New papers about near-infrared spectroscopy (NIRS) and imaging (NIRI)

Volume 1, Issue 1 (January-March 2013)

Felix Scholkmann | Biomedical Optics Research Laboratory (BORL), Division of Neonatology, University Hospital Zurich, 8091 Zurich, Switzerland, Felix.Scholkmann@usz.ch

Number of papers included: **99**

Note: The highlighted parts of the abstracts refer to the most important findings.

1. Zhang et al. (2013). **Brain and muscle oxygenation monitoring using near-infrared spectroscopy (NIRS) during all-night sleep**

Abstract: The hemodynamic changes during natural human sleep are still not well understood. NIRS is ideally suited for monitoring the hemodynamic changes during sleep due to the properties of local measurement, totally safe application and good tolerance to motion. Several studies have been conducted using NIRS in both normal subjects and patients with various sleep disorders during sleep to characterize the hemodynamic changing patterns during different sleep stages and during different symptoms such as obstructive apneas. Here we assessed brain and muscle oxygenation changes in 7 healthy adults during all-night sleep with combined polysomnography measurement to test the notion if hemodynamic changes in sleep are indeed brain specific. We found that muscle and brain showed similar hemodynamic changes during sleep initiation. A decrease in HbO2 and tissue oxygenation index (TOI) while an increase in HHb was observed immediately after sleep onset, and an opposite trend was found after transition with progression to deeper slow-wave sleep (SWS) stage. Spontaneous low frequency oscillations (LFO) and very low frequency oscillations (VLFO) were smaller (Levene's test, $p<0.05$) during SWS compared to light sleep (LS) and rapid-eye-movement (REM) sleep in both brain and muscle. Spectral analysis of the NIRS signals measured from brain and muscle also showed reductions in VLFO and LFO powers during SWS with respect to LS and REM sleep. These results indicate a systemic attenuation rather than local cerebral reduction of spontaneous hemodynamic activity in SWS. A systemic physiological mechanism may exist to regulate the hemodynamic changes in brain and muscle during sleep.

2. Vogt et al. (2013). **Mechanical indentation improves cerebral blood oxygenation signal quality of functional near-infrared spectroscopy (fNIRS) during breath holding**

Abstract: Functional near-infrared spectroscopy (fNIRS) is a well-known technique for non-invasively measuring cerebral blood oxygenation, and many studies have demonstrated that fNIRS signals can be related to cognitive function. However, the fNIRS signal is attenuated by the skin, while scalp blood content has been reported to influence cerebral oxygenation measurements. Mechanical indentation has been shown to increase light transmission through soft tissues by causing interstitial water and blood flow away from the compressed region. To study the effects of indentation on fNIRS, a commercial fNIRS system with 16 emitter/detector pairs was used to measure cerebral blood oxygenation at 2 Hz. This device used diffuse reflectance at 730 nm and 850 nm to calculate deoxy- and oxy-hemoglobin concentrations. A borosilicate glass hemisphere was epoxied over each sensor to function as both an indenter and a lens. After placing the indenter/sensor assembly on the forehead, a pair of plastic bands was placed on top of the fNIRS headband and strapped to the head to provide uniform pressure and tightened to approx. 15 N per strap. Cerebral blood oxygenation was recorded during a breath holding regime (15 second hold, 15 second rest, 6 cycles) in 4 human subjects both with and without the indenter array. Results showed that indentation increased raw signal intensity by 85 ± 35%, and that indentation increased amplitude of hemoglobin changes during breath cycles by 313% ± 105%. These results suggest that indentation improves sensing of cerebral blood oxygenation, and may potentially enable sensing of deeper brain tissues.

3. Kainerstorfer et al. (2013). **Applications of a novel hemodynamic model to functional brain studies with fNIRS and fMRI**

Abstract: We report time-domain applications of a new hemodynamic model by Fantini [1] that yields analytic expressions for signals that are measurable with hemodynamic-based neuroimaging techniques such as functional near-infrared spectroscopy (fNIRS) and functional magnetic resonance imaging (fMRI). We show how the model can be used to predict the perturbations in cerebral blood volume (CBV), blood flow (CBF), and metabolic rate of oxygen (CMRO2) that account for the initial dip and post-stimulus undershoot that have been reported in the fMRI and fNIRS literature. Furthermore, we have used data from the literature to perform a comparison between measured fNIRS and fMRI signals and the corresponding signals predicted by the new hemodynamic model. Results showed an excellent agreement between the model predictions and the reported measured data.

