

Web: nfsi-99.brain.hr

BOOK OF ABSTRACTS

2nd International Symposium on

N	ONINVASIVE
F	UNCTIONAL
S	OURCE
I	MAGING

within the Human Brain and Heart

September 3-7, 1999, Zagreb, Croatia

Editor: Selma Supek

**2nd International Symposium on Noninvasive Functional Source Imaging
within the Human Brain and Heart, Zagreb, Croatia, September 3-7, 1999**

Organizers

**Department of Physics, Faculty of Science, University of Zagreb
Croatian Institute for Brain Research, Faculty of Medicine, University of Zagreb**

Editor

Selma Supek

Publisher

Croatian Biophysical Society

Print

Grafija d.o.o., Zagreb

ISBN 853-97885-0-1

Copyright © 1999 Croatian Biophysical Society

All rights reserved.

No part of this book may be reproduced, stored in a retrieval system, or transmitted in any form or by any means electronic mechanical photocopying, microfilming, recording, or otherwise, without written permission from the Publisher.

Abstracts in this volume are printed as submitted by the authors.

Printed in Croatia

Cover: Croatian National Theater, Zagreb

Organizer

Department of Physics, Faculty of Science, University of Zagreb
Croatian Institute for Brain Research, Faculty of Medicine, University of Zagreb

Organizing Committee

Selma Supek, Department of Physics, Faculty of Science, Symposium Chair
Bešenski Nada, Clinical Hospital Rebro, Radiology
Brnjas-Kraljević Jasminka, Department of Biophysics, Faculty of Medicine
Demarin Vida, Clinical Hospital "Sestre Milosrdnice", Neurology
Folnegović-Šmalc Vera, Psychiatric Hospital Vrapče, Faculty of Medicine
Goldner Vladimir, Clinical Hospital Rebro, Cardiology
Išgum Velimir, Clinical Hospital Rebro, Neurophysiology
Jernej Branimir, Ruder Bošković Institute
Judaš Miloš, Faculty of Medicine, Anatomy
Kurjak Asim, General Hospital Sveti Duh, Obstetrics and Gynecology
Lončarić Sven, Faculty of Electrical Engineering and Computing
Magjarević Ratko, Faculty of Electrical Engineering and Computing
Miklić Pavle, Clinical Hospital Rebro, Neurosurgery
Radoš Marko, Clinical Hospital Rebro, Radiology
Šantić Ante, Faculty of Electrical Engineering and Computing
Spaventi Radan, Pliva - Research Institute

Supported by

Ministry of Health, Croatia
University of Zagreb
Croatian Biophysical Society
Croatian Physical Society
Croatian Medical and Biological Engineering Society
Croatian Society of Radiology
Croatian Society of Neurology
Croatian Society of Psychiatry
Croatian Psychological Association
Croatian Society of Cardiology

Scientific Program Committee

Aine Cheryl, USA
Doessel Olaf, Germany
Halgren Eric, USA
Johnston Peter, Australia
Kostović Ivica, Croatia
Nenonen Jukka, Finland
Nowak Hannes, Germany
Peters Maria, The Netherlands
Pfurtscheller Gert, Austria
Posse Stefan, Germany
Romani GianLuca, Italy
Salanius Stephan, Finland
Sekihara Kensuke, Japan
Sippens Arne, The Netherlands, USA
Supek Selma, Croatia
Tesche Claudia, Finland
Tilg Bernhard, Austria, USA
Van Leeuwen Peter, Germany
Van Oosterom Adriaan, The Netherlands
Vieth Juergen, Germany
Wach Paul, Austria

The Organizers of NFSI-99 gratefully acknowledge support from the following organizations:

Biomagnetic Technologies Inc.
Neuromag Ltd.
General Electric Medical Systems
Pliva d.d.
Nycomed
Croatia Airlines
Andrija Štampar School of Public Health
Croatian Institute for Brain Research
Department of Physics, Faculty of Science, University of Zagreb
Tourist Office Croatia
Tourist Office Zagreb
Zagrebački električni tramvaj - ZET
Đakovačka vina d.d.
Sloboda d.d., Osijek

Exhibitors

Biomagnetic Technologies Inc.	www.biomagtech.com
Neuromag Ltd.	www.neuromag.com
MEGIS Software GmbH	www.BESA.com
Pharmakon – AG	
Silicon Biomedical Instruments BV	
Tamaris d.o.o.	

Symposium venue

Sheraton Zagreb Hotel

Kneza Borne 2

10000 Zagreb

Croatia

Phone: +385-1-455 3535

Fax: +385-1-455 3-35

Oral Presentations

All oral presentations will be held in the Sheraton Zagreb Hotel Grand Ballroom, Section B (Ground floor).

Slides should be handed into the Slide Center at least 1 hour before the presentation. Slide preview is available in the slide preview room – Paris Meetingroom (7), 1st floor.

Poster Presentations

Poster presentations will be held in the Sheraton Zagreb Hotel, Grand Ballroom foyer.

Poster boards are HORIZONTAL - **1.5 m long** and **1 m high**. Pushpins will be provided. Posters should be mounted Monday morning at 9:00 am and removed by the end of Poster session. During the Poster Session (Monday, September 6, 1999 at 16:15-18:30) at least one of the authors is expected to be available at the poster.

Exhibition and Technical demonstrations

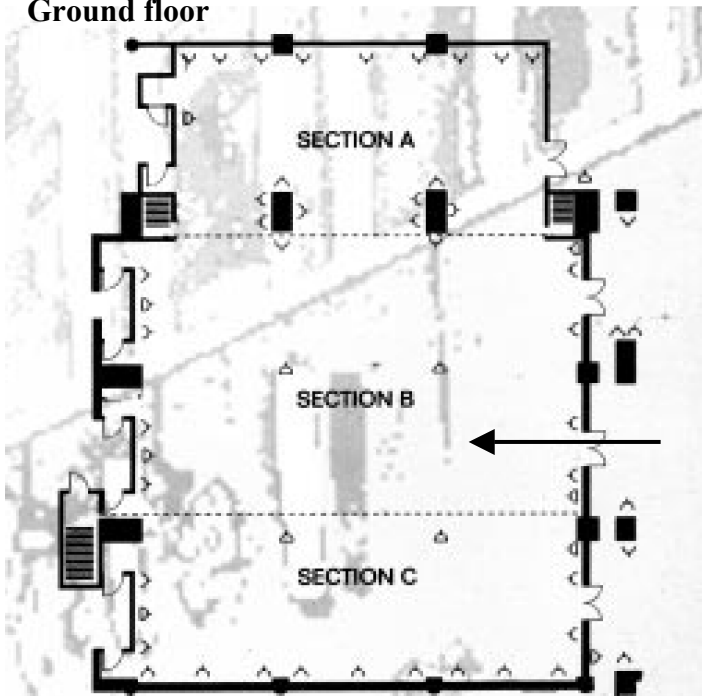
Exhibition will be held in the Sheraton Zagreb Hotel, Grand Ballroom foyer.

Technical demonstrations are scheduled for:

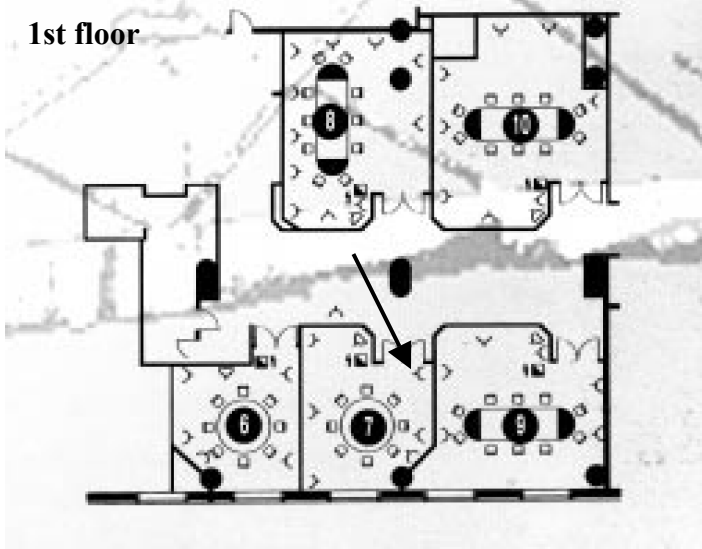
Friday, September 3, 1999, 16:45-18:30

Monday, September 6, 1999, 16:15-18:30

Ground floor



1st floor



Social Program

Friday, September 3, 1999

20:00 - 22:00 Cocktail and Welcome Reception

Sheraton Zagreb Hotel - Restaurant "Kralj Tomislav"

(included in the registration fee)

Saturday, September 4, 1999

19:00-21:00 Open House - Croatian Institute for Brain Research

Salata 12

(15 minutes walk from the Sheraton Zagreb Hotel; maps will be available)

Sunday, September 5, 1999

8:00 - 20:00 Whole-day excursion to the National Park of Plitvice Lakes

Departure from the Sheraton Zagreb Hotel at 8:00 am. Arrival to Plitvice around 10:30 - refreshment. Guided tour of the lakes, including a boat and panoramic train rides (3-4 hours). Lunch at the restaurant Licka kuca (meat - veal, fish - trout, and vegetarian menus). Departure around 17:30.

(included in the registration fee)

Monday, September 6, 1999

20:00 - Symposium Dinner

(buffet, detailed menu will be available at the registration desk, Croatian specialties)

Sheraton Zagreb Hotel, Restaurant "Kralj Tomislav"

Price: 26.00 USD

NFSI-99 PROGRAM

Thursday, September 2, 1999.

16:00-21:00 *Registration*

Friday, September 3, 1999.

08:00-09:30 *Registration*

09:30-10:00 Opening Session

INVITED TUTORIAL: MEG

Chair: Supek S.

10:00-10:45 A - 1 MEG: Principles, methods, and applications
Del Gratta C., and Romani G.L.
*Institute of Advanced Biomedical Technologies, and Department of Clinical
Sciences and Biomedical Imaging, University "G. D'Annunzio", Chieti, Italy*

10:45-11:00 Coffee Break

MEG - EMPIRICAL STUDIES

Chairmen: Halgren E. and Aine C.

11:00-11:30 A - 2 Basic Human Visual Studies in MEG: Past and Present
with Improved Automated Analysis
Aine, C.J.^{1,2}, Stephen, J.^{1,2}, Huang, M.^{1,2}, Christner, R.¹, Supek, S.^{3,4}
*¹Center for Functional Brain Imaging, VA Medical Center, Albuquerque, NM
87108 USA; ²Dept. of Radiology, University of New Mexico, Albuquerque,
NM 87131 USA; ³Department of Physics, Faculty of Science, Bijenicka cesta
32, 10000 Zagreb, Croatia; ⁴Croatian Institute for Brain Research, Salata
12, 10000 Zagreb, Croatia*

11:30-12:00 A - 3 MEG Study of Hippocampal Theta During a Working
Memory Task
Teschke, C.D.¹, Karhu, J.^{1,2}
*1Helsinki University of Technology, Espoo, Finland;
2Kuopio University Hospital, Kuopio, Finland*

12:00-12:15 A - 4 Estimating Neural Source of High-Frequency Magnetic
Oscillation Evoked by Posterior Tibial Nerve Stimulation Using
Time-Frequency MEG-MUSIC Algorithm
Sakuma K.¹, Sekihara K.², Hashimoto I.^{1,3}
*¹National Institute for Physiological Sciences, Okazaki, Japan; ²JST Mind
Articulation Project, Tokyo, Japan; ³Department of Psychophysiology, Tokyo
Institute of Psychiatry, Tokyo, Japan*

12:15-14:00 Lunch

**INVITED TUTORIAL: MEG /EEG, MCG/ECG MODELING
BIOELECTROMAGNETIC FORWARD AND INVERSE PROBLEMS**

Chairmen: Wach P. and Van Leeuwen P.

- 14:00-14:45 A - 5 Modeling aspects of bioelectric source imaging
Van Oosterom A.
Laboratory of Medical Physics & Biophysics, University of Nijmegen,
- 14:45-15:15 A - 6 On the effective passive conductivity of human tissues
Peters M.J., van Burik M.J., Stinstra J.G.
*Low Temperature Division, Faculty of Applied Physics, University of Twente,
P.O.Box 217, 7500 AE Enschede, The Netherlands*
- 15:15-15:30 A - 7 On Realistic a priori informed spatial basis functions in
minimum norm solutions.
C. Phillips^{1,2,3}, M.D. Rugg², K.J. Friston¹
*¹Wellcome Department of Cognitive Neurology, Institute of Neurology,
London, UK; ²Institute of Cognitive Neuroscience, UCL, London, UK
³Cyclotron Research Centre, University of Liege, Belgium*
- 15:30-15:45 Coffee Break

MEG/MCG MODELING STUDIES

Chairmen: Sekihara K: and Tilg B.

- 15:45-16:00 A - 8 Secondary Sources in the Skull
Van Burik M.J., Peters M.J.
*Low Temperature Department, Faculty of Applied Physics, University of
Twente, P.O. Box 217, 7500 AE, Enschede, The Netherlands*
- 16:00-16:15 A - 9 The Electrically Silent Cardiac Magnetic Field
¹Fischer G., ¹Tilg B., ¹Modre R., ²Fetzer J., ²Rucker W., ³Huiskamp G.,
¹Wach P.
*¹Institute of Biomedical Engineering, Technical University Graz, Graz,
Austria; ²Institute for Theory in Electrical Engineering, University Stuttgart ,
Stuttgart, Germany; ³Department of Clinical Neurophysiology, Utrecht
University Hospital, Utrecht, Netherlands*
- 16:15-16:30 A - 10 A Linearized Iterative Algorithm for Myocardial
Activation Time Imaging
Modre R.¹, Tilg B.^{1,2}, Fischer G.¹, Wach P.¹
*¹Institute of Biomedical Engineering, Technical University Graz, Graz,
Austria; ²Cardiac Electrophysiology Department, University of California
San Francisco, San Francisco, California, USA*

- 16:30-16:45 A - 11 Influence of randomly displaced BSPM leads and measurement noise on the identification of ventricular pre-excitation sites.
Jazbinšek V., Hren R.
Institute of Mathematics, Physics and Mechanics, University of Ljubljana, Slovenia
- 16:45-18:30 Technical Demonstrations
- 20:00-22:00 Cocktail and Welcome Reception
(Sheraton Zagreb Hotel, Restaurant "King Tomislav")

Saturday, September 4, 1999.

INVITED TUTORIAL AND REVIEW TALK: fMRI

Chair: Halgren E.

- 09:00-09:45 A - 12 Tutorial Introduction to Functional MRI (fMRI)
Savoy R.L.
The MGH-NMR Center
Building 149, 13th Street; Charlestown, MA 02129; USA
And The Rowland Institute for Science
100 Edwin H. Land Boulevard; Cambridge, MA 02142; USA
- 09:45-10:30 A - 13 A Review of fMRI Technological Developments
Jia-Hong Gao
Research Imaging Center
University of Texas Health Science Center, San Antonio, TX, USA
- 10:30-10:45 Coffee Break

fMRI - EMPIRICAL STUDIES

Chairmen: Vieth J. and Romani G.-L.

- 10:45-11:15 A - 14 Spatiotemporal Patterns of Human Brain Activation During the Processing of Words and Faces: Anatomically-Constrained and fMRI Biased Distributed Inverse Solutions for Whole-Head MEG
Halgren, E.^{1,3}, Marinkovic, K.¹, Dhond, P.¹, Fischl, B.², Dale, A.²
¹*Radiology, University of Utah, Salt Lake City, USA*, ²*MGH-NMR, Harvard Medical School, USA*, ³*INSERM E 9926, Marseilles, France*
- 11:15-11:30 A - 15 Selective BOLD Activation of the Receptive Speech Area Using a Novel Passive Listening Paradigm
Lowe, M.J., Lurito, J.T., Mathews, V.P., Phillips, M.D., and Dzemidzic, M.
Department of Radiology, Indiana University School of Medicine, Indianapolis, IN, USA
- 11:30-11:45 A - 16 On the organisation of the human somatosensory cortices: a fMRI study
Della Penna S.¹, Bonomo L.^{1,2}, Del Gratta C.^{1,2}, Ferretti A.¹, Franciotti R.¹, Rossini P.M.³, Tartaro A.^{1,2}, Torquati K.¹ and Romani G.L.^{1,2}

1-Institute of Advanced Biomedical Technologies, University of Chieti, Chieti, Italy; 2-Department of Clinical Sciences and Biomedical Imaging, University of Chieti, Chieti, Italy; 3-AFaR-IRCCS “San Giovanni di Dio”, Istituto Sacro Cuore di Gesù, Brescia, Italia.

- 11:45-12:00 A - 17 Single event functional MRI of supplementary motor and primary motor cortical areas. 30
^{1,4}Cunnington R, ²Windischberger C, ¹Erdler M, ¹Deecke L, and ^{2,3}Moser E.
¹Department of Neurology; ²NMR Unit, Institute for Medical Physics;
³Centre for Magnetic Resonance Imaging, University of Vienna, Austria; and
⁴Department of Psychology, Monash University, Clayton, Australia.
- 12:00-12:15 A - 18 Quantification of Supplementary Motor Area Activation with movements of different practice levels using Functional Magnetic Resonance Imaging at 3T
Erdler M. ¹, Windischberger C. ², Cunningham R. ¹, Edward V. ¹, Streibl B. ¹, Gartus A. ¹, Moser E. ^{2,3}, Deecke L. ¹, Beisteiner R. ¹
¹Department of Neurology; ²NMR - Group –Institute for Medical Physics;
³MR unit, General Hospital and University of Vienna, Vienna Austria
- 12:15-12:30 A - 19 Functional Discrimination of Thalamic Nuclei Using BOLD Contrast fMRI at 1.5 T
Dzemidzic, M., Lowe, M.J., Lurito, J.T., Mathews, V.P., and Phillips, M.D.
Department of Radiology, Indiana University School of Medicine, Indianapolis, IN, USA
- 12:30-14:00 Lunch
- 14:00-16:00 **MODELING WORKSHOP**
Workshop organizer: Scherg Michael
Workshop participants: Scherg M., Sekihara K., Edlinger G., Uutela K.
- A - 20 Combined functional imaging using MEG, EEG and fMRI
Scherg M. ¹, Goebel R. ³, Stippich Ch. ², D. Weckesser¹, H. Bornfleth¹, N. Ille¹, K. Drüen¹, S. Linek¹, P. Berg⁴
Departments of Neurology¹ and Neuroradiology², University Hospital Heidelberg, Heidelberg, Germany; Max Planck Institute for Brain Research³, Frankfurt, Germany; Department of Psychology⁴, Unversity of Konstanz, Konstanz, Germany
- A - 21 Application of Eigenspace Beamformer to Virtual Depth-Electrode Measurement Using MEG
Sekihara K. ¹, Poeppel D. ², Miyashita Y. ¹
¹JST Mind Articulation Project, Tokyo, Japan; ²University of Maryland, College Park, USA
- A - 22 Cortical oscillatory activity assessed by combined EEG and MEG recordings and High-Resolution ERD methods
Edlinger¹ G., Bastiaansen² M., Brunia² C., Neuper¹ C., Pfurtscheller¹ G.

¹*Department of Medical Informatics, Institute for Biomedical Engineering,
and Ludwig Boltzmann Institute for Medical Informatics and
Neuroinformatics, Graz University of Technology, Austria*
²*Psychonomics section, Tilburg University, Tilburg, Netherlands*

A - 23 Minimum l1-norm estimates in the analysis of MEG data
Uutela, K., Hämmäläinen, M.
Brain Research Unit, Helsinki University of Technology, Finland

16:00-16:15 Coffee Break

16:15-18:00 **ROUND-TABLE DISCUSSION**
Chair: Romani Gian Luca

19:00-21:00 OPEN HOUSE
Croatian Institute for Brain Research, Šalata 12

Sunday, September 5, 1999.

08:00-20:00 Whole day excursion to the National Park Plitvice Lakes

Monday, September 6, 1999.

MCG - CLINICAL STUDIES

Chairmen: van Oosterom A. and Nowak H.

09:00-09:30 A - 24 Cardiomagnetic Source Imaging Studies with Focal and
Distributed Source Models
Nenonen J.^{1,2}, Pesola K.^{1,2}, Lötjönen J.^{1,2}, Lauerma K.⁴, Hänninen,
H.^{2,3}, Korhonen, P.^{2,3}, Mäkiärvä, M.^{2,3}, Fenici, R.³, and Katila, T.^{1,2}
¹*Laboratory of Biomedical Engineering, Helsinki University of Technology,
02015 HUT, Espoo;* ²*Medical Engineering Centre, BioMag Laboratory,
3**Division of Cardiology, and* ⁴*Department of Radiology, Helsinki University
Central Hospital, 00290 Helsinki, Finland;* ⁵*Clinical Physiology -
Biomagnetism Center, Catholic University of Rome, Italy*

09:30-09:45 A - 25 Spatial and Temporal Changes during the QT-Interval in
the Magnetic Field of Patients with Coronary Artery Disease
Van Leeuwen P.¹, Hailer B.², Lange S.³, Donker D.⁴, Grönemeyer D.³
¹*Dept. of Biomagnetism, EFMT, Bochum, Germany;* ²*Department of
Internal Medicine, Philippsstift, Essen, Germany;* ³*Institute for
Microtherapy, University of Witten/Herdecke, Bochum, Germany;* ⁴*Dept. of
Cardiology, University Hospital Maastricht, Maastricht, Netherlands*

09:45-10:00 A - 26 Current density estimation on the left ventricular
epicardium: A potential method for ischemia localization
Pesola K.^{1,2}, Hänninen H.^{2,3}, Lauerma K.⁴, Lötjönen J.¹, Mäkiärvä M.^{2,3},
Nenonen J.^{1,2}, Takala P.^{1,2}, Voipio-Pulkki L.-M.⁵, Toivonen L.^{2,3}, Katila T.^{1,2}
¹*Laboratory of Biomedical Engineering, Helsinki University of Technology,
Espoo, Finland;* ²*Medical Engineering Centre, BioMag Laboratory,* ³*Division
of Cardiology,* ⁴*Division of Radiology, Helsinki University Central Hospital*

(HUCH), Helsinki, Finland; ⁵Turku University Central Hospital, Turku, Finland

- 10:00-10:15 A - 27 Validation of Noninvasive Functional Cardiac Electrical Source Imaging in a 43-year Old Male Patient
Tilg B.^{1,2}, Modre R.¹, Fischer G.¹, SippensGroenewegen A.², Mlynash M.², Roithinger F.X.², Reddy G.³, Roberts T.³, Wach P.¹, Lesh M.D.², Steiner ²
¹Institute of Biomedical Engineering, Technical University Graz, Graz, Austria; ²Section of Cardiac Electrophysiology, Department of Medicine, ³Department of Radiology, University of California San Francisco, San Francisco, California, USA
- 10:15-10:30 A - 28 Magnetocardiography under Clinical Conditions
Erné, S.N.¹, Kammrath, H.G.¹, Ziolkowski, M.², Tenner, U.¹, Müller, H.-P. ¹
¹Division for Technical Bioelectromagnetism, Central Institute for Biomedical Engineering, Ulm University, D – 89069 Ulm, Germany
²Szczecin Technical University, Al. Piastow 19, PL - 70310, Szczecin, Poland
- 10:30-10:45 A - 29 Topographic Presentation of the Dipolar Content of Cardiac Electric Field
Bacharova L.I, Chorvat D.I, Mateasik A.I, Titomir L.I.2
¹International Laser Center, Bratislava, Slovakia
²Institute of Problems of Information Transmission RAS, Moscow, Russia
- 10:45-11:00 Coffee Break

MEG/EEG - BASIC AND CLINICAL STUDIES

Chairmen: Tesche C. and Romani G. L.

- 11:00-11:30 A - 30 The Clinical Use of MEG Activity Associated with Brain Lesions
Vieth J.B., Kober H., Ganslandt O.¹⁾, Kamada K.
Dept. of experimental Neuropsychiatry and ¹⁾Neurosurgery, University of Erlangen-Nuernberg, Germany
- 11:30-12:00 A - 31 Applications of MEG to the Mapping of the Language Cortex
¹Papanicolaou, A.C., ¹Simos, P., ¹Breier, J.I., ¹Zouridakis, G., ¹Constantinou, J., ²Wheless, J.W., ²Maggio, W.W.
The University of Texas Health Science Center, Departments of Neurosurgery¹ and Neurology², Houston, Texas U.S.A.
- 12:00-12:15 A - 32 CFunctional Mapping of Speech Evoked Brain Activity by Magnetoencephalography and its Clinical Application
M. Möller¹, H. Kober², O. Ganslandt¹, Ch. Nimsky¹, R. Fahlbusch¹
¹Department of Neurosurgery, University of Erlangen-Nürnberg, Erlangen, Germany; ²Biomagnetism Group, University of Erlangen-Nürnberg, Erlangen, Germany

- 12:15-12:30 A - 33 Scalp current density(SCD) mapping of cerebral activity during object and space selection in humans
^{1,2}Zani A., ¹Avella C., ²Lilli S., ²Proverbio A.M.
¹*Cognitive Electrophysiology Lab, Istituto di Psicologia del CNR, Roma, Italy*
²*Cognitive Electrophysiology Lab, Department of Psychology, University of Trieste, Trieste, Italy*
- 12:30-12:45 A - 34 Spatio-temporal mapping of electrocortical activity during selective processing of colour and shape in humans
¹Proverbio A.M., ¹Burco F., ^{1,2}Zani A.
¹*Cognitive Electrophysiology Lab, Department of Psychology, Univ. of Trieste, 34123 Trieste, Italy;* ²*Cognitive Electrophysiology Lab, Istituto di Psicologia, CNR, Viale Marx 15, 00137 Rome, Ital*
- 12:45-14:00 Lunch
- 14:00-16:00 **CLINICAL APPLICATIONS WORKSHOP**
Workshop organizer: Papanicolaou Andy
Workshop participants: Aine C., Bowyer S., Ilmoniemi R., Kemna L., Papanicolaou A., Sterr A.
- A - 35 Are functional imaging procedures clinically useful?
Papanicolaou, A. C.
The University of Texas Medical School, Houston, USA
- A - 36 New Bioelectromagnetic Imaging Methods for Clinical Use
Ilmoniemi, Risto J. ¹ and Aronen, Hannu J. ^{1,2}
¹*BioMag Laboratory, Medical Engineering Centre, Helsinki University Central Hospital, P.O. Box 508, FIN-00029 HYKS, Finland*
E-mail: rji@biomag.helsinki.fi; ²*Department of Radiology, Helsinki University Central Hospital, P.O. Box 380, FIN-00029 HYKS, Finland; E-mail: hannu.aronen@huch.fi*
- A - 37 Clinical DC applications using MEG: Moving the curtains aside
Bowyer S.M.
Henry Ford Hospital, Detroit, MI
- A - 38 Functional Magnetic Resonance Imaging in Real Time on a Clinical Whole Body Scanner
S. Posse
Institute of Medicine, Research Center Jülich GmbH, D-52425 Jülich, Germany
- A - 39 Plasticity of Cortical Representations in Humans: Principles and Clinical Implications
Sterr, A.
Department of Psychology, University of Konstanz; Konstanz; Germany
Work was supported by the Deutsche Forschungsgemeinschaft

16:00-16:15 Coffee Break

16:15-18:30 **POSTER SESSION (MEG, MCG, ERP, fMRI)**
Chairmen: Peters M. and Nowak H.

