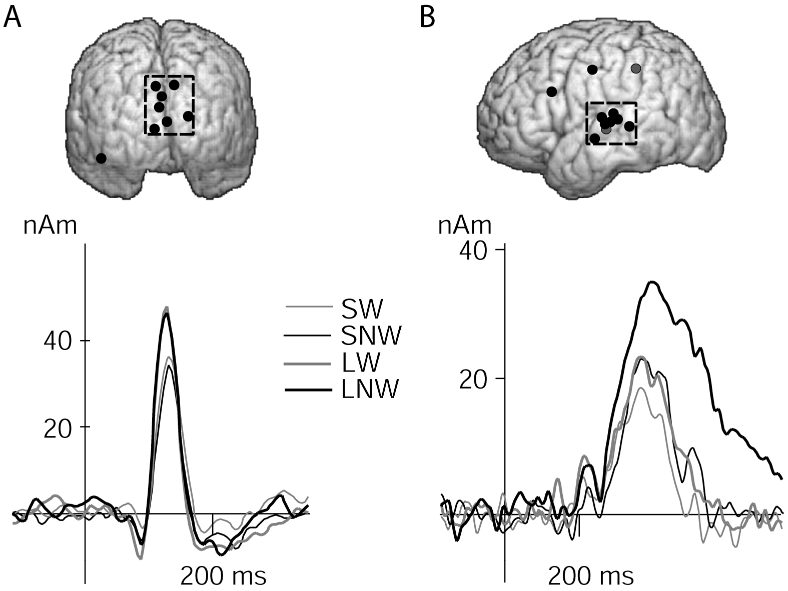


FIGURE 24 (A) Sources showing significantly stronger peak amplitude to LNW than SW stimuli within 200 ms after stimulus onset. The rectangular box depicts a cluster of these sources (from six participants) in the occipital lobe. The mean time course of activation across the six participants (below). (B) Sources showing a significant difference in amplitude for SW and LNW stimuli after 200 ms after stimulus onset. The rectangular box depicts a cluster of these sources in the left temporal lobe (from six participants). The mean time course of activation across the six participants (below).

5.6.3 Discussion

Study VI showed that, while activation in the occipital area reflected merely the length of the input string, the activation in the left temporal cortex was influenced by both the letter string length and its lexical status (stronger activation for non-words than words and for longer letter-strings than shorter letter-strings). The left superior temporal area has been associated with both phonological analysis and lexical-semantic processing during reading or visual word perception (Jobard et al., 2003; Vigneau et al., 2006). The time-window of N400 has been traditionally linked with semantic processes during reading

(Helenius et al., 1998; Kutas and Hillyard, 1980). The present findings suggest that this time-window also reflects phonological processing: The enhancement of the N400 response by length and lexical status is likely to reflect stronger demands on direct grapheme-to-phoneme decoding.

From the perspective of dual route models of reading, the combined length and lexicality effect in the superior temporal cortex could be interpreted as reflecting the combined use of sub-lexical and lexical reading routes. Non-word reading utilizes the sub-lexical route, i.e. grapheme-to-phoneme coding, whereas real words are read via the direct lexical route. The stronger length effect for non-words could be associated with the less favored role of the sub-lexical route – the direct route is suggested to be more efficient and faster when it can be used. However, there was no indication of anatomically separate routes of processing for words vs. non-words, as would be predicted by the dual route account. The activation of the same network by words and non-words supports connectionist models of reading where all letter-strings are supposed to be read via a single process. However, in this interactive approach, length effects are mainly accounted for by peripheral mechanisms including visual and articulatory factors. In our study, there was indeed a clear length effect in the occipital cortex, apparently reflecting visual processing, but also the later activation arising from the superior temporal cortex was modulated by letter string length. Thus, neither dual route account nor interactive connectionist account can totally explain the obtained results.

6 GENERAL DISCUSSION

This thesis investigated the cortical mechanisms underlying spoken and written language perception by means of a time-sensitive imaging method, magnetoencephalography. In the auditory experiments, a posterior superior temporal area bilaterally showed sensitivity to different features in the speech signal during the progression of neural activation. At around 100 ms, the neural activation as reflected in the prominent N100m response was sensitive to the phonetic aspects of the signal in simple synthetic sounds. The activation around 100 ms was modulated by the acoustic-phonetic/phonological properties in the speech signal also when whole words were used as stimuli. From 250 ms onwards, in the onset-phase of the N400m response, the neural processing was influenced by semantic information of spoken words. Interestingly, natural meaningless syllables also elicited activation in this time-window, especially when they perceptually and with regard to context, implied the beginning of a whole word.

Written words evoked an activation sequence including responses in the occipital, occipitotemporal and left temporal cortex. The physical properties of the words (letter-string length) affected neural signaling in the time window around 100 ms in the occipital cortex, similarly for words and non-words. However, the later activation arising from the temporal cortex was affected both by physical features and by the lexical status of the word (word vs. non-word), and was suggested to reflect on-line phonological and lexical-semantic processing.

In children, the neural activation evoked by both auditory and visual perceptual processes was clearly delayed as compared with adults. However, the activation sensitive to language stimuli in both modalities was localized in very similar regions as in adults. The correlation between developing reading and phonological skills and neural responses to auditory and visual language suggests interdependence of the maturing nervous system and the development of language skills.

6.1 What makes speech special?

Speech perception can be thought of as occurring at different levels of representation, although this does not necessitate hierarchy or specify the dependency between stages. At the lexical and semantic level, the special nature of speech, among other sounds such as laughter or bird song, can be readily appreciated. (In the latter case, the connection to word form and meaning is, at least, more ambiguous and there is no direct connection to written language.) However, when examining the sound structure of the speech signal at the level of acoustics, there is no distinctive marker separating speech from non-speech auditory signals. A unique combination of general acoustic features rather than a single invariant property of sound separates speech from other complex auditory signals (Stevens, 1980).

How is speech special from the perspective of neural processing? The neural coding of the relevant auditory features of speech is rather well characterized at the level of sub-cortical structures (Sachs, 1984). Based on animal studies (Rauschecker et al., 1995), it seems that higher centers in the auditory pathway are increasingly sensitive to complex features or feature combinations, e.g. to communication calls. Feature combinations are also likely to represent relevant properties in human speech. The sensitivity of individual neurons/neuronal populations to relevant feature combinations represents a possible 'hard-wired' mechanism for the encoding of speech sounds in the human brain. Drawing conclusions from animal communication studies concerning the representation of speech in the human brain is, however, not straightforward. Although the acoustics of monkey calls resemble human speech sounds in some respects, there are differences in the nature and use of the human speech signal as compared with animal communication sounds (human language and animal communication: Hauser et al., 2002; Yip, 2006). The existence of an intermediate stage of (core) phonology is likely to be unique to humans. The continuous acoustic signal is discretized into a limited set of speech sounds that can be combined in numerous ways to convey conceptual information.

The neurofunctional models of speech perception based on the location of activation are becoming increasingly complex in terms of regional specialization to different properties of the speech signal (Scott and Johnsrude, 2003). It has proved difficult to find neural mechanisms specific to speech analysis (Price et al., 2005) and sensitivity to speech has also been suggested to arise from the combined activation of several regions, coding for different non–speech-specific aspects of sounds. Whether speech specificity is represented as activation of a distinct region or as activation of a network of areas, the nature of neural processing requires including timing in the neurofunctional description of speech perception.

Our results (Study I) indicate that the neural populations posterior to the primary auditory area are sensitive to the presence of phonetic features in the sound signal at 100 ms. We found a combined increase in response strength and rise-time in the left hemisphere for simple speech sounds as compared to acoustically comparable complex non-speech sounds. In the right hemisphere, no difference between speech sounds and complex non-speech sounds was detected. This is readily interpreted as reflecting neural activation that no longer responds purely to the acoustic complexity of the stimulus, but to a combination of features that are relevant for identifying the speech status of the signal pre-lexically. In support of our findings, some fMRI studies have suggested a specialized role for areas posterior to the primary auditory cortex (including the planum temporale) in perception of speech and phonetic information (Benson et al., 2001; Vouloumanos et al., 2001; Zatorre et al., 1992). However, the issue of speech specificity seems not to be that simple; the same regions have shown sensitivity to spectral or temporal complexity, whether in speech or non-speech signals (Binder et al., 2000; Binder et al., 1996). Thus, it might be that speech-specific neural processing is not captured in a stationary description of brain networks. Taking into account the inertia of blood-flow measures, stimulus-dependent variation of transient neural responses such as the N100m may well go undetected in PET or fMRI. The different time windows accessible with the different imaging methods may have a considerable effect with regard to which part of the network is detected.

What are the features in speech that evoke the enhanced activation in the neuronal response around 100 ms? Our results suggested that the enhanced activation does not reflect the pure acoustic complexity of speech but rather indicates that the neuronal response is sensitive to the difference between speech and non-speech acoustic signals. This does not, however, explain how different phonological identities are coded in the brain. Using the MMN paradigm, it has been shown that, by about 150 ms, the neural activation is sensitive to phonologically meaningful distinctions between speech sounds (Phillips et al., 2000). It remains to be shown, what the critical features in speech sounds contributing to the ‘speech’ status of the signal are and further underlie the categorization of different speech sounds. Our results indicate that simple combinations of formant frequencies is not sufficient as these types of complex sounds evoked activation that differed from that evoked by speech. The question of phonological identity is further challenged by the problem of invariance in the speech signal.

One possible manifestation of speech specificity in the brain is the lateralization of processing to the left hemisphere. The bilaterality of pre-lexical processing of speech shown in fMRI/PET studies (Binder et al., 2000; Poeppel et al., 2004) indicates that both the left and the right hemisphere are intimately involved in early stages of speech perception. On the other hand, some neuroimaging studies show left lateralized processing of simple speech sounds (Gootjes et al., 1999; Vouloumanos et al., 2001), especially when attention is directed to linguistic features in the signal (Gandour et al., 2004; Poeppel et al., 1996; Zatorre et al., 1992). In agreement with these earlier findings, the auditory cortices were bilaterally involved in processing of both speech and non-speech auditory information in Study I. However, the balance was shifted towards the left hemisphere at around 100 ms only for speech sounds. This subtle but significant difference does not necessarily follow from a difference in the absolute amplitudes or neural resources devoted to processing speech. Indeed, it was shown earlier that the absolute amplitudes for both speech and complex non-speech sounds were higher in the right hemisphere – only the relative amplitudes shifted towards the left for speech (Vihla et al., 2000). Thus, for the acoustic signal of speech, the emphasis in the bilateral auditory network is shifted to the left hemisphere. Leftward lateralization for speech is further supported by studies showing that transformation from non-phonetic to phonetic (non-speech to speech) perception of identical sine-wave speech sounds is accompanied with increased activation in the left posterior superior temporal sulcus and gyrus (Dehaene-Lambertz et al., 2005; Möttönen et al., 2006). A change in cortical activation based on altered expectation for physically identical sounds agrees with our results from studies IV and V showing an effect of context (expectation) in the perceptual processing of speech.

The idea of bilateral activation with lateralized functional specificity agrees with presented theories on a 'division of labor' between the hemispheres for different aspects of sounds (Boemio et al., 2005; Zatorre and Belin, 2001). These views suggest that the underlying difference between hemispheres is in processing of temporal information – the left hemisphere is suggested to process temporal features modulated within tens of milliseconds while the right hemisphere is suggested to be specialized on spectral analysis or temporal features with larger scale modulations. This claim is based on data concerning continuous sounds. In our limited sample of speech sounds (two vowels and two CV-syllables), there was no indication of a difference in lateralization between steady-state sounds and transition sounds (or left hemisphere specificity for transition sounds).

6.2 Language comprehension – from percept to concept

The fundamental goal in speech perception is to access the lexical/semantic information in the long-term store. This is accomplished based on the original acoustic stream of sounds but the nature of representation necessary for this purpose is not known. Our studies indicate that the variety of acoustic events provided by the sub-cortical auditory pathway are mapped (finally) to an invariant sound sequence representing words at the semantic level within the 250 ms time-window from sound onset. Starting around this time, the semantic/lexical information seems to be available for cortical neural networks (Study V) as has been suggested also by earlier EEG and MEG studies (Hagoort and Brown, 2000b; Pylkkänen et al., 2002).

Activation around 400 ms (N400m response) has been shown to be influenced both by phonological and semantic manipulations (Connolly and Phillips, 1994; Dumay et al., 2001; Hagoort and Brown, 2000b; Helenius et al., 2002b; Perrin and Garcia-Larrea, 2003; Praamstra and Stegeman, 1993; Radeau et al., 1998). In study V, the activation at the onset phase of the N400m was specifically influenced by the semantic content of words, and not by the sound form (acoustic/phonetic/phonological features) that affected the signal before 250 ms. If the auditory signal of words has access to semantic information starting at ~250 ms, as suggested by our findings, the functional significance of phonological processing after 250 ms in the N400 time-window is not immediately clear. It might be that tasks requiring special attention to phonological properties (such as rhyme detection e.g. in Praamstra and Stegeman, 1993) engage processes that are not necessarily activated in pure spoken word perception. The different time-windows for the influences of sound form and meaning can be interpreted in terms of sequential stages in spoken word perception proceeding from acoustic/phonetic/phonological analysis to lexical-semantic processing, or more specifically, from processing of phonetic features to analysis of whole words. This is compatible with autonomous (or serial) accounts of spoken word recognition. However, in line with the interactionist frame-work, the preceding context clearly influenced spoken word analysis already pre-lexically, implying that lexical access is not based purely on bottom-up information.

Interestingly, meaningless syllables also induced an N400-type of response that is typically evoked by whole spoken words (Connolly and Phillips, 1994; Hagoort and Brown, 2000b; Helenius et al., 2002b). Moreover, this response was enhanced to more closely resemble word-like activation when it was presented in experimental blocks also including words and sentences and when acoustic-phonetic cues of word continuation were included in the signal. This result is in line with the idea of continuous processing of the speech signal so that all available information is used online to predict further incoming input: Behavioral experiments show that information at the level of phonetic features is used on-line to activate lexical candidates, even before all the information needed for a lexical entry is present (Marslen-Wilson and Warren, 1994).

At the neural level, this could mean that the networks responsible for processing the meaning of the sound sequence are contacted based on potentially meaningful streams of sounds. The neural response to syllables in the N400m time window could reflect this type of activation. When the input signal did not provide any further information needed for word recognition, the activation was diminished and faded away, significantly earlier than for words or sentences. Importantly, both the linguistic context (as would be expected based on interactive models of spoken word recognition) and the acoustic-phonetic cues (as would be expected based on more autonomous models of spoken word recognition) enhanced the activation. It is noteworthy that the timing of the influence by preceding linguistic (semantic) context was very similar, around 200–300 ms, for both words and meaningless syllables.

What is the nature of sound representation that is of interest for meaning-based neural analysis of speech? In the models of spoken word recognition, there are diverging views as to whether access to word-level information (word in the form of a sound sequence) is necessary before contact with lexical information, or whether there is a continuous interaction between the input signal and lexical information along the progression of the stream of sounds of a word. Evidence for a certain amount of separation between feature-level processes and processes related to lexical access in the brain were suggested by the fact that there was no influence of semantic information in the time window before 200 ms (Study V) although neural processes at this time seemed to be sensitive to the phonetic information in the signal (Study I). However, this does not mean that there is access to the phonemic level of processing before lexical entry: The sensitivity to a speech signal at around 100 ms was interpreted to reflect sensitivity of the underlying neural population to the combination of features relevant for speech sounds. This might well be the 'highest' necessary level of abstraction if it provides sufficient invariance to access the lexical information.

Indeed, studies showing sensitivity to phonemic/phonological information typically use tasks that explicitly require processing of sound categories of language (Näätänen et al., 1997; Phillips et al., 2000) (e.g. contrasting acoustic sound categories that also represent two phonological categories in the listener's native language vs. contrasting acoustic sound categories that do not convey linguistically relevant information.) These types of experiments have shown sensitivity of neural activation around 150 ms to phonological information in the native language (Näätänen et al., 1997). However, they only indicate availability of this type of information which is not necessarily part of processing during natural speech perception.

Phonological processing might have a different role in written word perception. During reading acquisition, it is necessary to pay attention to individual speech sounds (phonemes) in order to learn their symbolic representations (Bradley and Bryant, 1983; Share, 1995). Interestingly, the neural activation at around 400 ms for written words, arising from the superior temporal area, seems to reflect both lexical (semantic) and phonological processes. In our study, non-words evoked stronger and more long-lasting activation than words, but also 8-letter words evoked larger and longer-lasting activation than shorter 4-letter words (Study VI). The earlier activation in the occipital cortex reflected only the amount of visual information in the input string. Activation in the superior temporal gyrus has earlier been shown to reflect both lexical-semantic (Bavelier et al., 1997) and phonological processing (Paulesu et al., 2000; Price et al., 1996; Pugh et al., 1996) during written word perception. The time-window around 400 ms has been indicated to reflect mainly the semantic aspects of written words (Halgren et al., 1994; Helenius et al., 1998). Our results imply that the access to lexical (semantic) information is not independent of the process of grapheme-to-phoneme coding, which seemed to influence the activation around 400 ms in the left temporal cortex. Although it is not known whether the visual and auditory perceptual processes interact with the same neural resources to access meaning, our results highlight the importance of the left temporal region in the on-line perceptual transformation, not only in spoken word perception, but also in reading. Discussion and support for this contention from a developmental point of view is provided in the next chapter.