4. Sun et al. (2013). **Quantitative comparison of the hemodynamic activation elicited by cardinal and oblique gratings with functional near-infrared spectroscopy**

Abstract: Evidence has been accumulated for over a century indicating that the visual system of humans and many animals is more sensitive to contour stimulation at vertical or horizontal orientations than oblique orientations. However, the neural basis for this orientation anisotropy is still a subject of debate. In the present study, we recorded brain activity over the parietal-occipital and frontal lobes with functional near-infrared spectroscopy (fNIRS) when human participants were presented with gratings in different orientations. The oblique gratings induced a much larger change in the oxygenated hemoglobin concentration than vertical and horizontal gratings in the left occipital lobe. However, we did not find any significant orientation anisotropy in the frontal lobe. Our study showed that different quantitative changes in the hemoglobin concentrations occurred in response to differently oriented stimuli in the visual cortex and that fNIRS could potentially be a valuable tool in the assessment of the hemodynamic responses of the visual system.

5. Contini et al. (2013). **Investigation of verbal and visual working memory by multi-channel time-resolved functional near-infrared spectroscopy**

Abstract: Working memory (WM) is fundamental for a number of cognitive processes, such as comprehension, reasoning and learning. WM allows the short-term maintenance and manipulation of the information selected by attentional processes. The goal of this study was to examine by time-resolved fNIRS neural correlates of the verbal and visual WM during forward and backward digit span (DF and DB, respectively) tasks, and symbol span (SS) task. A neural dissociation was hypothesised between the maintenance and manipulation processes. In particular, a dorsolateral/ventrolateral prefrontal cortex (DLPFC/VLPFC) recruitment was expected during the DB task, whilst a lateralised involvement of Brodmann Area (BA) 10 was expected during the execution of the DF task. Thirteen subjects were monitored by a multi-channel, dual-wavelength (690 and 829 nm) time-resolved fNIRS system during 3 minutes long DF and DB tasks and 4 minutes long SS task. The participants' mean memory span was calculated for each task: DF: 6.46±1.05 digits; DB: 5.62±1.26 digits; SS: 4.69±1.32 symbols. No correlation was found between the span level and the heart rate data (measured by pulse oximeter). As expected, DB elicited a broad activated area, in the bilateral VLPFC and the right DLPFC, whereas a more localised activation was observed over the right hemisphere during either DF (BA 10) or SS (BA 10 and 44). The robust involvement of the DLPFC during DB, compared to DF, is compatible with previous findings and with the key role of the central executive subserving in manipulating processes.

6. Contini et al. (2013). **Multi-channel time-resolved functional near infrared spectroscopy system**

Abstract: A multichannel (16 sources and 8 detectors) time-domain fNIRS medical device is presented. The system was extensively characterized on tissue phantoms. Preliminary in vivo measurements on muscle and brain cortex are reported to test the ability of the system to noninvasively measure tissue hemodynamics.

7. Yennu et al. (2013). **Investigation of human frontal cortex under noxious thermal stimulation of temporo-mandibular joint using functional near infrared spectroscopy**

Abstract: According to American Academy of Orofacial Pain, 75% of the U.S. population experiences painful symptoms of temporo-mandibular joint and muscle disorder (TMJMD) during their lifetime. Thus, objective assessment of pain is crucial for efficient pain management. We used near infrared spectroscopy (NIRS) as a tool to explore hemodynamic responses in the frontal cortex to noxious thermal stimulation of temporomadibular joint (TMJ). NIRS experiments were performed on 9 healthy volunteers under both low pain stimulation (LPS) and high pain stimulation (HPS), using a temperature-controlled thermal stimulator. To induce thermal pain, a 16X16 mm2 thermode was strapped onto the right TMJ of each subject. Initially, subjects were asked to rate perceived pain on a scale of 0 to 10 for the temperatures from 41°C to 47°C. For the NIRS measurement, two magnitudes of temperatures, one rated as 3 and another rated as 7, were chosen as LPS and HPS, respectively. By analyzing the temporal profiles of changes in oxy-hemoglobin concentration (HbO) using cluster-based statistical tests, we were able to identify several regions of interest (ROI), (e.g., secondary somatosensory cortex and prefrontal cortex), where significant differences ($p<0.05$) between HbO responses to LPS and HPS are shown. In order to classify these two levels of pain, a neural-network-based classification algorithm was used. With leave-one-out cross validation from 9 subjects, the two levels of pain were identified with 100% mean sensitivity, 98% mean specificity and 99% mean accuracy to high pain. From the receiver operating characteristics curve, 0.99 mean area under curve was observed.