A - 40 A Multipurpose 67 Channel Biomagnetometer
Van Leeuwen P.¹, Hoormann J.², Hailer B.³, Mackert B.M.⁴, Stroink G.⁵
¹ Dept. of Biomagnetism, EFMT, Bochum, Germany; ² Institut für Arbeitsphysiologie, Dortmund, Germany; ³ Department of Internal Medicine, Philippsstift, Essen, Germany; ⁴ Neurophysics Group, Dept. of Neurology, Freie Universität Berlin, Germany; ⁵ Dept. of Physics, Dalhousie University, Halifax, Canada

A - 41 Magnetic Source Imaging Based on
Magnetocardiographic Recordings
Nowak H.^{1,2}, Leder U.³, Pohl P.³, Hauelsen J.²
¹JENASENSORIC, Jena, Germany; ²Biomagnetic Centre, University, Jena, Germany; ³Clinic of Internal Medicine, University, Jena, Germany

A - 42 Spatial mapping of beta oscillations in central EEG after
voluntary movement of different limbs
Neuper, C., Edlinger, G., Pfurtscheller, G.
Department of Medical Informatics, Institute for Biomedical Engineering,
and Ludwig Boltzmann Institute for Medical Informatics and
Neuroinformatics, Graz University of Technology, Austria

A - 43 ERP mapping of brain activation during phonological
processing
¹Proverbio A.M., ¹Lilli S., ², ¹Zani A.
¹Cognitive Electrophysiology Lab, Department of Psychology, University of
Trieste, Trieste, Italy; ²Cognitive Electrophysiology Lab, Istituto
di Psicologia del CNR, Roma, Italy

A - 44 Anatomically-Constrained MEG Activity to Faces with
Normal or Distorted Feature Arrangement and Facial Outline
Marinkovic K.¹, Dale, A.², Halgren, E.^{1,3}
¹Radiology, University of Utah, Salt Lake City, USA, ²MGH-NMR, Harvard
Medical School, USA, ³INSERM E 9926, Marseilles, France

A - 45 Dynamic Functional Imaging by Combined MEG, EEG
and fMRI in a Case of Cortical Myoclonus
Bornfleth H.¹, Scherg M.¹, Meinck H.M.¹, Stippich C.², Goebel R.³,
Weckesser D.¹, Drüen K.¹, Tauberschmidt E.¹, Berg P.⁴
Departments of Neurology¹ and Neuroradiology², University Hospital
Heidelberg, Heidelberg, Germany; Max Planck Institute for Brain Research³,
Frankfurt, Germany; Department of Psychology⁴, University of Konstanz,
Konstanz, Germany

A - 46 Signal to Noise Improvement in fMRI Analysis
Erné S.N.¹, Müller H.-P.¹, Kammrath H.G.¹, Tomczak R.², Wunderlich A.²

¹Central Institute for Biomedical Engineering, Ulm University, D-89069 Ulm, Germany ²Department for Diagnostic Radiology, University Clinic Ulm, D-89069 Ulm, Germany

A - 47 Influence of stimulus sequence in blocked-designed paradigms on fMRI localization results
Lanzenberger R.¹, Streibl B.¹, Cunnington R.¹, Windischberger C.², Edward V.¹, Erdler M.¹, Gartus A.¹, Moser E.^{2,3}, Beisteiner R.¹
¹ Department of Neurology, ² NRM-Group – Institute for Medical Physics;
³ MR-Unit General Hospital and University of Vienna, Vienna, Austria

A - 48 Physical Phantoms for Biomagnetic and Bioelectric Measurements
Tenner U.¹, Ern  S.N.¹, Hauelsen J.², Nowak H.², Brauer H.³
¹University of Ulm, Ulm, Germany; ²Friedrich-Schiller-University, Jena, Germany; ³Technical University of Ilmenau, Ilmenau, Germany

A - 49 Voxel conductivity changes in a FEM head model for MEG and EEG forward computations
Jens Hauelsen ¹, Ceon Ramon ², Hartmut Brauer ³, Hannes Nowak ¹
¹Biomagnetisches Zentrum, Friedrich-Schiller-Universit t, Jena, Germany
²Center for Bioengineering, University of Washington, Seattle, U.S.A.
³Inst fur Allgem. Und Theoret. Elektrotechnik, TU Ilmaneu, Germany

A - 50 Localization of tactile, electrical and pain evoked fields: A comparison using whole head MEG
Sterr, A., Kreyer, I. and Elbert, T.
Department of Psychology, University of Konstanz; Konstanz; Germany

A - 51 Extended Current Source Models for Biomagnetic Phantom Studies 64
Brauer, H.¹, Ziolkowski, M.², Hauelsen, J.³, Tenner, U.⁴, Nowak, H.³
¹ Technical University of Ilmenau, Ilmenau, Germany; ² Technical University of Szczecin, Szczecin, Poland; ³ Friedrich-Schiller-University, Jena, Germany; ⁴ University of Ulm, Ulm, Germany

20:00

Symposium Dinner
Sheraton Zagreb Hotel, Restaurant "King Tomislav"

Tuesday, September 7, 1999.

**INVITED TUTORIAL: TMS
TMS AND OTHER STUDIES**

Chairmen: Halgren E. and Ilmoniemi R.

- 09:00-09:45 A - 52 Transcranial Magnetic Stimulation – New Modality in Brain Mapping
Risto J. Ilmoniemi
Bio Mag Laboratory, Medical engineering Centre, Helsinki University Central Hospital
- 09:45-10:15 A - 53 Changes of Regional Cerebral Blood Flow Caused by Transcranial Magnetic Stimulation of the Visual Cortex
L.J. Kemna, FM. Mottaghy, S. Posse
Institute of Medicine, Research Center, Juelich, Germany; Department for Nuclear Medicine, University of Duesseldorf, Germany
- 10:15-10:30 A - 54 TMS Induced Changes in Early Somatosensory Evoked Responses
J. Karhu ^{1,2}, J. Rouhonen ¹, J. Virtanen ¹, M. Ollikainen ¹, R. Varonen ¹, R. Ilmoniemi ¹
¹Biomag Laboratory, Medical Engineering Centre, Helsinki University Central Hospital; ² Department of Clinical Neurophysiology, Kuopio University Hospital, Finland
- 10:30-11:00 A - 55 Morphological and Haemodynamic Investigations of the Fetal Brain
Kurjak A., Kos M.
Department of Obstetrics and Gynecology, Medical School University of Zagreb, Sveti duh Hospital, Zagreb, Croatia
- 11:00 Closing Remarks

CONTENTS

INVITED TUTORIAL: MEG

- A – 1 MEG: Principles, methods, and applications ----- 23
Del Gratta C., and Romani G.L.

MEG - EMPIRICAL STUDIES

- A – 2 Basic Human Visual Studies in MEG: Past and Present
with Improved Automated Analysis----- 24
Aine, C.J.^{1,2}, Stephen, J.^{1,2}, Huang, M.^{1,2}, Christner, R.¹, Supek, S.^{3,4}
- A – 3 MEG Study of Hippocampal Theta During a Working Memory Task ----- 25
Tesche, C.D.¹, Karhu, J.^{1,2}
- A – 4 Estimating Neural Source of High-Frequency Magnetic Oscillation
Evoked by Posterior Tibial Nerve Stimulation Using
Time-Frequency MEG-MUSIC Algorithm----- 26
Sakuma K.¹, Sekihara K.², Hashimoto I.^{1,3}

INVITED TUTORIAL: MEG /EEG, MCG/ECG MODELING BIOELECTROMAGNETIC FORWARD AND INVERSE PROBLEMS

- A – 5 Modeling aspects of bioelectric source imaging ----- 27
Van Oosterom A.
- A – 6 On the effective passive conductivity of human tissues ----- 28
Peters M.J., van Burik M.J., Stinstra J.G.
- A – 7 Realistic a priori informed spatial basis functions in
minimum norm solutions. ----- 29
C. Phillips^{1,2,3}, M.D. Rugg², K.J. Friston¹

MEG/MCG MODELING STUDIES

- A – 8 Secondary Sources in the Skull ----- 30
Van Burik M.J., Peters M.J.
- A – 9 The Electrically Silent Cardiac Magnetic Field----- 31
¹Fischer G., ¹Tilg B., ¹Modre R., ²Fetzer J., ²Rucker W., ³Huiskamp G., ¹Wach P.
- A – 10 A Linearized Iterative Algorithm for Myocardial Activation Time Imaging ----- 32
Modre R.¹, Tilg B.^{1,2}, Fischer G.¹, Wach P.¹

A – 11	Influence of randomly displaced BSPM leads and measurement noise on the identification of ventricular pre-excitation sites -----	33
	<i>Jazbinšek V., Hren R.</i>	

INVITED TUTORIAL AND REVIEW TALK: fMRI

A – 12	Tutorial Introduction to Functional MRI (fMRI) -----	34
	<i>Savoy R.L.</i>	
A – 13	A Review of fMRI Technological Developments -----	35
	<i>Jia-Hong Gao</i>	

fMRI - EMPIRICAL STUDIES

A – 14	Spatiotemporal Patterns of Human Brain Activation During the Processing of Words and Faces: Anatomically-Constrained and fMRI Biased Distributed Inverse Solutions for Whole-Head MEG -----	36
	<i>Halgren, E.^{1,3}, Marinkovic, K.¹, Dhond, P.¹, Fischl, B.², Dale, A.²</i>	
A – 15	Selective BOLD Activation of the Receptive Speech Area Using a Novel Passive Listening Paradigm -----	37
	<i>Lowe, M.J., Lurito, J.T., Mathews, V.P., Phillips, M.D., and Dziedzic, M.</i>	
A – 16	On the organisation of the human somatosensory cortices: a fMRI study -----	38
	<i>Della Penna S.¹, Bonomo L.^{1,2}, Del Gratta C.^{1,2}, Ferretti A.¹, Franciotti R.¹, Rossini P.M.³, Tartaro A.^{1,2}, Torquati K.¹ and Romani G.L.^{1,2}</i>	
A – 17	Single event functional MRI of supplementary motor and primary motor cortical areas. -----	39
	<i>^{1,4}Cunnington R, ²Windischberger C, ¹Erdler M, ¹Deecke L, and ^{2,3}Moser E.</i>	
A – 18	Quantification of Supplementary Motor Area Activation with movements of different practice levels using Functional Magnetic Resonance Imaging at 3T -----	40
	<i>Erdler M.¹, Windischberger C.², Cunnington R.¹, Edward V.¹, Streibl B.¹, Gartsch A.¹, Moser E.^{2,3}, Deecke L.¹, Beisteiner R.¹</i>	
A – 19	Functional Discrimination of Thalamic Nuclei Using BOLD Contrast fMRI at 1.5 T -----	41
	<i>Dziedzic, M., Lowe, M.J., Lurito, J.T., Mathews, V.P., and Phillips, M.D.</i>	

MODELING WORKSHOP

A – 20	Combined functional imaging using MEG, EEG and fMRI -----	42
	<i>Scherg M.¹, Goebel R.³, Stippich Ch.², D. Weckesser¹, H. Bornfleth¹, N. Ille¹, K. Drüen¹, S. Linek¹, P. Berg⁴</i>	

A – 21	Application of Eigenspace Beamformer to Virtual Depth-Electrode Measurement Using MEG-----	43
	<i>Sekihara K.¹, Poeppel D.², Miyashita Y.¹</i>	
A – 22	Cortical oscillatory activity assessed by combined EEG and MEG recordings and High-Resolution ERD methods -----	44
	<i>Edlinger¹ G., Bastiaansen² M., Brunia² C., Neuper¹ C., Pfurtscheller¹ G.</i>	
A – 23	Minimum l1-norm estimates in the analysis of MEG data -----	45
	<i>Uutela, K., Hämäläinen, M.</i>	

MCG - CLINICAL STUDIES

A – 24	Cardiomagnetic Source Imaging Studies with Focal and Distributed Source Models-----	46
	<i>Nenonen J.^{1,2}, Pesola K.^{1,2}, Lötjönen J.^{1,2}, Lauerma K.⁴, Hänninen, H.^{2,3}, Korhonen, P.^{2,3}, Mäkiärvä, M.^{2,3}, Fenici, R.⁵, and Katila, T.^{1,2}</i>	
A – 25	Spatial and Temporal Changes during the QT-Interval in the Magnetic Field of Patients with Coronary Artery Disease -----	47
	<i>Van Leeuwen P.¹, Hailer B.², Lange S.³, Donker D.⁴, Grönemeyer D.³</i>	
A – 26	Current density estimation on the left ventricular epicardium: A potential method for ischemia localization -----	48
	<i>Pesola K.^{1,2}, Hänninen H.^{2,3}, Lauerma K.⁴, Lötjönen J.¹, Mäkiärvä M.^{2,3}, Nenonen J.^{1,2}, Takala P.^{1,2}, Voipio-Pulkki L.-M.⁵, Toivonen L.^{2,3}, Katila T.^{1,2}</i>	
A – 27	Validation of Noninvasive Functional Cardiac Electrical Source Imaging in a 43-year Old Male Patient -----	49
	<i>Tilg B.^{1,2}, Modre R.¹, Fischer G.¹, SippensGroenewegen A.², Mlynash M.², Roithinger F.X.², Reddy G.³, Roberts T.³, Wach P.¹, Lesh M.D.², Steiner P.R.²</i>	
A – 28	Magnetocardiography under Clinical Conditions-----	50
	<i>Erné, S.N.¹, Kammrath, H.G.¹, Ziolkowski, M.², Tenner, U.¹, Müller, H.-P.¹</i>	
A – 29	Topographic Presentation of the Dipolar Content of Cardiac Electric Field-----	51
	<i>Bacharova L.1, Chorvat D.1, Mateasik A.1, Titomir L.I.2</i>	

MEG/EEG - BASIC AND CLINICAL STUDIES

A – 30	The Clinical Use of MEG Activity Associated with Brain Lesions-----	52
	<i>Vieth J.B., Kober H., Ganslandt O.¹⁾, Kamada K.</i>	
A – 31	Applications of MEG to the Mapping of the Language Cortex-----	53
	<i>Papanicolaou, A.C.,¹ Simos, P.,¹ Breier, J.I.,¹ Zouridakis, G.,¹ Constantinou, J.,² Wheless, J.W.,² Maggio, W.W.¹</i>	

A – 32	Functional Mapping of Speech Evoked Brain Activity by Magnetoencephalography and its Clinical Application -----	54
	<i>M. Möller¹, H. Kober², O. Ganslandt¹, Ch. Nimsky¹, R. Fahlbusch¹</i>	
A – 33	Scalp current density(SCD) mapping of cerebral activity during object and space selection in humans -----	55
	<i>1,2Zani A., 1Avella C., 2Lilli S., 2Proverbio A.M.</i>	
A – 34	Spatio-temporal mapping of electrocortical activity during selective processing of colour and shape in humans -----	56
	<i>1Proverbio A.M., 1Burco F., 1,2Zani A.</i>	

CLINICAL APPLICATIONS WORKSHOP

A – 35	Are functional imaging procedures clinically useful? -----	57
	<i>Papanicolaou, A. C.</i>	
A – 36	New Bioelectromagnetic Imaging Methods for Clinical Use -----	58
	<i>Ilmoniemi, Risto J.¹ and Aronen, Hannu J.^{1,2}</i>	
A – 37	Clinical DC applications using MEG: Moving the curtains aside -----	59
	<i>Bowyer S.M.</i>	
A – 38	Functional Magnetic Resonance Imaging in Real Time on a Clinical Whole Body Scanner -----	60
	<i>S. Posse</i>	
A – 39	Plasticity of Cortical Representations in Humans: Principles and Clinical Implications -----	61
	<i>Sterr, A.</i>	

POSTER SESSION (MEG, MCG, ERP, fMRI)

A – 40	A Multipurpose 67 Channel Biomagnetometer -----	62
	<i>Van Leeuwen P.¹, Hoormann J.², Hailer B.³, Mackert B.M.⁴, Stroink G.⁵</i>	
A – 41	Magnetic Source Imaging Based on Magnetocardiographic Recordings -----	63
	<i>Nowak H.^{1,2}, Leder U.³, Pohl P.³, Haueisen J.²</i>	
A – 42	Spatial mapping of beta oscillations in central EEG after voluntary movement of different limbs -----	64
	<i>Neuper, C., Edlinger, G., Pfurtscheller, G.</i>	
A – 43	ERP mapping of brain activation during phonological processing -----	65
	<i>1Proverbio A.M., 1Lilli S., 2, 1Zani A.</i>	

A – 44	Anatomically-Constrained MEG Activity to Faces with Normal or Distorted Feature Arrangement and Facial Outline -----	66
	<i>Marinkovic K.¹, Dale, A.², Halgren, E.^{1,3}</i>	
A – 45	Dynamic Functional Imaging by Combined MEG, EEG and fMRI in a Case of Cortical Myoclonus-----	67
	<i>Bornfleth H.¹, Scherg M.¹, Meinck H.M.¹, Stippich C.², Goebel R.³, Weckesser D.¹, Drüen K.¹, Tauberschmidt E.¹, Berg P.⁴</i>	
A – 46	Signal to Noise Improvement in fMRI Analysis-----	68
	<i>Erné S.N.¹, Müller H.-P.¹, Kammrath H.G.¹, Tomczak R.², Wunderlich A.²</i>	
A – 47	Influence of stimulus sequence in blocked-designed paradigms on fMRI localization results -----	69
	<i>Lanzenberger R.¹, Streibl B.¹, Cunningham R.¹, Windischberger C.², Edward V.¹, Erdler M.¹, Gartus A.¹, Moser E.^{2,3}, Beisteiner R.¹</i>	
A – 48	Physical Phantoms for Biomagnetic and Bioelectric Measurements-----	70
	<i>Tenner U.¹, Ern� S.N.¹, Haueisen J.², Nowak H.², Brauer H.³</i>	
A – 49	Voxel conductivity changes in aFEM head model for MEG and EEG forwards computations -----	71
	<i>Jens Haueisen ¹, Ceon Ramon ², Hartmut Brauer ³, Hannes Nowak ¹</i>	
A – 50	Localization of tactile, electrical and pain evoked fields: A comparison using whole head MEG-----	72
	<i>Sterr, A., Kreyer, I. and Elbert, T.</i>	
A – 51	Extended Current Source Models for Biomagnetic Phantom Studies -----	73
	<i>Brauer, H.¹, Ziolkowski, M.², Haueisen, J.³, Tenner, U.⁴, Nowak, H.³</i>	

INVITED TUTORIAL: TMS TMS AND OTHER STUDIES

A – 52	Transcranial Magnetic Stimulation – New Modality in Brain Mapping-----	74
	<i>Risto J. Ilmoniemi</i>	
A – 53	Changes of Regional Cerebral Blood Flow Caused by Transcranial Magnetic Stimulation of the Visual Cortex-----	75
	<i>L.J. Kemna, FM. Mottaghy, S. Posse</i>	
A – 54	TMS Induced Changes in Early Somatosensory Evoked Responses -----	76
	<i>J. Karhu ^{1,2}, J. Rouhonen ¹, J. Virtanen ¹, M. Ollikainen ¹, R. Varonen ¹, R. Ilmoniemi ¹</i>	
A – 55	Morphological and Haemodynamic Investigations of the Fetal Brain-----	77
	<i>Kurjak A., Kos M.</i>	

MEG: Principles, methods, and applications

Del Gratta C., and Romani G.L.

Institute of Advanced Biomedical Technologies, and Department of Clinical Sciences and Biomedical Imaging, University “G. D’Annunzio”, Chieti, Italy

MagnetoEncephaloGraphy (MEG) is proving to be an ideal means to investigate cerebral functions both in normal and pathological conditions. The technique can achieve accurate source localization on the basis of a relatively simple modeling. Furthermore, the method is non-invasive, and is reference-free, since the values of cerebral magnetic fields at several sites of the scalp are sampled with no need to refer them to any other specific value.

The quality of instrumentation nowadays available is definitively satisfactory, also for clinical use, and indeed, a clinical validation of the method is being carried out in many research areas. Systems covering the whole-head are available in several laboratories all over the world. These systems provide the possibility of a fast measurement of cerebral magnetic fields, often associated with that of scalp potentials, and the successive analysis of the data can be performed in a relatively short time period. The results of the analysis usually provide identification of an equivalent source (or more than one), accounting for the neural population elicited by the specific stimulation paradigm. Further integration of this source(s) with anatomical data obtained by means of MRI provides information on the functional organization of the cerebral cortex.

In this talk, some of the theoretical and experimental aspects of MEG will be described. The basics of magnetic field calculation and source estimation will be summarised, followed by an overview of the principles of MEG instrumentation. Finally, a review of some of the several applications of the method in basic and clinical research, that are being carried out in several institutions, in the areas that have mostly raised the interest of the clinicians, will be given.. An example of an integrated multimodal approach to a clinical case will be also illustrated with the aim at demonstrating the possibilities of the method when used in combination with other imaging diagnostic technologies.

Basic Human Visual Studies in MEG: Past and Present with Improved Automated Analysis

Aine, C.J.^{1,2}, Stephen, J.^{1,2}, Huang, M.^{1,2}, Christner, R.¹, Supek, S.^{3,4}

¹*Center for Functional Brain Imaging, VA Medical Center, Albuquerque, NM 87108 USA*

²*Dept. of Radiology, University of New Mexico, Albuquerque, NM 87131 USA*

³*Department of Physics, Faculty of Science, Bijenicka cesta 32, 10000 Zagreb, Croatia*

⁴*Croatian Institute for Brain Research, Salata 12, 10000 Zagreb, Croatia*

Modeling of human visual MEG data has been a challenge due to the existence of multiple sources and low signal-to-noise ratio, compared to other sensory responses. The use of traditional analysis procedures (i.e., manual selection of starting parameters) is both tedious and time-consuming. Our recent studies of the visual and somatosensory systems have benefited greatly from the development and testing of automated analysis procedures [1-2]. These procedures provide faster and easier analysis of the data and provide more assurance that the resultant models are the best models for the data.

Studies of visual cortex were conducted by selective and systematic manipulation of visual stimulus properties such as stimulus location, color, luminance, etc. [e.g., 3]. Stimulus durations were usually 250 ms with an ISI of 1 Hz, on average. Recording instruments ranged from the BTi 7 and 37-channel systems, and the Picker/Neuromag 122-channel system. Data analysis techniques ranged from manual least-squares minimization techniques to multistart downhill simplex search [1] and R-MUSIC [2].

Results from the visual studies indicate: 1) 3-6 different visual areas can be identified and localized that exhibit retinotopic organization (60-180 ms poststimulus); 2) the timecourses of sources arising from different visual areas differ as a function of stimulus position in the visual field, i.e., central or peripheral (e.g., peripheral stimulation causes earlier activation of the primary visual area and parietal cortex); and 3) the selective manipulation of stimulus parameters can preferentially activate sources in humans consistent with the 'ventral' versus 'dorsal' processing streams identified in non-human primates [4]. For example, isoluminant stimuli evoked activity localized to lateral lingual and fusiform gyri and the fusiform/inferotemporal border (ventral stream). Current studies are examining the relationship between different rates of alternation between the bands of circular sinusoid stimuli (i.e., bulls-eye patterns) and the eccentricity of the stimuli. The visual results have been interpreted within the framework of the specific receptive-field properties associated with these two streams, as originally discussed in [4]. Ungerleider, Mishkin, Desimone, and colleagues have emphasized that the representations of the periphery remain rather distinct and separate from foveal representations throughout cortex.

References:

- [1] Huang et al. Multi-start downhill simplex method for spatio-temporal source localization in magnetoencephalography. *Electroenceph. Clin. Neurophysiol.*, 1998, 108:32-44.
- [2] Moshier, J.C. and Leahy, R. Recursive MUSIC: A framework for EEG and MEG source localization. *IEEE BME*, 1998, 45:1342-1354.
- [3] Aine et al. Retinotopic organization of human visual cortex: Departures from the classical model. *Cerebral Cortex*, 1996, 6:354-361.
- [4] Ungerleider, L.G. and Mishkin, M. Two cortical visual systems. In D.J. Ingle, R.J. W. Mansfield and M.A. Goodale (Eds.). *The analysis of visual behavior* (pp. 549-586). Cambridge: MIT Press, 1982.

MEG Study of Hippocampal Theta During a Working Memory Task

Tesche, C.D.¹, Karhu, J.^{1,2}

1Helsinki University of Technology, Espoo, Finland;

2Kuopio University Hospital, Kuopio, Finland

We investigated magnetoencephalographic (MEG) responses during performance of a modified Sternberg working memory task [1]. A memory set of single digits (0, 1, ..., 9) was presented sequentially to the center of the visual field at interstimulus intervals of 1.2 s. The last memory-set digit was followed 3 s later by a "probe" digit. The size (1, 3, 5 or 7 elements) of each memory set was randomized between blocks. Subjects were instructed to lift the right (left) index finger if the probe was in (not in) the memory set. Data from 10 adult subjects were recorded with a whole-scalp 122-channel MEG array [2]. A multi-component signal-space (SSP) analysis [3] was used to derive waveforms characterizing stimulus-related responses recorded over visual and parietal cortex, movement-related responses recorded over sensorimotor cortex, and responses corresponding to activation of left and of right anterior hippocampus (for a discussion of the method as applied to hippocampal structures, see ref. [4]).