6.3 Language perception in the child brain

The sequence of auditory activation in children was clearly different from that in adults, especially in timing. Most importantly, speech sensitive activation was apparent much later in the neural response, in a prolonged activation at around 250 ms as compared with the transient response at around 100 ms in adults. Given the highly stable timing of auditory evoked components in adults (Hari, 1990), the clear difference in evoked response morphology in children is remarkable. The visual response sensitive to letter strings, arising from the occipitotemporal cortex both in adults and children, was also delayed in children (~200 ms) as compared with adults (~150 ms). As the evoked responses reflect activation of the underlying neural network, the delayed evoked response is likely to reflect maturational aspects of synaptic development that is known to continue well into adolescence (Huttenlocher and Dabholkar, 1997). In the visual domain, further increase in the delay between adults and children was observed when proceeding to higher-level processing. This finding is in line with protracted synaptic development of higher level sensory areas (Huttenlocher and Dabholkar, 1997). In the developing neural network, it is difficult to disentangle environmental influence from the effect of "biological" maturation. Accordingly, the immature neural networks, by definition, also reflect the level of exposure to print which evidently differs between adults and children.

What is the meaning of these structural and functional properties of the auditory and visual systems for language development? The development of spoken and written language involves fundamental differences. Speech perception is suggested to be built on innate perceptual abilities and critically influenced by environmental input early in infancy (Kuhl et al., 1992). Reading represents a postnatally learned ability, and neural processes related to written word perception are likely to be constructed during the development of literacy skills in later childhood (McCandliss et al., 2003). It might seem counter-intuitive that the neural correlates for the perception of auditory language showed more differences between adults and children than the neural correlates related to the perception of visual language – the auditory skills of a child are at least starting to develop earlier than word recognition and reading.

Visual functions used in reading are, however, only indirectly linked to language – via the use of spoken language. The complex transformation from the acoustic speech signal to linguistic units is a more or less automatic process while the connection between symbols and phonemes is actively built during reading acquisition. The time of learning to read represents an interesting period when a child's spoken language skills must interact with visual object recognition in order for him/her to develop optimal literacy skills. The experiments in different modalities are, thus, not fully comparable due to the different nature of auditory and visual linguistic signals. Rather, the two studies provide complementary information on the language development and construction of neural circuits for receiving linguistic information.

Interestingly, the visual response in the occipitotemporal cortex (that was sensitive to letter-strings) was not directly correlated with reading measures, but showed correlation with phonological skills. Smaller responses (closer to adult values) were linked with better phonological skills. This observation indicates a close relationship between neural resources underlying reading/word recognition and (auditory) speech processing in the early school years. Behaviorally, there is a well-documented interdependence between phonological skills and reading acquisition.

Phonological processing in adults seem to engage the superior temporal cortex in the left temporal lobe, whether evoked by visual (Pugh et al., 1996; Rumsey et al., 1997b) (Study VI) or auditory (Demonet et al., 1992) input. Our results indicate importance of the left temporal area and auditory functions also in reading acquisition: Earlier and shorter auditory responses in the left temporal cortex were coupled with faster reading. The activation of the superior temporal cortex in our auditory experiment reflects rather general processing: reading speed was correlated with neural responses to both simple speech and to non-speech sounds. The different response morphologies in adults and children (the prolonged 250 ms response vs. transient N100 response) however, suggest that the neural system in the immature brain may display features that are relevant to development and adaptation to the environment but are not present, at least to the same extent, in the mature system. Correlation between language skills and the neural response at ~200–500 ms further implies the importance of this time-window and prolonged activation for organizing the network for language processing, more precisely phonological skills and reading. The maturing auditory system is thus likely to provide the key 'processing resources' that are utilized to form the link between visual symbols and speech sounds.

What are the underlying neural phenomena causing the decrease of amplitude and shorter/faster evoked responses combined with increase in cognitive skills with development? The early school years are a period in brain development when afferent input could well be involved in structuring the connectivity in the maturing neural networks. Based on non-invasive brain imaging conducted from outside the skull, it is difficult to infer the cellular phenomena underlying the effects in evoked responses but the amplitude and latency effects could well reflect organization of activation within a network based on experience-dependent changes in neural connections. Judging from the timing and morphology of the evoked responses in our experiments, the neuronal populations responsible for category-specific responses (for visual words) attain more rapidly an adult-like structure than the auditory networks. This might reflect differences in the general properties of the two sensory systems, i.e. in the sub-cortical pathways. It can also be hypothesized that the basis for visual language skills is rapidly developed during the early school years, enabled by the neural substrates for spoken language. This would explain why the evoked responses for visual language appear more adult-like in children than those for auditory language. Rapid development of word recognition skills during the early school years has also been suggested by eye tracking studies (Aghababian and Nazir, 2000).

The derivative nature of the neural resources for written language, as compared with spoken language, would agree with the secondary (or second order) status of written language, both evolutionarily and developmentally. The visual system for written language is presumably organized in an activity-dependent manner, without any genetically coded maturational trajectory. The ontogenetic development of auditory function for communication (as of the basic visual functions) follows an evolutionarily set up system, extending from the prenatal period to maturity. From a more general perspective, the left temporal cortex is involved in diverse functions of language that are also known to develop until late childhood. Indeed, the posterior temporal areas were shown to be among the last brain regions to reach maturity, as measured with the thickness of grey matter (Gogtay et al., 2004).

6.4 When something goes wrong in language development

Developmental dyslexia is manifested in the early school years as delayed reading acquisition, and often persists to adult years as slow and error prone reading. The underlying dysfunction in dyslexia has been shown to be tightly linked to deficient skills in auditory language, i.e. processing of phonological information (Bradley and Bryant, 1978; Shankweiler et al., 1995). However, dyslexia is also accompanied by variable degrees of subtle sensory deficits, the role of which is not known (Ramus et al., 2003). Phonological problems have been further speculated to stem from dysfunction in basic auditory processing (Tallal, 1980; Tallal et al., 1993). The level of auditory processing of speech that is affected in dyslexia is controversial.

In our study, dyslexic individuals exhibited similar left-lateralized sensitivity to speech sounds at 100 ms as the control participants. However, they demonstrated abnormal inter-hemispheric timing and reduced right-hemisphere activation for both speech and non-speech sounds in this same time-window. The result can be interpreted to reflect a general auditory impairment that falls in the time window when the neural activation shows sensitivity to speech sounds and may thus specifically influence phonetic analysis. The timing and amplitude effects were interpreted to be connected: due to the delayed left hemisphere response, the N100m was evoked simultaneously in the two hemispheres, instead of the typical contralateral lead, thus possibly reducing the right-hemisphere activation due to weaker excitation via the corpus callosum (Mäkelä et al., 1993; Oe et al., 2002). Earlier MEG studies of dyslexic subjects have shown dysfunctions in the time window of the N100m response when processing rapidly presented (Nagarajan et al., 1999), or rapidly changing (Renvall and Hari, 2002) stimuli, as well as simple speech sounds (Helenius et al., 2002a).

What could be the underlying cause for the observed effect in our study? The N100m response is generated mainly in the area of the planum temporale (Liegeois-Chauvel et al., 1991), an area reported to display gross anatomical and cellular abnormalities in post mortem and MRI studies of dyslexic individuals (Galaburda, 1993; Galaburda et al., 1985; Hynd et al., 1990; Leonard et al., 1993). Any irregularity in the functioning of this general area is likely to cause abnormalities also in the neural response. However, the relationship between abnormalities in the planum temporale and dyslexia is probably more complex, varying e.g. with hand preference and general verbal ability (Eckert and Leonard, 2000; Rumsey et al., 1997a). In support of the idea of structural anomalies, recent MEG findings showed atypical symmetry of the N100m response location between hemispheres in dyslexic individuals (Heim et al., 2003).

Structural anomalies reflect abnormalities in the development of the nervous system caused by environmental or genetic factors. Indeed, studies of familial dyslexics have indicated a genetic origin for the disorder (Grigorenko, 2001; Taipale et al., 2003) in some individuals. In familial dyslexia, abnormal brain responses to speech sounds, that seem to be related to later reading problems, have been reported in newborns (Guttorm et al., 2005; Leppänen et al., 2002; Lyytinen et al., 2004). There are, however, a great number of dyslexic individuals without known familial background for the symptoms. The problems in reading and phonological processing are most reliably manifested in early school years during reading acquisition, and the underlying neural events are poorly characterized for this age group. In children with normal language development, the neural correlates of speech perception, as well as written word perception, demonstrated significant age-related delays and correlation with behavioral performance in reading/phonological skills (Study II and III). Delays in the processing of auditory information within the time-window of ~200–500 ms, that showed speech sensitive effects in our study, have been reported in language impaired children (Tonnquist-Uhlen, 1996). Moreover, the underlying source for this response indicated abnormal symmetry in dyslexic children (Paul et al., 2006). These findings support the conclusion that the prolonged auditory response at around 250 ms in children (in our study II) reflects important processes for normal language development.

The present results indicate that it is feasible to study the underlying neural phenomena related to normal and abnormal reading development with neuroimaging methods. More especially, the timing of neural events seems to carry developmentally and behaviorally important information. This was evident in study III where the areas sensitive to letter-strings were the same in adults and children, but the sequence of activation was progressively delayed in children. Likewise, in study II, the general location of speech sensitive activation was similar in adults and children but the timing of activation was remarkably different. The significantly higher inter-individual variability in children at both the behavioral (Wightman et al., 1989) and neurophysiological (Studies II and III) level makes it possible to examine phenomena that are not necessarily accessible in adults. Examining the brain responses at individual level is especially important when studying abnormal development since normally developed children of the same age also demonstrate substantial variation in amplitude, latency and also distribution of activation (Studies II and III). Both the temporal and occipitotemporal cortex in the left hemisphere seem to be tightly linked to the development of literacy skills. Further research on dyslexic children is needed to uncover the possible dysfunctions in the development of these areas related to reading disability. Understanding the development and maturation of normal auditory and visual language related processes in the brain is a necessary basis for the study of dysfunctional processes and their rehabilitation in the future.

YHTEENVETO

Kielen käsittely aivoissa – neuromagneettisia tutkimuksia aikuisilla ja lapsilla

Kielen havaitsemisen päämääränä on ymmärtää kuullun tai luetun viestin sisältö. Itse havaitseminen on meille näennäisen vaivatonta. Puheen tunnistaminen ja lukeminen ovat kuitenkin tulos monimutkaisesta aivokuorella tapahtuvasta laskennasta, jonka lähtökohtana on silmän ja korvan vastaanottama fysikaalinen signaali. Tässä väitöskirjassa tutkittiin kielen havaitsemiseen liittyviä aivotoimintoja aikuisilla ja lapsilla. Tutkimukset toteutettiin Teknillisen korkeakoulun Kylmälaboratoriossa, Aivotutkimusyksikössä. Aivojen sähköistä toimintaa erilaisille kielellisille ärsykkeille mitattiin magnetoenkefalografia (MEG) menetelmällä.

Kielellistä viestiä voidaan kuvata eri tasoilla. Esimerkiksi puhuttu sana voidaan nähdä kokonaisena merkitystä välittävänä yksikkönä (semanttinen edustus). Sanan voidaan myös kuvata koostuvan puheäänteistä, puhutun kielen perusyksiköistä (fonologinen edustus). Fysikaalisella tasolla äänisignaali koostuu mm. harmonisista signaaleista, kohinasta ja tauoista, joiden tietynlaiset yhdistelmät ovat ominaisia kielen äänteille (akustis-foneettinen edustus). Kielen havaitsemisen voidaankin ajatella etenevän näiden tasojen kautta tiedon luonteen muuntuessa tasojen välillä. Tällainen viitekehys kielen havaitsemisesta soveltuu käytettäväksi aivotutkimuksen lähtökohtana, jolloin voidaan testata hermoverkkojen sensitiivisyyttä näille kielellisen viestin eri piirteille aktivaatioketjun eri vaiheissa. Kielen havaitseminen ei kuitenkaan todennäköisesti etene tiukan porrastetusti vaan eri tasot ovat vuorovaikutuksessa keskenään.

Tutkimuksissa käytetty mittausmenetelmä, MEG, mittaa aivojen sähköisen toiminnan synnyttämiä pieniä magneettikenttiä ja niiden muutoksia millisekunnin tarkkuudella. Kun koehenkilölle esitetään ärsyke, esimerkiksi puhuttu tai kirjoitettu sana, MEG:llä voidaan mitata hermosolujen sähköisen toiminnan synnyttämiä herätevasteita (evoked response) tai sähköisen toiminnan sarja, vastejatkumo. Näiden vasteiden synnyttämät virtalähteet voidaan paikantaa ja kartoittaa aivokuorella etenevä aktivaatioketju.

Tämän väitöskirjan ensimmäinen keskeinen tavoite oli selvittää miten puheen havaitsemiseen liittyvä aktivaatioketju etenee aikuisten aivoissa. Voidaanko kuuloaivokuoren herätevasteissa havaita herkkyyttä erityisesti puheäänteen akustisille piirteille (Osatutkimus I)? Entä miten merkityksettömän puheäänteen herättämiin aivokuorivasteisiin vaikuttaa se että äänteet esitetään merkityksen käsittelyä tukevassa viitekehyksessä (Osatutkimus IV)? Missä vaiheessa aivojen aktivaatio heijastaa puhutun sanan äänneasun ja sanan merkityksen käsittelyä (Osatutkimus V)?

Ensimmäisessä osatutkimuksessa havaittiin, että 100 millisekuntia äänen esittämisen jälkeen syntyvä aivojen herätevaste vasemmalla kuuloaivokuorella on voimakkaampi puheäänteille kuin akustisesti vastaavanlaisille ei-kielellisille äänille. Tämä vaste syntyy ohimolohkon yläpinnalla, lähellä primaaria kuuloaivokuorta, joka on aivokuoren ensimmäinen kuuloaistimusta käsittelevä alue. Vaikka molemmat aivopuoliskot aktivoituivat keskimäärin yhtä voimakkaasti, ainoastaan vasemmassa aivopuoliskossa nähtiin voimakkain vaste puheäänille, heijastaen todennäköisesti suuremman hermosolujoukon pidempikestoista synkronista aktivaatiota. Lukivaikeuksisilla aikuisilla tämän varhaisen kuulovasteen ajoitus oli poikkeava sujuvasti lukeviin aikuisiin verrattuna: Aivopuoliskojen välinen ajoitus-ero, joka normaalisti heijastaa voimakkaampia yhteyksiä aivopuoliskon ja vastakkaisen korvan välillä (tässä tapauksessa oikeasta korvasta vasempaan aivopuoliskoon), näytti puuttuvan lukivaikeuksisilta, johtuen vasemman aivopuoliskon hitaammasta reaktiosta. Tämän voidaan tulkita johtuvan vasemman planum temporale alueen (PT) ja primaarin kuuloaivokuoren välisten yhteyksien rakenteellisista poikkeavuuksista ja/tai toimintahäiriöistä. Tulos viittaa yleisen äänenkäsittelyn poikkeavuuteen siinä aikaikkunassa, jossa sensitiivisyys puheen äänisignaalin erityispiirteille on jo syntynyt. Useat toiminnallista magneettikuvausta (functional magnetic resonance imaging, fMRI) hyödyntävät aivotutkimukset ovat pyrkineet selvittämään, löytyykö aivoista erityisesti puheen käsittelyyn erikoistunutta rakennetta, vai perustuuko puheen havaitseminen yleisiin, kaikille äänille yhteisiin mekanismeihin. Tulokset eivät ole olleet keskenään yhtäpitäviä, ja onkin esitetty, että puhesignaalin akustisen tiedon muuntaminen kielellistä havaitsemista palvelevaan muotoon tapahtuu usean eri alueen yhteisen toiminnan tuloksena. Tämän väitöskirjatutkimuksen tulokset viittaavat siihen, että puheäänteiden havaitsemisen taustalla voi olla hermosolujoukon hetkellinen samanaikainen puheäänteiden ominaispiirteille herkkä aktivaatio tietyssä aikaikkunassa riippumatta siitä onko vasteen synnyttämä aivoalue erikoistunut vain puheäänien havaitsemiseen. Tällaista nopeasti muuttuvaa sähköistä signaalia ei todennäköisesti havaittaisi verenvirtauksen muutoksiin perustuvalla fMRI-menetelmällä.