8. Tian et al. (2013). **EasyTopo: A toolbox for rapid diffuse optical topography based on a standard template of brain atlas**

Abstract: Diffuse optical topography remains a valid tool in functional near infrared spectroscopy (fNIRS) since it avoids solving the forward and inverse computational problems, which are encountered in diffuse optical tomography. Topography is particularly useful when a sparse array of optodes is used and depth specificity is not the primary interest. We have developed an easy toolbox for diffuse optical topography ("EasyTopo") based on a standard template of brain atlas. EasyTopo approximates the cortical layer of the brain as a hemispherical surface. Therefore, the stereotaxic coordinates of the brain surface and the co-registered fNIRS measurements (channels) are converted into the spherical coordinates, where 2D angular interpolation of the channel-wise data is implemented to obtain a topographic image of brain activation in the latitude-longitude space. Then, the interpolated image is projected back onto the brain surface in the original 3D stereotaxic coordinates. Compared with the existing 3D topography methods, EasyTopo is more computationally efficient and does not require any data extrapolation. Another advantage of EasyTopo is that the data between two spatially adjacent channels are interpolated along their included angles (i.e., along the angular direction) rather than along a straight line going under the brain surface. The former geometry in principle matches better with the realistic brain structure than the latter one. EasyTopo has been validated with both simulation and human experiments. Now this toolbox is publically available.

9. Pierro et al. (2013). **Frequency-resolved measurements of hemodynamic oscillations and quantitative analysis with a novel hemodynamic model**

Abstract: We present frequency-resolved measurements of the amplitude and phase of cerebral hemodynamic oscillations associated with paced breathing and measured with near-infrared spectroscopy on the forehead of a human subject. We have performed measurements at eleven paced breathing frequencies in the range 0.07-0.25 Hz. The resulting frequency spectra of the amplitude and phase of the hemodynamic oscillations were fit with a recently developed hemodynamic model,1 that was able to reproduce the measured spectra and to determine a number of associated physiological parameters. The parameters measured include the blood transit times in the capillary (0.87 s) and venous (1.0 s) compartments, and the high-pass cutoff frequency of cerebral autoregulation (0.087 Hz). We also illustrate the implications of the new hemodynamic model on the basis of a phasor representation of physiological and hemodynamic oscillations. The combination of frequency-resolved measurements of cerebral hemodynamics and the phasor-based, frequency-domain solution of the new hemodynamic model provides a novel tool for cerebral hemodynamic studies with a potential for assessing a variety of physiological, functional, and pathological conditions.

10. Funane et al. (2013). **Near-infrared spectroscopy system with non-contact source and detector for in vivo multi-distance measurement of deep biological tissue**

Abstract: A non-contact near-infrared spectroscopy (NIRS) scanning system with a phosphor cell placed on the skin for in vivo measurement of biological tissue was developed and evaluated. Because the phosphor is excited by the light that propagates in the tissue, and the excitation light is cut by optical filters, the light that propagates in the tissue is selectively detected. The non-contact system was extended to create a scanning system that can flexibly change source positions with a galvano scanner. The optical scanning system was used for non-contact measurement of the human forearm muscle, and the dependence of optical-density change (ΔOD) caused by the upper-arm occlusion and release on source-detector distance was observed. The obtained ΔOD demonstrates the effectiveness of using this system for multi-distance human-forearm measurement. Furthermore, a human forehead was measured with the system. To extract a deep-layer signal, a surface-layer subtraction method with short-distance regression was applied to measured data. On the basis of the correlation with a simultaneously measured laser-Doppler flowmetry signal, it was confirmed that the deep-layer signal was successfully extracted. The extraction result demonstrates that the optical scanning system can be used as a multi-distance NIRS system for measuring the human brain activity at the forehead.

11. Kida & Shinohara (2013). **Gentle touch activates the anterior prefrontal cortex: An NIRS study**

Abstract: Gentle touching of the hand activates emotion- and reward-related regions of the brain. The present study investigated activation of the prefrontal cortex by gentle sweeps of the palm or forearm with three materials (wood, velvet, paintbrush) using near-infrared spectroscopy (NIRS). Sweeps of the left palm with a sensuous velvet fabric increased the oxy-hemoglobin (oxy-Hb) concentration in the frontal-polar cortex (FPC) and a part of the orbitofrontal cortex (OFC), compared to a neutral touch produced by rounded wood. Pleasantness ratings were higher for the velvet than wood. In conclusion, the present study revealed the involvement of the FPC/OFC in pleasant emotion produced by gentle touch to the hand.

12. Selb et al. (2013). **Functional brain imaging with a supercontinuum time-domain NIRS system**

Abstract: We have developed the second generation of our time-domain near-infrared spectroscopy (TD-NIRS) system for baseline and functional brain imaging. The instrument uses a pulsed broadband supercontinuum laser emitting a large spectrum between 650 and 1700 nm, and a gated detection based on an intensified CCD camera. The source laser beam is split into two arms, below and above 776 nm. In each arm, a fast motorized

filter wheel enables selection of a bandpass filter at the required wavelength. Each filtered laser beam is then launched into one array of source fibers. The multiplexing through the array of fibers is implemented through a very compact home-made design consisting of two galvanometer mirrors followed by an achromatic doublet. Source fibers are then recombined one-by-one from both arms into the source optodes to be positioned on the head. The detection fibers are all imaged in parallel through a relay lens on an intensified CCD camera. By using detection fibers of different lengths, we introduce optical delays that enable simultaneous recording in different delay windows of the temporal point spread functions. We present the instrumentation and show its preliminary functional imaging capabilities. We also introduce a new probe where we use different fiber lengths on the source and the detector sides in order to record simultaneously both wavelengths from one location through different sets of fibers.