Neurophysiological data are often characterized as a sequence of evoked response peaks. In the present study, left and right anterior hippocampus showed evoked responses at 130 ms following both memory-set and probe stimuli. Reproducible bilateral activity also occurred at 240 ms following the probes. Set-size dependent responses were particularly prominent at 300–800 ms in right hippocampal waveforms. Power spectra of the stimulus-locked evoked responses contained features at 4–12 Hz. Blocking of ongoing (non-stimulus-locked) oscillatory activity was observed following stimulus presentation. Filtering of evoked response waveforms revealed resetting of stimulus-locked 4–8 Hz theta in right hippocampal waveforms coincident with presentation of the probe stimuli, with stimulus-locked responses initiated on the left 140 ms later. The duration of right hippocampal theta increased with memory set size for n=1 to n=5 elements, with no further increase for n=7.

A working memory task in rats elicits stimulus-locked resetting of rhythmic hippocampal activity (theta) [5]. Motivated by these results, we utilized the blocking of non-phase-locked activity following the memory-set probes in our normal human subjects as a window of opportunity for the characterization of stimulus-locked 4–8-Hz theta. Our results suggest that the increased duration of 4–8 Hz theta with set size following presentation of the probe may index involvement of hippocampus and associated structures in the scanning of a memory set. A limited time available for such a process, consistent with the involvement of working memory in on-line processing and generation of an immediate motor response, may then provide a natural limit on the capacity of working memory. This study was supported by grant NIH NINDS NS34533.

References:

[1] Sternberg, S. High-speed scanning in human memory, *Science*, 1966, 153:652–654.

[2] Ahonen, A.I., Hämäläinen, M., Kajola, M. et al. 122-channel SQUID instrument for investigating the magnetic signals from human brain, *Physica Scripta*, 1993, T49:198–205.

[3] Tesche, C.D., Uusitalo, M.A., Ilmoniemi, R.J. et al. Signal-space projections of MEG data characterize both distributed and well-localized neuronal sources, *Electroenceph clin Neurophysiol.*, 1995, 95:189–200.

[4] Tesche, C.D., Karhu, J., Tissari, S.O. Non-invasive detection of neuronal population activity in human hippocampus, *Cogn. Brain Res.*, 1996, 4:39–47.

[5] Givens, B. Stimulus-evoked resetting of the dentate theta rhythm: relation to working memory, *NeuroReport*, 1996, 8:159–163.

Estimating Neural Source of High-Frequency Magnetic Oscillation Evoked by Posterior Tibial Nerve Stimulation Using Time-Frequency MEG-MUSIC Algorithm

Sakuma K.¹, Sekihara K.², Hashimoto I.^{1,3}

¹National Institute for Physiological Sciences, Okazaki, Japan; ²JST Mind Articulation Project, Tokyo, Japan; ³Department of Psychophysiology, Tokyo Institute of Psychiatry, Tokyo, Japan

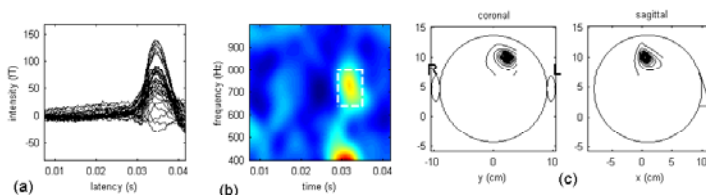
We recorded high frequency (500-800 Hz) primary cortical oscillations (HFO) evoked by posterior tibial nerve stimulation using magnetoencephalography [1]. Since the HFO has extremely low amplitude, it is difficult to precisely localize its source. The recently proposed time-frequency multiple signal classification (TF-MUSIC) algorithm [2] allows estimating the locations of neural sources from any time-frequency region of interest. We here applied the TF-MUSIC algorithm to this HFO source localization, and demonstrated the superiority of this method over the single dipole localization method.

Ten normal subjects were studied. Electrical stimuli with a 0.2 ms duration were delivered to the subject's right posterior tibial nerve at regular interval with a repetition rate of 4 Hz. The magnetic field was recorded with a bandpass filter (0.1-1200 Hz) from the vertex with a 37-channel MagnesTM biomagnetometer. An epoch of 60 ms duration was digitized at a 4167 Hz sampling rate and 9999 epochs were averaged (Fig. (a)). A spectrogram was calculated using this averaged data (Fig. (b)), and a region of interest (indicated by a square) was set so as to cover the target high-frequency component. The TF-MUSIC algorithm was then applied with this target time-frequency region (Fig. (c)). For comparison, the single moving dipole source analysis was also applied to digitally filtered (500-800 Hz) version of the same average data.

A single source was estimated very close to the primary somatosensory cortex (SI) area whose location was estimated from the P37m peak in the recorded waveforms. These results are in good agreement with the previous investigation conducted with the median nerve stimulation [3]. For this particular data, the single dipole method failed to localize a source near the SI area due to the low signal-to-noise ratio of the HFO. The HFO source was successfully localized in 6 out of 10 subjects with the TF-MUSIC algorithm as against in 4 out of 10 subjects with the single-dipole method.

References:

1. Sakuma, K., Hashimoto, I. *NeuroReport* 1999, in press.
2. Sekihara, K., Nagarajan, S., Poeppel, D., Miyashita, Y. *IEEE Trans. Med. Imaging*, in press.
3. Hashimoto, I., Mashiko, T., Imada, T. *Electroenceph. Clin. Neurophysiol.* 1996, 100: 189-203.



(a) Typical recordings. (b) Spectrogram obtained from recordings in (a). (c) TF-MUSIC localizer map.

Modeling aspects of bioelectric source imaging

van Oosterom A.

Laboratory of Medical Physics & Biophysics, University of Nijmegen,

This abstract summarizes an invited tutorial at the NFSI-99 meeting in Zagreb. Various notions will be discussed that are involved in the modeling that is required for the functional imaging of bioelectrical sources, be it in the world of EEG, ECG or otherwise (EMG, ENG, ...). These notions are relevant for the methods applied to recorded electric signals as well as for those using magnetic signals.

Necessity The necessity for using models to support the interpretation of observed bioelectric (magnetic) signals, as is the objective of bioelectric functional imaging, stems from the fundamental impossibility of deriving a unique specification of internal (bio-)electrical sources on the basis of observations on the body surface (ECG, EEG) or just outside the body (MCG, MEG): a multitude of different sources may give rise to identical data as observed outside the actual source region. To circumvent this problem a description of the bio-electric generator needs to be postulated *a priori*, the source model. In addition, a model needs to be involved describing the passive effects on the observed data of the body tissues that surround the active electric sources.

Source models Source models of different natures have been developed. They can be classed as having either a purely physical nature or as having a nature that is closely linked to the source properties that one may want to 'image'. It is the second type that is the most interesting one for an ultimate clinical application, but also the most challenging one.

Volume conduction models The tissues around the primary electric sources play an essential role in the wave forms that can be observed. The full documentation of the conductive properties of the tissues is simply impossible because of their complex nature, involving the inhomogeneity and anisotropy implied in their morphology. Simplifying models have been developed over the years which seem to be able to do sufficient justice to this complexity.

Forward Problem Both models having been formulated, this leads to the Forward Problem, *i.e.*, the computation of the potential or magnetic field distributions in the points of observation. Within the limitations of both models involved the computation of the transfer between sources and observed data does not pose a major problem: fast numerical algorithms have been developed that can solve the forward problem accurately.

Source Imaging The restrictions implied in the source models make it possible to compute (estimate) their parameters on the basis of observed data outside the source region. The latter procedure is (used to be) known as the Inverse Problem. Several of the methods studied at the moment result in a specification of the solution, the sources, in image format.

Perspective The fundamental impossibility mentioned above, caused by the physics involved, demands that the physiological basis of the source configurations used needs to be secured *a priori*. Moreover, the more interesting the sources are required to be, the heavier are the demands on the quality of the volume conductor model. This will be demonstrated in an application to cardiac source imaging.

On the effective passive conductivity of human tissues

Peters M.J., van Burik M.J., Stinstra J.G.

Low Temperature Division, Faculty of Applied Physics, University of Twente, P.O.Box 217, 7500 AE Enschede, The Netherlands

Biological materials are inhomogeneous materials with two domains: the extracellular and the intracellular space. Although the cells are of microscopic size, still they are much larger than the ions in the extracellular space so that the extracellular fluid can be considered as a dielectric continuum. The electrical properties of the intracellular fluid and the extracellular fluid are different. At low frequencies and small current densities, the currents tend to flow around the cell membranes rather than through them. Outside of the source region it is assumed that human tissues are Ohmic (linear with the electric field). Usually, values for the passive electric properties are taken from literature. However, the values given vary over a wide range. To narrow down the uncertainties, we will discuss the electric conductivity of human tissues for low frequencies taking the cellular structure into account.

Spherical particles suspended in a solvent are considered to be a relevant model of biological cells. Maxwell derived an expression for a dilute suspension of spheres within a uniform applied field. This expression has been experimentally tested for high concentrations of variously shaped objects and an agreement within 1% was found at concentrations up to 90%. The particles could be spheres, cubes, plates or cylinders. However, measurements of the conductivity of the cortex did not fit so well with the theory of Maxwell. It was found that the conductivity of the cortex is in good agreement with an expression that is known as Archie's law, which reads:

$$\sigma^* = \sigma_1 (1-p)^m,$$

where σ^* is the effective conductivity, p is the volume fraction of small suspended particles and σ_1 is the conductivity of the solvent. As no significant concentration gradients exist between the cerebrospinal fluid (CSF) and the interstitial fluid, the electrical conductivity is that of CSF. Archie's law was obtained from experiments in geology. Most of water-saturated rocks obey Archie's law. It will be shown that Archie's law is an expression for the conductivity of a densely packed suspension of spheres, ellipsoids and infinite long cylinders within a uniform field, assuming that no currents flow within the particles. The value of m depends on the shape of the particles. It is $3/2$ for spheres, 2 for very long cylinders with the axis perpendicular to the external field and 1 for cylinders with the axis parallel to the field. Maxwell's formula has been used repeatedly to estimate volume fractions from impedance data. It does not seem to be a reliable estimator of this parameter, p should be determined with other means, for instance iontophoresis. The cortex or a layer of subcutaneous fat can be modeled as densely packed spherical or spheroidal cells. The white matter, capillaries and muscles can be modeled as densely packed cylindrical particles and amniotic fluid as a dilute solution where the volume fraction of particles is dependent on the duration of pregnancy. From experiments it is found that for the cortex m is about $3/2$ [1]. The applied field is not uniform in the neighbourhood of sources, as is the case when we are modeling the volume conduction problem in ECG or EEG. As expected, this has an influence on the effective conductivity of the tissue nearby.

References:

[1] Nicholson, C. and Rice, M.E., The migration of substances in the neural microenvironment, *Annals of the New York Academy of Sciences*, 1986, 481:55-71.

Realistic a priori informed spatial basis functions in minimum norm solutions.

C. Phillips^{1,2,3}, M.D. Rugg², K.J. Friston¹

¹Wellcome Department of Cognitive Neurology, Institute of Neurology, London, UK

²Institute of Cognitive Neuroscience, UCL, London, UK

³Cyclotron Research Centre, University of Liege, Belgium

Linear inverse solutions have been applied extensively to solve the bioelectromagnetic inverse problem. In contrast to discrete dipole equivalent models, linear inverse solutions do not require any assumptions about the number of active sources and lead to a fully 3D representation of the electrical activity of the brain. However the problem is underdetermined: there are many more parameters to estimate (relative to the number of dipole locations considered) than data available (relative to the number of electrodes). In order to ensure the uniqueness of the solution, existing methods generally apply constraints on the solution, for example: minimum 2-norm, maximum smoothness[1], optimal resolution[2], etc. These methods provide solutions with relatively poor spatial resolution because they neglect, wholly or in part, anatomical information relevant to the real source distribution.

Our method aims to model the spatial source distribution by using a set of basis functions. By appropriately defining these basis functions, we are able to include a priori information about the sources and our solutions will *de facto* belong to the subspace spanned by these basis functions.

The priors enter as constraints of the covariance structure of the source power (over space), and are used to motivate the selection of a spatial basis set that maximises the information between the sources and their projection on that set. The orientation of each dipole is fixed and orthogonal to the cortical sheet, and therefore only the amplitude of the sources remains unknown. We then solve for the source distribution using two constraints: sources must correspond to dipoles localised to gray matter, and the 2D distribution of dipole strengths across the cortical surface must be spatially smooth.

In simulations conducted so far on noiseless instantaneous simulated data, we have obtained better resolution and more robust performance, even for deep sources, than could be achieved with other approaches [1,2]. Moreover the solutions are constrained to be anatomically realistic in orientation, amplitude and smoothness. We are planning to extend the approach to more realistic and noisy data, including a basis functions approach to constrain solutions in the temporal domain as well as in the spatial domain[3].

References:

1. Pascual-Marqui R.D., Michel C.M., Lehmann D. Low resolution electromagnetic tomography: a new method for localising electrical activity in the brain, *Int. J. Psychol.*, 1994, 18:49-65.
2. Grave de Peralta Menendez R., Hauk O., Gonzalez Andino S., Vogt H., Michel C., Linear inverse solutions with optimal resolution kernels applied to electromagnetic tomography, *Human Brain Mapping*, 1997, 5:454-467.
3. Phillips C., Rugg M.D., Friston K.J., A priori spatio-temporal basis functions in minimum norm solutions, HBM99 abstract, to be published.

Secondary Sources in the Skull

van Burik M.J., Peters M.J.

*Low Temperature Department, Faculty of Applied Physics, University of Twente,
P.O. Box 217, 7500 AE, Enschede, The Netherlands*

For the analysis of EEG and MEG mathematical models are used to describe the conduction of currents within the head. The head is not homogeneous. On the contrary, it consists of many regions of different conductivity. One of the most dominant regions is the skull. The conductivity of this structure is typically a factor of 20 to 80 lower than that of other tissues. Hence, it is a barrier for current flow and as a result the EEG at the scalp is strongly attenuated and smeared out. To take into account such influences, the skull has to be modelled. Customarily, this is done by using a head model with 3 or more surfaces and setting the conductivity of one of the compartments to that of the skull while assigning appropriate conductivity values to the other compartments. Within the boundary element method, the currents within the regions of different conductivity are modelled by placing secondary sources at their interfaces. The strength of the secondary sources is proportional to the step in conductivity and the applied potential difference, their orientation is perpendicular to the interface. The magnitude of the secondary sources depends on the position and moment of the primary sources, i.e. the sources that cause the EEG. If the primary sources are known and, simultaneously, the potential distribution on the scalp, the secondary sources can be estimated. Such an estimation will give insight into the influence of the skull.

A patient that was refractory to medical treatment of his epilepsy had to undergo surgery for resection of a small area of the brain. Invasive recordings of the potential inside the head were made to enable an accurate localisation of the seizure focus. The intracranial electrodes were placed subdurally on the surface of the brain, and into deep cerebral structures with depth electrodes. The electrodes were introduced in the head through two holes in the skull. Normally, the intracranial electrodes are used for recordings only. However, in this case, a small current was injected between two electrodes and this resulted in a measurable potential distribution on the scalp surface. The current injected between the pair of electrodes can be modelled by a current dipole and makes the primary source. Since the scalp EEG was measured during the injection of current at the electrodes in the brain, sufficient data is available for an estimation of the secondary sources.

The skull has two interfaces, one interface to the brain and one to the scalp. Using the boundary element method, secondary sources are placed at both interfaces since the conductivities of the brain and scalp differ from that of the skull. Because the surfaces are very close to each other we have chosen for a single layer of secondary sources. These sources are estimated on a surface that is placed between the inner and outer surface of the skull. A CT scan is used as basis for the geometrical model. Both the skull and the positions of the subdural and depth electrodes are clearly visible in the CT scan. This allows an accurate modelling.

While for some of the measurements distinct extremes are found underneath the two holes, for other measurements clear extremes are found at the base of the skull. Local extremes in the distribution of the secondary sources indicate that at those positions more current flows. High current densities can be expected at those positions in the skull where the conductivity is high compared to that of the surroundings or at those positions where the skull is locally thinner. While the former is typically the case for the two holes, the latter case is found at the base of the skull.

The Electrically Silent Cardiac Magnetic Field

**¹Fischer G., ¹Tilg B., ¹Modre R., ²Fetzer J., ²Rucker W., ³Huiskamp G.,
¹Wach P.**

¹Institute of Biomedical Engineering, Technical University Graz, Graz, Austria;

²Institute for Theory in Electrical Engineering, University Stuttgart, Stuttgart, Germany;

³Department of Clinical Neurophysiology, Utrecht University Hospital, Utrecht, Netherlands

It is commonly assumed that biomagnetic fields contain additional information compared to bioelectric fields. It was shown [1] that, a cylindrical strand of tissue with spiralling or helical fiber architecture of anisotropic conductivity produces an additional magnetic field component which does not occur when isotropic conductivity is assumed. This magnetic field component is associated with off-diagonal terms of the conductivity tensor which do not enter the calculation of the electric potential. Therefore, it is called electrically silent.

The human heart has a fibrous spiral- or helix-like structure but, to the author's best knowledge, no theoretical estimation exists, at which order of magnitude of strength electrically silent magnetic fields can be expected. In [2] a dipolar approximation of the silent field component is calculated from MCG recordings of healthy subjects. The magnetic dipole moment has been found to be in the order of magnitude of 100 nAm².

In the present study a BEM-FEM-coupling technique is applied in order to numerically investigate the cardiac magnetic field considering anisotropic volume conduction. First an eccentric spheres model of the left ventricle inside the torso is used assuming sigmoidal transmural variation of fiber angle within the ventricular wall [3]. Approximating the independent cardiac sources by a spherical function of first order and realistic magnitude, the magnetic dipole moment is found by 70 nAm². Results are then compared to calculations assuming isotropic cardiac conductivity. Choosing appropriate isotropic conductivity values the electric potential in 223 nodes on the outer sphere potential has the relative difference of 1.05 % comparing anisotropic (reference) and isotropic calculations. In contrast the relative difference of the magnetic field radial components in 130 observation points 0.01 m above the outer surface is 16.4 %.

Next investigations are extended to a realistic torso model including the heart with realistic fiber geometry [3]. An activation sequence of the heart has been calculated applying modified Beeler-Reuter equations. A 37-channel gradiometer system was synthetically arranged close to the anterior chest wall. The relative difference of the magnetic field maps assuming anisotropic and isotropic conductivity, respectively, is smaller than 5 % for all time steps. Again appropriate isotropic cardiac conductivities have been chosen.

Finally the effect of neglecting anisotropic cardiac volume conduction in the magnetocardiographic inverse problem is investigated estimating the epi- and endocardial activation time pattern. Results suggest, that applying an isotropic model of the cardiac muscle sufficient spatial and temporal resolution can be obtained in the solution.

[1] Roth, B.J. and Wikswo J.P. Electrically Silent Magnetic Fields, *Biophys. J.* 1986, 50:739-745.

[2] Brockmeier K., Schmitz L. et. al. Magnetocardiography and 32-Lead Potential Mapping: Repolarization in Normal Subjects During Pharmacologically Induced Stress, *J. Cardiovasc. Electr.* 1997, 8:615-626.

[3] Nielsen P.M.F., Le Grice I.J. et. al. Mathematical model of geometry and fibrous structure of the heart, *Am. J. Physiol.* 1991: 260:H1365-H1378.

A Linearized Iterative Algorithm for Myocardial Activation Time Imaging

Modre R.¹, Tilg B.^{1,2}, Fischer G.¹, Wach P.¹

¹*Institute of Biomedical Engineering, Technical University Graz, Graz, Austria*

²*Cardiac Electrophysiology Department, University of California San Francisco, San Francisco, California, USA*

Noninvasive Functional Cardiac Electrical Source Imaging uses magnetocardiogram (MCG) or body surface potential (BSP) in combination with morphological imaging data to reconstruct the electrical sources within the heart. The activation time pattern on the surface of the ventricle can be estimated applying a nonlinear optimization routine (E04UCF, NAG Ltd. UK) with a starting vector generated by the critical point theorem. The critical point theorem results in a low-quality estimate for the endocardial activation time pattern. As an alternative to the nonlinear approach in this study a linearized iterative algorithm for estimating the activation time pattern on the epicardium and endocardium was introduced and investigated.

The volume conductor was modeled applying an isotropic boundary element formulation including the blood masses, the lungs and the outer torso surface [1]. The transmembrane potential was described by a nonlinear analytical template function [2]. The activation time pattern on the surface (endocardium and epicardium) of the ventricle was estimated applying an iterative algorithm minimizing a cost function containing the residual norm, the corresponding semi-norm of the surface laplacian of the regularized solution and a second-order Tikhonov regularization parameter determining the weight of the semi-norm [2]. At each step of iteration the inverse problem was solved applying a Gauss-Newton method using a linearized version of the template function describing the transmembrane potential [3]. The linearized iterative algorithm was applied to synthetic MCG and BSP data. A reference activation time map on the surface of the ventricle (endocardium and epicardium) was estimated from a normal sinus rhythm MCG measured with the 68 channel cardiomagnetometer system at the Helsinki University Central Hospital (HUCH). This activation time map was used to simulate in the forward problem synthetic MCG and BSP data. Gaussian noise was added to this data.

From the synthetic MCG data applying the critical point theorem the correlation coefficients were found to be 0.56 for the epicardium and 0.3 for the endocardium, respectively. Using the critical point solution as a starting vector for the proposed linearized iterative method, the correlation coefficients were improved from 0.56 to 0.98 and from 0.30 to 0.99. Solutions estimated from synthetic BSP data showed similar improvements. The proposed linearized iterative inverse approach showed good computational performance and resulted in nearly the same inverse solution than the nonlinear approach.

References:

- [1] Fischer, G., Tilg, B., Wach, P., Modre, R., Leder, U., and Nowak, H. Application of high-order boundary elements to the electrocardiographic inverse problem, *Comput Meth Prog Bio*, 1999, 58:119-31.
- [2] Wach, P., Tilg, B., Lafer, G., and Fischer, G. Cardiac source imaging during re- and depolarization, In: Tilg, B., and Wach, P. NFSI99, *Biomed Technik* 1997, 42(Supplement 1):269-72.
- [3] Tautenhahn, U. On a general regularization scheme for nonlinear ill-posed problems: II. Regularization in Hilbert scales, *Inverse Problems*, 1998, 14:1607-16.

Influence of randomly displaced BSPM leads and measurement noise on the identification of ventricular pre-excitation sites.

Jazbinšek V., Hren R.

Institute of Mathematics, Physics and Mechanics, University of Ljubljana, Slovenia

The precise identification of the ventricular pre-excitation sites in patients suffering from Wolf-Parkinson-White (WPW) syndrome is a prerequisite for a successful radiofrequency ablation. Non-invasive body surface potential mapping (BSPM) can provide guidance in such a treatment. In this contribution, the influence of randomly displaced BSPM leads and measurement noise on the forward and inverse solution is investigated by means of a simulation study applied to the WPW pre-excitation sites.

We used Horaček standard torso model (700 triangles, 352 nodes) as a reference for 117 leads BSPM. Seven additional torso models with displaced leads are generated by randomly modifying those nodes that correspond to positions of BSPM leads on a surface of the standard torso model. We apply a root mean square (RMS) displacement value equal to 10 mm in all cases. BSPMs for 4 right lateral (RL) and 4 left lateral (LL) pre-excitation sites are simulated with an anatomically accurate model of the human ventricular myocardium in time sequences of 4 ms increments and up to 40 ms after the onset of activation (80 simulated BSPMs for each torso model. Measurement noise is introduced by adding 4 different RMS noise levels (5,10,20,50 μ V). We generate 10 different noise distributions for each noise level (additional $4 \times 10 \times 80 = 3200$ BSPMs per torso model). For each BSPM in a given torso we perform the inverse solution using current dipole source model within the standard torso. We get 3280 localization results (LRs) and localization errors (LEs), defined as a difference between LRs and corresponding pre-excitation sites.

Changes in BSPMs due to lead displacements are quantified with correlation coefficients (CCs) between displaced BSPMs and corresponding reference BSPMs. For noiseless BSPMs it is found that $CCs \pm SD$ for RL and LL pre-excitation sites, averaged over all time points and corresponding pre-excitation sites, are 0.980 ± 0.012 and 0.9971 ± 0.0004 , respectively. These results suggest that the 10 mm lead displacements have negligible influence on the forward solution of LL cases.

Average LEs for the reference BSPMs, at times 8, 28 ms after the onset and no noise added, are 1.8 ± 0.5 , 13.6 ± 4.0 mm for RL cases, and 12.9 ± 1.3 , 15.5 ± 2.9 mm for LL cases, respectively. Corresponding LRs, averaged over all displaced BSPMs, are 6.7 ± 2.6 , 15.4 ± 6.1 mm for RL cases, and 12.6 ± 1.6 , 15.2 ± 2.8 mm for LL cases. These results show that the current dipole model localizes RL cases better than LL cases in the early times after the onset, but in the later times LEs become comparable for both group of WPW cases.

The influence of lead displacements on LRs is estimated by comparing LRs obtained from displaced BSPMs with corresponding LRs calculated from the reference BSPMs. Results obtained from noiseless BSPMs averaged over all time points and all torso models are 6.5 ± 3.2 mm and 2.3 ± 1.0 mm for RL and LL cases, respectively. These findings show that displaced BSPM leads have larger influence on the inverse solution of RL than LL cases.

The influence of measurement noise depends on a signal to noise (S/N) ratio defined as a ratio between RMS value of BSPM and noise level. Results obtained by noisy BSPMs show that the measurement noise have a significant influence on the forward and inverse solution if S/N is less than 5. This affects BSPMs and LRs only in the early time interval after the onset, for example, up to 12 and 20 ms for the noise levels 5 and 10 μ V, respectively.

Tutorial Introduction to Functional MRI (fMRI)

Savoy R.L.

The MGH-NMR Center

Building 149, 13th Street; Charlestown, MA 02129; USA

And The Rowland Institute for Science

100 Edwin H. Land Boulevard; Cambridge, MA 02142; USA

This presentation will begin with a brief outline of the physics and physiology underlying the use of Magnetic Resonance Imaging (MRI) in the study of human brain function. The fundamental chain of ideas is that (1) neuronal activity causes local changes in cerebral (and subcortical) blood flow; (2) the oxygen utilization increase associated with neuronal activity is much smaller than the increase in oxygen delivery caused by the increased blood flow; (3) there is a consequent decrease in the concentration of deoxyhemoglobin in the venous vessels near this neuronal activity; (4) deoxygenated hemoglobin has a much greater magnetic susceptibility than oxygenated hemoglobin; (5) MRI is a flexible tool that can be used in different ways to detect the changes in blood flow directly, or to detect the distortions of the local magnetic fields caused by the changes in the concentration of deoxyhemoglobin. Thus, the non-invasive techniques of MRI can be used to create three dimensional maps of the activity of neurons in the human brain (albeit through the indirect means of detecting hemodynamic changes).