Osatutkimuksissa IV ja V tarkasteltiin rajapintaa sanan äänteellisen tason (fonologia) ja merkitystason (semantiikka) välillä. Koehenkilölle luotiin odotus joko äänneasusta tai merkityksestä esittämällä kolme peräkkäistä samanalkuista sanaa tai saman merkitysyhteyden jakavaa sanaa. Neljäntenä esitetty sana joko vastasi tai ei vastannut luotuja odotuksia. Kolmen peräkkäisen sanan esittäminen pienensi aktivaatiota ja neljännen, odotuksen rikkovan sanan esittäminen aiheutti aktivaation voimistumisen. Tulokset osoittivat että sanan äänneasu vaikutti aivovasteeseen ennen 250 millisekuntia kun taas merkitykselle herkkä aktivaatio alkoi 250 millisekunnin kohdalla. Sekä äänneasun että merkityksen vaikutukset näkyivät ohimolohkon takayläosaan paikantuvassa herätevasteessa, selvemmin vasemmassa aivopuoliskossa.

Yllättävästi, myös merkityksettömät luonnolliset puheäänteet (tavut) aiheuttivat yleisesti merkityksen käsittelyyn liitetyn herätevasteen 250 millisekunnin jälkeen. Tämä merkityksen virittäminen käynnistyi erityisesti kun merkityksettömiä tavuja esitettiin siten että niihin liitettiin sanan jatkuvuutta ennustavia akustis-foneettisia piirteitä. Tavut jotka esitettiin yhdessä kokonaisten sanojen ja lauseiden kanssa sekä lausesignaaliin alusta leikatut tavut herättivät enemmän aktivaatiota kuin tavut jotka äänitettiin erillisesti lausuttuina. Tulos tukee ajatusta, että kielen havaitseminen perustuu ennakoivaan prosessointiin, jossa hyödynnetään jatkuvasti saatavilla oleva tieto, sekä äänisignaalin sisältämä että kontekstin antama, merkityksen löytymiseksi. Hermoverkkojen tasolla tämä tarkoittaisi, että merkityksen käsittelyyn liittyvät prosessit rekrytoidaan jo mahdollisesti merkitystä sisältävään äänisignaaliin (sanan alkutavuun) perustuen. Tuloksen voidaan tulkita heijastavan myös 250 millisekunnin jälkeen syntyvän aktivaation mahdollista yhteyttä sanan muodon käsittelyyn, merkityksen sijaan.

Toinen väitöskirjatyön tavoite oli kuvata kielen hahmottamisen aivomekanismeja lapsilla. Onko puheäänen hahmotusketju lapsilla samanlainen kuin aikuisilla? Erityisesti, näyttäytyykö puheäänelle herkkä aktivaatio lapsilla samoin kuin aikuisilla (Osatutkimus II)? Entä onko kirjoitetun sanan hahmottamiseen liittyvä aktivaatioketju vastaava kun aikuisten aivoissa? Voidaanko lapsilla havaita kirjainjonoille herkkä aivovaste ohimo-takaraivolohko –alueella, jonka on aikuisilla osoitettu liittyvän nimenomaan kirjoitetun kielen havaitsemiseen (Osatutkimus III)? Näitä kysymyksiä tutkittiin 7–8 -vuotiailla lapsilla (ensiluokkalaisilla) kahdessa eri koeasetelmassa. Kummassakin tutkimuksessa lasten vasteita verrattiin aikuisten vasteisiin, jotka oli mitattu erillisenä kokeena täysin samanlaisella paradigmalla. MEG-mittauksen lisäksi tutkimuksessa arvioitiin lasten yleistä kognitiivista suorituskykyä, kielellisiä taitoja ja lukemista. Ensimmäisen luokan aikana lasten kognitiiviset taidot, erityisesti lukeminen, kehittyvät nopeasti. Lukemaan oppiminen edellyttää että lapsi kiinnittää huomiota sanan merkityksen lisäksi myös sanan äänneasuun (fonologinen tietoisuus) ja erityisesti, että lapsi oivaltaa puhutun sanan rakentuvat pienemmistä äänneosista (foneeminen tietoisuus), joita voidaan kuvata kirjoitetuilla symboleilla. Myös lukemaan oppiminen vuorostaan vahvistaa lapsen fonologisia taitoja. Puheen ja kirjoitetun kielen hahmotuksen taustalla olevat aivotoiminnot ovat siis erityisen kiinnostavia tässä ikäryhmässä.

Aiemmat lasten kuuloviestin käsittelyä koskevat herätevastetutkimukset (event related potential, ERP) osoittavat, että lasten kuulovasteet poikkeavat ajoitukseltaan selvästi aikuisten kuulovasteista. Lasten kuulovasteita on kuitenkin tutkittu vain harvoin MEG-menetelmällä, jolla voidaan myös paikantaa aktivaation lähde. Keskeisintä olisi selvittää, millaisia toimintoja nämä aikuisista poikkeavat kuulovasteet heijastavat ja onko niillä merkitystä lapsen kielellisen kehityksen kannalta. Tässä väitöskirjatutkimuksessa voitiin todeta, yhtäpitävästi aiempien tutkimustulosten kanssa, että äänteiden havaitseminen herätti lasten aivoissa selvästi erilaisen aktivaatioketjun kuin aikuisten aivoissa. Lasten aktivaatioketjussa painottui myöhempi, pidempikestoinen vastekomponentti kun taas aikuisilla nähtiin nopea lyhytkestoinen aktivaatio. Osalla lapsista pitkäkestoista aktivaatiota edelsi aikuisten vastetta muistuttava varhainen, lyhytkestoinen vaste. Puheäänen piirteille herkkä aivoaktivaatio, joka aikuisilla oli voimakkaimmillaan 100 ms äänen esittämisestä, syntyi lapsilla kuitenkin vasta 270 millisekuntia äänen esittämisestä. Lisäksi lapsilla puhe aiheutti voimakkaamman vasteen molemmissa aivopuoliskoissa kun aikuisilla herkkyys näkyi vain vasemmassa aivopuoliskossa. Aktivaation sijainti kummassakin aivopuoliskossa oli aikuisilla ja lapsilla kuitenkin samankaltainen. Tuloksista voidaan päätellä, että kehittymässä oleva hermoverkko ilmentää toimintoja, joita ei havaita aikuisilla ja jotka näin ollen heijastavat hermoston kehitykseen liittyviä prosesseja. Erityisen huomionarvoista on tätä olettamusta tukeva tutkimuksessa havaittu yhteys lasten puheäänelle herkän aivoaktivaation keston ja lukunopeuden välillä: Nopeammilla lukijoilla vasteen kesto oli lyhyempi. Yhteys havaittiin vain vasemman aivopuoliskon vasteiden ja lukemisen välillä vahvistaen käsitystä vasemman aivopuoliskon roolista kielen kannalta merkityksellisen äänteellisen tiedon käsittelyssä. Tämä lapsille tyypillinen, selvästi aikuisten aktivaatiota pitkäkestoisempi herätevaste heijastaa siis ilmeisesti lukemisen sujuvuuden kannalta tärkeitä hermostollisia prosesseja, liittyen mahdollisesti aivojen kuulojärjestelmän organisointiin kielellisten taitojen kannalta optimaalisella tavalla. Tätä olettamusta tukevat tutkimustulokset, joiden mukaan lukivaikeuksisilla ja kielenkehityksen erityisvaikeuksia omaavilla lapsilla on poikkeavia kuuloherätevasteita tässä samassa aikaikkunassa (noin 200–300 millisekuntia äänen esittämisestä). Tulokset osoittivat, että kuulovasteiden taustalla olevat aivoprosessit ovat vielä kehittymässä 7–8 -vuotiailla lapsilla, ja viittaavat kehityseroihin aivopuoliskojen välillä. Oikeassa aivopuoliskossa lähes kaikilla lapsilla nähtiin varhainen lyhytkestoinen aikuisten kuulovastetta vastaava aktivaatio, kun taas vasemmalla tällainen havaittiin vain muutamalla lapsella. Koska äänet esitettiin vain oikeaan korvaan, tämä saattaa heijastaa eroa myös vastakkaispuoleisten ja saman puoleisten hermoratojen kypsymisessä.

Lukeminen on evolutiivisesti uusi kyky ja sen voidaan ajatella perustuvan hermoverkkoihin, jotka viritetään kirjoitetun tekstin havaitsemiselle yksilönkehityksen aikana. Kirjoitetun sanan hahmottamiseen liittyvää aktivaatioketjua ei ole aikaisemmin juurikaan tutkittu lukemaan opettelevilla lapsilla. Aikuisilla kirjainjonon näkemiseen liittyvä aktivaatioketju aivokuorella alkaa takaraivolohkon takaosasta, jossa hermosolujen aktivaatio syntyy noin 100 millisekuntia kirjainjonon esittämisen jälkeen ja heijastaa yleisten visuaalisten piirteiden käsittelyä. Seuraava aktivaatiohuippu nähdään takaraivo-ohimolohkon rajapinnalla noin 150 millisekuntia kirjainjonon esittämisestä ja edelleen ohimolohkossa noin 200–500 millisekuntia kirjainjonon esittämisestä. Näillä alueilla aivoaktivaatio syntyi erityisesti kirjainjonoille. Jälkimmäisen alueen tiedetään osallistuvan myös merkityksen käsittelyyn. Tämän väitöskirjatutkimuksen tulokset osoittavat, että kirjainjonot aiheuttivat lapsilla aktivaatioketjun joka paikantui hyvin samanlaisille alueille kuin aikuisten aktivaatioketju. Aktivaation ajoitus oli kuitenkin viivästynyt aikuisten aktivaatioketjuun nähden. Erityisen huomionarvoista oli, että ero aikuisten aktivaation ajoitukseen kasvoi edettäessä aktivaatioketjussa aina seuraavalle prosessointitasolle. Tulos on yhtäpitävä hermoverkkojen kypsymistä kartoittavien tutkimusten kanssa, jotka osoittavat että varhaiset sensorisen tiedonkäsittelyn alueet kypsyvät aikaisemmin kuin myöhemmin aktivoituvat, korkeamman tason tiedonkäsittelyyn liittyvät alueet. Vain noin puolella lapsista havaittiin kirjainjonoille sensitiivinen aktivaatiohuippu takaraivolohkon ja ohimolohkon välisellä alueella. Vasteen näkyminen sinänsä ei ollut suoraan yhteydessä lasten lukutaitoon, mutta niillä lapsilla joilla kirjainjonoille herkkä aktivaatio näkyi, sen voimakkuus oli yhteydessä fonologisiin taitoihin. Pienempi vaste (lähempänä aikuisten vasteen voimakkuutta) liittyi parempaan suoriutumiseen fonologisissa tehtävissä. Näistä tuloksista voidaan tehdä se kiinnostava johtopäätös, että puheäänteiden käsittelytaidot, joiden tiedetään liittyvän lukemaan oppimiseen, näyttäisivät muokkaavan lukemiseen liittyviä aivoalueita lukemaan opettelevilla lapsilla.

Väitöskirjatyön viimeisessä osatutkimuksessa (VI) tarkasteltiin kirjoitetun sanan hahmottamiseen liittyvien aivoalueiden herkkyyttä toisaalta kirjainjonojen pituudelle ja toisaalta niiden tuttuudelle eli sille sisältyykö sana aikuisen henkilön sanastoon (esimerkiksi kissa) vai ei (epäsana esimerkiksi heikäle). Yhtäpitävästi aiempien tutkimustulosten kanssa, noin 100 millisekuntia sanan esittämisen jälkeen syntyvät vasteet takaraivolohkon takaosissa reagoivat vain sanan pituudelle. Vasemmassa ohimolohkossa syntyvä pidempiaikainen aktivaatio reagoi sekä sanan pituudelle että sen tuttuudelle. Aktivaatio kesti kauemmin kun sanat olivat pitkiä ja kun ne eivät olleet oikeita sanoja; pisimmän aktivaation aiheuttivat pitkät epäsanat. Tuloksen voidaan ajatella heijastavan fonologista prosessointia, tarkemmin ottaen äänne-kirjain vastaavuuksien käsittelyä.

Tämän väitöskirjatyön tulokset osoittavat, että aivotutkimuksen avulla voidaan kuvata kielen havaitsemisen taustalla olevia, eri piirteiden käsittelylle herkkiä aktivaatioketjun vaiheita. Erityisesti aivoaktivaation ajoitus näyttää kuvastavan kehityksellisesti merkityksellisiä toimintoja. Tämä näkyi sekä puhutun että kirjoitetun kielen käsittelyssä, joissa lasten aktivaatioketju oli sijainniltaan aikuisten kaltainen, mutta ajoitukseltaan viivästynyt ja pidempikestoinen. Suurempi vaihtelu sekä lasten aivovasteissa että behavioraalisissa taidoissa mahdollisti näiden välisen vuorovaikutussuhteen tutkimisen, mikä ei aikuisilla aina ole mahdollista. Kielelliseltä kehitykseltään normaaleilla, saman ikäryhmän lapsilla havaittiin huomattavia eroja aktivaation ajoituksessa, voimakkuudessa ja sijainnissa. Yksilötason tarkastelu onkin erityisen tärkeää kun tutkitaan epänormaalia kielen kehittymistä. Tämän väitöskirjatyön kuvaamat, aikuisten ja lasten kielen hahmottamisen aivomekanismit, luovat pohjaa poikkeavan kielen kehityksen aivomekanismien jatkotutkimuksille.

REFERENCES

Adams, M. (1990). Beginning to read, thinking and learning about print (London, The MIT Press).

Aghababian, V., and Nazir, T. A. (2000). Developing normal reading skills: aspects of the visual processes underlying word recognition. Journal of Experimental Child Psychology 76, 123-150.

Ahonen, T., Tuovinen, S., and Leppäsaari, T. (1999). Nopean sarjallisen nimeämisen testi (Jyväskylä, Haukkarannan koulu, Niilo Mäki Instituutti).

Aine, C. J., Supek, S., and George, J. S. (1995). Temporal dynamics of visual-evoked neuromagnetic sources: effects of stimulus parameters and selective attention. The International Journal of Neuroscience 80, 79-104.

Albrecht, R., Suchodoletz, W., and Uwer, R. (2000). The development of auditory evoked dipole source activity from childhood to adulthood. Clinical Neurophysiology 111, 2268-2276.

Alho, K. (1995). Cerebral generators of mismatch negativity (MMN) and its magnetic counterpart (MMNm) elicited by sound changes. Ear and Hearing 16, 38-51.

Allen, P., and Wightman, F. (1992). Spectral pattern discrimination by children. Journal of Speech and Hearing Research 35, 222-233.

Allen, P., Wightman, F., Kistler, D., and Dolan, T. (1989). Frequency resolution in children. Journal of Speech and Hearing Research 32, 317-322.

Allison, T., Hume, A. L., Wood, C. C., and Goff, W. R. (1984). Developmental and aging changes in somatosensory, auditory and visual evoked potentials. Electroencephalography and Clinical Neurophysiology 58, 14-24.

Allison, T., McCarthy, G., Nobre, A., Puce, A., and Belger, A. (1994). Human extrastriate visual cortex and the perception of faces, words, numbers, and colors. Cerebral Cortex 4, 544-554.

Allison, T., Puce, A., Spencer, D. D., and McCarthy, G. (1999). Electrophysiological studies of human face perception. I: Potentials generated in occipitotemporal cortex by face and non-face stimuli. Cerebral Cortex 9, 415-430.

Aulanko, R., Hari, R., Lounasmaa, O. V., Näätänen, R., and Sams, M. (1993). Phonetic invariance in the human auditory cortex. Neuroreport 4, 1356-1358.

Baldeweg, T., Richardson, A., Watkins, S., Foale, C., and Gruzelier, J. (1999). Impaired auditory frequency discrimination in dyslexia detected with mismatch evoked potentials. Annals of Neurology 45, 495-503.

Barkovich, A. J., and Kjos, B. O. (1988). Normal postnatal development of the corpus callosum as demonstrated by MR imaging. AJNR. American Journal of Neuroradiology 9, 487-491.

Bavelier, D., Corina, D., Jezzard, P., Padmanabhan, S., Clark, V. P., Karni, A., Prinster, A., Braun, A., Lalwani, A., Rauschecker, J., et al. (1997). Sentence reading: A functional MRI study at 4 tesla. Journal of Cognitive Neuroscience 9, 664-686.

Belin, P., and Zatorre, R. J. (2000). 'What', 'where' and 'how' in auditory cortex. Nature Neuroscience 3, 965-966.

Belin, P., Zatorre, R. J., Lafaille, P., Ahad, P., and Pike, B. (2000). Voice-selective areas in human auditory cortex. Nature 403, 309-312.