13. Meng et al. (2013). **Monitoring cerebral tissue oxygen saturation during surgery: a clinician's perspective**

Abstract: Organ protection and physiology optimization are important goals when taking care of anesthetized patients undergoing surgery. Postoperative cognitive dysfunction and perioperative stroke are unwarranted potential outcomes. Neurovascular coupling, the match between cerebral metabolic demand and substrate supply, should be regarded as the essential cerebral physiology which needs to be monitored during surgery. The brain-targeting near-infrared spectroscopy (NIRS) technology has the potential to fulfill this goal. Proposition of why and how to monitor essential cerebral physiology via advanced NIRS technologies is discussed. We also discussed the limits of the current NIRS technologies which merely measure cerebral tissue oxygen saturation in pooled cerebral arterial, capillary, and venous blood.

14. Ganesan et al. (2013). **Use of diffuse optical spectroscopy to monitor muscle and brain oxygenation dynamics during isometric and isokinetic exercise**

Abstract: The use of near-infrared time-resolved spectroscopy (TRS-20, Hamamatsu Corporation) in two resistance type exercise applications in human subjects is described. First, using isometric flexion of the biceps, we compared the magnitude and relevance of tissue hemoglobin concentration and oxygen saturation (stO2) changes when assuming constant scattering versus continuous measurement of reduced scattering coefficients at three wavelengths. It was found that the assumption of constant scattering resulted in significant errors in hemoglobin concentration assessment during sustained isometric contractions. Secondly, we tested the effect of blood flow restriction (BFR) on oxygenation in a muscle (vastus medialis oblique, VMO) and in the prefrontal cortex (PFC) of the brain. The BFR training technique resulted in considerably more fatigability in subjects, and correlated with reduced muscle stO2 between sets of exertion. Additionally, exercise with BFR resulted in greater PFC deoxygenation than a condition with equivalent work performance but no BFR. These experiments demonstrate novel applications for diffuse optical spectroscopy in strength testing and targeted muscle rehabilitation.

15. Meng et al. (2013). **Digital lock-in detection system based on single photon counting for near-infrared functional brain imaging**

Abstract: Near infrared (NIR) diffuse optical imaging (DOI) are increasingly used to detect hemodynamic changes in the cerebral cortex induced by brain activity. For the sake of capturing the dynamic changes in real-time imaging applications, such as brain imaging, digital lock-in detection technique could be applied. Using particular modulation and sampling constraints and averaging filters, one can achieve optimal noise reduction and discrimination between sources in different modulation frequencies. In this paper, we designed and developed a compact dual-wavelength continuous wave DOI system based on the single photon counting digital lock-in detection technique. According to the frequency division multiplexing light source coding technique, sine

waves with different frequencies are generated so as to amplitude-modulate two laser sources with different wavelengths. The diffuse light is detected by photomultiplier tubes (PMTs) and the data is collected by the detection channels simultaneously. A digital lock-in detection circuit for photon counting measurement module and a DDS (Direct Digital Synthesizer) signal generation module were separately implemented in two FPGA development platforms. To validate the feasibility and functionality of the developed system, a series of experimental tests were performed. Preliminary results show that the system could be used to reconstruct the absorption coefficient and could separate the response of the dual wavelength sources which were modulated by sine signals of different frequencies effectively. In addition, several imaging experiments were performed on the semi-infinite solid phantom to find the "best imaging position" for a given source-detector placement.

16. Kim et al. (2013). **The effect of oxygen administration on regional cerebral oxygen saturation after stellate ganglion block on the non-blocked side**