This technology has led to an explosion in the field of Human Brain Mapping. Thousands of images of a given brain can be made in a typical 1-2 hour fMRI session. The "signal" being sought in this data is often weak and a substantial body of data analysis techniques has been developed to find areas of significant change, and to visualize the collection of activated areas. A large portion of the tutorial lecture will describe both the basic and advanced techniques of this kind of data analysis.

The other major component of the tutorial will address issues in experimental design. The various approaches to experimental design are strongly coupled with various approaches to data analysis. Procedures modeled on the earlier technology of Positron Emission Tomography (PET), which necessarily use block designs, are still important in functional MRI. Additionally, procedures modeled on event related experiments of EEG and MEG can be implemented in functional MRI. There are many ways in which the characteristics of the hemodynamic response guide both experimental design and data analysis for investigators who wish to use brief stimuli to probe specific cognitive events. Correlational analysis permits the interpretation of imaging data based on the actual behavioral responses, sometimes collected long after the imaging experiment itself has ended. Variations on the theme of Principal Component Analysis raise the promise of being able to detect spatio-temporal regularities in the imaging data which were not intentionally built in to the experimental design.

Two kinds of applications will be mentioned. One group will be related to specific experiments in visual perception, attention and cognition. Another group will emphasize the role that clever experimental design and data analysis play in clinical studies.

There is, as yet, no definitive text in Functional MRI, and each edited collection has strong and weak chapters. Nonetheless, two recent books [1,2] collectively serve as detailed introductions to most of the current issues in fMRI.

- [1] Functional MRI. Moonen, C.T.W and Bandettini, P.A. (Editors). Heidelberg, Springer-Verlag, 1999.
- [2] Human Brain Function. Frackowiak, R.S.J., Friston, K.J., Frith, C.D., Dolan, R.J., and Mazziotta, J.C. (Editors). San Diego, Academic Press, 1997.

A Review of fMRI Technological Developments

Jia-Hong Gao

Research Imaging Center

University of Texas Health Science Center, San Antonio, TX, USA

Functional MRI (fMRI) has become a powerful tool for studying, in vivo, the functional organization of the human brain. Although fMRI initially followed leads set by PET and SPECT, fMRI has leapt beyond its nuclear forerunners.

In 1992, Kwong et al. [1] and Ogawa et al. [2] first mapped human brain activity using fMRI techniques without any administration of tracer (contrast agent). Their technique relied solely on the endogenous contrast that result from physiologic changes in the brain during activation. Task-associated changes in brain neural activity are associated with local changes in blood flow, blood volume, blood oxygenation, and carbohydrate metabolism. MRI is sensitive to blood flow, blood volume, and the blood oxygenation state of hemoglobin, all of which can be used to generate noninvasive images of human brain activity. By choosing different MRI imaging pulse sequences, blood oxygenation level dependent (BOLD) and cerebral blood flow (CBF) based fMRI techniques can be routinely used in the fMRI community to study brain activation. In most cases, these techniques have been performed using a blocked task paradigm. A comparison study of BOLD and CBF based fMRI has shown that a high linear correlation exists between CBF and BOLD signal changes.

Most recently, both BOLD and CBF based event-related fMRI (ER-fMRI) were developed to study the transit hemodynamic response to a short stimulus [3-5]. There is tremendous advantage to using ER-fMRI compared with the traditional blocked task designed fMRI in studies of working memory, attention, language, and many other aspects of human cognitive performance. These techniques are particularly useful when studying some unexpected single event, such as epileptic activity or drug responses. The combination of event related potentials (ERP) and ER-fMRI techniques enable us to gain substantial temporal and spatial resolution when imaging the responses to various stimuli. These gains will lead us to a better understanding of where and when brain activation happens. In addition to the “traditional” task-minus-rest fMRI procedure, by performing a covariance analysis, single state MR images can also provide information to aid in understanding human brain connectivity. The use of trans-cranial magnetic stimulation (TMS) coupled with the information from the fMRI studies of the brain response to the TMS is now at the forefront of methods used to study connectivity. As BOLD effects increase with increasing magnetic field strength, higher field magnets (> 3 T) are gaining popularity in the fMRI community. Currently, more than a dozen 3 T machines are already operational and are being used for fMRI research. In addition, several labs have been successfully performing fMRI studies using machines with even higher field strengths of 4-8 T.

References

- [1] Kwong KK, Belliveau JW et al: Dynamic magnetic resonance imaging of human brain activity during primary sensory stimulation. *Proc. Natl. Acad. Sci. (USA)* 1992, 89:5675.
- [2] Ogawa S, Tank DW et al: Intrinsic signal changes accompanying sensory stimulation: Functional brain mapping with magnetic resonance imaging. *Proc. Natl. Acad. Sci. (USA)* 1992, 89:5951.
- [3] Buckner RL, Bandettini PA et al., Detection of cortical activation during averaged single trials of a cognitive task using functional magnetic resonance imaging. *Proc. Natl. Acad. Sci. (USA)* 1996, 93:14878-14883.
- [4] Dale A, Buckner RL. Selective averaging of rapidly presented individual trials using fMRI. *Human Brain Mapp* 1997: 5:329-340.
- [5] Liu HL, Gao JH. Perfusion based event-related fMRI, *Magn. Reson. Med.* in press (1999).

Spatiotemporal Patterns of Human Brain Activation During the Processing of Words and Faces: Anatomically-Constrained and fMRI Biased Distributed Inverse Solutions for Whole-Head MEG

Halgren, E.^{1,3}, Marinkovic, K.¹, Dhond, P.¹, Fischl, B.², Dale, A.²

¹Radiology, University of Utah, Salt Lake City, USA, ²MGH-NMR, Harvard Medical School, USA,

³INSERM E 9926, Marseilles, France

The construction of accurate spatio-temporal maps of human brain activity during higher cognitive tasks requires combining a technique such as fMRI which has good spatial localization but low temporal resolution (>1 s), with a technique like MEG, which has temporal resolution as fine as the sampling rate, but uncertain localization. Furthermore, since intracranial EEG (iEEG) recordings have clearly shown that many areas show rapid, sustained and distributed engagement during cognitive tasks, the assumption that the MEG signal can be represented by one or a few equivalent current dipoles cannot be used to restrict the inverse solution (1). One solution to these problems is to calculate a distributed minimum norm pseudo-inverse from the MEG signal, for dipoles that lie in the cortex and (optionally) perpendicular to its surface (2). This anatomically-constrained MEG inverse solution (aMEG) can be focussed by adding fMRI as a functional prior (fMEG). aMEG and fMEG are averaged across subjects by aligning sulcal patterns (3). The physiology and biophysics of MEG and fMRI allow that they could be generated by the same cortical areas, but it is by no means certain. Simulations have shown that fMRI-invisible MEG sources can cause grossly inaccurate solutions if activity from that source is forced to lie in an area of fMRI activation (4). Thus, only a partial bias is used in the studies reported here.

aMEG, fMEG, fMRI and/or iEEG have been acquired in a series of tasks involving single words or faces, or words in sentences, and exploring perception, memory, phonemic, and semantic processing. The aMEG activation, integrated across time, usually resembles the fMRI activation in the same subjects and tasks, except for greater lateral anterior temporal aMEG activation. This may be due to susceptibility artifacts in the fMRI and/or mis-assignment of activation by the minimum norm solution. The spatiotemporal aMEG and fMEG patterns are strikingly similar to those which had been observed with iEEG in similar tasks (1). Initially confined to primary visual cortex, activity rapidly spreads to temporal, parietal and frontal sites within less than 60 ms. Most sites remain active for long periods of time, resulting in parallel activation, especially in ventral fronto-temporal cortices which also show the strongest effects of repetition, emotional valence, phonemic regularity, and semantic congruity. The main difference between tasks is a powerful lateralization of activation, with face processing evoking primarily right hemisphere activation, and word processing left. The ventral fronto-temporal aMEG/fMEG/fMRI activation in all cognitive contrasts may be generated by the same brain systems as the N2/N3/N4/LPC ERP components, and thus may reflect template-matching/ semantic memory access/ contextual integration/ cognitive closure, respectively.

1. Halgren, E., et al. *J. Physiol. (Paris)*, 1994, 88: 1-50, 51-80.

2. Dale, A.M., & Sereno, M.I. *J. Cog. Neurosci.* 1993, 5:162-176.

3. Fischl, B., Sereno, M.I., & Dale, A.M. *Human Brain Mapping* 1999, in press.

4. Liu, A.K., Belliveau, J.W., & Dale, A.M. *Proc. Natl. Acad. Sci. USA* 1998, 95:8945-50.

Supported by NIH NS18741 and HFSP0 RG 25/96.

Selective BOLD Activation of the Receptive Speech Area Using a Novel Passive Listening Paradigm

Lowe, M.J., Lurito, J.T., Mathews, V.P., Phillips, M.D., and Dzemidzic, M.

Department of Radiology, Indiana University School of Medicine, Indianapolis, IN, USA

Functional magnetic resonance imaging (fMRI) has been successfully applied in the identification of the cortical areas involved in motor and sensory [1], as well as higher cognitive functions, including language [2]. The goal of this study is to evaluate a novel fMRI method for the selective localization of areas involved in the receptive speech.

Functional imaging was performed on six right-handed healthy subjects on a 1.5 tesla General Electric Echosped scanner (GE Medical Systems, Waukesha, WI, USA), with gradient echo echo-planar imaging sequence. Time series data were obtained using blood-oxygenation level dependent (BOLD) contrast in 15 slice (whole brain) acquisitions with the following parameters: repetition time 2 s; echo time 50 ms; field-of-view 24x24 cm; matrix 64x64; bandwidth 62.5 kHz; flip angle 90°. All presented paradigms followed 32 second-“off”/32 second-“on” patterns giving a boxcar reference function for expected activation patterns. Auditory stimuli were presented via MR compatible stereoscopic sound system (Avotec Inc., Jensen Beach, FL, USA). Three different “on”/“off” patterns were used: 1) simple narrative text interleaved with scanner noise; 2) simple narrative text interleaved with narrative text played backward, 3) narrative text played backward interleaved with scanner noise. The MRI time series at each pixel was fit using the least squares fit to a boxcar reference function, a slope, and an intercept [3]. A Student’s t-statistic for each pixel was formed from the ratio of the fit amplitude to its error. Statistical maps were interpolated to 256³ cubic voxels and transformed to Talairach space. Activation maps were superimposed on high-resolution 3D T₁-weighted images with a single pixel confidence level of 99.9 %.

For all subjects, stimulus 2 produced a strong asymmetric focus of activation in the posterior portion of the left superior temporal gyrus, Brodmann area 22, which is the classical location of Wernicke’s area. Similar pattern of activation across the three stimuli was noted for more anterior temporal lobe foci. A strong focus of activation in the primary auditory cortex noted for stimuli 1 and 3, was not observed for stimulus 2, as expected across the three conditions for an auditory processing region. In addition to the primary auditory cortex, stimuli 1 and 3 activated the medial geniculate nucleus of the thalamus. Our results show that receptive language and auditory regions of the cortex can be selectively activated with a simple, robust, and potentially powerful technique with major clinical and research applications.

References:

- [1] Puce, A., Constable, T., Luby, M.L., McCarthy, G., Nobre, A.C., Spencer, D.D., Gore, J.C., and Allison, T., Functional magnetic resonance imaging of sensory and motor cortex: comparison with electrophysiologic localization, *J. Neurosurg.*, 1995, 83: 262-270.
- [2] Fitzgerald, D.B., Cosgrove, G.R., Ronner, S., Jiang, H., Buchbinder, B.R., Belliveau, J.W., Rosen, B.R., and Benson, R.R., Location of language in the cortex: a comparison between functional MR imaging and electrocortical stimulation, *AJNR*, 1997, 18: 1529-1539.
- [3] Lowe, M.J. and Russell, D.P., Treatment of baseline drifts in fMRI time series analysis, *J. Comp. Assist. Tomogr.*, 1999, 23: 463-473.

On the organisation of the human somatosensory cortices: a fMRI study

Della Penna S.¹, Bonomo L.^{1,2}, Del Gratta C.^{1,2}, Ferretti A.¹, Franciotti R.¹, Rossini P.M.³, Tartaro A.^{1,2}, Torquati K.¹ and Romani G.L.^{1,2}

1-Institute of Advanced Biomedical Technologies, University of Chieti, Chieti, Italy; 2-Department of Clinical Sciences and Biomedical Imaging, University of Chieti, Chieti, Italy; 3-AFaR-IRCCS “San Giovanni di Dio”, Istituto Sacro Cuore di Gesù, Brescia, Italia.

In this work we studied the ability of the fMRI method to localise the SI and SII areas in healthy humans following upper and lower limb sensory stimulation.

We tested seven healthy adult volunteers. They lied down in a relaxed state, during both the stimulation and the rest conditions, their eyes kept closed. Stimulation consisted of current pulses 0.2 ms duration and 1.9 Hz frequency. Stimuli were set at a level slightly above motor threshold (about 15 mA amplitude) and were delivered via Ag/AgCl electrodes, producing mixed cutaneous and proprioceptive either median or tibial nerve stimulation. The fMRI study was performed by delivering to subjects trains of stimuli according to a boxcar on-off paradigm. The fMRI scans were performed by using a 1.5 Tesla equipment and FID echoplanar imaging technique (TR= 0.8 s, TE= 54 ms). Each scan consisted of 22 slices, 3 mm thickness, located from the bicommissural line to the vertex. The functional images were processed to obtain t-test zscore statistical images.

In all the subjects tested, statistical image showed areas activated in the parietal lobe contralateral to the stimulated limb, where the primary somatosensory cortex is located. Areas activated with a statistical significance were also detected in the supratemporal plane, where the secondary somatosensory cortex is located. The location of these areas are consistent with the results obtained by means of electrical (EEG) and magnetic (MEG) measurements, as reported in the literature.

Single event functional MRI of supplementary motor and primary motor cortical areas.

^{1,4}Cunnington R, ²Windischberger C, ¹Erdler M, ¹Deecke L, and ^{2,3}Moser E.

¹Department of Neurology; ²NMR Unit, Institute for Medical Physics; ³Centre for Magnetic Resonance Imaging, University of Vienna, Austria; and ⁴Department of Psychology, Monash University, Clayton, Australia.

The roles of premotor, supplementary motor and primary motor cortical areas in the organisation and control of voluntary movement have been studied using many different methods, all of which have differing strengths and weaknesses. Functional MRI provides high spatial resolution for localising sources of activation, and has the potential to provide reasonable temporal resolution; however, most studies of motor activation to date have used relatively long image repetition times and box-car type designs alternating between periods of rest and activation, thereby failing to take advantage of the potential improvement in temporal resolution of fMRI over other techniques based on the analysis of regional cerebral blood flow, such as PET.

The aim of this study was to examine activation associated with single movements of the 5th finger with both high temporal and spatial resolution. Single brain slices including regions of primary motor and premotor cortex were acquired either every 80 ms (for 4 mm square pixels) or 160 ms (for higher resolution 2 mm square pixels) while subjects performed a single extension of the 5th finger in response to an auditory cue.

It was then possible to plot blood oxygenation level (BOLD) changes over time within each pixel of the acquired slice (either 2 or 4 mm square regions of brain). Using the model-free fuzzy-clustering analysis (EvIdent 5.0: Institute for Biodiagnostics, National Research Council, Winnipeg, Canada), it was possible to extract different BOLD response time-courses which were related to the movement task, and to find the extent to which pixels within different brain regions showed these task-related activation time-courses.

Five right-handed healthy subjects were examined on a 3 T BRUKER Medspec S300 (Ettlingen, Germany) equipped with a whole-body gradient system and a birdcage head coil. Imaging was performed using a phase-corrected single-shot gradient-echo blipped EPI sequence. A single slice of 5mm thickness and FOV 256 by 256 mm was acquired using two different matrix sizes: 64x64 pixel (RBW=100kHz; TR=80 ms; 1500 repetitions) and 128x128 pixel (RBW=200kHz; TR=160 ms; 750 repetitions). Echo time (40 ms) and total acquisition time (60 s) were constant.

Fuzzy-clustering analysis was able to identify time-courses relating to physiological artefacts, such as heart rate and respiration, as well as activation time-courses relating to the finger movement task. Signal intensity changes of 5-10% were found, depending upon the duration of the finger movement performed. Activation time-courses with a peak following movement execution were found within primary motor cortex and SMA. Additional time-courses, most likely reflecting activation before movement onset and with peaks before those observed in primary motor cortex, were found in the SMA. Our results show that single-event fMRI, in conjunction with fuzzy-clustering analysis, is a powerful technique which is able to detect event-related activation patterns for single trials with both high temporal and spatial resolution.

Quantification of Supplementary Motor Area Activation with movements of different practice levels using Functional Magnetic Resonance Imaging at 3T

Erdler M.¹, Windischberger C.², Cunnington R.¹, Edward V.¹, Streibl B.¹, Gartus A.¹, Moser E.^{2,3}, Deecke L.¹, Beisteiner R.¹

¹Department of Neurology; ²NMR - Group –Institute for Medical Physics; ³MR unit, General Hospital and University of Vienna, Vienna Austria

Several studies described the effect of short and long term practice of movements on the activity of supplementary motor area (SMA). It was demonstrated that SMA activity decreases with higher levels of practice [e.g. 1]. The goal of this study was to quantify this effect objectively. 6 subjects took part in the experiments. They performed repetitive tapping of the 2nd and of the 5th finger paced by the scanner noise at a constant frequency of 1.6 Hz. Subjects were instructed to strictly avoid comovements of adjacent fingers. Tapping was performed in a blocked design (block duration 20 sec), alternating 2nd and 5th finger blocks were separated by blocks of rest. The measurements were carried out on a 3 Tesla BRUKER Medspect S300 scanner using a phase-corrected blipped GE single shot EPI sequence (TE/TR=84/4000ms, 128*128 matrix, 256*256 FOV, 13 adjacent axial slices, slice thickness 3mm). Images were realigned using AIR v3 with 3D sinc interpolation. Data was analyzed using a correlation technique. Active pixels in SMA were counted separately for the 2nd and the 5th finger tapping.

In all 6 subjects the number of active pixels in the SMA was larger when tapping the 5th finger. Over all subjects the cumulated number of SMA pixels was 21 pixels for the 2nd finger and 129 pixels for the 5th finger which corresponds to a 6 fold increase in pixel counts. A t-test confirmed a significant group difference ($t(5) = 2.58$, $p < 0.05$). Table 1 shows detailed results for each subject.

Subject #	# of pixels in SMA, 2 nd finger	# of pixels in SMA, 5 th finger
1	4	52
2	2	6
3	9	13
4	2	18
5	2	29
6	2	11

Table 1: the number of pixels in SMA are given for 2nd finger tapping and 5th finger tapping.

The large difference between the pixel counts demonstrates a high sensitivity of high field fMRI for activation changes in small brain areas. The results confirm dependance of SMA activation on practice levels of movements. This is probably due to increased demands for motor control with less trained movements as the optimum activation of appropriate sets of muscles with appropriate intensity and optimized coordination is not adequately stored.

[1] Hund, M. & von Cramon, D.Y. Dynamic changes of motor learning in piano players and normal controls visualized by 3T-fMRI. 4th Int conference on Functional Mapping of the Human Brain, Book of Abstracts, 1998, Montreal, Canada

Functional Discrimination of Thalamic Nuclei Using BOLD Contrast fMRI at 1.5 T

Dzemidzic, M., Lowe, M.J., Lurito, J.T., Mathews, V.P., and Phillips, M.D.

Department of Radiology, Indiana University School of Medicine, Indianapolis, IN, USA

Functional magnetic resonance imaging (fMRI) techniques have been used to detect neuronal activation in small gray matter structures of the thalamus at 1.5 tesla (T) and higher field strength [1,2]. Chen *et al.* [2] showed that at 4 T, the lateral geniculate nucleus of the thalamus and the pulvinar of the thalamus could be distinguished. The goal of this study is to demonstrate that blood-oxygenation level dependent (BOLD) contrast fMRI technique can be used to discriminate among adjacent thalamic nuclei at 1.5T.

Six normal subjects were studied in a protocol designed to detect thalamic activation in simple auditory and visual tasks. Time series BOLD-weighted data were obtained with Gradient Echo Echoplanar magnetic resonance imaging on a 1.5T General Electric Echospeed scanner. Single (3.5mm thick) axial slice through the lateral and medial geniculate nuclei was chosen on a whole head 3D Spoiled Grass T₁-weighted scan. Subjects were presented paradigms following 36-sec. "off"/36-sec. "on" patterns giving a boxcar reference function for expected activation patterns. Auditory stimuli consisted of fragments of narrative text (activation) interleaved with the ambient scanner noise (control). Visual stimuli included interleaved periods of black background with a colored fixation point (control) and a background of checkerboard pattern switching at 8 Hz with a colored fixation point (activation). All acquired data were spatially filtered with a Hamming-window to increase contrast-to-noise ratio [3]. The MRI time series at each pixel was fit using the least squares fit to a boxcar reference function, a slope, and an intercept. The ratio of the amplitude and error of the fit to the reference function needed to assign a Student's *t* to each pixel was used to calculate activation maps. A cluster analysis was applied to define the extent of the activation within a region-of-interest and to use the centroid of the cluster as the location of the primary activation.

Spatial correlation of significantly activated regions to high-resolution volumetric scans of the thalamus shows that the lateral geniculate nucleus is detected with 99.9% confidence in all subjects during execution of the visual task while bilateral medial geniculate nucleus is detected in all subjects during execution of the auditory task. This is the first illustration that the BOLD contrast at 1.5T can discriminate among adjacent thalamic nuclei. Implications on spatial resolution and subcortical contrast will be presented.

References:

- [1] Guimaraes, A.R., Melcher, J.R., Talavage, T.M., Baker, J.R., Ledden, P., Rosen, B.R., Kiang, N.Y., Fullerton, B.C., and Weisskoff, R.M., Imaging subcortical auditory activity in humans, *Hum. Brain Mapp.*, 1998, 6: 33-41.
- [2] Chen W., Cato, T., Zhu, X.H., Strupp J., Ogawa, S., and Ugurbil, K., Mapping of lateral geniculate nucleus activation during visual stimulation in human brain using fMRI, *Magn. Reson. Med.*, 1998, 39: 89-96.
- [3] Lowe, M.J. and Sorenson, J.A., Spatially filtering functional magnetic resonance imaging data, *Magn. Res. Med.*, 1997, 37: 723-729.

This work was supported by the Whitaker foundation.

Combined functional imaging using MEG, EEG and fMRI

Scherg M.¹, Goebel R.³, Stippich Ch.², D. Weckesser¹, H. Bornfleth¹, N. Ille¹, K. Drüen¹, S. Linek¹, P. Berg⁴

Departments of Neurology¹ and Neuroradiology², University Hospital Heidelberg, Heidelberg, Germany; Max Planck Institute for Brain Research³, Frankfurt, Germany; Department of Psychology⁴, Unversity of Konstanz, Konstanz, Germany

Modern neuroimaging methods, e.g. PET and fMRI, have demonstrated the highly specific functional organisation of the human brain. This multifocal organisation lends itself to a discrete multiple source model with fixed dipoles or regional sources as initially proposed by Scherg and von Cramon (1985, 1986) based on the anatomy, cycoarchitectonics and lesions studies. There are three main concepts in brain electromagnetic source analysis (BESA) using a multiple source model: 1. Data reduction to equivalent locations, orientations and source waveforms of the active brain regions. 2. The source waveforms provide a temporal dynamic image. They reflect an estimate of the compound activity of the active brain regions. 3. Hypothesis testing: the intrinsic data reduction permits the placing of sources into different brain regions to probe for the presence of source currents contributing to the surface signals.

Using this concept, MEG and EEG modeling benefits substantially from locations derived from fMRI BOLD clusters. However, errors in the scaling and coregistration of MRI and fMRI must be minimized for an adequate comparison and seeding of dipoles from fMRI BOLD clusters. Using examples from presurgical mapping and a visual flow-field experiment, possibilities and pitfalls can be illustrated. MEG and EEG source waveforms add crucial information in showing which fMRI clusters are involved in fast dynamic brain processes.

Application of Eigenspace Beamformer to Virtual Depth-Electrode Measurement Using MEG

Sekihara K.¹, Poeppel D.², Miyashita Y.¹

¹*JST Mind Articulation Project, Tokyo, Japan;* ²*University of Maryland, College Park, USA*

We have developed a method that can estimate the time course of a neural activity at a predetermined location with a high signal-to-noise ratio. Using this method, an MEG sensor array can perform like a virtual depth electrode *in vivo*. The developed method consists of two steps: the first step estimating the orientation of a neural source and the second step estimating its activity time course. The second step uses the eigenspace beamformer [1], which is known to give the signal-to-noise ratio higher than that from the conventional minimum-variance (MV) beamformer [2].

Let us define the measured data as $\mathbf{b}(t)$, its covariance matrix as $\mathbf{R}$, the noise covariance matrix as $\mathbf{C}$, and the lead-field matrix at $\mathbf{x}$ as $\mathbf{L}(\mathbf{x}) = [\mathbf{l}^o(\mathbf{x}), \mathbf{l}^a(\mathbf{x})]$. We first solve the generalized eigenvalue problem. $\mathbf{R}\mathbf{e}_j = \lambda\mathbf{C}\mathbf{e}_j$, and form matrices $\mathbf{E}_S$ and $\mathbf{E}_N$ whose columns consist of the signal- and noise-level eigenvectors, respectively. Let us define a diagonal matrix whose diagonal elements are signal-level eigenvalues as $\mathbf{\Lambda}_S$. Then, an eigenvector corresponding to the minimum eigenvalue of the matrix pencil $[\mathbf{L}^T(\mathbf{x})\mathbf{E}_N\mathbf{E}_N^T\mathbf{L}(\mathbf{x}), \mathbf{L}^T(\mathbf{x})\mathbf{C}^{-1}\mathbf{L}(\mathbf{x})]$ gives the orientation of the source at $\mathbf{x}$ [3]. Denoting this eigenvector as $\mathbf{u}$, the time course of the source at $\mathbf{x}$, $s(t)$, can be obtained by $s(t) = [\mathbf{l}^T(\mathbf{x})\mathbf{E}_S\mathbf{\Lambda}_S\mathbf{E}_S^T\mathbf{b}(t)]/[\mathbf{l}^T(\mathbf{x})\mathbf{E}_S\mathbf{\Lambda}_S^{-1}\mathbf{E}_S^T\mathbf{l}(\mathbf{x})]$, where $\mathbf{l}(\mathbf{x}) = \mathbf{L}(\mathbf{x})\mathbf{u}$.