Bendor, D., and Wang, X. (2005). The neuronal representation of pitch in primate auditory cortex. Nature 436, 1161-1165.

Benes, F. M., Turtle, M., Khan, Y., and Farol, P. (1994). Myelination of a key relay zone in the hippocampal formation occurs in the human brain during childhood, adolescence, and adulthood. Archives of General Psychiatry 51, 477-484.

Benson, R. R., Richardson, M., Whalen, D. H., and Lai, S. (2006). Phonetic processing areas revealed by sinewave speech and acoustically similar non-speech. Neuroimage 31, 342-353.

Benson, R. R., Whalen, D. H., Richardson, M., Swainson, B., Clark, V. P., Lai, S., and Liberman, A. M. (2001). Parametrically dissociating speech and nonspeech perception in the brain using fMRI. Brain and Language 78, 364-396.

Bertelson, P., Morais, J., Alegria, J., and Content, A. (1985). Phonetic analysis capacity and learning to read. Nature 313, 73-74.

Bilecen, D., Scheffler, K., Schmid, N., Tschopp, K., and Seelig, J. (1998). Tonotopic organization of the human auditory cortex as detected by BOLD-FMRI. Hearing Research 126, 19-27.

Binder, J. R., Frost, J. A., Hammeke, T. A., Bellgowan, P. S., Springer, J. A., Kaufman, J. N., and Possing, E. T. (2000). Human temporal lobe activation by speech and nonspeech sounds. Cerebral Cortex 10, 512-528.

Binder, J. R., Frost, J. A., Hammeke, T. A., Rao, S. M., and Cox, R. W. (1996). Function of the left planum temporale in auditory and linguistic processing. Brain 119, 1239-1247.

Bird, C. R., Hedberg, M., Drayer, B. P., Keller, P. J., Flom, R. A., and Hodak, J. A. (1989). MR assessment of myelination in infants and children: usefulness of marker sites. AJNR. American Journal of Neuroradiology 10, 731-740.

Boemio, A., Fromm, S., Braun, A., and Poeppel, D. (2005). Hierarchical and asymmetric temporal sensitivity in human auditory cortices. Nature Neuroscience 8, 389-395.

Bonte, M., and Blomert, L. (2004). Developmental changes in ERP correlates of spoken word recognition during early school years: a phonological priming study. Clinical Neurophysiology 115, 409-423.

Booth, J. R., Burman, D. D., Meyer, J. R., Gitelman, D. R., Parrish, T. B., and Mesulam, M. M. (2002). Modality independence of word comprehension. Human Brain Mapping 16, 251-261.

Bradley, L., and Bryant, P. (1983). Categorizing sounds and learning to read - A causal connection. Nature 301, 419-421.

Bradley, L., and Bryant, P. E. (1978). Difficulties in auditory organisation as a possible cause of reading backwardness. Nature 271, 746-747.

Bradley, L., and Bryant, P. E. (1979). Independence of reading and spelling in backward and normal readers. Developmental Medicine & Child neurology 21, 504-514.

Brecelj, J. (2003). From immature to mature pattern ERG and VEP. Documenta Ophthalmologica. Advances in Ophthalmology 107, 215-224.

Brecelj, J., Strucl, M., Zidar, I., and Tekavcic-Pompe, M. (2002). Pattern ERG and VEP maturation in school children. Clinical Neurophysiology 113, 1764-1770.

Brodmann, K. (1909). Vergleichende Lokalisationelehr der Grosshirnrinde in ihren Prinzipien dargestellt auf Grund des Zellenbaues. (Leipzig, J.A. Barth).

Brody, B. A., Kinney, H. C., Kloman, A. S., and Gilles, F. H. (1987). Sequence of central nervous system myelination in human infancy. I. An autopsy study of myelination. Journal of Neuropathology and Experimental Neurology 46, 283-301.

Brunswick, N., McCrory, E., Price, C. J., Frith, C. D., and Frith, U. (1999). Explicit and implicit processing of words and pseudowords by adult developmental dyslexics: A search for Wernicke's Wortschatz? Brain 122, 1901-1917.

Brunswick, N., and Rippon, G. (1994). Auditory event-related potentials, dichotic listening performance and handedness as indices of lateralisation in dyslexic and normal readers. International Journal of Psychophysiology 18, 265-275.

Budd, T. W., Barry, R. J., Gordon, E., Rennie, C., and Michie, P. T. (1998). Decrement of the N1 auditory event-related potential with stimulus repetition: habituation vs. refractoriness. International Journal of Psychophysiology 31, 51-68.

Buxhoeveden, D. P., and Casanova, M. F. (2002). The minicolumn hypothesis in neuroscience. Brain 125, 935-951.

Cabeza, R., and Nyberg, L. (2000). Imaging cognition II: An empirical review of 275 PET and fMRI studies. Journal of Cognitive Neuroscience 12, 1-47.

Casey, B. J., Galvan, A., and Hare, T. A. (2005). Changes in cerebral functional organization during cognitive development. Current Opinion in Neurobiology 15, 239-244.

Castro-Caldas, A., Petersson, K. M., Reis, A., Stone-Elander, S., and Ingvar, M. (1998). The illiterate brain. Learning to read and write during childhood influences the functional organization of the adult brain. Brain 121, 1053-1063.

Catani, M., Jones, D. K., and ffytche, D. H. (2005). Perisylvian language networks of the human brain. Annals of Neurology 57, 8-16.

Ceponiene, R., Alku, P., Westerfield, M., Torki, M., and Townsend, J. (2005). ERPs differentiate syllable and nonphonetic sound processing in children and adults. Psychophysiology 42, 391-406.

Ceponiene, R., Rinne, T., and Näätänen, R. (2002). Maturation of cortical sound processing as indexed by event-related potentials. Clinical Neurophysiology 113, 870-882.

Chang, E. F., and Merzenich, M. M. (2003). Environmental noise retards auditory cortical development. Science 300, 498-502.

Chechik, G., Anderson, M. J., Bar-Yosef, O., Young, E. D., Tishby, N., and Nelken, I. (2006). Reduction of information redundancy in the ascending auditory pathway. Neuron 51, 359-368.

Chee, M. W., O'Craven, K. M., Bergida, R., Rosen, B. R., and Savoy, R. L. (1999). Auditory and visual word processing studied with fMRI. Human Brain Mapping 7, 15-28.

Chomsky, N. (2002). On Nature and Language (Cambridge, UK, Cambridge University Press).

Coch, D., and Holcomb, P. J. (2003). The N400 in beginning readers. Developmental Psychobiology 43, 146-166.

Cohen, D. (1968). Magnetoencephalography: evidence of magnetic fields produced by alpha-rhythm currents. Science 161, 784-786.

Cohen, L., and Dehaene, S. (2004). Specialization within the ventral stream: the case for the visual word form area. Neuroimage 22, 466-476.

Cohen, L., Dehaene, S., Naccache, L., Lehericy, S., Dehaene-Lambertz, G., Henaff, M. A., and Michel, F. (2000). The visual word form area: spatial and temporal characterization of an initial stage of reading in normal subjects and posterior split-brain patients. Brain 123, 291-307.

Cohen, L., Lehericy, S., Chochon, F., Lemer, C., Rivaud, S., and Dehaene, S. (2002). Language-specific tuning of visual cortex? Functional properties of the Visual Word Form Area. Brain 125, 1054-1069.

Coltheart, M., Curtis, B., Atkins, P., and Haller, M. (1993). Models of reading aloud: Dual-route and parallel-distributed-processing approaches. Psychological Review 100, 589-608.

Coltheart, M., and Rastle, K. (1994). Serial processing in reading aloud: Evidence for dual-route models of reading. Journal of Experimental Psychology: Human Perception, and Performance 20, 1197-1211.

Connolly, J., and Phillips, N. (1994). Event-related potential components reflect phonological and semantic processing of the terminal word of spoken sentences. Journal of Cognitive Neuroscience 6, 256-266.

Crognale, M. A. (2002). Development, maturation, and aging of chromatic visual pathways: VEP results. Journal of Vision 2, 438-450.

Cunningham, J., Nicol, T., Zecker, S., and Kraus, N. (2000). Speech-evoked neurophysiologic responses in children with learning problems: development and behavioral correlates of perception. Ear and Hearing 21, 554-568.

Cutting, J. E., and Pisoni, D. B. (1978). An Information-Processing Approach to Speech Perception. In Speech and Language in the Laboratory, School, and Clinic, J. F. Kavanagh, and W. Strange, eds. (Cambridge, The MIT Press), pp. 39-72.

D'Arcy, R. C., Connolly, J. F., Service, E., Hawco, C. S., and Houlihan, M. E. (2004). Separating phonological and semantic processing in auditory sentence processing: a high-resolution event-related brain potential study. Human Brain Mapping 22, 40-51.

Davis, M. H., and Johnsrude, I. S. (2003). Hierarchical processing in spoken language comprehension. The Journal of Neuroscience 23, 3423-3431.

de Haan, M., Johnson, M. H., and Halit, H. (2003). Development of face-sensitive event-related potentials during infancy: a review. International Journal of Psychophysiology 51, 45-58.

Dehaene-Lambertz, G., Pallier, C., Serniclaes, W., Sprenger-Charolles, L., Jobert, A., and Dehaene, S. (2005). Neural correlates of switching from auditory to speech perception. Neuroimage 24, 21-33.

Deiber, M. P., Ibanez, V., Fischer, C., Perrin, F., and Mauguiere, F. (1988). Sequential mapping favours the hypothesis of distinct generators for Na and Pa middle latency auditory evoked potentials. Electroencephalography and Clinical Neurophysiology 71, 187-197.

Delgutte, B. (1984). Speech coding in the auditory nerve: II. Processing schemes for vowel-like sounds. The Journal of the Acoustical Society of America 75, 879-886.

Demonet, J. F., Chollet, F., Ramsay, S., Cardebat, D., Nespoulous, J. L., Wise, R., Rascol, A., and Frackowiak, R. (1992). The anatomy of phonological and semantic processing in normal subjects. Brain 115 (Pt 6), 1753-1768.

Denckla, M. B., and Rudel, R. G. (1976). Rapid "automatized" naming (R.A.N): dyslexia differentiated from other learning disabilities. Neuropsychologia 14, 471-479.

Diehl, R. L., Lotto, A. J., and Holt, L. L. (2004). Speech perception. Annu Rev Psychol 55, 149-179.

Dorsaint-Pierre, R., Penhune, V. B., Watkins, K. E., Neelin, P., Lerch, J. P., Bouffard, M., and Zatorre, R. J. (2006). Asymmetries of the planum temporale and Heschl's gyrus: relationship to language lateralization. Brain 129, 1164-1176.

Dumay, N., Benraiss, A., Barriol, B., Colin, C., Radeau, M., and Besson, M. (2001). Behavioral and electrophysiological study of phonological priming between bisyllabic spoken words. Journal of Cognitive Neuroscience 13, 121-143.

Dykman, R. A., and Ackerman, P. T. (1992). Diagnosing dyslexia: IQ regression plus cut-points. Journal of Learning Disabilities 25, 574-576.

Eckert, M. A., and Leonard, C. M. (2000). Structural imaging in dyslexia: the planum temporale. Mental Retardation and Developmental Disabilities Research Reviews 6, 198-206.

Eden, G. F., Stein, J. F., Wood, H. M., and Wood, F. B. (1994). Differences in eye movements and reading problems in dyslexic and normal children. Vision Research 34, 1345-1358.

Eden, G. F., VanMeter, J. W., Rumsey, J. M., Maisog, J. M., Woods, R. P., and Zeffiro, T. A. (1996). Abnormal processing of visual motion in dyslexia revealed by functional brain imaging. Nature 382, 66-69.

Eggermont, J. (1974). Basic Principles of electrocochleography. In Electrocochleography basic principles and clinical application, J. J. Eggermont, D. V. Odenthal, P. H. Schmidt, and A. Spoor, eds. (Acta Oto-Laryngol Suppl), pp. 1-84.

Eggermont, J. J. (1988). On the rate of maturation of sensory evoked potentials. Electroencephalography and Clinical Neurophysiology 70, 293-305.

Eggermont, J. J. (2001). Between sound and perception: reviewing the search for a neural code. Hearing Research 157, 1-42.

Ehri, L. C. (1992). Reconceptualizing the development of sight word reading and its relationship to recoding. In Reading acquisition, P. Gough, L. Ehri, and R. Treiman, eds. (Hillsdale, NJ, Lawrence Erlbaum Associates Inc.).

Ehri, L. C. (1998). Grapheme-phoneme knowledge is essential for learning to read words in English. In Word recognition in beginning literacy, J. L. Metsala, and L. C. Ehri, eds. (Mahwah, NJ, Erlbaum), pp. 3-40.

Eimas, P. D., Siqueland, E. R., Jusczyk, P., and Vigorito, J. (1971). Speech perception in infants. Science 171, 303-306.

Elberling, C., Bak, C., Kofoed, B., Lebech, J., and Saermark, K. (1982). Auditory magnetic fields from the human cerebral cortex: location and strength of an equivalent current dipole. Acta Neurol Scand 65, 553-569.

Elliot, H. (1969). Textbook of Neuroanatomy. (Philadelphia, Lippincott).

Eulitz, C., Diesch, E., Pantev, C., Hampson, S., and Elbert, T. (1995). Magnetic and electric brain activity evoked by the processing of tone and vowel stimuli. The Journal of Neuroscience 15, 2748-2755.

Fiez, J. A., and Petersen, S. E. (1998). Neuroimaging studies of word reading. Proceedings of the National Academy of Sciences of the United States of America 95, 914-921.

Fletcher, J. M., Francis, D. J., Rourke, B. P., Shaywitz, S. E., and Shaywitz, B. A. (1992). The validity of discrepancy-based definitions of reading disabilities. Journal of Learning Disabilities 25, 555-561, 573.

Fletcher, J. M., Shaywitz, S. E., Shankweiler, D. P., Katz, L., Liberman, I. Y., Stuebing, K. K., Francis, D. J., Flower, A. E., and Shaywitz, B. A. (1994). Cognitive profiles of reading disability: Comparisons of discrepancy and low achievement definitions. Journal of Educational Psychology 86, 6-23.

Fodor, J. A. (1983). The modularity of Mind (Cambridge MA, MIT Press).

Formisano, E., Kim, D. S., Di Salle, F., van de Moortele, P. F., Ugurbil, K., and Goebel, R. (2003). Mirror-symmetric tonotopic maps in human primary auditory cortex. Neuron 40, 859-869.

Fowler, C. (1994). Speech perception: direct realist theory. In The Encyclopedia of Language and Linguistics., R. Asher, ed. (Oxford, Pergamon).

Frith, U. (1985). Beneath the surface of developmental dyslexia. In Surface dyslexia: Cognitive and neuropsychological studies of phonological reading, K. E. Patterson, J. C. Marshall, and M. Coltheart, eds. (London, Lawrence Erlbaum), pp. 301-330.

Galaburda, A., and Sanides, F. (1980). Cytoarchitectonic organization of the human auditory cortex. The Journal of Comparative Neurology 190, 597-610.

Galaburda, A. M. (1993). Neuroanatomic basis of developmental dyslexia. Neurologic Clinics 11, 161-173.

Galaburda, A. M., Sanides, F., and Geschwind, N. (1978). Human brain. Cytoarchitectonic left-right asymmetries in the temporal speech region. Archives of Neurology 35, 812-817.

Galaburda, A. M., Sherman, G. F., Rosen, G. D., Aboitiz, F., and Geschwind, N. (1985). Developmental dyslexia: four consecutive patients with cortical anomalies. Annals of Neurology 18, 222-233.

Gandour, J., Tong, Y., Wong, D., Talavage, T., Dzemidzic, M., Xu, Y., Li, X., and Lowe, M. (2004). Hemispheric roles in the perception of speech prosody. Neuroimage 23, 344-357.

Geschwind, N., and Levitsky, W. (1968). Human brain: left-right asymmetries in temporal speech region. Science 161, 186-187.

Giedd, J. N., Blumenthal, J., Jeffries, N. O., Castellanos, F. X., Liu, H., Zijdenbos, A., Paus, T., Evans, A. C., and Rapoport, J. L. (1999). Brain development during childhood and adolescence: a longitudinal MRI study. Nature Neuroscience 2, 861-863.

Giraud, A. L., Lorenzi, C., Ashburner, J., Wable, J., Johnsrude, I., Frackowiak, R., and Kleinschmidt, A. (2000). Representation of the temporal envelope of sounds in the human brain. Journal of Neurophysiology 84, 1588-1598.

Gogtay, N., Giedd, J. N., Lusk, L., Hayashi, K. M., Greenstein, D., Vaituzis, A. C., Nugent, T. F., 3rd., Herman, D. H., Clasen, L. S., Toga, A. W., *et al.* (2004). Dynamic mapping of human cortical development during childhood through early adulthood. Proceedings of the National Academy of Sciences of the United States of America 101, 8174-8179.