Abstract: BACKGROUND: Stellate ganglion block (SGB) causes sympathetic denervation of the head, neck, and upper extremities. In some studies, it has been reported that cerebral blood flow on the non-blocked side decreases after SGB, so when performing an SGB for pain management of the head, neck, and arm, the increased risk of cerebral ischemia should be considered. OBJECTIVES: To examine the influence of administration of oxygen via nasal cannula after SGB on regional cerebral oxygen saturation (rSO2) of the non-blocked and blocked sides using near-infrared spectroscopy (NIRS). STUDY DESIGN: Prospective observational study. SETTING: Outpatient department for interventional pain management at Yonsei University College of Medicine, Seoul, Korea. METHODS: Thirty-eight patients with disease entities in the head, neck, and upper extremity and 3 volunteers were studied. SGB was performed with 10 mL of 1% lidocaine using an anterior paratracheal approach at the C6 transverse process level. A successful block was determined based on the appearance of Horner syndrome at 15 minutes after SGB. Oxygen was supplied at a rate of 5 L/min via nasal cannula starting 15 minutes after SGB. rSO2, blood pressure (BP), and heart rate (HR) were obtained at 5-minute intervals for 30 minutes using NIRS, a non-invasive blood pressure manometer, an electrocardiogram, and a pulse oximetry. RESULTS: On the non-blocked side, when compared to the baseline values, there were significant decreases in the rSO2 ($P < 0.001$) and after administration of oxygen, there were significant increases of the rSO2 compared to the rSO2 at 15 minutes ($P < 0.001$). The lowest rSO2 at 15 minutes on the non-blocked side recovered to greater than the baseline value 5 minutes after starting oxygen administration. On the blocked side, when compared to the baseline values, there were significant increases at all time points ($P < 0.001$) and after administration of oxygen there were significant increases compared to the rSO2 at 15 minutes ($P < 0.001$). The rSO2 on the blocked side and the non-blocked side were significantly different at 15 minutes ($P = 0.015$). After oxygen administration, there were no significant differences of rSO2 between the 2 sides. LIMITATIONS: This study is limited by its sample size and observational design. It is difficult to precisely define the importance of the effect of SGB and oxygen administration on rSO2 change as we did not examine how the intensity of the nerve block changed with the passage of time. CONCLUSION: SGB leads to decreased cerebral blood flow of the non-blocked hemisphere, and oxygen administration seems to be a simple method to compensate for this response.

17. Sutoh et al. (2013). **Changes in Self-Regulation-Related Prefrontal Activities in Eating Disorders: A Near Infrared Spectroscopy Study**

Abstract: Objective: The aim of this study is to clarify the symptomatology of the eating disorders examining the prefrontal function and activity associated with self-regulation among participants with or without eating disorders. Methods: Ten patients with anorexia nervosa, fourteen with bulimia nervosa, and fourteen healthy control participants performed two cognitive tasks assessing self-regulatory functions, an auditorily distracted word fluency task and a rock-paper-scissors task under the measurements on prefrontal oxyhemoglobin concentration with near infrared spectroscopy. The psychiatric symptoms of patient groups were assessed with several questionnaires. Results: Patients with bulimia nervosa showed decreased performances and prefrontal

hyper activation patterns. Prefrontal activities showed a moderate negative correlation with task performances not in the patient groups but only in the healthy participants. The prefrontal activities of the patient groups showed positive correlations with some symptom scale aspects. Conclusions: The decreased cognitive abilities and characteristic prefrontal activation patterns associated with self-regulatory functions were shown in patients with bulimia nervosa, which correlated with their symptoms. These findings suggest inefficient prefrontal self-regulatory function of bulimia nervosa that associate with its symptoms.

18. Karim et al. (2013). **Neuroimaging to detect cortical projection of vestibular response to caloric stimulation in young and older adults using functional near-infrared spectroscopy (fNIRS)**

Abstract: Functional near-infrared spectroscopy (fNIRS) is a non-invasive and portable neuroimaging technique. The method uses non-ionizing laser light in the range of red to near-infrared to detect changes in cerebral blood oxygenation. In this study, we used fNIRS to investigate cortical hemodynamic changes in the temporo-parietal and frontal regions during caloric vestibular stimulation. Caloric stimulation has previously been investigated using functional magnetic resonance imaging (fMRI) and positron emission tomography (PET), which serves as a validation of the fNIRS imaging modality toward the measurement of vestibular related brain regions. To date, only a single study has used fNIRS during caloric irrigations, which observed blood volume changes in the temporal–parietal area in healthy younger subjects. In this current study, fNIRS was used to measure cortical vestibular activation in 10 right-handed younger subjects (5 male and 5 female, age 25 +/− 6 years) and 10 right-handed older subjects (6 male and 4 female, age 74 +/− 5 years). We investigated both warm (44 °C) and cool (30 °C) unilateral caloric vestibular stimulation. Consistent with previous reports, we found that warm (44 °C) caloric irrigation caused a bilateral activation. In addition, we found that cool (30 °C) caloric irrigation caused contralateral activation of the temporo-parietal area. This study is the first to investigate age effects of the caloric stimulation on brain activity. We found that the older subjects had stronger bilateral effects than the younger subjects. Our results confirm previous fMRI and PET studies that showed cortical activation during caloric vestibular irrigation is dependent on side of irrigation, and temperature of irrigation. Furthermore, our results demonstrate that fNIRS is a viable technique in measuring cortical effects during vestibular tasks.