The auditory-evoked fields (Fig. 1(a)) were measured using the 37-channel MagnesTM magnetometer installed at University of California, San Francisco. The time course of the N1m-source estimated by applying the proposed method is shown in Fig. 1(b). For comparison, we also applied the direct-matrix-inversion-type MV beamformer expressed as $s(t) = [\mathbf{l}^T(\mathbf{x})\mathbf{R}^{-1}\mathbf{b}(t)]/[\mathbf{l}^T(\mathbf{x})\mathbf{R}^{-1}\mathbf{l}(\mathbf{x})]$. The results from the MV beamformer (Fig. 1(c)) are noisy and almost meaningless. In contrast, the proposed eigenspace beamformer gives reasonable results, indicating the superiority of the proposed method.

References:

1. Yu, J.L., Yeh, C.C. *IEEE Trans. Signal Process.* 1995, 43: 2453-2461.
2. Frost, O.L. *Proceedings of the IEEE* 1972, 60: 926-935.
3. Ferrara, E.R., Parks, T.M. *IEEE Trans. Antennas and Propagation* 1983, 31: 231-236.

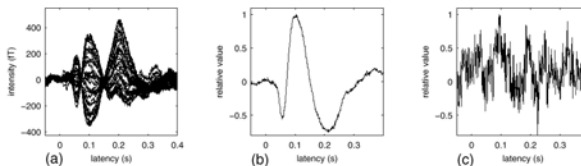


Figure 1: (a) Measured auditory field. Results from (a) the proposed method, and (c) the MV method.

Cortical oscillatory activity assessed by combined EEG and MEG recordings and High-Resolution ERD methods

Edlinger¹ G., Bastiaansen² M., Brunia² C., Neuper¹ C., Pfurtscheller¹ G.

¹*Department of Medical Informatics, Institute for Biomedical Engineering, and Ludwig Boltzmann Institute for Medical Informatics and Neuroinformatics, Graz University of Technology, Austria*

²*Psychonomics section, Tilburg University, Tilburg, Netherlands*

Event-related desynchronization (ERD) is a phenomenon of the awake brain and was quantified for the first time by [1]. ERD of alpha band rhythms can be seen as a correlate of activated cortical neurons and was reported during sensory, motor and cognitive processing. Combined EEG and MEG recordings have (at least partly) higher information content for identifying brain source activity than single EEG and MEG recordings. In order to investigate the usefulness of simultaneous EEG and MEG recordings the topographical differences in EEG and/or MEG maps based on simplex and complex self-paced finger movements are investigated. A total of 36 scalp electrodes and 150 gradiometers (CTF systems) are used simultaneously for recording EEG and MEG at the MEG center KNAW in Amsterdam, Netherlands. Data sets of six subjects are recorded. Optical switches detect the movement of index finger. Magnetic resonance images are available for constructing realistically shaped head models. All computations are performed using the boundary element method.

It is assumed that most of the ongoing EEG observed on the scalp (by EEG recordings) or outside the head (by MEG recordings) is due to superficially located neo-cortical sources. Dipole layers can describe the sources. Based on findings by [2, 3, 4] mainly radially orientated dipole-layers (with respect to the cortical surface) contribute to the observed ERD/ERS. Hence high-resolution ERD methods based on distributed cortical sources ([5]) combining biomagnetic and bioelectric data are applied to the acquired data sets. The aggregation of electric and magnetic lead field matrices is based on a procedure described by [6]. Results indicate that High-resolution ERD results based on combined measurements yield reliable and more stable inversely computed cortical source distributions than results obtained by EEG and MEG only.

[1] Pfurtscheller, G. and Aranibar, A. Event-related cortical desynchronization detected by power measurements of scalp EEG., *Electroencephalogr.Clin.Neurophysiol.*, 1977, 42:817-826.

[2] Pfurtscheller, G., Stancák, A. Jr, and Neuper, C. Post-movement beta synchronization. A correlate of an idling motor area?, *Electroencephalogr.Clin.Neurophysiol.*, 1996, 98:281-293.

[3] Edlinger, G., Pfurtscheller, G., van, Burik M., and Wach, P. Post-movement EEG synchronization studied with different high resolution methods., *Brain Topogr.*, 1997, 10:103-113.

[4] Edlinger, G., Wach, P., and Pfurtscheller, G. On the realization of an analytic high-resolution EEG., *IEEE Trans.Biomed.Eng.*, 1998, 45:736-745.

[5] Hämäläinen, M.S. and Ilmoniemi, R. J.Interpreting magnetic fields of the brain: Estimates of current distributions. Helsinki University of Technology. TKK-F-A559. 1984.

[6] Fuchs, M., Wagner, M., Wischmann, H. A., Köhler, T., Theissen, A., Drenckhahn, R., and Buchner, H. Improving source reconstructions by combining bioelectric and biomagnetic data., *Electroencephalogr.Clin.Neurophysiol.*, 1998, 107:93-111.

This work was supported by the Austrian "Fonds zur Förderung wissenschaftlicher Forschung", project P11571 and P12407.

Minimum l1-norm estimates in the analysis of MEG data

Uutela, K., Hämäläinen, M.

Brain Research Unit, Helsinki University of Technology, Finland

Neural currents can be estimated from magnetoencephalographic (MEG) measurements by employing a suitable source model. We have recently developed software to conveniently calculate minimum l1-norm estimates from MEG data. The result is the maximum a posteriori probability current estimate corresponding to an exponential a priori probability distribution for source strengths [1].

Compared with minimum l2-norm estimates, the l1-norm estimate explains the data with a few focal sources, which may well account for the currents activated in studies of sensory projection areas. Because the computation of the l1-norm estimate using traditional methods is very time consuming, we have developed a novel computational approach [2] which is sufficiently fast for on-line analysis of MEG data.

We analyzed the properties of baseline estimate noise and the spread of the estimate corresponding of a single focal source with stimulation studies. Because the l1-norm estimate is nonlinear, these results can not be directly generalized. An extended source or several distributed sources producing very similar magnetic fields typically yield an estimate with single, strong focal source.

We have used the method to study responses of several sensory modalities and activity during some cognitive tasks, and the results are promising. Strong active areas can be easily detected and the activity caused by measurement artifacts can be usually distinguished. Our method also facilitates the combination of measurements of several subjects or stimulus conditions.

References:

- [1] Matsuura, K., and Okabe, Y. Selective minimum-norm solution of the biomagnetic inverse problem, *IEEE Trans. Biomed. Eng.*, 1995, 42:608-615.
- [2] Uutela, K., Hämäläinen, M., and Somersalo, E. Visualization of Magnetoencephalographic Data using Minimum Current Estimates, *NeuroImage*, 1999, in press.

Cardiomagnetic Source Imaging Studies with Focal and Distributed Source Models

Nenonen J.^{1,2}, Pesola K.^{1,2}, Lötjönen J.^{1,2}, Lauerma K.⁴, Hänninen, H.^{2,3}, Korhonen, P.^{2,3}, Mäkijärvi, M.^{2,3}, Fenici, R.⁵, and Katila, T.^{1,2}

¹*Laboratory of Biomedical Engineering, Helsinki University of Technology, 02015 HUT, Espoo;*

²*Medical Engineering Centre, BioMag Laboratory,*

³*Division of Cardiology, and* ⁴*Department*

of Radiology, Helsinki University Central Hospital, 00290 Helsinki, Finland

⁵*Clinical Physiology - Biomagnetism Center, Catholic University of Rome, Italy*

During the recent years, magnetocardiographic (MCG) source imaging has received increasing interest [1]. Presently, the MCG is employed at some hospitals to test and further develop its clinical use [2]. The BioMag Laboratory at the Helsinki University Central Hospital (HUCH) is equipped with state-of-the-art facilities both for basic research and for clinical applications in functional cardiomagnetic studies [3]. We describe briefly the cardiomagnetic source imaging studies in association with the ongoing patient studies at the BioMag Laboratory.

We focus on three patient groups: 1) Fifteen patients have been studied with a non-magnetic pacing catheter, inserted in the heart during routine electrophysiological studies. 2) Nine patients suffering from chronic ischemia have been studied. The MCG and the BSPM data were recorded at resting state, and during ergometer exercise to induce acute ischemia. 3) Four arrhythmia patients undergoing open-chest surgery have been studied. Activation isochrones were reconstructed, and the results were compared directly with the epicardial activation maps recorded during the surgery.

Boundary-element torso models were generated for each patient individually using medical imaging data. Both focal (single current dipole) and distributed (equivalent current density, uniform double-layer) source models have been investigated.

In all 28 patients referred above, an invasively obtained localization result was used as the 'golden standard' to validate the MCG and BSPM inverse solutions. Both dipole locations [4] and estimated current densities on the heart surfaces [5] showed a good agreement with invasive data. The results suggest that the source imaging methods are valuable for providing advance information in pre-ablative evaluation of the patients.

References:

- [1] Hämaläinen, M.S., Nenonen, J. Magnetic source imaging. In: Webster, J., Ed. Encyclopedia of Electrical Engineering, Vol. 12. Wiley & Sons. New York, 1999, pp. 133–148.
- [2] Stroink, G., Moshage, W., Achenbach, S. Cardiomagnetism. In: Andrä, W., Nowak, H., Eds. Magnetism in Medicine. Wiley VCH, Berlin, 1998, pp. 136–189.
- [3] Nenonen, J. Multimodal cardiac source imaging studies in the BioMag Laboratory. Biomed. Technik, 1997, 42: 29–32.
- [4] Pesola, K., Nenonen, J., Fenici, R., Lötjönen, J., Mäkijärvi, M., Fenici, P., Korhonen, P., Lauerma, K., Valkonen, M., Toivonen, L., Katila, T. Bioelectromagnetic localization of the pacing catheter in the heart. Phys. Med. Biol., in press.
- [5] Pesola, K., Hänninen, H., Lauerma, K., Lötjönen, J., Mäkijärvi, M., Nenonen, J., Takala, P., Voipio-Pulkki, L.-M., Toivonen, L., Katila, T. Current density estimation on the left ventricular epicardium: A potential method for ischemia localization. This volume.

Spatial and Temporal Changes during the QT-Interval in the Magnetic Field of Patients with Coronary Artery Disease

Van Leeuwen P.¹, Hailer B.², Lange S.³, Donker D.⁴, Grönemeyer D.³

¹ Dept. of Biomagnetism, EFMT, Bochum, Germany; ² Department of Internal Medicine, Philippsstift, Essen, Germany; ³ Institute for Microtherapy, University of Witten/Herdecke, Bochum, Germany; ⁴ Dept. of Cardiology, University Hospital Maastricht, Maastricht, Netherlands

In the diagnosis of coronary artery disease, a number of standard noninvasive methods, such as ECG, nuclear imaging and (stress-) echocardiography are available. However, they have varying sensitivity and specificity, are not always practically applicable and may be associated with risk. On the basis of the noninvasive registration of cardiac activity with magnetocardiography, we have explored several approaches in the examination of patients with coronary artery disease.

We investigated healthy subjects without a history or evidence of cardiovascular disease (normal group, n=20), patients with significant narrowing ($\geq 75\%$) of at least 1 coronary artery but without prior myocardial infarction (CAD group, n=22) and patients with prior myocardial infarction (MI group, n=20). Magnetocardiograms (MCG) were recorded in all subjects for 60 s at rest using a 37-channel system (bandpass 1-200 Hz, sampling rate 1 kHz). On the basis of each subject's averaged data, the following methods were used to evaluate disease status. Magnetic field maps (MFM) were reconstructed and examined over the QRST interval on the basis of field strength, orientation and width. For a subset of subjects, the orientation and strength of equivalent current dipoles (ECD) were calculated at selected times between Q onset and T offset. Furthermore, in all subjects QT interval dispersion and the spatial variability of the QT interval duration were examined.

Of the spatial features of the magnetic field, orientation was altered in both patient groups throughout de- and repolarization, strength at repolarization begin. On the basis of $>10\%$ deviations from the normal course, the sensitivity of MFM orientation was 85% and 68% respectively for the MI and CAD groups, the specificity 85%. Those CAD patients who consistently showed fewer deviations from the normal values were less likely to have multivessel disease. ECD orientation was also similar for normal subjects. In all patients of the MI group and most in the CAD group, it deviated from the normal values at least one of the time points, in particular at T maximum and T offset. Sensitivity was 100% for MI and 80% for CAD, specificity was 90%. Of the temporal features, QT dispersion values were significantly higher in the patient groups ($p<0.05$ for CAD, $p<0.005$ for MI). When taking the spatial distribution of QT interval duration into account, discrimination between the normal and patient groups improved ($p<0.005$ and $p<0.0005$, respectively).

Various spatial and temporal features of the MCG may be examined during the QT interval to reveal differences between healthy subjects and patients with CAD. Of the magnetic field map characteristics, orientation during repolarization seems particularly sensitive to disease-induced changes. This is consistent with findings showing that magnetic iso-integral maps are more sensitive in the ST-T interval in patients after MI [1]. Also, body surface potential mapping may identify patients with CAD who have no changes in 12-lead ECG at rest [2]. Here we found that both the map features and variability in QT duration were altered in a large portion of patients who displayed no changes in ECG. This implies that MCG at rest may be used to identify patients with CAD not only after suffering myocardial damage due to MI but also those with normal left ventricular function but documented hemodynamically relevant stenosis of the coronary arteries.

References:

- [1] Lant, J., Stroink, G., ten Voorde, B.J., Horacek, B.M., Montague, T.J. Complementary nature of electrocardiographic and magnetocardiographic data, *J Electrocardiol*, 1990, 23:315-322.
- [2] Green, L.S., Lux, B.L., Haws, C.W. Detection and localization of coronary artery disease with body surface mapping in patients with normal electrocardiograms, *Circulation*, 1987, 76:1290-1297.

Current density estimation on the left ventricular epicardium: A potential method for ischemia localization

**Pesola K.^{1,2}, Hänninen H.^{2,3}, Lauerma K.⁴, Lötjönen J.¹, Mäkijärvi M.^{2,3},
Nenonen J.^{1,2}, Takala P.^{1,2}, Voipio-Pulkki L.-M.⁵, Toivonen L.^{2,3}, Katila
T.^{1,2}**

¹Laboratory of Biomedical Engineering, Helsinki University of Technology, Espoo, Finland;

²Medical Engineering Centre, BioMag Laboratory, ³Division of Cardiology, ⁴Division of Radiology,
Helsinki University Central Hospital (HUCH), Helsinki, Finland;

⁵Turku University Central Hospital, Turku, Finland

We have applied a multiple dipole source model in current density estimation (CDE) in the human heart from magnetocardiographic (MCG) measurements. A similar model has been applied previously, e.g., in localizing epicardial current sources [1] and in detecting decreased current amplitude in myocardial infarction (MI) patients [2]. In our study, the calculation points were located on the epicardial surface of the left ventricle. Triangulated, homogeneous torso models were used to model the volume conductor. The dipole moments were solved from magnetic field data using Tikhonov regularization. Simulated MCG data with realistic amount of measurement noise was used to study different regularization operators. Higher order regularization was found to be superior to zero order regularization. Promising results were obtained using a simple discrete approximation of the surface Laplacian [3] as the regularization operator.

In addition to simulations, CDE was applied in 13 coronary artery disease (CAD) patients. Four of the patients had single vessel disease with no previous MI. Nine patients had regional or global left ventricular dysfunction caused by severe chronic myocardial ischemia. MCG measurements were performed at rest and after stress with the 67-channel cardiomagnetometer in BioMag Laboratory at HUCH. Stress testing was performed using a non-magnetic stress ergometer, pedaled in supine position. Injury current density estimates were calculated in the ST-segment of the difference signal using individualized realistic left ventricle and torso models acquired from magnetic resonance imaging (MRI). In single vessel CAD patients, CDEs were compared to the areas of occlusion. In the other patient group, left ventricular function, and it's viability in dyskinetic areas were evaluated using MRI, single photon emission tomography (SPECT) and positron emission tomography (PET). The calculated CDEs were compared to the reference information about the ischemic areas in the left ventricle. The results of the study showed that CDE is a potential method to model ischemic myocardial injury currents.

References:

- [1] Ferguson, A.S., Vardy, D., et al. A regularized minimum norm method for calculating distributions of source currents on epicardial surfaces, In: Baumgartner, C., et al. Biomagnetism: Fundamental Research and Clinical Applications, Elsevier Science/IOS Press, 1995.
- [2] Leder, U., Pohl, H.P., et al. Noninvasive biomagnetic imaging in coronary artery disease based on individual current density maps of the heart, *Int. J. Cardiol.*, 1998, 64:83-92.
- [3] Huiskamp, G. Difference formulas for the surface Laplacian on a triangulated surface, *J. Comp. Phys.*, 1991, 95:477-496.

Validation of Noninvasive Functional Cardiac Electrical Source Imaging in a 43-year Old Male Patient

**Tilg B.^{1,2}, Modre R.¹, Fischer G.¹, SippensGroenewegen A.², Mlynash M.²,
Roithinger F.X.², Reddy G.³, Roberts T.³, Wach P.¹, Lesh M.D.², Steiner P.R.²**

¹*Institute of Biomedical Engineering, Technical University Graz, Graz, Austria*

²*Section of Cardiac Electrophysiology, Department of Medicine, ³Department of Radiology,
University of California San Francisco, San Francisco, California, USA*

Different approaches for electrical source imaging from electro- (ECG) and magnetocardiographic (MCG) mapping data have been developed during the last two decades. The most established inverse formulations are imaging of the activation time (AT) and epicardial potential pattern [3, 5]. Recently, an open chest validation study in humans was presented [4]. However, closed-chest validation in humans has not yet been reported. In this study, we compared noninvasively estimated and measured AT maps on the endocardium of the right ventricle (RV).

A 43-year old male without structural heart disease underwent an electrophysiological study for paroxysmal atrial fibrillation. A 164-point endocardial sinus rhythm AT map of the RV was measured with an electroanatomical catheter mapping system (CARTO Biosense/Johnson&Johnson [1]). The 62-channel ECG mapping data was simultaneously recorded. The MCG was measured on the anterior chest surface with a 37-channel magnetic field mapping system in a shielded room. The torso was imaged with a 1.5 Tesla magnetic resonance (MR) scanner. The entire volume conductor was modeled with 528 pseudo-subparametric high-order boundary elements (BEs). The endocardial surface of the RV was meshed with 70 BEs (212 nodal points). The AT pattern was estimated from the ECG and MCG data on the entire surface of the ventricle (246 BEs, 744 nodal points) applying the critical point theorem and a nonlinear optimization routine (E04UCF, NAG Ltd.) [3, 5].

The reconstructed and invasively recorded endocardial AT sequence of the RV showed good qualitative agreement. The measured and estimated AT interval was 51 and 53·10⁻³s, respectively. The inverse solutions from ECG and MCG data were also quite similar. The endo- and epicardial AT pattern of the left ventricle were found to be in accordance with previously published results [2].

A recently introduced electroanatomical catheter mapping system offers an excellent tool for a closed-chest validation of the electro- and magnetocardiographic inverse problem [1]. The favourable results achieved for sinus rhythm activity let one to expect that similar agreement can be obtained with ectopic or preexcited ventricular activation.

References:

- [1] Ben-Haim, S.A., Osadchy, D., Schuster, I., Gepstein, L., Hayam G., and Josephson, M.E. Nonfluoroscopic, in vivo navigation and mapping technology. *Nature Med.*, 1996, 2: 1393-1395.
- [2] Durrer D., van Dam R., Freud G., Janse M., Meijer F., Arzbacher R. Total excitation of the isolated human heart. *Circ.*, 1970, 41: 899-912.
- [3] Huiskamp, G., and Greensite, F. A new method for myocardial activation imaging, *IEEE Trans. Biomed. Eng.*, 1997, 44: 433-446.
- [4] Ostendorp, T., Pesola, K. Non-invasive determination of the activation time sequence of the heart: validation by comparison with invasive human data. In: *Computers in Cardiology 1998*, New York, NY, USA, IEEE, 25: 313-316.
- [5] Tilg, B. Noninvasive functional cardiac electrical source imaging. Thesis for Habilitation, Technical University Graz, Aachen, Verlag Shaker, 1998.

Magnetocardiography under Clinical Conditions

Erné, S.N.¹, Kammrath, H.G.¹, Ziolkowski, M.², Tenner, U.¹, Müller, H.-P.¹

¹*Division for Technical Bioelectromagnetism, Central Institute for Biomedical Engineering,
Ulm University, D – 89069 Ulm, Germany*

²*Szczecin Technical University, Al. Piastow 19, PL - 70310, Szczecin, Poland*

During the last years several algorithms and analysis procedures were developed for the evaluation of biomagnetic and bioelectric data. To obtain clinical validation, an MCG system especially designed for clinical studies on large patient number has been installed in Ulm.

This MCG system is using a map of 55 magnetic channels, three orthogonal electrocardiographic (ECG) leads and a breathing channel. For a raw patient positioning a set of laser markers is used. The patient positioning unit (PPU) determines the patient position relative to the sensor array using three coils on a cross that is fixed along the sternum of the patient. The corresponding PPU measurement takes only few seconds before the five minutes MCG measurement starts.

At the beginning the Biomagnetic Analysis Console (BAC) software was used [1]. Now, the standard analysis tool is the Open Magnetic and Electric Graphic Analysis (OMEGA) software [2]. This software contains established time series analysis algorithms with their extensions to MCG data as well as tools for the localization of cardiac electromagnetic sources.

The OMEGA software is using different analysis algorithms under exactly defined preprocessing conditions on the same data set to pursue synergetic interactions. As analysis methods are included frequency analysis, binomial filtering, Simson analysis, heart beat variability, principle component analysis, smoothness test as well as the visualization of the field distribution. Spatio-temporal analysis and current source localization methods are implemented as well. These methods are using localized (dipole) sources or distributed sources. Tools for generating 3D models obtained from Magnetic Resonance Imaging (MRI) are included. 2D/3D visualization of the results of the electromagnetic source reconstruction in the morphologic environment is also possible.

Within a training study some 70 MCG measurements have been performed. The volunteers have been selected having no reported cardiac diseases. During the course of the training study the measurement protocol was iteratively improved. An optimized recording strategy and an optimized measurement position for the patient has been defined and can be set up within a few minutes, so that an MCG measurement can be performed within 10 minutes.

[1] K. Martin, S.N. Ern , C. Law, J. Mallick, B. Tatar, Multiple Modality Biomagnetic Analysis System, 10th International Conference on Biomagnetism, BIOMAG '96, Santa Fe, USA, 1996.

[2] U. Tenner, H. Kammrath, S.N. Ern , OMEGA Open Magnetic and Electric Graphic Analysis, 8th International Congress on Holter and Noninvasive Electrocardiology, Ulm, Germany, 1998.

Topographic Presentation of the Dipolar Content of Cardiac Electric Field

Bacharova L.1, Chorvat D.1, Mateasik A.1, Titomir L.I.2

1International Laser Center, Bratislava, Slovakia

2Institute of Problems of Information Transmission RAS, Moscow, Russia

To demonstrate a bio-mathematical model for the topographic presentation of orthogonal electrocardiograms and to present reference values of dipolar electrocardiogram of ventricular depolarization.

In dipolar electrocarditopography (DECARTO), orthogonal ECG signals are transformed by means of a simple mathematical model to represent the equivalent generator of the cardiac electric field as a uniform double layer with time varying size and location on a spherical surface approximating the ventricular wall, called the image sphere. Ventricular activation is represented by time series of maps of activated points on the image surface. More compact, but also easily perceived visualization of the same data may be obtained in the form of summary maps of cardiac excitation, or chronotopocardiograms. Decartograms can be presented in a form of discrete spherical image surface in a shape of rectangle, other planar projection of sphere, or in 3D presentation. The reference values were calculated from a sample of healthy population (total number 123 subjects, 54 women, 69 men), for the Frank orthogonal electrocardiogram.

Electrocardiotopograms are presented in the form of a rectangle (matrix of 11 lines, 24 columns). For each point of this matrix the value of relative frequency (probability) of its occurrence in activated state is given in a sample of healthy population.

Visualization of physically corrected orthogonal ECG lead signals as vectorcardiographic loops and determination of the spatial localization of instantaneous vector end-points enable the physician to find the bridge in his conceptual model between characteristics of myocardial activation propagation and abstract representation of the cardiac electric field. Treatment of the same signals as dipolar electrocardiograms aids in finding topographical relations between body surface electrical events and the activation process in the myocardium. This approach aids also in understanding and analysis of body surface potential maps obtained by separate procedures.

References:

[1] Titomir, L.I., Ruttkay-Nedecky, I.: Chronotopocardiography: A new method for presentation of orthogonal electrocardiograms and vectorcardiograms. *Int. J. Bio-Medical Computing*, 1987, 20:275-282.

The Clinical Use of MEG Activity Associated with Brain Lesions

Vieth J.B., Kober H., Ganslandt O.¹⁾, Kamada K.

*Dept. of experimental Neuropsychiatry and ¹⁾Neurosurgery,
University of Erlangen-Nuernberg, Germany*

In border zones of brain lesions abnormal focal spontaneous brain activity may occur in the MEG (and the EEG), as slow and fast wave lesional activity, and as epileptic spike and seizure activity. Clinically it is very important to know the location and the extent of these abnormal sources, but also the exact location of the normal evoked and event related activity around brain lesions, especially when they should be removed surgically.

In order to localize focal normal or abnormal brain activity the multisource problem must be handled. Therefore we developed two three-dimensionally working spatio-temporal averaging MEG tools: (1) the dipole-density-plot (DDP), which is showing the concentration of dipoles over the analyzing time, and (2) the current localization by spatial filtering (CLSF), which is showing the current intensity for either individual time instants or over the analyzing time, the current-density-plot (CDP).

Thus we were able to show clinical applications with different progress towards clinical usefulness and relevance. The applications were validated by using structural lesions when applicable.

Normal activity:

1. Routine application is established with the intraoperatively used neuronavigator to determine the relation of tumors to the cortical somato-sensory, motory, auditory and cortical speech areas. The validation showed in 50 cases the coincidence of the the somato-sensory MEG approach exactly with the results of intraoperatively used evoked epicortical potentials approach in the postcentral gyrus.
2. In two studies we found in subjects (6 cases) and tumor patients (15 cases) a typical constant dislocation of around 1 cm between the neuronal activity (MEG) and the venous drainage marking of the functional MRI (fMRI).