Goodale, M. A., and Milner, A. D. (1992). Separate visual pathways for perception and action. Trends in Neurosciences 15, 20-25.

Gootjes, L., Raij, T., Salmelin, R., and Hari, R. (1999). Left-hemisphere dominance for processing of vowels: a whole-scalp neuromagnetic study. Neuroreport 10, 2987-2991.

Gordon, K. A., Papsin, B. C., and Harrison, R. V. (2003). Activity-dependent developmental plasticity of the auditory brain stem in children who use cochlear implants. Ear and Hearing 24, 485-500.

Goswami, U., Ziegler, J. C., Dalton, L., and Schneider, W. (2003). Nonword reading across orthographies: How flexible is the choice of reading development in English and German. Applied Psycholinguistics 24, 235-247.

Griffiths, T. D., Warren, J. D., Scott, S. K., Nelken, I., and King, A. J. (2004). Cortical processing of complex sound: a way forward? Trends Neurosci 27, 181-185.

Grigorenko, E. L. (2001). Developmental dyslexia: an update on genes, brains, and environments. Journal of Child Psychology and Psychiatry, and allied disciplines 42, 91-125.

Grill-Spector, K., Kushnir, T., Hendler, T., Edelman, S., Itzchak, Y., and Malach, R. (1998). A sequence of object-processing stages revealed by fMRI in the human occipital lobe. Human Brain Mapping 6, 316-328.

Grosjean, F. (1980). Spoken word recognition processes and the gating paradigm. Perception & Psychophysics 28, 267-283.

Grossi, G., Coch, D., Coffey-Corina, S., Holcomb, P. J., and Neville, H. J. (2001). Phonological processing in visual rhyming: a developmental erp study. Journal of Cognitive Neuroscience 13, 610-625.

Guttorm, T. K., Leppänen, P. H., Poikkeus, A. M., Eklund, K. M., Lyytinen, P., and Lyytinen, H. (2005). Brain event-related potentials (ERPs) measured at birth predict later language development in children with and without familial risk for dyslexia. Cortex 41, 291-303.

Hackett, T. A., Preuss, T. M., and Kaas, J. H. (2001). Architectonic identification of the core region in auditory cortex of macaques, chimpanzees, and humans. The Journal of Comparative Neurology 441, 197-222.

Hackett, T. A., Stepniewska, I., and Kaas, J. H. (1998). Subdivisions of auditory cortex and ipsilateral cortical connections of the parabelt auditory cortex in macaque monkeys. The Journal of Comparative Neurology 394, 475-495.

Hagoort, P., and Brown, C. M. (2000a). ERP effects of listening to speech compared to reading: the P600/SPS to syntactic violations in spoken sentences and rapid serial visual presentation. Neuropsychologia 38, 1531-1549.

Hagoort, P., and Brown, C. M. (2000b). ERP effects of listening to speech: semantic ERP effects. Neuropsychologia 38, 1518-1530.

Hagoort, P., Indefrey, P., Brown, C., Herzog, H., Steinmetz, H., and Seitz, R. J. (1999). The neural circuitry involved in the reading of German words and pseudowords: A PET study. Journal of Cognitive Neuroscience 11, 383-398.

Halgren, E., Baudena, P., Heit, G., Clarke, J. M., Marinkovic, K., and Clarke, M. (1994). Spatio-temporal stages in face and word processing. I. Depth-recorded potentials in the human occipital, temporal and parietal lobes [corrected]. Journal of Physiology, Paris 88, 1-50.

Halgren, E., Raij, T., Marinkovic, K., Jousmäki, V., and Hari, R. (2000). Cognitive response profile of the human fusiform face area as determined by MEG. Cerebral Cortex 10, 69-81.

Hall, D. A., Hart, H. C., and Johnsrude, I. S. (2003). Relationships between human auditory cortical structure and function. Audiology & Neuro-otology 8, 1-18.

Hall, D. A., Johnsrude, I. S., Haggard, M. P., Palmer, A. R., Akeroyd, M. A., and Summerfield, A. Q. (2002). Spectral and temporal processing in human auditory cortex. Cerebral Cortex 12, 140-149.

Hari, R. (1990). The neuromagnetic method in the study of the human auditory cortex. In Auditory Evoked Magnetic Fields and Electric Potentials, F. Grandori, M. Hoke, and G. L. Romani, eds. (Basel, Karger), pp. 222-282.

Hari, R. (1993). Magnetoencephalography as a tool of clinical neurophysiology. In Electroencephalography: Basic Principles, Clinical Applications, and Related Fields, E. Niedermeyer, and F. L. D. Silva, eds. (Baltimore, Williams & Wilkins), pp. 1035-1061.

Hari, R., Hämäläinen, M., Ilmoniemi, R., Kaukoranta, E., Reinikainen, K., Salminen, J., Alho, K., Näätänen, R., and Sams, M. (1984). Responses of the primary auditory cortex to pitch changes in a sequence of tone pips: neuromagnetic recordings in man. Neuroscience Letters 50, 127-132.

Hari, R., Kaila, K., Katila, T., Tuomisto, T., and Varpula, T. (1982). Interstimulus interval dependence of the auditory vertex response and its magnetic counterpart: implications for their neural generation. Electroencephalography and Clinical Neurophysiology 54, 561-569.

Hari, R., Pelizzone, M., Mäkelä, J. P., Hallström, J., Leinonen, L., and Lounasmaa, O. V. (1987). Neuromagnetic responses of the human auditory cortex to on- and offsets of noise bursts. Audiology 26, 31-43.

Hari, R., Renvall, H., and Tanskanen, T. (2001). Left minineglect in dyslexic adults. Brain 124, 1373-1380.

Harley, T. (2001). The Psychology of Language. From Data to Theory (Hove, East Sussex, Psychology Press Ltd).

Hashimoto, T., Kashii, S., Kikuchi, M., Honda, Y., Nagamine, T., and Shibasaki, H. (1999). Temporal profile of visual evoked responses to pattern-reversal stimulation analyzed with a whole-head magnetometer. Experimental Brain Research 125, 375-382.

Hauser, M. D., Chomsky, N., and Fitch, W. T. (2002). The faculty of language: what is it, who has it, and how did it evolve? Science 298, 1569-1579.

Haxby, J. V., Gobbini, M. I., Furey, M. L., Ishai, A., Schouten, J. L., and Pietrini, P. (2001). Distributed and overlapping representations of faces and objects in ventral temporal cortex. Science 293, 2425-2430.

Haxby, J. V., Grady, C. L., Horwitz, B., Ungerleider, L. G., Mishkin, M., Carson, R. E., Herscovitch, P., Schapiro, M. B., and Rapoport, S. I. (1991). Dissociation of object and spatial visual processing pathways in human extrastriate cortex. Proceedings of the National Academy of Sciences of the United States of America 88, 1621-1625.

Haxby, J. V., Ungerleider, L. G., Clark, V. P., Schouten, J. L., Hoffman, E. A., and Martin, A. (1999). The effect of face inversion on activity in human neural systems for face and object perception. Neuron 22, 189-199.

Hebb, D. O. (1949). The Organization of Behavior (New York, Wiley).

Heim, S., Eulitz, C., and Elbert, T. (2003). Altered hemispheric asymmetry of auditory N100m in adults with developmental dyslexia. Neuroreport 14, 501-504.

Helenius, P., Salmelin, R., Richardson, U., Leinonen, S., and Lyytinen, H. (2002a). Abnormal auditory cortical activation in dyslexia 100 msec after speech onset. Journal of Cognitive Neuroscience 14, 603-617.

Helenius, P., Salmelin, R., Service, E., and Connolly, J. F. (1998). Distinct time courses of word and context comprehension in the left temporal cortex. Brain 121, 1133-1142.

Helenius, P., Salmelin, R., Service, E., and Connolly, J. F. (1999a). Semantic cortical activation in dyslexic readers. Journal of Cognitive Neuroscience 11, 535-550.

Helenius, P., Salmelin, R., Service, E., Connolly, J. F., Leinonen, S., and Lyytinen, H. (2002b). Cortical activation during spoken-word segmentation in nonreading-impaired and dyslexic adults. The Journal of Neuroscience 22, 2936-2944.

Helenius, P., Tarkiainen, A., Cornelissen, P., Hansen, P. C., and Salmelin, R. (1999b). Dissociation of normal feature analysis and deficient processing of letter-strings in dyslexic adults. Cerebral Cortex 9, 476-483.

Helmholtz, H. (1867). Handbuch der physiologischen Optik (Leipzig, Voss).

Hickok, G., and Poeppel, D. (2000). Towards a functional neuroanatomy of speech perception. Trends in Cognitive Sciences 4, 131-138.

Hickok, G., and Poeppel, D. (2004). Dorsal and ventral streams: a framework for understanding aspects of the functional anatomy of language. Cognition 92, 67-99.

Hickok, G., and Poeppel, D. (2007). The cortical organization of speech processing. Nature Reviews. Neuroscience 8, 393-402.

Hillenbrand, J., Getty, L. A., Clark, M. J., and Wheeler, K. (1995). Acoustic characteristics of American English vowels. The Journal of the Acoustical Society of America 97, 3099-3111.

Holcomb, P. J., Coffey, S. A., and Neville, H. J. (1992). Visual and auditory sentence processing: A developmental analysis using event-related brain potentials. Developmental Neuropsychology 8, 203-241.

Holopainen, L., Ahonen, T., and Lyytinen, H. (2001). Predicting delay in reading achievement in a highly transparent language. J Learn Disabil 34, 401-413.

Horton, J. C., and Hedley-Whyte, E. T. (1984). Mapping of cytochrome oxidase patches and ocular dominance columns in human visual cortex. Philosophical Transactions of the Royal Society of London. Series B, Biological sciences 304, 255-272.

Hubel, D. H., and Wiesel, T. N. (1962). Receptive fields, binocular interaction and functional architecture in the cat's visual cortex. The Journal of Physiology 160, 106-154.

Hupe, J. M., James, A. C., Payne, B. R., Lomber, S. G., Girard, P., and Bullier, J. (1998). Cortical feedback improves discrimination between figure and background by V1, V2 and V3 neurons. Nature 394, 784-787.

Huppi, P. S., Warfield, S., Kikinis, R., Barnes, P. D., Zientara, G. P., Jolesz, F. A., Tsuji, M. K., and Volpe, J. J. (1998). Quantitative magnetic resonance imaging of brain development in premature and mature newborns. Annals of Neurology 43, 224-235.

Huttenlocher, P. R. (1979). Synaptic density in human frontal cortex - developmental changes and effects of aging. Brain Research 163, 195-205.

Huttenlocher, P. R., and Dabholkar, A. S. (1997). Regional differences in synaptogenesis in human cerebral cortex. The Journal of Comparative Neurology 387, 167-178.

Hynd, G. W., Semrud-Clikeman, M., Lorys, A. R., Novey, E. S., and Eliopulos, D. (1990). Brain morphology in developmental dyslexia and attention deficit disorder/hyperactivity. Archives of Neurology 47, 919-926.

Hämäläinen, M., Hari, R., Ilmoniemi, R. J., Knuutila, L., and Lounasmaa, O. V. (1993). Magnetoencephalography - theory, instrumentation, and applications to noninvasive studies of the working human brain. Reviews of Modern Physics 65, 413 - 497.

Indefrey, P., Kleinschmidt, A., Merboldt, K. D., Kruger, G., Brown, C., Hagoort, P., and Frahm, J. (1997). Equivalent responses to lexical and nonlexical visual stimuli in occipital cortex: a functional magnetic resonance imaging study. Neuroimage 5, 78-81.

Ishai, A., Schmidt, C. F., and Boesiger, P. (2005). Face perception is mediated by a distributed cortical network. Brain Research Bulletin 67, 87-93.

Ishai, A., Ungerleider, L. G., Martin, A., Schouten, J. L., and Haxby, J. V. (1999). Distributed representation of objects in the human ventral visual pathway. Proceedings of the National Academy of Sciences of the United States of America 96, 9379-9384.

Jacquemot, C., Pallier, C., LeBihan, D., Dehaene, S., and Dupoux, E. (2003). Phonological grammar shapes the auditory cortex: a functional magnetic resonance imaging study. The Journal of Neuroscience 23, 9541-9546.

Jancke, L., Wustenberg, T., Scheich, H., and Heinze, H. J. (2002). Phonetic perception and the temporal cortex. Neuroimage 15, 733-746.

Jernigan, T. L., Trauner, D. A., Hesselink, J. R., and Tallal, P. A. (1991). Maturation of human cerebrum observed in vivo during adolescence. Brain 114, 2037-2049.

Jobard, G., Crivello, F., and Tzourio-Mazoyer, N. (2003). Evaluation of the dual route theory of reading: a metanalysis of 35 neuroimaging studies. Neuroimage 20, 693-712.

Johnstone, S. J., Barry, R. J., Anderson, J. W., and Coyle, S. F. (1996). Age-related changes in child and adolescent event-related potential component morphology, amplitude and latency to standard and target stimuli in an auditory oddball task. International Journal of Psychophysiology 24, 223-238.

Jones, E. G. (2000). Microcolumns in the cerebral cortex. Proceedings of the National Academy of Sciences of the United States of America 97, 5019-5021.

Jusczyk, P. W., and Luce, P. A. (2002). Speech perception and spoken word recognition: past and present. Ear and Hearing 23, 2-40.

Juszyk, P. (1997). The discovery of spoken language (Cambridge, MA, MIT Press).

Juszyk, P., Luce, P., and Charles-Luce, J. (1994). Infant's sensitivity to phonotactic patterns in the native language. Journal of Memory and Language 33, 630-645.

Kaas, J. H., and Hackett, T. A. (1999). 'What' and 'where' processing in auditory cortex. Nature Neuroscience 2, 1045-1047.

Kaas, J. H., and Hackett, T. A. (2000). Subdivisions of auditory cortex and processing streams in primates. Proceedings of the National Academy of Sciences of the United States of America 97, 11793-11799.

Kajamies, A., Poskiparta, E., Annevirta, T., Dufva, M., & Vauras, M. (2003). YTTE. Luetun ja kuullun ymmärtämisen ja lukemisen sujuvuuden arviointi. [Test of reading fluency and comprehension and listening comprenension]. (Turku, University of Turku, Centre for Learning research).

Kanwisher, N., McDermott, J., and Chun, M. M. (1997). The fusiform face area: a module in human extrastriate cortex specialized for face perception. The Journal of Neuroscience 17, 4302-4311.

Kaplan, E., and Shapley, R. M. (1986). The primate retina contains two types of ganglion cells, with high and low contrast sensitivity. Proceedings of the National Academy of Sciences of the United States of America 83, 2755-2757.

Kaukoranta, E., Hari, R., and Lounasmaa, O. V. (1987). Responses of the human auditory cortex to vowel onset after fricative consonants. Experimental Brain Research 69, 19-23.

Kileny, P., Paccioretti, D., and Wilson, A. F. (1987). Effects of cortical lesions on middle-latency auditory evoked responses (MLR). Electroencephalography and Clinical Neurophysiology 66, 108-120.

Klatt, D. H. (1979). Speech perception: A model of acoustic-phonetic analysis and lexical access. Journal of Phonetics 7, 279-312.

Klingberg, T., Hedehus, M., Temple, E., Salz, T., Gabrieli, J. D., Moseley, M. E., and Poldrack, R. A. (2000). Microstructure of temporo-parietal white matter as a basis for reading ability: evidence from diffusion tensor magnetic resonance imaging. Neuron 25, 493-500.

Kolb, B., and Whishaw, I. Q. (1996). Fundamentals of human neuropsychology, 4th edn (New York, W.H. Freeman and Company).

Kraus, N., and McGee, T. (1992). Electrophysiology of the Human Auditory System. In The Mammalian Auditory Pathway: Neurophysiology, A. Popper, and R. Fay, eds. (New Yourk, Springer-Verlag).

Kraus, N., McGee, T., Carrell, T., Sharma, A., Micco, A., and Nicol, T. (1993). Speech-evoked cortical potentials in children. Journal of the American Academy of Audiology 4, 238-248.

Kraus, N., Ozdamar, O., Hier, D., and Stein, L. (1982). Auditory middle latency responses (MLRs) in patients with cortical lesions. Electroencephalography and Clinical Neurophysiology 54, 275-287.

Kuhl, P. K. (1991). Human adults and human infants show a "perceptual magnet effect" for the prototypes of speech categories, monkeys do not. Perception & Psychophysics 50, 93-107.

Kuhl, P. K. (2004). Early language acquisition: cracking the speech code. Nature Reviews. Neuroscience 5, 831-843.

Kuhl, P. K., and Miller, J. D. (1975). Speech perception by the chinchilla: voiced-voiceless distinction in alveolar plosive consonants. Science 190, 69-72.