19. Tong et al. (2013). **Evaluating the effects of systemic low frequency oscillations measured in the periphery on the independent component analysis results of resting state networks**

Abstract: Independent component analysis (ICA) is widely used in resting state functional connectivity studies. ICA is a data-driven method, which uses no a priori anatomical or functional assumptions. However, as a result, it still relies on the user to distinguish the independent components (ICs) corresponding to neuronal activation, peripherally originating signals (without directly attributable neuronal origin, such as respiration, cardiac pulsation and Mayer wave), and acquisition artifacts. In this concurrent near infrared spectroscopy (NIRS)/functional MRI (fMRI) resting state study, we developed a method to systematically and quantitatively identify the ICs that show strong contributions from signals originating in the periphery. We applied group ICA (MELODIC from FSL) to the resting state data of 10 healthy participants. The systemic low frequency oscillation (LFO) detected simultaneously at each participant's fingertip by NIRS was used as a regressor to correlate with every subject-specific IC time course. The ICs that had high correlation with the systemic LFO were those closely associated with previously described sensorimotor, visual, and auditory networks. The ICs associated with the default mode and frontoparietal networks were less affected by the peripheral signals. The consistency and reproducibility of the results were evaluated using bootstrapping. This result demonstrates that systemic, low frequency oscillations in hemodynamic properties overlay the time courses of many spatial patterns identified in ICA analyses, which complicates the detection and interpretation of connectivity in these regions of the brain.

20. Cristia et al. (2013). **An Online Database of Infant Functional Near InfraRed Spectroscopy Studies: A Community-Augmented Systematic Review**

Abstract: Until recently, imaging the infant brain was very challenging. Functional Near InfraRed Spectroscopy (fNIRS) is a promising, relatively novel technique, whose use is rapidly expanding. As an emergent field, it is particularly important to share methodological knowledge to ensure replicable and robust results. In this paper, we present a community-augmented database which will facilitate precisely this exchange. We tabulated articles and theses reporting empirical fNIRS research carried out on infants below three years of age along several methodological variables. The resulting spreadsheet has been uploaded in a format allowing individuals to continue adding new results, and download the most recent version of the table. Thus, this database is ideal to carry out systematic reviews. We illustrate its academic utility by focusing on the factors affecting three key variables: infant attrition, the reliability of oxygenated and deoxygenated responses, and signal-to-noise ratios. We then discuss strengths and weaknesses of the DBIfNIRS, and conclude by suggesting a set of simple guidelines aimed to facilitate methodological convergence through the standardization of reports.

21. Carter et al. (2013). **Target predictability, sustained attention, and response inhibition**

Abstract: We examined whether the sustained attention to response task is a better measure of response inhibition or sustained attention. Participants performed a number detection task for 37.3 min using either a Sustained Attention to Response Task (SART; high Go low No-Go) or a more traditionally formatted vigilance task (TFT; high No-Go low Go) response format. Participants performed these tasks using either a regular fixed ordered stimuli set (1–9, sequentially repeated), in which the target number appeared predictably, or a random order (1–9, random presentation), in which the target number appeared at random. We utilized functional near infrared spectroscopy (fNIRS) to measure cerebral oxygenation levels in the right and left frontal areas. We also used post-task participant reports of arousal, and conscious thoughts occurring during the tasks. Performance differed for the both response format and target predictability. Greater right than left frontal hemisphere activation occurred in the TFT than the SART with time-on-task. In addition, the SART response format resulted in elevated self-reports of task-related thoughts than the TFT response format. The results suggest the SART, random or fixed ordered, places high response inhibition, not necessarily sustained attention, demands on participants. Elevated levels of task-related thoughts during the SART format condition in comparison to the TFT condition does not appear to be in accord with the claim that the SART induces mindlessness.

22. Minagawa-Kawai et al. (2012). **Inights on NIRS sensitivity from a cross-linguistic study on the emergence of phonological grammar**

Abstract: Each language has a unique set of phonemic categories and phonotactic rules which determine permissible sound sequences in that language. Behavioral research demonstrates that one's native language shapes the perception of both sound categories and sound sequences in adults, and neuroimaging results further indicate that the processing of native phonemes and phonotactics involves a left-dominant perisylvian brain network. Recent work using a novel technique, functional Near InfraRed Spectroscopy (NIRS), has suggested that a left-dominant network becomes evident towards the end of the first year of life as infants process phonemic contrasts. The present research project attempted to assess whether the same pattern would be seen for native phonotactics. We measured brain responses in Japanese- and French-learning infants to two contrasts: Abuna vs. Abna (a phonotactic contrast that is native in French, but not in Japanese) and Abuna vs. Abuuna (a vowel length contrast that is native in Japanese, but not in French). Results did not show a significant response to either contrast in either group, unlike both previous behavioral research on phonotactic processing and NIRS work on phonemic processing. To understand these null results, we performed similar NIRS experiments with Japanese adult participants. These data suggest that the infant null results arise from an interaction of multiple factors, involving the suitability of the experimental paradigm for NIRS measurements and stimulus perceptibility. We discuss the challenges facing this novel technique, particularly

focusing on the optimal stimulus presentation which could yield strong enough hemodynamic responses when using the change detection paradigm.