Abnormal activity:

1. In presurgical evaluation of epileptic patients we (19 cases) and C.C. Gallen (29 cases) showed, the easy performable localization of the epileptogenic lesion. The clinical relevance still depends on the statistical testing of the reliability of the easy obtainable MEG localization of the epileptogenic lesion compared to the localiazation of the irritative and the epileptogenic zone.
 2. Our further studies showed, that clinical relevance might be possible for the localization of the functional lesions associated with strokes, transient ischemic attacks (also "silent" ones), white matter lesions (MS, lacunar infarcts), and those in Rolandic epilepsy (in addition to sharp waves also activity of functional lesional activity).
 3. In patients with brain infarctions and tumors we looked for the significance of metabolic MR spectroscopy localizations of lactate and aspartate in comparison to the abnormal MEG activity. The results revealed a correlation of the intensity of the abnormal MEG and the concentration of aspartate showing a relatively large border zone.
- So, some clinical MEG applications reached the level of routine work, but other applications still need a broader testing for clinically accepted relevance.

Applications of MEG to the Mapping of the Language Cortex

**Papanicolaou, A.C.,¹ Simos, P.,¹ Breier, J.I.,¹ Zouridakis, G.,¹
Constantinou, J.,² Wheless, J.W.,² Maggio, W.W.¹**

*The University of Texas Health Science Center, Departments of Neurosurgery¹ and Neurology²,
Houston, Texas U.S.A.*

Two complimentary procedures, one involving visual and the other auditory activation tasks, have been developed for mapping the receptive language cortex in individual normal subjects, in epileptic and other neurosurgical patients and in children with developmental dyslexia. The reliability of the cortical maps was first established in a series of normative studies involving over 100 normal volunteers. The specific aims of the first study were: (1) to verify that early components of Evoked Fields (EFs) to visually and aurally presented words were due to activation of the primary visual and auditory cortex, respectively; and (2) that the degree of activation resulting in the early (EF) components was bilaterally symmetrical, whereas late EF components, associated with either aurally or visually presented words, reflected predominantly left hemisphere activation involving the posterior temporal and parietal cortex. Both aims were achieved. The aim of the second and third studies was to replicate the first and to control for the possibility that the hemispheric asymmetry in the degree of activation that accounts for the late EF components were not language-specific but, instead, a peculiar feature of all late EF components. In the second study, subjects performed an auditory word recognition task and a control task involving recognition of non-linguistic sounds. In the third study, subjects performed a visual recognition task involving the same words as in the second and a control task involving recognition of faces. In both experiments, the overwhelming majority of individuals showed bilaterally symmetric activation profiles in the control tasks but clearly asymmetric profiles involving Wernicke's area in both linguistic tasks. The three studies considered together demonstrated the reliability and the validity of the MEG mapping procedures for groups of normal subjects. The test-retest reliability of the procedures was then confirmed in a fourth study. All of these studies are summarized in a recent publication [1]. Subsequently, two validation studies were initiated, the first for the purpose of determining the accuracy of MEG in predicting hemispheric dominance for language and the second for assessing its accuracy in identifying the language-specific regions within the dominant hemisphere. Thus far, 25 epilepsy patients have participated in the first study. In all 25 cases, we have obtained excellent agreement between the predictions of MEG regarding hemispheric dominance and the results of the "Wada procedure" (which is considered to be the "gold standard" for such determinations). In the second study, 14 patients have been thus far enrolled. In all 14 cases, the cortical regions within the dominant hemisphere identified by MEG as language-specific have also been found to be such using direct, cortical stimulation mapping, intraoperatively. These results clearly support the notion that MEG-derived maps are valid and highly specific. In addition, we have obtained evidence, with 18 dyslexics, that although the cortical maps are essentially identical in normal readers and dyslexics for aural language processing, all dyslexics have distinctly different maps from those of normal readers for tasks that require reading. The implications of these clinical investigations for the future of MEG as a diagnostic modality will be discussed.

[1] Papanicolaou, A.C., Simos, P.G., et al. Magnetoencephalographic mapping of the language specific cortex, *Journal of Neurosurgery*, 1999, 90:85-93.

Functional Mapping of Speech Evoked Brain Activity by Magnetoencephalography and its Clinical Application

M. Möller¹, H. Kober², O. Ganslandt¹, Ch. Nimsky¹, R. Fahlbusch¹

¹Department of Neurosurgery, University of Erlangen-Nürnberg, Erlangen, Germany

²Biomagnetism Group, University of Erlangen-Nürnberg, Erlangen, Germany

Rationale: In this study we investigated the speech related cortex activation by magnetoencephalography (MEG) to localize the motor and sensory speech area and to identify the speech dominant hemisphere in neurosurgical patients and subjects. To avoid postoperative speech disorder in brain tumor patients we applied presurgical functional mapping of speech related sources and used the localization intraoperatively in a neuronavigation system.

Methods: We investigated 27 cases (11 healthy subjects and 16 brain tumor patients) simultaneously over both hemispheres with a 2x37 channel biomagnetic system. All subjects and 14 patients were tested by the Edinburgh Handedness Inventory. Patients had to name pictograms and to read mono-syllable words silently in two separate sessions. About 280 meaningful and 140 meaningless stimuli were randomized displayed for 800 ms with an interstimulus interval of 2351 ms and a variation of 500 ms on a screen in front of the subject's face. Motion and eye movement artefacts were manually removed. The recorded data was digitally notch-filtered at 50 Hz. To enhance speech-relevant magnetic signals the averaged meaningless dataset was subtracted from the meaningful. We developed a laterality index between left and right cortex activation to determine the speech dominant hemisphere individually for each patient. MEG-results were superimposed on MR-images by a contour-fit program and intraoperatively displayed in a neuronavigation system in three cases.

Results: The exact analysis of the time course of cortex activation revealed early activation occipital in the visual cortex and in the right fusiform gyrus. Sources at a latency around 350 ms could be localized in the sensory speech area (Wernicke). Motor speech area (Broca) was activated around 500 ms. Further activity could mainly be located in the frontal lobe and insula. In all subjects and in 15 of 16 patients the left Wernicke area was clearly identified, the Broca area could be located in the left hemisphere in 10 subjects and in 12 patients. We also found right activation in the posterior temporal lobe and in the inferior frontal gyrus whereas these activations were not as strong as those in the left hemisphere. The laterality index of Wernicke and Broca signal intensity identified speech dominance in the left hemisphere in all investigated cases. In three patients MEG-localizations were displayed in a neuronavigation-system and used as intraoperative landmarks. Postoperatively no deterioration of the speech ability could be observed.

Discussion: Functional mapping by MEG is a noninvasive and accurate method to investigate the exact time course during speech processing and to localize speech related sources. In neurosurgical application MEG can help estimating the risk of postoperative speech disorder in patients with brain tumors in the vicinity of speech-eloquent areas by identifying the speech dominant hemisphere and assists in planning the extension of surgery by localizing language-related brain areas preoperatively. The intraoperative use of MEG-localizations in a neuronavigation-system can support the orientation in the operation field and so reduce the risk of postoperative aphasia.

Scalp current density(SCD) mapping of cerebral activity during object and space selection in humans

1,2Zani A., 1Avella C., 2Lilli S., 2Proverbio A.M.

1Cognitive Electrophysiology Lab, Istituto di Psicologia del CNR, Roma, Italy

2Cognitive Electrophysiology Lab, Department of Psychology, University of Trieste, Trieste, Italy

In the present study we investigated object and space brain selection mechanisms by recording event-related potentials (ERPs) of the brain in humans with an high-density electrode montage (32 channels). The same stimuli (1 and 6 cpd equiluminant black-and-white gratings presented in the two upper hemifields of the visual space) were presented in two different tasks in which participants had to attend selectively and respond to either one spatial frequency (*object selection*) independent of its location or one location (*space selection*) independent of stimulus spatial frequency.

Consistent with previous studies, attention modulation showed early attention effects in both types of selection mechanisms. In particular, in the spatial location task, attention modulated P1 amplitude as early as 100ms at extra-striate sites [1], as shown by scalp current density (SCD) maps, whereas in the frequency selection task, attention modulation started as early as 60-80 msec at both striate and extra-striate areas [2].

Reaction times (RTs) were about 100 ms faster in the location than the frequency selection task. Different morphologies and SCD topographical distribution characterized ERPs obtained in the two selection modes over the posterior regions of the scalp. ERPs for space selection were characterized by a prominent P1 peaking at about 140 ms, followed by a tiny N1 and a very early P300 component. Conversely, ERPs for object selection showed an early PN80 deflection followed by a prominent selection negativity (SN) and a delayed late positive component (LPC). Spatio-temporal SCD mapping in the P1-PN80 range for the two attention modes showed topographies centered at lateral-occipital sites (extra-striate areas) for space selection and at mesial-occipital, posterior-temporal, and parietal-occipital sites (striate and extra-striate areas) for object selection. SCD mapping in the SN latency range for object selection showed a neat focus centered at the inferior-lateral-occipital electrode sites at Inion level (IN3/IN4) progressively shifting in time toward the lateral-occipital (OL/OR) and posterior-temporal (T5/T6) locations.

These findings suggest two anatomically and functionally distinct neural mechanisms for space and object selection. These data are different from those obtained in space and object feature-conjunction selection tasks e.g., [3] where the selection of space and object is carried out in parallel but not independently from one another. This further supports the view [2, 3] that attention-conjunction effects are not simply additive in nature but reflect complex interactions between different neural attentional mechanisms.

References:

- [1] Heinze, H.J., Mangun, G.R., et al. 1994 Combined spatial and temporal imaging of brain activity during visual selective attention in humans, *Nature*, 1994, 372:543-546.
- [2] Zani, A. and Proverbio, A.M. ERP signs of early selective attention effects to check size, *EEG Clin. Neurophysiol.*, 1995, 95:277-292.
- [3] Zani, A. and Proverbio, A.M. Attention modulation of early components of ERPs to lateralized gratings in the upper and lower visual quadrants, *J. Psychophysiol.*, 1997, 11:21-32.

Spatio-temporal mapping of electrocortical activity during selective processing of colour and shape in humans

¹Proverbio A.M., ¹Burco F., ^{1,2}Zani A.

¹*Cognitive Electrophysiology Lab, Department of Psychology, Univ. of Trieste, 34123 Trieste, Italy*

²*Cognitive Electrophysiology Lab, Istituto di Psicologia, CNR, Viale Marx 15, 00137 Rome, Italy*

High spatial resolution neuroimaging techniques have indicated that different brain regions are activated during selective processing of shapes and/or colour: i.e., bilateral temporal regions (areas 22), left parietal region (area 39), left dorsal occipital region (area 18) and bilateral parahippocampal regions for the former, and bilateral occipital regions (areas 18 and 19) for the latter [1]. Studies of selection of colour or combinations of colour and other features (e.g., check size [2], orientation [3]) with high temporal resolution event-related potentials (ERPs) have indicated the timing of colour selective neural processing modulation, starting as early as 100 msec post-stimulus in form of a P130, and continuing with a prominent selection negativity (SN) and a broadly distributed P300. This is consistent with the view of early selection effects for non-spatial stimulus features [4]. Dipole modelling analysis applied to the high resolution electrode montage localized the sources of the early P130 and SN at the dorsolateral occipital and ventral occipital (close to the collateral sulcus) regions [2], respectively, consistent with neuroimaging findings.

In the present study, we further investigated colour processing from an ecological point of view. ERPs were recorded with a 32 channels montage from the scalp of 8 healthy young volunteers who viewed and selectively attended different sorts of pictures of familiar objects and animals presented in different colours (a 'prototypical' one - e.g., a green crocodile - and other samples of the same shape in different colours - e.g., pink and yellow crocodiles) in the central visual field of a PC monitor. Volunteers had to select and respond to the pictures either on the basis of the colour (colour selection) independent of their shape, or on the basis of the shape represented (object selection) independent of its colour. ERP results indicated that selection of the two dimensions occurred in parallel but not independently of one another, and affected the amplitude of the occipital P1 (P110), N1 (N166) and SN (N278) components, and the central-parietal P300 one. Overall, object selection produced larger and later N2 and P300 components, as opposed to colour selection, thus indicating that object processing is more source demanding. Very interestingly, SN responses to colour selection were significantly affected by object content, but not viceversa. More specifically, when engaged in selecting a colour (e.g., green) and a shape (object or animal) was displayed that "prototypically" had that colour in nature (e.g., a green crocodile), volunteers' SN responses resulted significantly larger than when the shape presented was not "prototypical" in that colour (e.g., a green lamb) especially over the left hemisphere.

Spatio-temporal mapping revealed that for colour selection SN displayed two foci bilaterally centered at ventral mesial- and lateral-occipital sites (IN1, IN3 and IN2, IN4), whereas for shape selection this component was more diffusely bilaterally distributed at ventral (IN1, IN3, and IN2, IN4) and dorsal mesial- and lateral-occipital, and posterior temporal sites (O1, OL, T5, and O2, OR, T6). Mapping of 'prototypical colour' attentional difference waves (i.e., prototypical minus universal) displayed a large focus centered at ventral lateral-occipital sites. The focus was mostly asymmetrically spread toward the left hemisphere.

[1] Corbetta, M., Miezin, F.M., Shulman, G.L., and Petersen, S.E., Attentional modulation of neural processing of shape, color, and velocity in humans. *Science*, 1990, 248: 1556-1559.

[2] Karayanidis, F., and Michie, P.T., Evidence of visual processing negativity with attention to orientation and color in central space. *Electroencephalogr Clin Neurophysiol*, 1997, 103: 282-297.

[3] Anllo-Vento, L., Luck, S.J., and Hillyard, S.A., Spatio-temporal dynamics of attention to color: Evidence from human electrophysiology. *Hum Brain Map*, 1998, 6: 216-238.

[4] Zani, A., and Proverbio, A.M., ERP signs of early selective attention effects to check size. *Electroencephalogr Clin Neurophysiol*, 1995, 95: 277-292.

Are functional imaging procedures clinically useful?

Papanicolaou, A. C.

The University of Texas Medical School, Houston, USA

Functional imaging through quantitative electroencephalography (EEG), Transcranial Magnetic Stimulation (TMS), Magnetoencephalography (MEG), also known as Magnetic Source Imaging (MSI), Positron Emission Tomography (PET), Single Photon Emission Computed Tomography (SPECT) and functional Magnetic Resonance Imaging (fMRI), has made tremendous progress during the last decade. Especially impressive has been the progress made in imaging the profiles of brain activation during performance of cognitive tasks. Such profiles, if sufficiently reliable and sufficiently task-specific, may be construed as outlines of the brain mechanisms of higher functions whether linguistic, mnemonic or perceptual. Aside from the indisputable contribution of such images to Cognitive Neuroscience, they may also prove practically useful in clinical practice, as an adjunct of as a substitute of more traditional but invasive procedures like the Wada procedure for determining hemispheric dominance for memory and language or the intraoperative electrical stimulation mapping procedures for determining what cortical regions, within a hemisphere partake in the mechanism of verbal functions.

The purpose of this workshop is to discuss how close is each of the various functional imaging methods to fulfilling the requirements of clinical diagnostic procedures, namely, reliability, validity, sensitivity and specificity. Evidence, involving extensive neurosurgical patient samples, to the effect that MEG may be as efficient in determining hemispheric dominance for language as the traditional Wada procedure and as efficient in identifying specific regions involved in these functions, within the dominant hemisphere, as the traditional intraoperative stimulation mapping, will be presented. Moreover, further plans of improving and extending these procedures to mapping non-linguistic functions, or functions, like memory, involving difficult to image medial brain regions, , will be discussed.

Similar discussions, in the context of this workshop, regarding the promise and the accomplishments of other functional imaging modalities and other forms of their clinical applications, will hopefully result in a fair assessment of the relative efficacy of each method, for each particular clinical application, thus fulfilling the express purpose of this workshop.

New Bioelectromagnetic Imaging Methods for Clinical Use

Ilmoniemi, Risto J.¹ and Aronen, Hannu J.^{1,2}

¹*BioMag Laboratory, Medical Engineering Centre, Helsinki University Central Hospital, P.O. Box 508, FIN-00029 HYKS, Finland; E-mail: rji@biomag.helsinki.fi*

²*Department of Radiology, Helsinki University Central Hospital, P.O. Box 380, FIN-00029 HYKS, Finland; E-mail: hannu.aronen@huch.fi*

Magnetoencephalography (MEG) and electroencephalography (EEG) allow the direct measurement of electrical cerebral activity. Combined with anatomical information from magnetic resonance imaging (MRI) and functional MRI (fMRI), a detailed picture of the spatiotemporal pattern of brain activity can be obtained. On the other hand, transcranial magnetic stimulation (TMS) can be applied to the brain in order to activate cortical neurons, allowing a wide range of studies of reactivity, functional organization and dynamics of neuronal processing.

We have integrated to our 122-channel MEG (Neuromag Ltd.) array a 64-channel EEG system, being thus able to record the complete electromagnetic map of brain activity in one shot. Present clinical applications of MEG include presurgical localization of functional brain areas and the characterization of epilepsy prior to surgery. We have compared MEG and functional MRI localization of somatosensory activation, concluding that the combination of MEG and fMRI is far more reliable than the use of either method alone in the mapping of brain activation patterns. In stroke patients, we have studied the functions of the primary and secondary somatosensory cortices, finding changes in cortical responses that accompany the recovery of the patient's symptoms.

We have combined stereotactic TMS with 60-channel high-resolution EEG, being able to measure cortical TMS-evoked responses. The local response provides an index of reactivity of the cortex while distant activity gives a measure of connectivity. The traditional use of TMS has included the evaluation of motor pathways. For example, in multiple sclerosis, the longer-than-normal central motor conduction time can be used as a diagnostic indicator. In head injuries and in stroke, on the other hand, TMS may be used to evaluate the severity of pyramidal tract damage.

The combination of stereotactic TMS and high-resolution EEG will provide new diagnostic possibilities. It has been suggested that TMS responses may be used for the early prediction of stroke recovery. TMS may also provide an effective method for locating functional areas prior to brain surgery. Local reactivity to TMS may be altered in patients with stroke, epilepsy, migraine, or degenerative diseases. Any defects in white matter tracts (caused, *e.g.*, by multiple sclerosis, stroke, trauma or neoplasia) may cause changes in functional connectivity, which can be directly studied by combined TMS and EEG measurements.

Our research strategy is to develop and validate imaging facilities that allow us to explore brain function in health and in disease. Standardized material from normal subjects have been collected. We can also follow changes in brain function in various pathological conditions such as brain tumor and ischemic strokes. The existing clinical applications of MEG, *i.e.*, presurgical localization of functional areas and the characterization of epileptic activity, require the use of 3D conventional MRI. The combination of fMRI and MEG enables us to compare fMRI and MEG results and, using fMRI as a constraint for the MEG inverse solution, source localization can be significantly improved. The integration of various functional brain imaging techniques offers the most precise spatiotemporal window into the function of the human brain.

Clinical DC applications using MEG: Moving the curtains aside

Bowyer S.M.

Henry Ford Hospital, Detroit, MI

Direct Current Magnetoencephalography is the somewhat misused term describing extremely low frequency phenomena. DC changes take place in the cellular environment over a long period of time. Biomedical data analysis is usually conducted using a variety of filters such as: band passes, notch filters, and high or low-pass filters. These filters act like curtains by blocking out signals that until now have been considered unimportant. The information contained in these signals however, may be useful in the clinical evaluation of a number of neurological disorders such as: Migraine [1], Epilepsy [2], Stroke [3], TIA [4], Anoxia [5], and Nerve and Muscle injury [6]. Modern Electroencephalographic (EEG) recordings are not capable of resolving the DC signal, due to electrode/skin interface noise. Until recently Electroencephalographic (ECoG) has been the only reliable method for observing extremely slow signals from the brain; however this requires direct contact with the cortical surface. MEG has emerged as an alternative modality capable of observing DC signals arising from the human brain, in a non-invasive manner. In 1987, KMA Welch predicted that if SCD was the underlying mechanism of migraine, then MEG technology could be used to detect migraine [1]. For the past 11 years the Henry Ford Hospital-Oakland University (HFH-OU) group has been using a 7-channel Neuromagnetometer, to conduct DC-MEG studies [7,8]. In migraine patients we have found that the data revealed a reduction of spontaneous EEG and MEG activity during migraine with aura [9]. Gardner-Medwin et al. (1991) measured DC magnetic fields from rabbit cortex in vivo during SCD [10], to better understand MEG signals of SCD. Recently we have used a micro squid to characterize the MEG signals from a gyrencephalic and a lissencephalic brain during propagation of SCD [11,12]. Using rats, Chen et al (1992) detected DC MEG signals arising from ischemia[3], and Takinashi et al (1991), detected DC MEG signals during anoxia[5]. Curio et al. (1993) found observable DC-MEG signals arising from nerve and muscle injuries [6]. In 1998, in studies of human subjects, both Saligram et al.[2] and Wübbler et al.[13] used changes in position of the subject to extract the DC amplitude of the underlying DC field. These studies have increased our understanding of waveforms arising from direct current changes in the cellular environment.

DC-MEG signals were observed in spontaneous and evoked migraine auras using two different BTi neuromagnetometers, Model 607 and WHS magnes 2500. These signals were consistent with those expected to arise during the propagation of an underlying hyperexcited wave, such as SCD. These DC-MEG shifts were not seen in the controls. The MEG field patterns seen in the evoked data were of similar morphology to those observed in the spontaneous data and can be interpreted as arising from similar underlying electrical activity. Further studies utilizing the larger 148-channel neuromagnetometer array, will help to obtain a more concise picture of what may be occurring in the cortex of migraine-with-aura patients

References

- [1]Welch, et al.: The concept of migraine as a state of central neuronal hyperexcitability. *Neurol Clin*; 8: 817-82, 1990.
- [2]Saligram U, et al.: Measurement and quantification of interictal and postictal DC magnetic field shifts in unilateral temporal lobe epilepsy. 11th International Biomagnetism Conference 1998, Sendai, Japan. In press.
- [3]Chen Q, et al.: Magnetoencephalography of focal ischemia, *Stroke* 23:1299-1303 1992.
- [4]Vieth J, et al.:Functional 3D localization of cerebrovascular accidents by magnetoencephalography (MEG), *NeurolRes*1992;14(2Suppl):132-4
- [5]Takanashi Y, et al.: Magnetic fields associated with anoxic depolarisation in anesthetized rats, *Brain Res*, 562:13-16, 1991
- [6]Curio G, et al.: Non-invasive neuromagnetic monitoring of nerve and muscle injury currents, *EEG Clin. Neurophysiol.* 89:154-160, 1993.
- [7]Barkley GL, et al.: Techniques for DC Magnetoencephalography, *J of Clinical Neurophysiol.* 8(2):189-199, 1991.
- [8]Tepley N, et al.: A technique for sequential measurements of DC neuromagnetic, *EEG Clin. Neurophysiol.* 99:16-18, 1996.
- [9]Barkley GL, et al.: Magnetoencephalographic Studies of Migraine, *Headache* 30(7):428-434, 1990.
- [10]Gardner-Medwin AR, et al.: Magnetic fields associated with spreading depression in anesthetized rabbits, *Brain Res* 540:153-158, 1991.
- [11]Bowyer SM, et. al: Currents underlying MEG signals of spreading cortical depression in a rabbit model. 11th International Biomagnetism Conference 1998, Sendai, Japan. In press.
- [12]Bowyer SM, et. al: Currents underlying MEG signals of spreading cortical depression in swine. 11th International Biomagnetism Conference 1998, Sendai, Japan. In press.
- [13] Wübbeler G, et al.: Mesurement of near-DC Biomagnetic Fields of the head unisg a horizontal moculation of the body postion. 11th International Biomagnetism Conference 1998, Sendai, Japan. In press.

Functional Magnetic Resonance Imaging in Real Time on a Clinical Whole Body Scanner

S. Posse

Institute of Medicine, Research Center Jülich GmbH, D-52425 Jülich, Germany

Real-time fMRI is a new modality which enables online assessment of subject performance and data quality. It facilitates rapid optimization of measurement parameters and paradigms. It also has the potential to facilitate fMRI in the clinical setting, thus saving cost and time.

We have implemented and tested real-time fMRI on a conventional 1.5 Tesla Vision scanner (Siemens Medical Systems, Germany) using a variety of external hardware platforms (from PC to Supercomputer depending on application) for real-time data analysis. Activation tasks using single block design included standard sensory and motor paradigms (visual stimulation, finger tapping, foot movements, auditory attention etc.) and higher cognitive tasks such as word generation and mood induction.

Multi-slice echo-planar imaging with real-time image reconstruction was performed on more than 50 subject. Enhanced functional sensitivity as compared to conventional echo-planar imaging was obtained by using real-time single-shot spectroscopic imaging of water relaxation [1]. Dynamic brain activation maps were computed using "sliding-window" correlation analysis [2]. For time critical applications, such as automatic optimization of the reference vector [3], higher order detrending of nonstimulus correlated signals and motion correction [4], which cannot be performed simultaneously in real-time on a workstation, parts of the software were implemented on a Cray T3E massively-parallel computer.

Signal changes in sensory and motor cortices in response to visual stimulation, finger tapping, foot movements and auditory attention were clearly observable within seconds of task initiation. Visual activation in response to brief light flashes (as short as 500 ms) was observable in real time. Even signal changes in response to single finger movements were observable in real time in primary motor cortex and supplementary motor cortex. Lateralized signal changes in response to a word generation paradigm were reproducibly measurable using single block design. In preliminary experiments even mood related signal changes in subcortical regions were measurable in real time. In conclusion, real-time fMRI is a new tool which enables robust and rapid functional mapping of primary sensory and motor cortices, and localization of higher cognitive functions.

References:

- Posse, S., et al., Magn. Reson. Med. (in press)
- Gembris, D., et al., Proc. Intern. Soc. for Magn. Res. in Med. 1998,1486
- Gembris, D. et. al., Neuroimage (in press)
- Mathiak, K, Posse, S, Neuroimage (in press)

In collaboration with Siemens Medical Systems, Erlangen, Germany.

Supported by EU grant BIOMED II PL 950870.

Plasticity of Cortical Representations in Humans: Principles and Clinical Implications

Sterr, A.

Department of Psychology, University of Konstanz; Konstanz; Germany

The brain has the potential to reorganize the functional organization of its neural networks and even to alter its structure in response to experience. On a microscopic scale, structural changes include alterations in synaptic efficacy, synapse formation, synaptic plasticity, spine density, and alterations in dendritic length. As a consequence, supportive tissue elements such as astrocytes and blood vessels are also changed. The representational maps can alter their functional organization also in the macroscopic range. These maps are not only highly plastic during ‘critical periods’ in the development of cortical structures but maintain limited ability to respond to alterations in afferent input throughout life. Reorganization of cortical representations is linked to altered perception and behavior. In most cases the perceptual consequences are adaptive in nature but maladaptive consequences have also been described e.g. in tinnitus or focal hand dystonia.