Kuhl, P. K., and Miller, J. D. (1978). Speech perception by the chinchilla: identification function for synthetic VOT stimuli. The Journal of the Acoustical Society of America 63, 905-917.

Kuhl, P. K., Williams, K. A., Lacerda, F., Stevens, K. N., and Lindblom, B. (1992). Linguistic experience alters phonetic perception in infants by 6 months of age. Science 255, 606-608.

Kujala, A., Alho, K., Service, E., Ilmoniemi, R. J., and Connolly, J. F. (2004). Activation in the anterior left auditory cortex associated with phonological analysis of speech input: localization of the phonological mismatch negativity response with MEG. Brain Research. Cognitive Brain Research 21, 106-113.

Kujala, T., Belitz, S., Tervaniemi, M., and Näätänen, R. (2003). Auditory sensory memory disorder in dyslexic adults as indexed by the mismatch negativity. The European Journal of Neuroscience 17, 1323-1327.

Kujala, T., Myllyviita, K., Tervaniemi, M., Alho, K., Kallio, J., and Näätänen, R. (2000). Basic auditory dysfunction in dyslexia as demonstrated by brain activity measurements. Psychophysiology 37, 262-266.

Kuriki, S., and Murase, M. (1989). Neuromagnetic study of the auditory responses in right and left hemispheres of the human brain evoked by pure tones and speech sounds. Experimental Brain Research 77, 127-134.

Kurtzberg, D., Hilpert, P. L., Kreuzer, J. A., and Vaughan, H. G., Jr. (1984). Differential maturation of cortical auditory evoked potentials to speech sounds in normal fullterm and very low-birthweight infants. Developmental Medicine & Child neurology 26, 466-475.

Kutas, M., and Hillyard, S. A. (1980). Reading senseless sentences: brain potentials reflect semantic incongruity. Science 207, 203-205.

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

Langner, G. (1992). Periodicity coding in the auditory system. Hearing Research 60, 115-142.

Larsen, J. P., Hoien, T., Lundberg, I., and Odegaard, H. (1990). MRI evaluation of the size and symmetry of the planum temporale in adolescents with developmental dyslexia. Brain and Language 39, 289-301.

Leinonen, S., Müller, K., Leppänen, P. H. T., Aro, M., Ahonen, T., and Lyytinen, H. (2001). Heterogeneity in adult dyslexic readers: Relating processing skills to the speed and accuracy of oral text reading. Reading and Writing: An Interdisciplinary Journal 14, 265-296.

Leonard, C. M., Voeller, K. K. S., Lombardino, L. J., Morris, M. K., Hynd, G. W., Alexander, A. W., Andersen, H. G., Garofalakis, M., Honeyman, J. C., Mao, J., *et al.* (1993). Anomalous cerebral structure in dyslexia revealed with MRI. Archives of Neurology 50, 461-469.

Leppänen, P. H., Richardson, U., Pihko, E., Eklund, K. M., Guttorm, T. K., Aro, M., and Lyytinen, H. (2002). Brain responses to changes in speech sound durations differ between infants with and without familial risk for dyslexia. Developmental Neuropsychology 22, 407-422.

Liberman, A. M. (1996). Introduction: some assumptions about speech and how they changed. In Speech: A Special Code (Cambridge, MA, MIT Press).

Liberman, A. M., Cooper, F. S., Shankweiler, D. P., and Studdert-Kennedy, M. (1967). Perception of the speech code. Psychological Review 74, 431-461.

Liberman, A. M., Harris, K. S., Kinney, J. A., and Lane, H. (1961). The discrimination of relative onset-time of the components of certain speech and nonspeech patterns. Journal of Experimental Psychology 61, 379-388.

Liberman, A. M., and Mattingly, I. G. (1985). The motor theory of speech perception revised. Cognition 21, 1-36.

Licht, R., Bakker, D. J., Kok, A., and Bouma, A. (1988). The development of lateral event-related potentials (ERPs) related to word naming: a four year longitudinal study. Neuropsychologia 26, 327-340.

Lieberman, P. (1963). Some effects of semantic and grammatical context on the production and perception of speech. Language and Speech 6, 172-187.

Liegeois-Chauvel, C., Musolino, A., and Chauvel, P. (1991). Localization of the primary auditory area in man. Brain 114, 139-151.

Lindeman, J. (1998). ALLU - Ala-asteen Lukutesti [ALLU - Reading Test for Primary School] (University of Turku, Finland, The Center for Learning Research).

Liu, J., Harris, A., and Kanwisher, N. (2002). Stages of processing in face perception: an MEG study. Nature Neuroscience 5, 910-916.

Logothetis, N. K. (1999). Vision: a window on consciousness. Scientific American 281, 69-75.

Lovegrove, W. J., Bowling, A., Badcock, D., and Blackwood, M. (1980). Specific reading disability: differences in contrast sensitivity as a function of spatial frequency. Science 210, 439-440.

Luce, P. A., and Pisoni, D. B. (1998). Recognizing spoken words: the neighborhood activation model. Ear and Hearing 19, 1-36.

Luo, H., and Poeppel, D. (2007). Phase patterns of neuronal responses reliably discriminate speech in human auditory cortex. Neuron 54, 1001-1010.

Lütkenhöner, B., and Steinsträter, O. (1998). High-precision neuromagnetic study of the functional organization of the human auditory cortex. Audiology & Neuro-otology 3, 191-213.

Lyytinen, H. (1997). In search of the precursors of Dyslexia. In Dyslexia: Biology, Cognition and intervention., M. Snowling, and C. Hulme, eds. (London, Whurr Publishers).

Lyytinen, H., Aro, M., Eklund, K., Erskine, J., Guttorm, T., Laakso, M. L., Leppänen, P. H., Lyytinen, P., Poikkeus, A. M., and Torppa, M. (2004). The development of children at familial risk for dyslexia: birth to early school age. Annals of Dyslexia 54, 184-220.

Madrid, M., and Crognale, M. A. (2000). Long-term maturation of visual pathways. Visual Neuroscience 17, 831-837.

Malach, R., Reppas, J. B., Benson, R. R., Kwong, K. K., Jiang, H., Kennedy, W. A., Ledden, P. J., Brady, T. J., Rosen, B. R., and Tootell, R. B. (1995). Object-related activity revealed by functional magnetic resonance imaging in human occipital cortex. Proceedings of the National Academy of Sciences of the United States of America 92, 8135-8139.

Manis, F. R., Seidenberg, M. S., Doi, L. M., McBride-Chang, C., and Petersen, A. (1996). On the bases of two subtypes of developmental [corrected] dyslexia. Cognition 58, 157-195.

Marinkovic, K., Dhond, R. P., Dale, A. M., Glessner, M., Carr, V., and Halgren, E. (2003). Spatiotemporal dynamics of modality-specific and supramodal word processing. Neuron 38, 487-497.

Marslen-Wilson, W. (1989). Access and integration: projecting sound onto meaning. In Lexical Representation and Process., W. Marslen-Wilson, ed. (Cambridge, MA, MIT Press), pp. 3-24.

Marslen-Wilson, W., and Tyler, L. K. (1980). The temporal structure of spoken language understanding. Cognition 8, 1-71.

Marslen-Wilson, W., and Warren, P. (1994). Levels of perceptual representation and process in lexical access: words, phonemes, and features. Psychological Review 101, 653-675.

Marslen-Wilson, W. D. (1987). Functional parallelism in spoken word-recognition. Cognition 25, 71-102.

Massaro, D. W., and Cohen, M. M. (1991). Integration versus interactive activation: the joint influence of stimulus and context in perception. Cognitive Psychology 23, 558-614.

Maunsell, J. H. (1992). Functional visual streams. Current Opinion in Neurobiology 2, 506-510.

Maurer, U., Brem, S., Kranz, F., Bucher, K., Benz, R., Halder, P., Steinhausen, H. C., and Brandeis, D. (2006). Coarse neural tuning for print peaks when children learn to read. Neuroimage 33, 749-758.

Maye, J., Werker, J. F., and Gerken, L. (2002). Infant sensitivity to distributional information can affect phonetic discrimination. Cognition 82, B101-111.

McAnally, K. I., and Stein, J. F. (1996). Auditory temporal coding in dyslexia. Proceedings. Biological Sciences 263, 961-965.

McCandliss, B. D., Cohen, L., and Dehaene, S. (2003). The visual word form area: expertise for reading in the fusiform gyrus. Trends in Cognitive Sciences 7, 293-299.

McClelland, J. L., and Elman, J. L. (1986). The TRACE model of speech perception. Cognitive Psychology 18, 1-86.

McConkie, G. W., and Rayner, K. (1976). Asymmetry of the perceptual span in reading. Bulletin of the Psychonomic Society 8, 365-368.

McEvoy, L., Levänen, S., and Loveless, N. (1997). Temporal characteristics of auditory sensory memory: neuromagnetic evidence. Psychophysiology 34, 308-316.

Merzenich, M. M., and Brugge, J. F. (1973). Representation of the cochlear partition of the superior temporal plane of the macaque monkey. Brain Research 50, 275-296.

Miller, J. D., Wier, C. C., Pastore, R. E., Kelly, W. J., and Dooling, R. J. (1976). Discrimination and labeling of noise-buzz sequences with varying noise-lead times: an example of categorical perception. The Journal of the Acoustical Society of America 60, 410-417.

Miller, J. L., and Eimas, P. D. (1995). Speech perception: from signal to word. Annu Rev Psychol 46, 467-492.

Mody, M., Studdert-Kennedy, M., and Brady, S. (1997). Speech perception deficits in poor readers: auditory processing or phonological coding? Journal of Experimental Child Psychology 64, 199-231.

Moore, J. K. (2002). Maturation of human auditory cortex: implications for speech perception. The Annals of Otology, Rhinology & Laryngology. Supplement 189, 7-10.

Moore, J. K., and Guan, Y. L. (2001). Cytoarchitectural and axonal maturation in human auditory cortex. Journal of the Association for Research in Otolaryngology 2, 297-311.

Morais, J., Bertelson, P., Cary, L., and Alegria, J. (1986). Literacy training and speech segmentation. Cognition 24, 45-64.

Morais, J., and Kolinsky, R. (1994). Perception and awareness in phonological processing: the case of the phoneme. Cognition 50, 287-297.

Morosan, P., Rademacher, J., Schleicher, A., Amunts, K., Schormann, T., and Zilles, K. (2001). Human primary auditory cortex: cytoarchitectonic subdivisions and mapping into a spatial reference system. Neuroimage 13, 684-701.

Morton, J. (1989). An information-processing account of reading acquisition. In From reading to neurons, A. M. Galaburda, ed. (Cambridge, MA, MIT Press), pp. 43-66.

Moskowitz, A., and Sokol, S. (1983). Developmental changes in the human visual system as reflected by the latency of the pattern reversal VEP. Electroencephalography and Clinical Neurophysiology 56, 1-15.

Mountcastle, V. B. (1957). Modality and topographic properties of single neurons of cat's somatic sensory cortex. Journal of Neurophysiology 20, 408-434.

Mountcastle, V. B. (1997). The columnar organization of the neocortex. Brain 120, 701-722.

Muter, V., Hulme, C., Snowling, M., and Taylor, S. (1998). Segmentation, not rhyming, predicts early progress in learning to read. Journal of Experimental Child Psychology 71, 3-27.

Mäkelä, J., Ahonen, A., Hämäläinen, M., Hari, R., Ilmoniemi, R., Kajola, M., Knuutila, J., Lounasmaa, O., McEvoy, L., Salmelin, R., *et al.* (1993). Functional differences between auditory cortices of the two hemispheres revealed by wholehead neuromagnetic recordings. Human Brain Mapping 1, 48-56.

Mäkelä, J. P., and Hari, R. (1992). Neuromagnetic auditory evoked responses after a stroke in the right temporal lobe. Neuroreport 3, 94-96.

Mäkelä, J. P., Hämäläinen, M., Hari, R., and McEvoy, L. (1994). Whole-head mapping of middle-latency auditory evoked magnetic fields. Electroencephalography and Clinical Neurophysiology 92, 414-421.

Möttönen, R., Calvert, G. A., Jääskeläinen, I. P., Matthews, P. M., Thesen, T., Tuomainen, J., and Sams, M. (2006). Perceiving identical sounds as speech or non-speech modulates activity in the left posterior superior temporal sulcus. Neuroimage 30, 563-569.

Nagarajan, S., Mahncke, H., Salz, T., Tallal, P., Roberts, T., and Merzenich, M. M. (1999). Cortical auditory signal processing in poor readers. Proceedings of the National Academy of Sciences of the United States of America 96, 6483-6488.

Nakamura, A., Kakigi, R., Hoshiyama, M., Koyama, S., Kitamura, Y., and Shimojo, M. (1997). Visual evoked cortical magnetic fields to pattern reversal stimulation. Brain Research. Cognitive Brain Research 6, 9-22.

Nelken, I. (2004). Processing of complex stimuli and natural scenes in the auditory cortex. Current Opinion in Neurobiology 14, 474-480.

Neville, H., and Bavelier, D. (2002). Human brain plasticity: evidence from sensory deprivation and altered language experience. Progress in Brain Research 138, 177-188.

Nicholls, J. G., Martin, R. A., and Wallace, B. G. (1992). From Neuron to Brain, 3rd edn (Sunderland, MA, Sinauer Associates, Inc.).

Niemi, J., Laine, M., and Tuominen, J. (1994). Cognitive morphology in Finnish: Foundations of a new model. Language and Cognitive Processes 9, 423-446.

Nobre, A. C., Allison, T., and McCarthy, G. (1994). Word recognition in the human inferior temporal lobe. Nature 372, 260-263.

Nobre, A. C., and McCarthy, G. (1994). Language-related ERPs: scalp distributions and modulations by word type and semantic priming. Journal of Cognitive Neuroscience 6, 233-255.

Norris, D., McQueen, J. M., and Cutler, A. (2000). Merging information in speech recognition: feedback is never necessary. The Behavioral Brain Sciences 23, 299-325; discussion 325-270.

Näätänen, R. (1992). Attention and brain function (Hillsdale, NJ, Erlbaum).

Näätänen, R., Lehtokoski, A., Lennes, M., Cheour, M., Huotilainen, M., Iivonen, A., Vainio, M., Alku, P., Ilmoniemi, R. J., Luuk, A., *et al.* (1997). Language-specific phoneme representations revealed by electric and magnetic brain responses. Nature 385, 432-434.

Näätänen, R., and Picton, T. (1987). The N1 wave of the human electric and magnetic response to sound: a review and an analysis of the component structure. Psychophysiology 24, 375-425.

Obleser, J., Elbert, T., and Eulitz, C. (2004a). Attentional influences on functional mapping of speech sounds in human auditory cortex. BMC Neuroscience 5, 24.

Obleser, J., Lahiri, A., and Eulitz, C. (2004b). Magnetic brain response mirrors extraction of phonological features from spoken vowels. Journal of Cognitive Neuroscience 16, 31-39.

Odom, J. V., Bach, M., Barber, C., Brigell, M., Marmor, M. F., Tormene, A. P., Holder, G. E., and Vaegan (2004). Visual evoked potentials standard (2004). Documenta Ophthalmologica. Advances in Ophthalmology 108, 115-123.

Oe, H., Kandori, A., Yamada, N., Miyashita, T., Tsukada, K., and Naritomi, H. (2002). Interhemispheric connection of auditory neural pathways assessed by auditory evoked magnetic fields in patients with fronto-temporal lobe infarction. Neuroscience Research 44, 483-488.

Orton, S. T. (1925). Word blindness in school children. Archives of Neurology and Psychiatry 14, 581-615.

Paetau, R., Ahonen, A., Salonen, O., and Sams, M. (1995). Auditory evoked magnetic fields to tones and pseudowords in healthy children and adults. Journal of Clinical Neurophysiology 12, 177-185.

Pandya, D. N. (1995). Anatomy of the auditory cortex. Revue Neurologique 151, 486-494.

Pandya, D. N., and Sanides, F. (1973). Architectonic parcellation of the temporal operculum in rhesus monkey and its projection pattern. Zeitschrift für Anatomie und Entwicklungsgeschichte 139, 127-161.

Pantev, C., Hoke, M., Lutkenhoner, B., and Lehnertz, K. (1989). Tonotopic organization of the auditory cortex: pitch versus frequency representation. Science 246, 486-488.

Pantev, C., Lutkenhoner, B., Hoke, M., and Lehnertz, K. (1986). Comparison between simultaneously recorded auditory-evoked magnetic fields and potentials elicited by ipsilateral, contralateral and binaural tone burst stimulation. Audiology 25, 54-61.

Pascual-Leone, A., Amedi, A., Fregni, F., and Merabet, L. B. (2005). The plastic human brain cortex. Annual Review of Neuroscience 28, 377-401.

Pascual-Leone, A., and Walsh, V. (2001). Fast backprojections from the motion to the primary visual area necessary for visual awareness. Science 292, 510-512.