23. Winther Schytz et al. (2013). **Low-frequency oscillations and vasoreactivity of cortical vessels in obstructive sleep apnea during wakefulness: A near infrared spectroscopy study**

Abstract: Objectives: Effective nasal continuous positive airway pressure (CPAP) therapy reduces the cardiovascular outcomes associated with obstructive sleep apnea (OSA), but the mechanism behind this effect is unclear. We investigated if OSA patients during wakefulness showed signs of increased sympathetic activity and decreased vasoreactivity in cerebral cortical vessels as measured with near-infrared spectroscopy (NIRS), and if this may be reversed by CPAP treatment. Subjects and methods: 23 OSA patients (mean age, 55 y) naive to CPAP were included in a prospective interventional study. The OSA patients received CPAP therapy for at least two months. Cortical low-frequency oscillation (LFO) amplitudes and vasoreactivity during a breath hold test were measured with NIRS and were compared between baseline and after CPAP treatment. Baseline values also were compared to 13 healthy controls (mean age, 52 y). Results: We found a decrease in LFO amplitudes after CPAP therapy (P = 0.022) in OSA patients. We found no differences in LFO amplitudes between OSA patients and healthy controls (P = 0.934). There were no differences in peak vascular response following breath hold tests in OSA patients before and after CPAP therapy (P = 0.158) or compared to healthy controls (P = 0.740). Conclusion: Our NIRS study revealed a decrease in LFO amplitude following two months of CPAP treatment in OSA patients, which may reflect a decrease in sympathetic activity affecting cortical vessels.

24. Lloyd-Fox et al. (2013). **Reduced neural sensitivity to social stimuli in infants at risk for autism**

Abstract: In the hope of discovering early markers of autism, attention has recently turned to the study of infants at risk owing to being the younger siblings of children with autism. Because the condition is highly heritable, later-born siblings of diagnosed children are at substantially higher risk for developing autism or the broader autism phenotype than the general population. Currently, there are no strong predictors of autism in early infancy and diagnosis is not reliable until around 3 years of age. Because indicators of brain functioning may be sensitive predictors, and atypical social interactions are characteristic of the syndrome, we examined whether temporal lobe specialization for processing visual and auditory social stimuli during infancy differs in infants at risk. In a functional near-infrared spectroscopy study, infants aged 4–6 months at risk for autism showed less selective neural responses to social stimuli (auditory and visual) than low-risk controls. These group differences could not be attributed to overall levels of attention, developmental stage or chronological age. Our results provide the first demonstration of specific differences in localizable brain function within the first 6 months of life in a group of infants at risk for autism. Further, these differences closely resemble known patterns of neural atypicality in children and adults with autism. Future work will determine whether these differences in infant neural responses to social stimuli predict either later autism or the broader autism phenotype frequently seen in unaffected family members.

25. Rodrigo et al. (2013). **Differentiating functions of the lateral and medial prefrontal cortex in motor response inhibition**

Abstract: The right inferior frontal gyrus is generally considered a critical region for motor response inhibition. Recent studies, however, suggest that the role of this cortical area in response inhibition may be overstated and that the contributions of other aspects of the prefrontal cortex are often overlooked. The current study used optical imaging to identify regions of the prefrontal cortex beyond the right inferior frontal gyrus which may serve to support motor response inhibition. Forty-three right-handed healthy adults completed a manual Go/No-Go task while evoked oxygenation of the prefrontal cortex was measured using 16-channel functional near-infrared spectroscopy. During motor response inhibition, the right inferior frontal gyrus, and to a lesser extent

the homologous contralateral region, showed increased activation relative to a baseline task. Conversely, the medial prefrontal cortex was significantly deactivated, and the extent of reduced activity in this region was associated with fewer errors on the response inhibition task. These findings suggest a more substantial role of the left inferior frontal gyrus in response inhibition and possibly a distinct function of the middle frontal gyrus subserving error detection on manual motor control tasks.