Animal and non-invasive studies in humans on brain plasticity have uncovered the basic principles which guide representational reorganization. This knowledge provides powerful opportunities for clinical applications e.g. after brain injury or in regards to the treatment of maladaptive consequences of brain plasticity. The talk will focus on the empirical evidence for brain plasticity and the implications of this knowledge for clinical applications.

Work was supported by the Deutsche Forschungsgemeinschaft

A Multipurpose 67 Channel Biomagnetometer

Van Leeuwen P.¹, Hoormann J.², Hailer B.³, Mackert B.M.⁴, Stroink G.⁵

¹ Dept. of Biomagnetism, EFMT, Bochum, Germany; ² Institut für Arbeitsphysiologie, Dortmund, Germany; ³ Department of Internal Medicine, Philippsstift, Essen, Germany; ⁴ Neurophysics Group, Dept. of Neurology, Freie Universität Berlin, Germany; ⁵ Dept. of Physics, Dalhousie University, Halifax, Canada

The trend in the development of large scale multichannel biomagnetometers over recent years has been focused on whole head systems [1,2,3]. Such systems have hundreds of channels with magnetometer as well as gradiometer sensing coils and they implement both hardware and software techniques for noise and artifact suppression. However, as they are designed for magnetoencephalographic applications, the shape of the dewar tip restricts their use to the examination of the activity of the central nervous system. Accordingly there is a need for a corresponding sensor for the registration of biomagnetic signals from other organ systems. In the following we describe such a system and its possible fields of application.

The BTi 1300C is a 67 channel magnetometer system based on the technology of the Magnes 2500WH which is a 148 channel whole head system [1]. The sensors of the 1300C are arranged concentrically on a slightly curved surface (r_c 52 cm) which has a diameter of 32.4 cm and covers an area of 800 cm². The diameter of the sensing coils is 28 mm, their spacing is approximately 38 mm. The distance of the coils to the bottom of the dewar is ≤ 16 mm. Environmental noise cancellation is possible on the basis of an array of ambient noise detectors. Intrinsic system noise is specified as ≤ 10 fT/ $\sqrt{\text{Hz}}$ average over frequency and across all channels. Simultaneous acquisition of the magnetic channels and up to 48 external channels at acquisition rates over 4 KHz is possible.

The 1300C was primarily designed for the registration of magnetocardiographic signals. Dewar tip shape allows for appropriate coverage of the frontal thorax with a single placement of the sensor. This permits the reconstruction and analysis of comprehensive cardiac magnetic field maps in the frontal plane and corresponding localization of activity. System sensitivity as well as sensor shape and size also facilitate the acquisition of fetal cardiac and adult gastroenterological activity. With a single sensor placement, fetal cardiac signals can be easily identified in the raw signal: in the second trimester QRS complexes and often P-waves are evident, later in pregnancy T-waves may be found. In gastroenterological acquisitions we have demonstrated slow wave activity with a 3 cpm peak consistent with spontaneous gastric activity. Neurological applications include the registration of peripheral and central neural activity. The relatively flat shape of the sensor is suited for magnetoneurography. We have measured tibial nerve somatosensory evoked magnetic fields at the body surface over the lower back allowing visualization of the propagation of compound action currents deep inside the body along fibers of plexus, nerve roots and cauda equina. Furthermore the system does not preclude magnetoencephalography: for example, stimulus locked auditory fields have been registered and evaluated. Thus, measurements in various areas of application have been successfully performed with the 1300C and have demonstrated the viability of such a multipurpose biomagnetic system.

References

- [1] Buchanan, D.S., Warden, L., Johnson, R.T. Optimized design for a whole head biomagnetism sensor. In: Aine, C., Okada, Y.C., Stroink, G., Swithenby, S., Wood, C. Advances in Biomagnetism Research: Biomag '96, New York, Springer, 1998: in print.
- [2] Vrba, J., Angus, V., Betts, K., et al. 143 channel whole cortex MEG system. In: Aine, C., Okada, Y.C., Stroink, G., Swithenby, S., Wood, C. Advances in Biomagnetism Research: Biomag '96, New York, Springer, 1998: in print.
- [3] Hämäläinen, M.S. An integrated MEG EEG system for clinical studies, Biomed Tech, 1997, 42 (1):68-71.

Magnetic Source Imaging Based on Magnetocardiographic Recordings

Nowak H.^{1,2}, Leder U.³, Pohl P.³, Haueisen J.²

¹JENASENSORIC, Jena, Germany

²Biomagnetic Centre, University, Jena, Germany

³Clinic of Internal Medicine, University, Jena, Germany

The application of inverse-solution-based analysis of magnetic fields has become known as Magnetic Source Imaging (MSI), a combination of magnetocardiography (MCG) with magnetic resonance imaging (MRI) as a source imaging technique. Multisensor magnetocardiography achieved by sophisticated solutions of the inverse problem of electrocardiography may be of additional diagnostic value in clinical cardiology. This method can be applied as a non-invasive imaging procedure to detect electrically unstable myocardium e.g. after infarction [1]. Furthermore, the non-invasive pre-interventional examination of patients suffering from coronary artery disease may provide an application of magnetic source imaging which is as fascinating as it is difficult.

Magnetocardiograms were taken using a multisensor device (Philips). The device consists of two sensor heads, each holding 31 sensors. The recording time was set to 100 to 600 s (1000 Hz sampling rate). The sensor heads were tilted by about 30°. The coordinates of the torso relative to the multichannel system were determined by localising the center coordinates of 10 coilsets. MRIs were taken with a 1.5 T machine (Philips Gyroscan® ACS II). Prior to investigation, coilsets were replaced by oil pills. A series of 40 to 60 transverse slices (5 mm thick, T1 weighted turbo field echo scan) were taken. The scan time window was placed in the late enddiastolic heart phase at R upstroke. The data processing, i.e. segmentation of three-dimensional surfaces, calculation of current densities, and presentation of results was done with the software package Curry® made by Philips.

Images of distributed cardiac source activity were obtained in 23 patients after myocardial infarction and in 25 patients/normals without a history of infarction. The presence of infarction (ECG, history, elevated blood level of cardiac enzymes) was proven by angiography. Constraints (minimum norm, lead field normalisation, noise regularisation, anatomical restriction) were used to obtain a unique solution. Current density was assigned to patches of the left ventricular endocardial surface. The resultant images were compared to regional wall motion in left ventriculography.

The vast majority of myocardial segments with wall motion abnormalities (hypokinesia, akinesia, dyskinesia) were identified by magnetic source imaging (low current density). However, in some segments (predominantly inferior) disagreement was found. The subjects without a history of infarction had only few segments with abnormal low current density.

The study demonstrates that inverse solutions aimed at current density calculations on realistic myocardial surfaces have the potential to identify and image electrical properties of the myocardium in coronary artery disease. However, further development of reconstruction algorithms and clinical studies including other reference procedures (PET, scintigraphy) are of paramount importance to the method.

References:

[1] Leder, U., Haueisen, J., Huck, M. and Nowak, H. Non-invasive imaging of arrhythmogenic left-ventricular myocardium after infarction. THE LANCET, 1998, 352, 1825

Spatial mapping of beta oscillations in central EEG after voluntary movement of different limbs

Neuper, C., Edlinger, G., Pfurtscheller, G.

Department of Medical Informatics, Institute for Biomedical Engineering, and Ludwig Boltzmann Institute for Medical Informatics and Neuroinformatics, Graz University of Technology, Austria

After performance of a voluntary movement bursts of central beta activity in the 13- to 30-Hz frequency range can be found. Previous studies suggest that these short-lasting bursts of beta oscillations occur in the first second after termination of movement and display largest amplitudes close to the corresponding primary sensorimotor area [1,2]. Moreover, there is some evidence that the frequencies of these induced beta oscillations depend on the recording site within the sensorimotor strip [3]. The aim of this study was to analyze the somatotopic organization of the frequency of post-movement beta oscillations.

Event-related EEG changes after movements of different limbs were investigated using a self-paced movement paradigm. EEG was recorded from 60 electrodes placed over central and related areas, equally spaced with approximately 2.5cm distance. EEG data were processed time-locked to movement-offset. In order to identify the dominant frequency of induced beta oscillations, the continuous wavelet transformation was used. The surface Laplacian method was applied to bandpass-filtered single-trial EEG data. Spatial maps and band power time courses were analyzed by quantifying the event-related (de)synchronization (ERD/ERS). For selected subjects, the spatial distribution of the beta band ERS was calculated for the cortical surface of a realistic head model constructed from MR images [4].

The findings suggest that the induced beta oscillations are slightly slower close to the hand representation area as compared to more medial sites. The frequency of the beta activity appears to differentiate signals from various sensorimotor areas corresponding to the functional cortical representation of different limbs (motor homunculus).

References:

- [1] Salmelin, R., Härmäläinen, M., Kajola, M. and Hari, R., Functional segregation of movement-related rhythmic activity in the human brain, *Neuroimage*, 1995, 2: 237-243.
- [2] Neuper, C. and Pfurtscheller, G., Post-movement synchronization of beta rhythms in the EEG over the cortical foot area in man, *Neurosci. Lett.*, 1996, 216: 17-20.
- [3] Pfurtscheller, G., Pichler-Zalaudek, K. and Neuper, C. ERD and ERS in voluntary movement of different limbs. In: Pfurtscheller, G., Lopes da Silva, F.H. (Eds.), *Event-Related Desynchronization and Related Oscillatory Phenomena of the Brain*, Handbook of Electroenceph. and Clin. Neurophysiol., Revised Edition Vol. 6., Elsevier, Amsterdam. in press 1999.
- [4] Edlinger, G., Pfurtscheller, G., van Burik, M. and Wach, P., Post-Movement EEG Synchronization studied with different high-resolution methods, 1997, *Brain Topogr.*, 10 (2): 103-113.

This work was supported by the Austrian "Fonds zur Förderung wissenschaftlicher Forschung", project P11571 and P12407.

ERP mapping of brain activation during phonological processing

¹Proverbio A.M., ¹Lilli S., ², ¹Zani A.

¹Cognitive Electrophysiology Lab, Department of Psychology, University of Trieste, Trieste, Italy

²Cognitive Electrophysiology Lab, Istituto di Psicologia del CNR, Roma, Italy

Event-related potentials (ERPs) of the brain were recorded with a 32channels montage in healthy young volunteers during a phonological decision task. Participants were required to judge whether a visually presented three letters syllable was included or not in a target word by making a two-choices button-press. Syllables were randomly presented in upper case in the central visual field. Half of them were included in the target words at the beginning, in the middle, or in the final part. Their pronunciation was the same whether in isolation or within the word. Target words were not actually presented to subjects, but suggested by means of a unique definition visually presented on a computer screen.

ERPs to stems correctly judged as included in the target word displayed a large P300 component. Spatio-temporal mapping showed a large focus centered at central-parietal scalp areas. In contrast, ERPs to stems not included in the target words elicited a series of negative potentials, very likely reflecting the response to phonological incongruence. Spatio-temporal mapping of ERP waves showed that the effect of phonological incongruence on ERPs amplitude was evident as early as 185 msec centered over left and right lateral-occipital (OL/OR electrode sites, halfway between O1/O2 and T5/T6 electrode sites) areas. Neuroimaging CT scanning evidence is forthcoming to suggest that these sites fall on the extrastriate areas of the occipital lobes [1]. These high-temporal resolution ERPs indicate an early timing of activation for extrastriate regions during visually-coded phonological processing.

Overall, these data suggest that at a very early stage of linguistic analysis, phonological processing of simple word-stems may be carried out on the basis of a purely visual code, and that this coded processing is carried out by extrastriate regions of the occipital lobes of the brain, indicated by neuroimaging studies (PET) as the locus of word form system analysis [2].

References

- [1] Homan R.W., Herman J., and Purdy P., Cerebral location of international 10-20 system electrode placement, *EEG and Clin. Neurophysiol.*, 1987, 66: 376-382.
- [2] Petersen S.E., Fox, P.T., Posner, M.I., Mintun, M. and Raichle, M.E., Positron emission tomography studies of the processing of single words, *J. Cognitive Neurosci.*, 1996, 1: 153-170.

Anatomically-Constrained MEG Activity to Faces with Normal or Distorted Feature Arrangement and Facial Outline

Marinkovic K.¹, Dale, A.², Halgren, E.^{1,3}

¹Radiology, University of Utah, Salt Lake City, USA, ²MGH-NMR, Harvard Medical School, USA, ³INSERM E 9926, Marseilles, France

The importance of the fusiform gyrus for face processing has been demonstrated with a variety of brain-imaging techniques and its activation has shown to be face-specific when compared to complex meaningful visual stimuli including animal faces, objects and animal bodies. The purpose of this study was to identify the spatiotemporal pattern of cortical activation to normal or inverted human faces and face-like stimuli with distorted feature localization or facial outline in order to obtain more finely tuned face-specificity.

Four right-handed men were instructed to passively observe six different types of grayscale stimuli including normal face photographs (NF), faces with unnaturally rearranged features (URF), blank faces (preserved normal face outline with no features: BL), inverted faces (INV), normal facial features presented in an egg-shaped oval (EGG) and randomly distorted stimuli so that they were no longer recognizable as faces (RND). All of the stimuli were presented on a gray background, had the same size, face-like shape and subtending 2.8° - 4° in the same location in the visual field. There were six different stimuli in each of the six conditions, with a hundred presentations per condition. Pictures were presented for 225 ms once per second. MEG signals were recorded with a whole head 306-channel Neuromag magnetometer. Each person's cortical surface was reconstructed from high-resolution T1 MRI scans [1] and used to constrain a minimum norm inverse solution [2].

Activation spread from the retinotopic areas to the temporal pole along the inferoventral temporal lobe (tl) on the right and posterior superior temporal sulcus (sts) on the left at about 115 ms, followed by strong inferoventral tl activation, especially on the right at about 165 ms, with the second peak at about 240 ms. Overall, the activation to the NF was right-lateralized, with more right anterior tl activation, as compared to the more posterior sts activity on the left. The activity evoked by the URF images was not clearly lateralized and it included more posterior tl sites as compared to NF. Blank faces evoked much less overall activation than NF which differed from NF by a focal activation at 240 ms in the posterior middle temporal gyrus. INV also evoked a less lateralized activity, with more posterior and inferior parietal activation on the right as compared to NF. EGG-shaped faces with normal features evoked very comparable activity to NF, although the NF evoked more activity on the right at 240 ms. Finally, the randomized images (RND) evoked quite a different pattern as compared to NF, involving the posterior temporo-occipito-parietal junction and not activating the inferoventral anterior temporal lobe.

In sum, normal faces evoked a right-lateralized activity in the posterior and inferoventral temporal lobe. Images with correct feature locations but lacking a facial outline evoked activity most comparable to that evoked by normal faces. In contrast, a facial outline without features was not effective in evoking an activation similar to NF.

[1] Dale, A.M., Fischl, B., and Sereno, M.I. Cortical surface-based analysis. I. Segmentation and surface reconstruction, *NeuroImage*, 1999 9:179-94.

[2]. Dale, A.M., and Sereno, M.I. Improved localization of cortical activity by combining EEG and MEG with MRI cortical surface reconstruction: A linear approach, *J. Cog. Neurosci.* 1993, 5:162-176.

Supported by USPHS NS18741 and HFSP0 RG 25/96. Thanks to C. Rabbal, P.Dhond, D. Post, K. Paulson and J.D. Lewine

Dynamic Functional Imaging by Combined MEG, EEG and fMRI in a Case of Cortical Myoclonus

**Bornfleth H.¹, Scherg M.¹, Meinck H.M.¹, Stippich C.², Goebel R.³,
Weckesser D.¹, Drüen K.¹, Tauberschmidt E.¹, Berg P.⁴**

Departments of Neurology¹ and Neuroradiology², University Hospital Heidelberg, Heidelberg, Germany; Max Planck Institute for Brain Research³, Frankfurt, Germany; Department of Psychology⁴, University of Konstanz, Konstanz, Germany

The independent recording of EEG/MEG and fMRI allows to combine the superior spatial resolution of fMRI with the excellent temporal resolution of EEG/MEG. EEG and MEG signals reflect the spatio-temporal overlap of the brain activities involved in performing a specific task. A discrete, reductionist model can be generated by assigning an equivalent source to each active region or area. The case of cortical myoclonus studied here showed a complex temporal pattern of cortical activation preceding myoclonic jerks, or following somatosensory stimulation. Locations and orientations of equivalent sources were revealed by spatio-temporal multiple source analysis (MSA). fMRI blood oxygen level-dependent (BOLD) clusters were used for the seeding of dipoles and for the validation of independently obtained MSA solutions.

In a 49-year old female with myoclonic epilepsy continuous EEG (29 channels), MEG (Neuromag-122) and EMG (FDI right and left) were recorded simultaneously. Electrode positions and reference points on the head were digitized using a Polhemus 3D digitizing system. Four head coils were used to obtain the transformation matrix from the MEG device coordinate system to the device-independent head coordinate system. MRI was acquired using a Picker Edge 1.5T EPI system. fMRI was obtained during a motor task and tactile stimulation. Coregistration with MRI was achieved by fitting the digitized surface points, coils and electrodes to the skin surface reconstructed from MRI. When electrode and coil thicknesses as well as linear distortion of the MRI were considered, mean fitting errors of less than 2 mm were obtained. Jerk-locked averaging to spontaneous myoclonus in the muscles of both hands, averaging of SEP/SEFs to median nerve and tactile finger stimulation, source analysis, MRI coregistration and fMRI analysis were performed using the BESA99 and BrainVoyager programs. Equivalent sources were modeled using a four-shell ellipsoidal volume conductor model of the head for the EEG and a spherical model for MEG. The head center for both models was determined from the T1-weighted MR images.

MSA succeeded in separating the temporal activation patterns underlying both EEG and MEG with consistent waveforms. Unilateral jerks in hand muscles were preceded by central rhythmic activity which could be modeled by deep equivalent generators comprising premotor cortex and SMA. The cascade of fast activities involved the contralateral motor and premotor cortex, postcentral gyrus and the descending pathway. Somatosensory stimulation triggered a dynamic network involving contralateral somatosensory, motor and premotor cortex, followed within a few milliseconds by ipsilateral motor cortex. Equivalent sources obtained by MSA were localized in close proximity to the BOLD clusters in fMRI. fMRI could thus be used to validate the MSA results on the one hand. On the other hand, MRI-seeded sources can help to establish initial multiple source models and provide probes to estimate the dynamics of the underlying brain activation.

Signal to Noise Improvement in fMRI Analysis

Ern  S.N.¹, M ller H.-P.¹, Kammrath H.G.¹, Tomczak R.², Wunderlich A.²

¹*Central Institute for Biomedical Engineering, Ulm University, D-89069 Ulm, Germany*

²*Department for Diagnostic Radiology, University Clinic Ulm, D-89069 Ulm, Germany*

During the last years interest has grown in novel methods for mapping human brain function based on the technique of functional magnetic resonance imaging (fMRI). The methods have good spatial resolution. The resolution is limited most likely only by the precision of the adjustment of the blood flow in time and space to the metabolic demands of neuronal activity.

To evaluate the fMRI image series sophisticated algorithms and great computational power are needed to separate the pathological irregularities from artefacts resulting from patient movement or MRI detection techniques. Additionally, variable visualisation possibilities are necessary to allow for an interpretation of the results.

In the work presented here, algorithms have been developed that allow for fast and user independent motion correction of fMRI image series. Some 60 volumes each consisting of some 16 slices can be motion corrected within a few minutes.

A new analysis algorithm to detect brain activation, based on an improvement of the signal to noise ratio has been developed. The noise reduction is obtained by averaging of voxels that are assumed to belong to the same activated morphologic region. The analysis is based on a cluster analysis that works with categorised data analysis. Here the similarity of the voxels is defined on the basis of several properties:

- Intensity of stimulus correlated signals.
- Correlation of the time course of the voxels.
- Geometrical distance (near voxels are more likely to belong to the same structure).

Finally, the activation can be estimated either statistically (Kolmogorov-Smirnov test) or deterministic (amplitude of the stimulus correlated signals).

These and other analysis algorithms are implemented in the FAMIS (Functional Analysis and Morphologic Imaging Software). It contains several parts for fMRI data processing and for the visualisation of the results:

- Algorithms for motion correction caused by translation as well as by rotational patient movements.
- A visualisation package for the morphologic MRI data sets.
- Algorithms to detect brain activation.
- Integration of functional results to the morphologic environment.

As a first validation data base, some ten fMRI data sets have been analysed.

Influence of stimulus sequence in blocked-designed paradigms on fMRI localization results

**Lanzenberger R.¹, Streibl B.¹, Cunnington R.¹, Windischberger C.²,
Edward V.¹, Erdler M.¹, Gartus A.¹, Moser E.^{2,3}, Beisteiner R.¹**

¹ Department of Neurology, ² NRM-Group – Institute for Medical Physics; ³ MR-Unit
General Hospital and University of Vienna, Vienna, Austria

Blocked designs are a widely-used paradigm in fMRI research [1]. However, the effects of block order when investigating two or more different tasks have not yet been thoroughly investigated. We compared the localization of cortical activation in a single task repetitive blocked design with the localization in a double task alternating blocked design. The blocks consisted of tapping the right 2nd or 5th finger. The purpose of this study was to investigate changes in activation centers and strengths due to different stimulus order.

Fifteen healthy right-handed subjects (10 male, 5 female) participated in the present study. In a “single finger” paradigm, they performed three blocks of repetitive tapping of either the 2nd or 5th finger alternating with rest. In a “double finger” paradigm, a 2nd–rest–5th–rest sequence was cycled three times. Finger tapping was paced by the sound of the scanner at the frequency of 1.6 Hz and instructions to start and stop tapping were given verbally. The durations of the finger tapping and rest periods were 20 seconds each.

The measurements were performed on a 3 Tesla BRUKER MR-Unit using a GE single shot EPI sequence (TE/TR=84.1/4000ms, 128*128 matrix, 256*256 FOV; 10 axial slices, slice thickness 3 mm).

Images were realigned with a 3Dsinc interpolation using the software package AIR 3.0 (Automated Image Registration). Correlation analysis was performed with the software package EVIDENT 5.0 using a correlation threshold of 0.6 and a box-car reference function. Activations in the left primary sensory-motorcortex were determined separately for the 2nd and 5th finger. The center of mass of all related pixels for the analyzed slices of every subject was computed using in-house software and displayed as 3D vectors.

In order to reduce the effect of differing brain sizes, we computed the difference in location between the two fingers in all three spatial dimensions. A t-test for vector components showed a significant difference between the single and double finger paradigms ($t(15) = 2.6$, $p = 0.021$) for the anterior-posterior direction. In order to evaluate the activity levels of 2nd and 5th finger, also we tested the number of pixels. A t-test for activity confirmed a significant difference between the stimulation paradigms ($t(15) = 2.83$, $p = 0.013$).

These results suggest that changes in block sequence can significantly affect the magnitude and localization of activation. Follow-up studies with more subjects would be useful for a comprehensive assessment.

[1] Wexler, B.E., Fulbright, R.K., Lacadie, C.M.. An fMRI study of the human cortical motor system response to increasing functional demands, Magnetic Resonance Imaging, 1997, 15:385-396

Physical Phantoms for Biomagnetic and Bioelectric Measurements

Tenner U.¹, Erné S.N.¹, Haueisen J.², Nowak H.², Brauer H.³

¹University of Ulm, Ulm, Germany

²Friedrich-Schiller-University, Jena, Germany

³Technical University of Ilmenau, Ilmenau, Germany

Due to the non-uniqueness of the inverse problem, source reconstruction is only possible under restricted conditions regarding volume conductors and sources.

The simplest source model is the current dipole which is a good approximation for focal sources. Current topics of research in bioelectromagnetism are algorithms for reconstruction of extended current sources by solving the inverse problem. It is useful to perform magnetic and electrical measurements with physical phantoms under well-defined conditions to validate the models and to calibrate the measuring systems. One advantage of physical phantom measurements over pure simulation studies, is that the former takes into account real world influences such as environmental noise and 3-D positioning errors, thus providing an error estimation of the entire source reconstruction procedure.

We developed four physical phantoms for biomagnetic investigations.

- A tank model with octagonal cross section for basic studies.
- A realistically shaped thorax phantom including 138 surface electrodes (Ag/AgCl) to perform magnetic field mapping (MFM) and body surface potential mapping (BSPM) simultaneously as well as to separate magnetic and electrical studies.
- A spherical model with a diameter of 100 mm to characterize the minimum distance resolution between two dipole sources and validate the localization algorithms used in basic research on animals.
- A head model consisting of a plastic cylinder with a rounded top for testing helmet systems.

We developed five special source modules, that can be interchangeably fixed on a ground plate at a defined position at the interior back of the phantom or in the head model. Four of the source modules consist of a set of multiple dipoles. The other module consists of an extended current source (butterfly source model) with variable position and orientation.

The thorax phantom was filled with NaCl solution. A special polymer membrane was used to model different conductive compartments in the thorax. Different conductivities were established by filling the partial subvolumina with different NaCl concentrations. The membran allows free ionic current flow while keeping the conductivity differences in the compartments.

Magnetic Resonance Images (MRI) data of the physical phantom models were used to obtain geometric description of the volume conductor for the Boundary Element Method.

The described physical phantoms has proved to be suitable for estimating the accuracy of biomagnetic measuring systems.

Voxel conductivity changes in aFEM head model for MEG and EEG forwards computations

Jens Hauelsen ¹, Ceon Ramon ², Hartmut Brauer ³, Hannes Nowak ¹

¹Biomagnetisches Zentrum, Friedrich-Schiller-Universität, Jena, Germany

²Center for Bioengineering, University of Washington, Seattle, U.S.A.

³Inst für Allgem. Und Theoret. Elektrotechnik, TU Ilmaneu, Germany

The *in vivo* conductivity values of the different tissues of the human head are needed for forward and inverse modeling in magnetoencephalography (MEG) and electroencephalography (EEG). However, *in vivo* conductivity values are difficult to obtain and the values in the literature are not always reliable. A technique which extracts the conductivity tensor information from diffusion tensor magnetic resonance imaging (MRI) proposed by Tuch et al. [1] is likely to overcome these problems. With this technique individual conductivity tensor information for every patient can be used for modeling in MEG and EEG. This technique does not rely on tissue classification or compartment segmentation but on the overlay of anatomical and conductivity tensor information obtained by MRI. However, this modeling technique is influenced by the signal to noise ratio of the two MRI data sets and the errors introduced by overlaying the anatomical and the conductivity tensor MRI information.