Patterson, R. D., Uppenkamp, S., Johnsrude, I. S., and Griffiths, T. D. (2002). The processing of temporal pitch and melody information in auditory cortex. Neuron 36, 767-776.

Paul, I., Bott, C., Heim, S., Eulitz, C., and Elbert, T. (2006). Reduced hemispheric asymmetry of the auditory N260m in dyslexia. Neuropsychologia 44, 785-794.

Paulesu, E., Frith, C. D., and Frackowiak, R. S. (1993). The neural correlates of the verbal component of working memory. Nature 362, 342-345.

Paulesu, E., McCrory, E., Fazio, F., Menoncello, L., Brunswick, N., Cappa, S. F., Cotelli, M., Cossu, G., Corte, F., Lorusso, M., *et al.* (2000). A cultural effect on brain function. Nature Neuroscience 3, 91-96.

Paus, T., Collins, D. L., Evans, A. C., Leonard, G., Pike, B., and Zijdenbos, A. (2001). Maturation of white matter in the human brain: a review of magnetic resonance studies. Brain Research Bulletin 54, 255-266.

Paus, T., Zijdenbos, A., Worsley, K., Collins, D. L., Blumenthal, J., Giedd, J. N., Rapoport, J. L., and Evans, A. C. (1999). Structural maturation of neural pathways in children and adolescents: in vivo study. Science 283, 1908-1911.

Penfield, W., and Rasmussen, T. (1950). The Cerebral Cortex of Man. A Clinical Study of Localization of Function. (New Yourk, Macmillan).

Perfetti, C. (1992). The representation problem in reading acquisition. In Reading acquisition, P. B. Gough, L. C. Ehri, and R. Treiman, eds. (Hillsdale, NJ, Erlbaum), pp. 145-174.

Perfetti, C. A. (1999). Comprehending written language: a blueprint of the reader. In The Neurocognition of Language, C. Brown, and P. Hagoort, eds. (New York, Oxford University Press).

Perrin, F., and Garcia-Larrea, L. (2003). Modulation of the N400 potential during auditory phonological/semantic interaction. Brain Research. Cognitive Brain Research 17, 36-47.

Petersen, S. E., Fox, P. T., Snyder, A. Z., and Raichle, M. E. (1990). Activation of extrastriate and frontal cortical areas by visual words and word-like stimuli. Science 249, 1041-1044.

Pfefferbaum, A., Mathalon, D. H., Sullivan, E. V., Rawles, J. M., Zipursky, R. B., and Lim, K. O. (1994). A quantitative magnetic resonance imaging study of changes in brain morphology from infancy to late adulthood. Archives of Neurology 51, 874-887.

Phillips, C. (2001). Levels of representation in the electrophysiology of speech perception. Cognitive Science 25, 711--731.

Phillips, C., Pellathy, T., Marantz, A., Yellin, E., Wexler, K., Poeppel, D., McGinnis, M., and Roberts, T. (2000). Auditory cortex accesses phonological categories: an MEG mismatch study. Journal of Cognitive Neuroscience 12, 1038-1055.

Piattelli-Palmarini, M. (1994). Ever since language and learning: afterthoughts on the Piaget-Chomsky debate. Cognition 50, 315-346.

Picton, T. W., Hillyard, S. A., Krausz, H. I., and Galambos, R. (1974). Human auditory evoked potentials. I. Evaluation of components. Electroencephalography and Clinical Neurophysiology 36, 179-190.

Picton, T. W., Stapells, D. R., and Campbell, K. B. (1981). Auditory evoked potentials from the human cochlea and brainstem. The Journal of Otolaryngology. Supplement 9, 1-41.

Pisoni, D. B. (1977). Identification and discrimination of the relative onset time of two component tones: implications for voicing perception in stops. The Journal of the Acoustical Society of America 61, 1352-1361.

Plaut, D. C., McClelland, J. L., Seidenberg, M. S., and Patterson, K. E. (1996). Understanding normal and impaired word reading: Computational principles in quasi-regular domains. Psychological Review 103, 56-115.

Poeppel, D., Guillemin, A., Thompson, J., Fritz, J., Bavelier, D., and Braun, A. R. (2004). Auditory lexical decision, categorical perception, and FM direction discrimination differentially engage left and right auditory cortex. Neuropsychologia 42, 183-200.

Poeppel, D., and Hickok, G. (2004). Towards a new functional anatomy of language. Cognition 92, 1-12.

Poeppel, D., Yellin, E., Phillips, C., Roberts, T. P., Rowley, H. A., Wexler, K., and Marantz, A. (1996). Task-induced asymmetry of the auditory evoked M100 neuromagnetic field elicited by speech sounds. Brain Research. Cognitive Brain Research 4, 231-242.

Polk, T. A., Stallcup, M., Aguirre, G. K., Alsop, D. C., D'Esposito, M., Detre, J. A., and Farah, M. J. (2002). Neural specialization for letter recognition. Journal of Cognitive Neuroscience 14, 145-159.

Ponton, C., Eggermont, J. J., Khosla, D., Kwong, B., and Don, M. (2002). Maturation of human central auditory system activity: separating auditory evoked potentials by dipole source modeling. Clinical Neurophysiology 113, 407-420.

Ponton, C. W., and Eggermont, J. J. (2001). Of kittens and kids: altered cortical maturation following profound deafness and cochlear implant use. Audiology & Neuro-otology 6, 363-380.

Ponton, C. W., Eggermont, J. J., Kwong, B., and Don, M. (2000). Maturation of human central auditory system activity: evidence from multi-channel evoked potentials. Clinical Neurophysiology 111, 220-236.

Popper, A. N., and Fay, R. R. (1992). The Mammalian Auditory Pathway: Neurophysiology (New Yourk, Springer-Verlag).

Poskiparta, E., Niemi, P., and Vauras, M. (1999). Who benefits from training in linguistic awareness in the first grade, and what components show training effects? Journal of Learning Disabilities 32, 437-446, 456.

Poskiparta, E., Niemi, P. & Lepola, J. (1994). Diagnostiset testit 1. Lukeminen ja kirjoittaminen. [Diagnostic tests 1. Reading and spelling] (Turku, University of Turku, Centre for Learning Research).

Praamstra, P., Meyer, A., and Levelt, W. (1994). Neurophysiological manifestations of phonological processing: latency variation of a negative ERP component timelocked to phonological mismatch. Journal of Cognitive Neuroscience 6, 204-219.

Praamstra, P., and Stegeman, D. F. (1993). Phonological effects on the auditory N400 event-related brain potential. Brain Research. Cognitive Brain Research 1, 73-86.

Price, C., Thierry, G., and Griffiths, T. (2005). Speech-specific auditory processing: where is it? Trends in Cognitive Sciences 9, 271-276.

Price, C. J., and Devlin, J. T. (2003). The myth of the visual word form area. Neuroimage 19, 473-481.

Price, C. J., and Devlin, J. T. (2004). The pro and cons of labelling a left occipitotemporal region: "the visual word form area". Neuroimage 22, 477-479.

Price, C. J., Wise, R. J., and Frackowiak, R. S. (1996). Demonstrating the implicit processing of visually presented words and pseudowords. Cerebral Cortex 6, 62-70.

Price, D. J., Kennedy, H., Dehay, C., Zhou, L., Mercier, M., Jossin, Y., Goffinet, A. M., Tissir, F., Blakey, D., and Molnar, Z. (2006). The development of cortical connections. The European Journal of Neuroscience 23, 910-920.

Puce, A., Allison, T., Asgari, M., Gore, J. C., and McCarthy, G. (1996). Differential sensitivity of human visual cortex to faces, letterstrings, and textures: a functional magnetic resonance imaging study. The Journal of Neuroscience 16, 5205-5215.

Pugh, K. R., Shaywitz, B. A., Shaywitz, S. E., Constable, R. T., Skudlarski, P., Fulbright, R. K., Bronen, R. A., Shankweiler, D. P., Katz, L., Fletcher, J. M., and Gore, J. C. (1996). Cerebral organization of component processes in reading. Brain 119, 1221-1238.

Purves, D., Augustine, G. J., Fitzpatrick, D., Katz, L. C., LaMantia, A.-S., McNamara, J. O., and Williams, S. M. (2000). Neuroscience, 2nd edn (Sunderland, MA, Sinauer Associates, Inc.).

Pylkkänen, L., Stringfellow, A., and Marantz, A. (2002). Neuromagnetic evidence for the timing of lexical activation: an MEG component sensitive to phonotactic probability but not to neighborhood density. Brain and Language 81, 666-678.

Radeau, M., Besson, M., Fonteneau, E., and Castro, S. L. (1998). Semantic, repetition and rime priming between spoken words: behavioral and electrophysiological evidence. Biological Psychology 48, 183-204.

Rademacher, J., Morosan, P., Schormann, T., Schleicher, A., Werner, C., Freund, H. J., and Zilles, K. (2001). Probabilistic mapping and volume measurement of human primary auditory cortex. Neuroimage 13, 669-683.

Rakic, P., Bourgeois, J. P., Eckenhoff, M. F., Zecevic, N., and Goldman-Rakic, P. S. (1986). Concurrent overproduction of synapses in diverse regions of the primate cerebral cortex. Science 232, 232-235.

Ramus, F., Rosen, S., Dakin, S. C., Day, B. L., Castellote, J. M., White, S., and Frith, U. (2003). Theories of developmental dyslexia: insights from a multiple case study of dyslexic adults. Brain 126, 841-865.

Rash, B. G., and Grove, E. A. (2006). Area and layer patterning in the developing cerebral cortex. Current Opinion in Neurobiology 16, 25-34.

Rauschecker, J. P. (1998). Cortical processing of complex sounds. Current Opinion in Neurobiology 8, 516-521.

Rauschecker, J. P., and Tian, B. (2000). Mechanisms and streams for processing of "what" and "where" in auditory cortex. Proceedings of the National Academy of Sciences of the United States of America 97, 11800-11806.

Rauschecker, J. P., Tian, B., and Hauser, M. (1995). Processing of complex sounds in the macaque nonprimary auditory cortex. Science 268, 111-114.

Rauschecker, J. P., Tian, B., Pons, T., and Mishkin, M. (1997). Serial and parallel processing in rhesus monkey auditory cortex. The Journal of Comparative Neurology 382, 89-103.

Rayner, K., Well, A. D., and Pollatsek, A. (1980). Asymmetry of the effective visual field in reading. Perception & Psychophysics 27, 537-544.

Reiss, A. L., Abrams, M. T., Singer, H. S., Ross, J. L., and Denckla, M. B. (1996). Brain development, gender and IQ in children. A volumetric imaging study. Brain 119, 1763-1774.

Renvall, H., and Hari, R. (2002). Auditory cortical responses to speech-like stimuli in dyslexic adults. Journal of Cognitive Neuroscience 14, 757-768.

Ridder, W. H., 3rd., Borsting, E., Cooper, M., McNeel, B., and Huang, E. (1997). Not all dyslexics are created equal. Optometry and Vision Science 74, 99-104.

Ritter, W., Vaughan, H. G., Jr., and Costa, L. D. (1968). Orienting and habituation to auditory stimuli: a study of short term changes in average evoked responses. Electroencephalography and Clinical Neurophysiology 25, 550-556.

Rojas, D. C., Walker, J. R., Sheeder, J. L., Teale, P. D., and Reite, M. L. (1998). Developmental changes in refractoriness of the neuromagnetic M100 in children. Neuroreport 9, 1543-1547.

Romani, G. L., Williamson, S. J., and Kaufman, L. (1982). Tonotopic organization of the human auditory cortex. Science 216, 1339-1340.

Romanski, L. M., Tian, B., Fritz, J., Mishkin, M., Goldman-Rakic, P. S., and Rauschecker, J. P. (1999). Dual streams of auditory afferents target multiple domains in the primate prefrontal cortex. Nature Neuroscience 2, 1131-1136.

Rotteveel, J. J., Colon, E. J., Notermans, S. L., Stoelinga, G. B., de Graaf, R., and Visco, Y. (1986). The central auditory conduction at term date and three months after birth. IV. Auditory cortical responses. Scandinavian Audiology 15, 85-95.

Rugg, M. D. (1984). Event-related potentials in phonological matching tasks. Brain and Language 23, 225-240.

Rugg, M. D., and Barrett, S. E. (1987). Event-related potentials and the interaction between orthographic and phonological information in a rhyme-judgment task. Brain and Language 32, 336-361.

Rumsey, J. M., Donohue, B. C., Brady, D. R., Nace, K., Giedd, J. N., and Andreason, P. (1997a). A magnetic resonance imaging study of planum temporale asymmetry in men with developmental dyslexia. Archives of Neurology 54, 1481-1489.

Rumsey, J. M., Horwitz, B., Donohue, B. C., Nace, K., Maisog, J. M., and Andreason, P. (1997b). Phonological and orthographic components of word recognition. A PET-rCBF study. Brain 120, 739-759.

Sable, J. J., Low, K. A., Maclin, E. L., Fabiani, M., and Gratton, G. (2004). Latent inhibition mediates N1 attenuation to repeating sounds. Psychophysiology 41, 636-642.

Sachs, M. B. (1984). Neural coding of complex sounds: speech. Annual Review of Physiology 46, 261-273.

Saffran, J. R. (2001). Words in a sea of sounds: the output of infant statistical learning. Cognition 81, 149-169.

Saffran, J. R., Aslin, R. N., and Newport, E. L. (1996). Statistical learning by 8-month-old infants. Science 274, 1926-1928.

Salmelin, R. (2007). Clinical neurophysiology of language: the MEG approach. Clinical Neurophysiology 118, 237-254.

Salmelin, R., Service, E., Kiesilä, P., Uutela, K., and Salonen, O. (1996). Impaired visual word processing in dyslexia revealed with magnetoencephalography. Annals of Neurology 40, 157-162.

Samuel, A. G. (1990). Using perceptual-restoration effects to explore the architecture of perception. In Cognitive models of speech processing., G. G. M. Altmann, ed. (Cambridge, MA, MIT Press), pp. 295-314.

Samuel, A. G. (1996). Does lexical information influence the perceptual restoration of phonemes? Journal of Experimental Psychology: General 125, 28-51.

Samuel, A. G. (1997). Lexical activation produces potent phonemic percepts. Cognitive Psychology 32, 97-127.

Scarborough, H. S. (1984). Continuity between childhood dyslexia and adult reading. British Journal of Psychology 75, 329-348.

Scherg, M., Hari, R., and Hämäläinen, M. (1989). Frequency-specific sources of the auditory N19-P30 detected by a multiple source analysis of evoked magnetic fields and potentials. In Advances in Biomagnetism., S. J. Williamson, M. Hoke, G. Stroink, and M. Kotani, eds. (New Yourk, Plenum Press), pp. 97-100.

Schlaggar, B. L., Brown, T. T., Lugar, H. M., Visscher, K. M., Miezin, F. M., and Petersen, S. E. (2002). Functional neuroanatomical differences between adults and school-age children in the processing of single words. Science 296, 1476-1479.

Schmolesky, M. T., Wang, Y., Hanes, D. P., Thompson, K. G., Leutgeb, S., Schall, J. D., and Leventhal, A. G. (1998). Signal timing across the macaque visual system. Journal of Neurophysiology 79, 3272-3278.

Schneider, B. A., Trehub, S. E., Morrongiello, B. A., and Thorpe, L. A. (1989). Developmental changes in masked thresholds. The Journal of the Acoustical Society of America 86, 1733-1742.

Schulte-Korne, G., Deimel, W., Bartling, J., and Remschmidt, H. (2001). Speech perception deficit in dyslexic adults as measured by mismatch negativity (MMN). International Journal of Psychophysiology 40, 77-87.

Schultz, R. T., Cho, N. K., Staib, L. H., Kier, L. E., Fletcher, J. M., Shaywitz, S. E., Shankweiler, D. P., Katz, L., Gore, J. C., Duncan, J. S., and et al. (1994). Brain morphology in normal and dyslexic children: the influence of sex and age. Annals of Neurology 35, 732-742.

Scott, S. K., Blank, C. C., Rosen, S., and Wise, R. J. (2000). Identification of a pathway for intelligible speech in the left temporal lobe. Brain 123, 2400-2406.

Scott, S. K., and Johnsrude, I. S. (2003). The neuroanatomical and functional organization of speech perception. Trends in Neurosciences 26, 100-107.

Seidenberg, M. S., and McClelland, J. L. (1989). Distributed, developmental model of word recognition and naming. Psychological Review 96, 523-568.

Seki, K., Nakasato, N., Fujita, S., Hatanaka, K., Kawamura, T., Kanno, A., and Yoshimoto, T. (1996). Neuromagnetic evidence that the P100 component of the pattern reversal visual evoked response originates in the bottom of the calcarine fissure. Electroencephalography and Clinical Neurophysiology 100, 436-442.

Sereno, M. I., Dale, A. M., Reppas, J. B., Kwong, K. K., Belliveau, J. W., Brady, T. J., Rosen, B. R., and Tootell, R. B. (1995). Borders of multiple visual areas in humans revealed by functional magnetic resonance imaging. Science 268, 889-893.

Seymour, P. H., Aro, M., and Erskine, J. M. (2003). Foundation literacy acquisition in European orthographies. Br J Psychol 94, 143-174.

Shankweiler, D. P., Crain, S., Katz, L., Flower, A. E., Liberman, A. M., Brady, S. A., Thornton, R., Lundquist, E., Dreyer, L., Fletcher, J. M., *et al.* (1995). Cognitive profiles of reading-disabled children: Comparison of language skills in phonology, morphology, and syntax. Psychological Science 6, 149-156.

Share, D. L. (1995). Phonological recoding and self-teaching: sine qua non of reading acquisition. Cognition 55, 151-218; discussion 219-126.

Share, D. L. (2004). Orthographic learning at a glance: on the time course and developmental onset of self-teaching. J Exp Child Psychol 87, 267-298.

Sharma, A., Kraus, N., McGee, T. J., and Nicol, T. G. (1997). Developmental changes in P1 and N1 central auditory responses elicited by consonant-vowel syllables. Electroencephalography and Clinical Neurophysiology 104, 540-545.

Shaywitz, B. A., Shaywitz, S. E., Blachman, B. A., Pugh, K. R., Fulbright, R. K., Skudlarski, P., Mencl, W. E., Constable, R. T., Holahan, J. M., Marchione, K. E., *et al.* (2004). Development of left occipitotemporal systems for skilled reading in children after a phonologically- based intervention. Biological Psychiatry 55, 926-933.

Shaywitz, B. A., Shaywitz, S. E., Pugh, K. R., Mencl, W. E., Fulbright, R. K., Skudlarski, P., Constable, R. T., Marchione, K. E., Fletcher, J. M., Lyon, G. R., and Gore, J. C. (2002). Disruption of posterior brain systems for reading in children with developmental dyslexia. Biol Psychiatry 52, 101-110.

Shaywitz, S. E., Escobar, M. D., Shaywitz, B. A., Fletcher, J. M., and Makuch, R. (1992). Evidence that dyslexia may represent the lower tail of a normal distribution of reading ability. The New England Journal of Medicine 326, 145-150.

Shaywitz, S. E., Shaywitz, B. A., Pugh, K. R., Fulbright, R. K., Constable, R. T., Mencl, W. E., Shankweiler, D. P., Liberman, A. M., Skudlarski, P., Fletcher, J. M., *et al.* (1998). Functional disruption in the organization of the brain for reading in dyslexia. Proceedings of the National Academy of Sciences of the United States of America 95, 2636-2641.

Shtyrov, Y., Kujala, T., Palva, S., Ilmoniemi, R. J., and Näätänen, R. (2000). Discrimination of speech and of complex nonspeech sounds of different temporal structure in the left and right cerebral hemispheres. Neuroimage 12, 657-663.

Silven, M., Ahtola, A., and Niemi, P. (2003). Early words, multiword utterances and maternal reading strategies as predictors of mastering word inflections in Finnish. Journal of Child Language 30, 253-279.

Silvén, M., Poskiparta, E., & Niemi, P. (2004). The odds of becoming a precocious reader in Finnish. Journal of Educational Psychology 96, 152-164.

Simos, P. G., Breier, J. I., Fletcher, J. M., Foorman, B. R., Mouzaki, A., and Papanicolaou, A. C. (2001). Age-related changes in regional brain activation during phonological decoding and printed word recognition. Developmental Neuropsychology 19, 191-210.

Snowling, M. J. (1981). Phonemic deficits in developmental dyslexia. Psychological Research 43, 219-234.

Sowell, E. R., Thompson, P. M., Holmes, C. J., Batth, R., Jernigan, T. L., and Toga, A. W. (1999). Localizing age-related changes in brain structure between childhood and adolescence using statistical parametric mapping. Neuroimage 9, 587-597.

Sowell, E. R., Thompson, P. M., Leonard, C. M., Welcome, S. E., Kan, E., and Toga, A. W. (2004). Longitudinal mapping of cortical thickness and brain growth in normal children. The Journal of Neuroscience 24, 8223-8231.

Spitsyna, G., Warren, J. E., Scott, S. K., Turkheimer, F. E., and Wise, R. J. (2006). Converging language streams in the human temporal lobe. The Journal of Neuroscience 26, 7328-7336.

Sprenger-Charolles, L., Siegel, L. S., Bechennec, D., and Serniclaes, W. (2003). Development of phonological and orthographic processing in reading aloud, in silent reading, and in spelling: a four-year longitudinal study. Journal of Experimental Child Psychology 84, 194-217.

Stanovich, K. E., and Siegel, L. S. (1988). Explaining the differences between the dyslexic and the garden variety poor reader. The phonological variable difference model. Journal of Learning Disability 21, 590-604.

Starr, A., and Amlie, R. (1981). The evaluation of newborn brainstem and cochlear functions by auditory brainstem potentials. In Progress in Perinatal Neurology, R. Korobkin, and C. Guilleminault, eds. (Baltimore, Williams and Wilkins), pp. 65-84.

Stein, J., and Walsh, V. (1997). To see but not to read; the magnocellular theory of dyslexia. Trends in Neurosciences 20, 147-152.

Stevens, K. N. (1980). Acoustic correlates of some phonetic categories. The Journal of the Acoustical Society of America 68, 836-842.

Sur, M., and Rubenstein, J. L. (2005). Patterning and plasticity of the cerebral cortex. Science 310, 805-810.

Sutton, S., Tueting, P., Zubin, J., and John, E. R. (1967). Information delivery and the sensory evoked potential. Science 155, 1436-1439.

Taipale, M., Kaminen, N., Nopola-Hemmi, J., Haltia, T., Myllyluoma, B., Lyytinen, H., Muller, K., Kaaranen, M., Lindsberg, P. J., Hannula-Jouppi, K., and Kere, J. (2003). A candidate gene for developmental dyslexia encodes a nuclear tetratricopeptide repeat domain protein dynamically regulated in brain. Proceedings of the National Academy of Sciences of the United States of America 100, 11553-11558.

Takeshita, K., Nagamine, T., Thuy, D. H., Satow, T., Matsuhashi, M., Yamamoto, J., Takayama, M., Fujiwara, N., and Shibasaki, H. (2002). Maturational change of parallel auditory processing in school-aged children revealed by simultaneous recording of magnetic and electric cortical responses. Clinical Neurophysiology 113, 1470-1484.

Talavage, T. M., Ledden, P. J., Benson, R. R., Rosen, B. R., and Melcher, J. R. (2000). Frequency-dependent responses exhibited by multiple regions in human auditory cortex. Hearing Research 150, 225-244.

Tallal, P. (1980). Auditory temporal perception, phonics, and reading disabilities in children. Brain and Language 9, 182-198.

Tallal, P., Miller, S., and Fitch, R. H. (1993). Neurobiological basis of speech: a case for the preeminence of temporal processing. Annals of the New York Academy of Sciences 682, 27-47.

Tanskanen, T., Näsänen, R., Montez, T., Päällysaho, J., and Hari, R. (2005). Face recognition and cortical responses show similar sensitivity to noise spatial frequency. Cerebral Cortex 15, 526-534.

Tarkiainen, A., Cornelissen, P. L., and Salmelin, R. (2002). Dynamics of visual feature analysis and object-level processing in face versus letter-string perception. Brain 125, 1125-1136.

Tarkiainen, A., Helenius, P., Hansen, P. C., Cornelissen, P. L., and Salmelin, R. (1999). Dynamics of letter string perception in the human occipitotemporal cortex. Brain 122, 2119-2132.

Tarkiainen, A., Liljestrom, M., Seppa, M., and Salmelin, R. (2003). The 3D topography of MEG source localization accuracy: effects of conductor model and noise. Clinical Neurophysiology 114, 1977-1992.

Taylor, M. J., Batty, M., and Itier, R. J. (2004). The Faces of Development: A Review of Early Face Processing over Childhood. Journal of Cognitive Neuroscience 16, 1426-1442.

Temple, E., Poldrack, R. A., Protopapas, A., Nagarajan, S., Salz, T., Tallal, P., Merzenich, M. M., and Gabrieli, J. D. (2000). Disruption of the neural response to rapid acoustic stimuli in dyslexia: evidence from functional MRI. Proceedings of the National Academy of Sciences of the United States of America 97, 13907-13912.

Thivard, L., Belin, P., Zilbovicius, M., Poline, J. B., and Samson, Y. (2000). A cortical region sensitive to auditory spectral motion. Neuroreport 11, 2969-2972.

Tiitinen, H., Sivonen, P., Alku, P., Virtanen, J., and Näätänen, R. (1999). Electromagnetic recordings reveal latency differences in speech and tone processing in humans. Brain Research. Cognitive Brain Research 8, 355-363.

Tobimatsu, S., and Celesia, G. G. (2006). Studies of human visual pathophysiology with visual evoked potentials. Clinical Neurophysiology 117, 1414-1433.

Toga, A. W., Thompson, P. M., and Sowell, E. R. (2006). Mapping brain maturation. Trends in Neurosciences 29, 148-159.

Tonnquist-Uhlen, I. (1996). Topography of auditory evoked long-latency potentials in children with severe language impairment: the P2 and N2 components. Ear and Hearing 17, 314-326.

Tonnquist-Uhlen, I., Borg, E., and Spens, K. E. (1995). Topography of auditory evoked long-latency potentials in normal children, with particular reference to the N1 component. Electroencephalography and Clinical Neurophysiology 95, 34-41.

Tootell, R. B., and Hadjikhani, N. (2001). Where is 'dorsal V4' in human visual cortex? Retinotopic, topographic and functional evidence. Cerebral Cortex 11, 298-311.

Treiman, R., and Zukowski, A. (1996). Children's sensitivity to syllables, onsets, rimes, and phonemes. Journal of Experimental Child Psychology 62, 193-215.

Tsao, F. M., Liu, H. M., and Kuhl, P. K. (2004). Speech perception in infancy predicts language development in the second year of life: a longitudinal study. Child Development 75, 1067-1084.

Turkeltaub, P. E., Gareau, L., Flowers, D. L., Zeffiro, T. A., and Eden, G. F. (2003). Development of neural mechanisms for reading. Nature Neuroscience 6, 767-773.

Ungerleider, L. G., and Haxby, J. V. (1994). 'What' and 'where' in the human brain. Current Opinion in Neurobiology 4, 157-165.

Ungerleider, L. G., and Mishkin, M. (1982). Two cortical visual systems. In Analysis of Visual Behavior, D. Ingle, M. A. Goodale, and R. J. W. Mansfield, eds. (Cambridge Mass, MIT Press).

Wagner, R. K., and Torgesen, J. K. (1987). The nature of phonological processing and its causal role in the acquisition of reading skills. Psychological Bulletin 101, 192-212.

Wallace, M. N., Johnston, P. W., and Palmer, A. R. (2002). Histochemical identification of cortical areas in the auditory region of the human brain. Experimental Brain Research 143, 499-508.

Vanni, S., Warnking, J., Dojat, M., Delon-Martin, C., Bullier, J., and Segebarth, C. (2004). Sequence of pattern onset responses in the human visual areas: an fMRI constrained VEP source analysis. Neuroimage 21, 801-817.

Warren, R. M., Obusek, C. J., Farmer, R. M., and Warren, R. P. (1969). Auditory sequence: confusion of patterns other than speech or music. Science 164, 586-587.

Vaughan, H. G., Jr., and Ritter, W. (1970). The sources of auditory evoked responses recorded from the human scalp. Electroencephalography and Clinical Neurophysiology 28, 360-367.

Wechsler, D. (1974). Wechsler Intelligence Scale for Children - Revised: Manual (New York, Psychological Corporation. [Finnish translation, Psykologien Kustannus Oy, 1984]).

Wechsler, D. (1981). Wechsler adult intelligence scale - Revised: Manual. (New York, Psychological Corporation. [Finnish translation, Psykologien Kustannus Oy, 1992]).

Wechsler, D. (1987). Wechsler memory scale - revised: Manual. (New York, Psychological Corporation. [Finnish translation, Psykologien Kustannus Oy, 1997]).

Vellutino, F. R., Fletcher, J. M., Snowling, M. J., and Scanlon, D. M. (2004). Specific reading disability (dyslexia): what have we learned in the past four decades? Journal of Child Psychology and Psychiatry, and allied disciplines 45, 2-40.

Verhaart, W. J. (1950). Fiber analysis of the basal ganglia. The Journal of Comparative Neurology 93, 425-440.

Werker, J. F., and Tees, R. C. (1984). Cross-language speech perception: evidence for perceptual reorganization during the first year of life. Infant Behavior & Development 7, 49-63.

Werker, J. F., and Tees, R. C. (1999). Influences on infant speech processing: toward a new synthesis. Annu Rev Psychol 50, 509-535.

Wernicke, C. (1874). Der aphasische symptomencomplex. (Breslau, Poland, M.Cohn and Weigert.).

Wessinger, C. M., VanMeter, J., Tian, B., Van Lare, J., Pekar, J., and Rauschecker, J. P. (2001). Hierarchical organization of the human auditory cortex revealed by functional magnetic resonance imaging. Journal of Cognitive Neuroscience 13, 1-7.

Wever, E. G. (1949). Theory of Hearing (New York, Wiley).

Wiesel, T. N. (1982). Postnatal development of the visual cortex and the influence of environment. Nature 299, 583-591.

Wightman, F., Allen, P., Dolan, T., Kistler, D., and Jamieson, D. (1989). Temporal resolution in children. Child Development 60, 611-624.

Vigneau, M., Beaucousin, V., Herve, P. Y., Duffau, H., Crivello, F., Houde, O., Mazoyer, B., and Tzourio-Mazoyer, N. (2006). Meta-analyzing left hemisphere language areas: phonology, semantics, and sentence processing. Neuroimage 30, 1414-1432.

Vihla, M., Lounasmaa, O. V., and Salmelin, R. (2000). Cortical processing of change detection: dissociation between natural vowels and two-frequency complex tones. Proceedings of the National Academy of Sciences of the United States of America 97, 10590-10594.

Vihla, M., and Salmelin, R. (2003). Hemispheric balance in processing attended and non-attended vowels and complex tones. Brain Research. Cognitive Brain Research 16, 167-173.

Wimmer, H., Landerl, K., Linortner, R., and Hummer, P. (1991). The relationship of phonemic awareness to reading acquisition: more consequence than precondition but still important. Cognition 40, 219-249.

Wolf, M. (1986). Rapid alternating stimulus naming in the developmental dyslexias. Brain and Language 27, 360-379.

Wolf, M., and Obregon, M. (1992). Early naming deficits, developmental dyslexia, and a specific deficit hypothesis. Brain and Language 42, 219-247.

von Bekesy, G. (1960). Experiments in Hearing (New York, McGraw-Hill).

von Economo, C., and Koskinas, G. N. (1925). Die Cytoarchitektonic der Hirnrinde des Erwachsenen Menschen (Berlin, Springer-Verlag).

Vouloumanos, A., Kiehl, K. A., Werker, J. F., and Liddle, P. F. (2001). Detection of sounds in the auditory stream: event-related fMRI evidence for differential activation to speech and nonspeech. Journal of Cognitive Neuroscience 13, 994-1005.

Wunderlich, J. L., Cone-Wesson, B. K., and Shepherd, R. (2006). Maturation of the cortical auditory evoked potential in infants and young children. Hearing Research 212, 185-202.

Yakovlev, P. I., and Lecours, A. R. (1967). The myelogenetic cycles of regional maturation of the brain. In Regional Development of the Brain in Early Life, A. Minkowski, ed. (Oxford, Blackwell Scientific).

Yao, H., and Dan, Y. (2005). Synaptic learning rules, cortical circuits, and visual function. Neuroscientist 11, 206-216.

Yip, M. J. (2006). The search for phonology in other species. Trends in Cognitive Sciences 10, 442-446.

Zatorre, R. J., and Belin, P. (2001). Spectral and temporal processing in human auditory cortex. Cerebral Cortex 11, 946-953.

Zatorre, R. J., Bouffard, M., and Belin, P. (2004). Sensitivity to auditory object features in human temporal neocortex. The Journal of Neuroscience 24, 3637-3642.

Zatorre, R. J., Evans, A. C., Meyer, E., and Gjedde, A. (1992). Lateralization of phonetic and pitch discrimination in speech processing. Science 256, 846-849.

Zimmerman, J. E., Theine, P., and Harding, J. T. (1970). Design and operation of stable rf-biased superconducting point-contact quantum devices, and a note on the properties of perfectly clean metal contacts. Journal of Applied Physics 41, 1572-1580.