In order to quantify the influence of such possible errors we computed neuromagnetic fields and electric scalp potentials using an isotropic high resolution finite element method (FEM) model of the human head. Since we expected the largest influence in the vicinity of the source, the aim of this study was to examine the influence of local tissue conductivity changes in the vicinity of the source on the neuromagnetic field and the electric scalp potential. We varied the conductivity value of single voxels in the vicinity of the source and computed subsequently correlation coefficients and amplitude changes of fields and potentials. A single dipole was located in gray matter (0.33 S/m) and gray matter voxels in the vicinity of the dipole were changed to csf (1.78 S/m) or white matter (0.14 S/m).

As expected, conductivity changes in voxels adjacent to the dipole produced the largest influence on both the magnetic field and the electric potential. In those voxels, the magnetic field amplitude was more influenced than the electric potential amplitude. Furthermore, only conductivity changes in those voxels showed a significant influence on the magnetic field and the electric potential topology (correlation coefficient).

According to our experiences, the lowest correlation coefficient obtained (0.98) could produce a dipolar source mislocalization of up to 1.5 cm while a correlation coefficient of 0.999 (one voxel away from the source) will result in not more than approximately 1 mm mislocalization. Thus, only large changes in the conductivity in the voxels adjacent to the dipolar source will yield significant errors in source localization procedures.

In conclusion, it seems that relatively small conductivity changes as possibly introduced by low signal to noise ratio or artefacts in the conductivity tensor MRI do not have a significant influence on MEG/EEG source localizations.

References:

[1] Tuch, D.S., Wedeen, V.J., Dale, A.M., and Belliveau, J.W. Electrical conductivity tensor map of the human brain using NMR diffusion imaging: An effective medium approach. In: Proc. Sixth Ann. Meeting Int. Soc. Magn. Res. Med., Sydney, Australia, 1998.

Localization of tactile, electrical and pain evoked fields: A comparison using whole head MEG

Sterr, A., Kreyer, I. and Elbert, T.

Department of Psychology, University of Konstanz; Konstanz; Germany

Noninvasive functional brain mapping and neuromagnetic source imaging in particular can reveal various aspects of somatotopy in the human cortex. For this purpose, electrical or tactile stimulation has been applied to the peripheral sites. Both stimulation methods have assets and drawbacks and both may produce different outcome. Here, we compare within subjects tactualy (TL) electrically (EL) and pain-induced (PN) evoked magnetic fields (EFs) applied to either thumb (D1) or little finger (D5). A whole head Neuromagnetometer (148 channels, BTi) was employed allowing simultaneous monitoring of ipsi- and contralateral activation. The aim of the study was (1) to characterize discrepancies and similarities between the different EFs and their source localization and (2) to determine the magnitude of ipsilateral activation. Five male right-handed student subjects participated in the study. A 2x3 design comprising the experimental variables **STIMULUS MODALITY** (tactile (TL), electrical non painful (EL) and electrical painful (PN) and **STIMULUS LOCATION** (D₁ vs. D₅ of the right hand) was used. Six conditions (TL-D₁; EL-D₁; PN-D₁; TL-D₅; EL-D₅; PN-D₅) were presented block wise according to a fixed irregular order. In each block 250 trials were presented with a randomized ISI of 450-550 ms. The study was approved by the ethics committee of the University of Konstanz and informed consent was signed by all subjects prior to investigation. Data recording was performed in supine position. The frequency range was set to 0.1-200Hz with 520.5 Hz sampling rate. Stimulus locked epochs of 300 ms (151.21 ms pre- & 147.85 ms post-trigger interval) were averaged and 30 Hz low-pass filtered to obtain condition-specific EFs. For each hemisphere a single moving dipole model was calculated for a subset of 37 laterally located channels. The parameters of the “best fit” within latency range between 30-80ms were submitted to further statistical analysis. Latencies differed for the different **STIMULATION MODALITIES** ($F_{(2,4)}=6.1$; $p<0.05$) in that EL- and PN-latencies were shorter than TL-latencies (EL vs TL: $t=2.8$; $p<0.05$; PN vs TL: $t=1.1$; $p<0.05$; EL vs PN: ns.). No effects were found for amplitudes (root mean squares across selected channels) and dipole moments, respectively. Each of the three methods of stimulation produced the expected somatotopic pattern of the hand representation. However, Euclidean distances between D₁ and D₅ were the same for EL (1.31 ± 0.78 cm) and TL (1.35 ± 0.41 cm) but larger for PN (1.89 ± 1.07). Neither for EL and TL nor for PN was it possible to model an ipsilateral component within the given latency range of 30-80 ms. Our results suggest that pneumatic as well as electrically evoked fields do not differ systematically. The somatotopic organization of the fingers in area 3b was depicted reliably by TL as well as EL and both methods lead to comparable estimations for the expansion of the hand representation. The representation of painful stimuli seems to evoke different aspects of the somatotopic map. However, given that our results are based on a 5-subject sample, further studies are necessary to detail these findings.

Work was supported by the Deutsche Forschungsgemeinschaft.

Extended Current Source Models for Biomagnetic Phantom Studies

Brauer, H.¹, Ziolkowski, M.², Haueisen, J.³, Tenner, U.⁴, Nowak, H.³

¹Technical University of Ilmenau, Ilmenau, Germany

²Technical University of Szczecin, Szczecin, Poland

³Friedrich-Schiller-University, Jena, Germany

⁴University of Ulm, Ulm, Germany

Diagnostic use of measured biomagnetic or bioelectric data requires finding solutions of inverse problems. Inverse algorithms for reconstruction of extended current sources within realistically shaped volume conductors are one of actual research topics in bioelectromagnetism. The estimation of current density distributions using reliable and stable source reconstruction techniques is also a vital problem in clinical diagnosis.

In last years we developed several physical torso phantoms as well as physical source models which were used for both biomagnetic and bioelectric measurements. Usually the source models consist of single current dipoles or multiple current dipoles. But actually there are required extended source models which enable us to describe current distributions in regions of interest (heart or brain).

We applied two types of source configuration. First one is a set of 12 dipoles placed in an array of 3-by-4 dipoles which can be driven simultaneously by an external current generator. By choosing different channels and slightly modifying the dipole orientations we are able to adopt the source model more or less to the desired current distribution. The second kind of source models consists of special configurations of polymer membranes contacted with platinum electrodes. Via these electrodes the electric current is transformed to an ionic current flow inside the membrane which could have, in principle, an arbitrary shape. By modifying the membrane shape we receive a well-defined current distribution in space. The preparation of wholes in the membrane as well as modifying their shape allow directly influencing the desired current distribution.

The aim of this paper are forward simulations of these physical source models. To derive equivalent generator models which could be used in the inverse algorithms we described the extended sources by large sets of point-like current dipoles. Their optimal numbers for best approximation of the measured magnetic (and/or electric) fields were estimated by computer simulations. As a result we received numerical descriptions of the extended, physical source models which now can be applied to the different source reconstruction techniques. By means of these phantom studies we are able to investigate capabilities and limitations of reconstruction methods which are already in use in clinical practice. Because we know the impressed current distributions (of the physical models) very well it is much easier now to evaluate the applied inverse methods.

Further investigations will deal with the development of real 3D source models. So far the proposed source models cannot describe volume current distributions because the actual used membranes are very thin. But nevertheless, the proposed membrane models are real extended current sources which are very helpful for evaluation or validation of source reconstruction methods. On the other hand such inverse methods which can be applied to reconstruction of extended sources still have to be developed.

Transcranial Magnetic Stimulation – New Modality in Brain Mapping

Risto J. Ilmoniemi

Bio Mag Laboratory, Medical engineering Centre, Helsinki University Central Hospital

Recent progress is leading to novel approaches in the use of transcranial magnetic stimulation (TMS) for functional brain imaging. While more traditional methods are based on sensory stimulation or task performance and the recording of subsequent brain activity, TMS can be used to stimulate the brain directly or to block or modulate ongoing activity. TMS-evoked activity can be recorded by EEG, PET, or fMRI. In addition to providing indices of cortical reactivity, these methods allow one to study brain connectivity. It has already been demonstrated with both EEG and PET that localized magnetic stimulation of the cortex leads to neuronal activation at cortical sites that receive neuronal input from the stimulated site.

Anatomical structures seen in MRI and activation sites determined by PET, fMRI or MEG/EEG can be used for the selection of TMS target areas in the brain. With an accurate stereotactic system, the coordinate systems in the different imaging modalities can be combined. Although PET and fMRI provide significant benefits in locating TMS-evoked activity, their use will be limited by the relatively high cost and complexity of the equipment. We expect, however, that the combination of TMS and high-resolution EEG will often be the method of choice for basic neuroscience and for clinical diagnosis, for example in the assessment of brain connectivity in patients suffering from neurodegenerative diseases or head injuries.

TMS can be used in three quite different ways: 1) by studying the electrophysiological response either locally or as mediated by neuronal pathways from the stimulated spot, 2) by disturbing ongoing neuronal signal processing in the brain in order to study cortical areas that are important for specific tasks (temporary lesions), or 3) by treating patients with targeted repetitive stimulation (therapy). Many variations and combinations of these paradigms exist.

In this tutorial, after a history of the field and some fundamentals of the technique, two points will be emphasized. First, frameless stereotaxy, computer-assisted operation, and the integration of TMS with MRI and other brain-imaging modalities is transforming TMS into a true brain-mapping tool. Second, the integration of TMS with EEG, PET and other functional imaging methods will open an exciting new area of research as the reactivity and connectivity of the cortex can be studied noninvasively for the first time.

Changes of Regional Cerebral Blood Flow Caused by Transcranial Magnetic Stimulation of the Visual Cortex

L.J. Kemna, FM. Mottaghy, S. Posse

Institute of Medicine, Research Center, Juelich, Germany; Department for Nuclear Medicine, University of Duesseldorf, Germany

During the last two years pioneering works have appeared which combine TMS and rTMS with fMRI [2], PET [1] and EEG [3] to demonstrate activation in the stimulated area and in distant regions. The studies dealing with PET and rTMS used the motor or prefrontal cortex as target for TMS stimulation. Blood flow increases have been found using intensities above motor threshold, decreases below threshold. These results suggest, that it should be possible to investigate connectivity in the visual system using TMS combined with PET or fMRI.

We investigated the influence of TMS on the primary visual cortex in 9 volunteers during PET. As a previous group analysis in 8 subjects at 70 % maximum output of the Magstim round coil and 4 Hz did not produce measurable results, we decided to carry out single-subject analyses at different stimulus intensities: 70 and 100 % maximum output for 30 sec using 4 Hz, 2 cm above theinion, beginning with the injection of O-15-butanol. During the control condition another coil outside the Siemens HR+ PET scanner produced a discharge click. The subjects had their eyes closed in all conditions. We used MPITool and SPM96 for single-subject and group analyses.

All but one volunteer reported phosphenes at 100 % output, while only about half of them saw these appearances at 70 % and then they were very faint. Most subjects noticed a moving component in the phosphene that increased during the single runs and from run to run, the phosphenes growing ever weaker. The single-subject analyses showed clear interindividual differences at 100 % TMS output, which can grossly be arranged in two groups: Volunteers with blood flow increase and volunteers with a decrease beneath the coil during stimulation. All showed activation in the somatosensory and auditory cortices on both sides as well as deactivations in the mesial frontal lobes.

The group analysis in the first group showed blood flow increases in the vicinity of the calcarine sulcus in V1/V2, in the pulvinar and in V5 more prominent on the left side. As a surprise to us we also found increases in the dorsomedial parts of the cerebellum as far as 4 cm away from the coil. The second group showed blood flow decreases in the occipital pole bilaterally and no certain cerebellar activation or deactivation. At lower pulse intensity (70 % maximum) only frontal deactivations and auditory activations could be observed.

We conclude that rTMS produces measurable blood flow changes in the visual cortex at higher stimulus intensities than in motor cortex. Considerable interindividual differences in the pattern of activation must be expected which favors single-subject analysis. We have clearly demonstrated indirect activation of structures outside of the area of rTMS stimulation, suggesting that combination of rTMS with PET can be used to investigate connectivity in the visual system. However, it is desirable to use fMRI which enables use of shorter rTMS trains and investigation of the temporal dynamics of induced brain activations.

More recently, we developed Functional Imaging in REal time (FIRE) on a clinical whole body scanner which enables detection of functional activation within 10 s of stimulation in visual cortex during the ongoing scan (4). This would enable interactive positioning of the TMS coil to optimize stimulus response, rapid verification of stimulus thresholds on individual subjects and online control of data quality (e.g. head motion).

References:

- Paus-T, et al., Transcranial magnetic stimulation..., J-Neurosci. 1997; 17: 3178-84
- Bohning-DE, et al, Echoplanar BOLD fMRI..., Invest-Radiol. 1998; 33: 336-40
- Ilmoniemi-RJ, et al., Neuronal responses to magnetic..., Neurorreport. 1997; 8: 3537-40
- S. Posse, et al., Real Time fMRI ..., Abstract book: ISMRM.; 162 (1998)

TMS Induced Changes in Early Somatosensory Evoked Responses

J. Karhu^{1,2}, J. Rouhonen¹, J. Virtanen¹, M. Ollikainen¹, R. Varonen¹, R. Ilmoniemi¹

¹Biomag Laboratory, Medical Engineering Centre, Helsinki University Central Hospital

²Department of Clinical Neurophysiology, Kuopio University Hospital, Finland

Transcranial Magnetic Stimulation (TMS) pulse is relatively focal and very brief (sub-millisecond) and the induced field elicits a highly synchronous burst of local neuronal discharges in brain. TMS has been used to evaluate motor conduction by stimulating motor cortex and recording peripheral muscle movement (1), and to study the impairment of performance in cognitive tasks by disturbing focal cortical areas with TMS (2). We have combined TMS with high-resolution electroencephalography (EEG) to examine cortical reactivity and functional neuronal connections within human brain (3). In this study we show that the early cortical responses to somatosensory input can be modulated significantly by accurately timed TMS.

Magnetic pulses were delivered to right motor cortex of six healthy right-handed adults and also two the left motor cortex in two of these subjects (21–39 years; five males) who provided informed consent. The location for figure-of-eight stimulator coil with 40-mm-diameter wings was found by recording muscle movement from contralateral small hand muscles. During recordings, the stimulation intensity was dropped below the motor threshold. Right median nerve was stimulated through transcutaneous electrodes at the wrist. Constant current pulses (0.3 ms duration) at interstimulus intervals of 1 s were delivered 5 ms prior to TMS and 30 and 50 ms after the TMS. In control sessions, magnetic and electric pulses were delivered separately. The effect of auditory click elicited by magnetic stimulator was also controlled separately. EEG responses were monitored continuously from 60 electrodes with a custom-made instrumentation. Data were bandpass filtered at 1 – 250 Hz and sampled at 1450 Hz. About 150 responses were averaged time-locked to the median nerve stimulation. The amplitudes and latencies of EEG responses were measured from the channel of maximum amplitude. For cortical activation maps, electrode and stimulator coil locations were digitized with respect to external head landmarks (Polhemus, USA). Individual magnetic resonance images (MRI) were acquired (Siemens Vision, 1.5 T) and used for 3-D reconstruction of cortical surfaces. Minimum-norm estimates of current distribution constrained to cortical surface were then calculated to evaluate the distribution and spreading of electric activity (Curry, Neuroscan).

All subjects showed normal, contralateral, highly localized somatosensory evoked magnetic responses (SEPs) at 20–40 ms right median nerve stimulation. The average magnitude of the earliest N20 response ($2.03 \pm 0.43 \mu\text{V}$) was suppressed significantly by TMS pulse delivered to opposite hemisphere 5 ms *after* the hand stimulation ($0.78 \pm 0.36 \mu\text{V}$). In two subjects N 20 was almost abolished by the following TMS. In contrast, there were no similar effects to the magnitude of P30 (SEP: $4.93 \pm 1 \mu\text{V}$ vs. SEP+TMS: $4.72 \pm 1.16 \mu\text{V}$) or to the latencies of responses. The TMS delivered prior to median nerve stimulation showed dissociated effects enhancing P30 in electrodes over motor areas and suppressing responses in electrodes over somatosensory cortex in postcentral areas.

Transcallosal spreading of TMS-evoked neuronal activity delivered *after* the hand stimulation strongly suppresses the first cortical somatosensory responses whereas the immediately following responses are not modulated. Ipsi- and contralateral TMS directed to hand area *prior* to hand stimulation seems to have a dissociated effect to responses over sensory and motor areas. These data support parallel, not sequential, early processing of somatosensory stimuli both in multiple somatosensory areas and even in topographically overlapping sites (4). The combination of TMS and EEG allows the study of TMS effects to neuronal activity in functionally connected brain areas with a millisecond-level accuracy.

References

1. Barker, A.T., Jalinous, R., Freeston, I.L. Lancet 1985, 1: 1106-1107.
2. Amassian, V.E., Cracco, R.Q., Maccabee, J. et al. Electroenceph. Clin. Neurophysiol.. 1989, 74: 458-462.
3. Ilmoniemi, R.J., Virtanen, J., Ruohonen, J. et al. NeuroRep. 1997, 8: 3537-3540.
4. Tesche, C.D., Karhu, J. Brain Res. 1997, 744: 23-31; Karhu, J., Tesche C.D. J. Neurophysiol. 1999, in press.

Morphological and Haemodynamic Investigations of the Fetal Brain

Kurjak A., Kos M.

Department of Obstetrics and Gynecology, Medical School University of Zagreb, Sveti duh Hospital, Zagreb, Croatia

Morphological and haemodynamic investigations of the fetal brain offer the opportunity of following the patophysiological processes connected to hypoxemia. It is especially important in connection to the possibility to predict the reversible and irreversible neurological damage (i.e., the short and long term prognosis of children endangered in that fashion). It is easy today to recognize the phenomenon of fetal blood redistribution and vasocentralisation, the fundamental compensational mechanism in all conditions of decreased intrauterine oxygen supply, by ultrasonographic and Doppler measurements. Doppler findings imply the increased blood flow resistance and the decreased blood flow in peripheral tissues and organs caused by vasoconstriction. At the same time, the resistance is lowered and the blood flow is increased through the brain circulation because of the reflex vasodilatation. These criteria are widely accepted as diagnostic signs of threatening or initial fetal hypoxia. With the advancing of this condition and further worsening of oxygen supply intrauterine neurological damage ensues. Previous compensational lowering of resistance and vasodilatation in brain circulation quickly becomes the state of progressive resistance increase and fatal reduction of blood flow through brain blood vessels. This is the consequence of hypoxic vasoparesis caused by brain oedema marking the terminal stage connected with irreversible neurological damage. By means of Doppler measurements we shall register maximally increased indexes of resistance and pulsatility at the level of anterior, medium, and posterior cerebral artery, usually with the absence of diastolic blood flow. Ultrasonographically we shall usually see changes in brain morphology - well-developed intraventricular haemorrhage and brain oedema with accompanying collapse of subarachnoidal space.

INDEX BY AUTHORS

A

Aine C. J., 24
Aronen 58
Avella C., 55

B

Bacharova L., 51
Bastiaansen M., 44
Beisteiner R., 40, 69
Berg P. 42, 67
Bonomo L., 38
Bornfleth H., 42, 67
Bowyer, S. M., 59
Brauer H., 70, 71, 73
Breier, J. I., 53
Brunia C., 44
Burco F., 56

C

Chorvat D., 51
Christner R., 24
Constantinou, J., 53
Cunnington R., 39, 40, 69

D

Dale A. M., 36, 66
Deecke L., 39, 40
Del Gratta C., 23, 38
Della Penna S., 38
Dhond P., 36
Donker D., 47
Drüen K., 42, 67
Dzemidzic M., 37, 41

E

Edlinger G., 64
Edward V., 40, 69
Elbert, T., 72
Erdler M., 39, 40, 69
Erné, S. N., 50, 68, 70

F

Fahlbusch, R., 54
Fenici, R., 46
Ferretti A., 38
Fetzer J., 31
Fischer G., 31, 32, 49
Fischl B., 36
Franciotti R., 38
Friston K. J., 29

G

Ganslandt O., 52, 54
Gao J. H., 35
Gartus A., 40, 69
Göbel R., 42, 67
Grönemeyer D., 47

H

Hailer B., 47, 62
Halgren, E, 36, 66
Hämäläinen M., 45
Hänninen, H., 46, 48
Hannu J., 58
Hashimoto I., 26
Haueisen J., 63, 70, 71, 73
Hoormann J., 62
Hren R., 33
Huang M., 24
Huiskamp G., 31

I

Ille N., 42
Ilmoniemi R. J, 58, 74, 76

J

Jazbinšek V., 33

K

Kamada K., 52

Kammrath H. G., 50, 68
Karhu, J., 25, 76
Katila, T., 46, 48
Kemna L. J., 75
Kober H., 52, 54
Korhonen, P., 46
Kos M., 77
Kreyer, I., 72
Kurjak A., 77

L

Lange S., 47
Lanzenberger R., 69
Lauerma K., 46, 48
Leder U., 63
Lesh M. D., 49
Lilli S., 55, 65
Linek S., 42
Lötjönen J., 46, 48
Lowe M. J., 37, 41
Lurito J. T., 37, 41

M

Mackert B. M. 62
Maggio, W. W., 53
Mäkijärvi, M., 46, 48
Marinkovic K., 36, 66
Mateasik A., 51
Mathews V. P., 37, 41
Meinck H. M., 67
Miyashita Y., 43
Mlynash M., 49
Modre R., 31, 32, 49
Möller M., 54
Moser E., 39, 40, 69
Mottaghy F. M., 75
Müller H. P., 50, 68

N

Nenonen J., 46, 48
Neuper C., 44, 64
Nimsky Ch., 54
Nowak H, 63, 70, 71, 73

O

Ollikainen M., 76

P

Papanicolaou A. C., 53, 57
Peoppel D., 43
Pesola K., 46, 48
Peters M., J., 28, 30
Pfurtscheller G., 44, 64
Phillips C., 29
Phillips M. D., 37, 41
Pohl P., 63
Posse S., 60, 75
Proverbio A.. M. 55, 56, 65

R

Ramon C., 71
Reddy G., 49
Roberts T., 49
Roithinger F. X., 49
Romani G. L., 23, 38
Rossini P. M., 38
Rouhonen J., 76
Rucker W., 31
Rugg M. D., 29

S

Sakuma K., 26
Savoy R. L., 34
Scherg M., 42, 67
Sekihara K., 26, 43
Simos P., 53
Sippens Groenewegen A., 49
Steiner P. R., 49
Stephen J., 24
Sterr A., 61, 72
Stinstra J. G., 28
Stippich C., 42, 67
Streibl B., 40, 69
Stroink G., 62
Supek S., 24

T

Takala P., 48
Tartaro A., 38
Tauberschmidt E., 67
Tenner, U., 50, 70, 73
Tesche, C. D. 24
Tilg B., 31, 32, 49
Titomir L. I., 51
Toivonen L., 48

Tomczak R., 68
Torquati K., 38

U

Uutela K., 45

V

van Burik M. J., 28, 30
Van Leeuwen P., 47, 62
van Oosterom A., 27
Varonen R., 76
Vieth J. B., 52
Virtanen J., 76

Voipio-Pulkki L.-M., 48

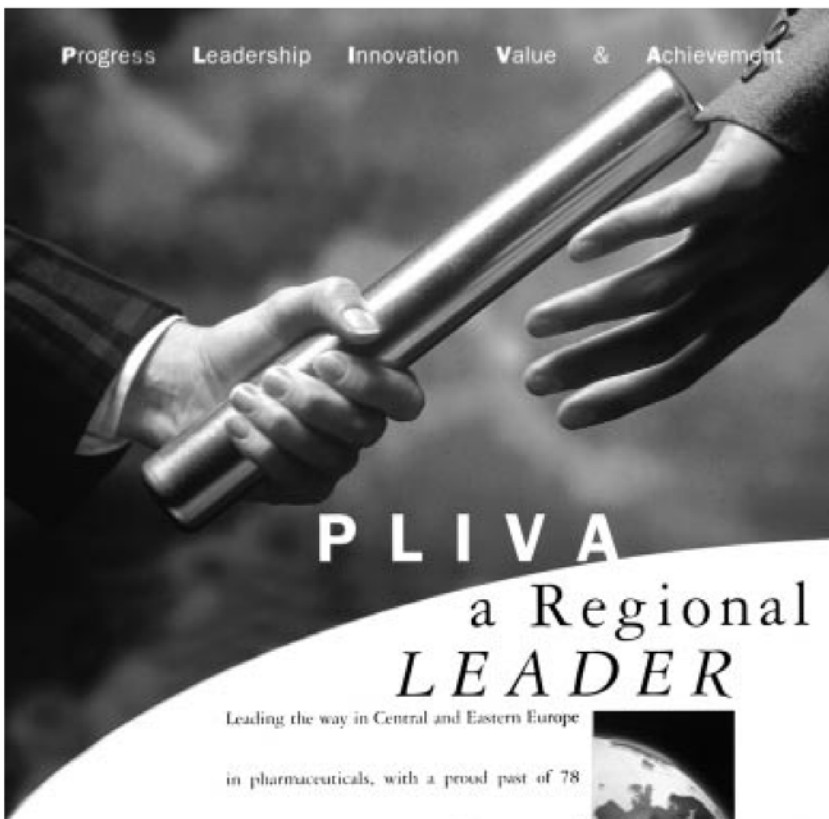
W

Wach P., 49
Weckesser D., 42, 67
Wheless, J. W., 53
Windischberger C., 39, 40, 69
Wunderlich A., 68

Z

Zani A., 55, 56, 65
Ziolkowski, M., 50, 73
Zouridakis, G., 53

Progress Leadership Innovation Value & Achievement



PLIVA

a Regional
LEADER

Leading the way in Central and Eastern Europe

in pharmaceuticals, with a proud past of 78

years of Progress, prominent Achievements and

further Innovation in all fields of our work.

Value and the well being of people is at the top

of our priorities.



Design: Pridel & Partners Ltd. Photo: Stockphoto

For more information, please contact:
Public Relations Department
Ul. Grada Vukovara 49, Zagreb, CROATIA
Tel. 385 1 61 20 852, Fax. 385 1 61 60 358