26. Aoki et al. (2013). **Correlation between prefrontal cortex activity during working memory tasks and natural mood independent of personality effects: An optical topography study**

Abstract: Interactions between mood and cognition have drawn much attention in the fields of psychology and neuroscience. Recent neuroimaging studies have examined a neural basis of the mood–cognition interaction that which emphasize the role of the prefrontal cortex (PFC). Although these studies have shown that natural mood variations among participants are correlated with PFC activity during cognitive tasks, they did not control for personality differences. Our aim in this study was to clarify the relationship between natural mood and PFC activity by partialling out the effects of personality. Forty healthy adults completed self-report questionnaires assessing natural mood (the Profile of Mood States) and personality (the NEO Five-Factor Inventory and the Behavioral Inhibition/Activation Systems scales). They performed verbal and spatial working memory (WM) tasks while their PFC activity was measured using optical topography, a non-invasive, low-constraint neuroimaging tool. Correlation analysis showed that the level of negative mood was inversely associated with PFC activity during the verbal WM task, which replicated our previous findings. Furthermore, the negative correlation between negative mood and PFC activity remained significant after controlling for participants' personality traits, suggesting that natural mood is an independent contributing factor of PFC activity during verbal WM tasks.

27. Duan et al. (2013). **Time-domain schemes of optical topography: methodology, simulative and experimental validation**

Abstract: To cope with the low quantification in the established optical topography that originates from the excessively simplified computation model based on the modified Lambert-Beer's Law (MLBL), we propose a least-squares fitting scheme for time-domain optical topography that seeks for data matching between the time-resolved measurement and the model prediction calculated by analytically solving the time-domain diffusion equation in semi-infinite geometry. Our simulative and phantom experiments demonstrate that the proposed curve-fitting method is overall superior to the conventional MLBL-based one in quantitative performance.

28. Zhang et al. (2013). **Real-time multispectral diffuse optical tomography system for imaging epileptic activity and connectivity**

Abstract: We describe a multispectral continuous-wave diffuse optical tomography (DOT) system that can be used for in vivo three-dimensional (3-D) imaging of seizure dynamics. Fast 3-D data acquisition is realized through a time multiplexing approach based on a parallel lighting configuration - our system can achieve 0.12ms per source per wavelength and up to 14Hz sampling rate for a full set of data for 3-D DOT image reconstruction. The system is validated using both static and dynamic tissue-like phantoms. In vivo rat experiments using both focal and generalized models of seizure are also demonstrated. In the focal seizure experiment, hemodynamic seizure focus was clearly detected and tracked. In the generalized seizure experiment, early hemodynamic responses with heterogeneous patterns were detected several minutes preceding the EEG onset of seizures and widespread hemodynamic changes were found evolving from local regions. Connectivity changes were also found during the development of seizures. This study demonstrates that DOT represents a powerful tool for investigating seizure generation and propagation, elucidating the causes and mechanism of seizures.

29. Fedele et al. (2013). **Monochromatic ultra-slow oscillations in the human electroencephalogram**

Abstract: Introduction: Ultra-slow electroencephalographic oscillations (< 0.1 Hz) have been extensively investigated in humans and animals and were found to occur in a variety of conditions. Despite the ample evidence for their presence in the human brain, less is known about their biological mechanisms. Here, we report on the existence of monochromatic ultra-slow oscillations (MUSO) in the human scalp electroencephalogram (EEG). Methods: In order to address the biological MUSO origin we performed simultaneous recordings with multi-channel EEG, near infrared spectroscopy (NIRS) and non-invasive continuous measurement of arterial blood pressure in 10 healthy subjects. To test the relevance of hemodynamic contribution to MUSO variability, we performed recordings before and after a 60 degrees bed tilting manoeuvre. Results: MUSO were detected in 8 out of 10 subjects during restful wakefulness. The striking signature of these oscillations was their almost monochromatic spectral profile restricted to the frequency range 0.08 - 0.15 Hz. The spatial topography of MUSO was complex, showing multiple foci variable across subjects. Application of spatio-spectral decomposition revealed multiple MUSO components in a given subject. These oscillations were most pronounced after the application of spatial derivatives, such as bipolar or Laplacian montages. While the peak frequency of NIRS and blood pressure was often similar across subjects, the peak frequencies of MUSO differed considerably from both NIRS and blood pressure oscillations. In 8/10 subjects we observed a coherence between MUSO and Oxy-Hb (NIRS)/arterial blood pressure. After a 60 degrees tilt we observed a significative correlation at the MUSO spectral power peak between EEG and blood pressure. Discussion: We hypothesize that MUSOs can occur due to the modulation of the blood-brain barrier DC potential by mechanical fluctuations related to hemodynamics or due to skin vasomotion. The discovery of such possibly extra-neuronal pronounced oscillations opens an avenue for studying hemodynamic responses with EEG technology and in addition poses a number of questions concerning the interpretation of previously recorded low-frequency neuronal oscillations in humans.

30. Massaro et al. (2013). **Brain Perfusion in Encephalopathic Newborns after Therapeutic Hypothermia**

Abstract: BACKGROUND AND PURPOSE: Cerebral perfusion patterns in neonates with HIE after therapeutic hypothermia have not been well described. The objectives of this study were to compare global and regional perfusion between infants with HIE and neonate controls and to relate measures of cerebral perfusion to brain injury on conventional MR imaging in neonates with HIE. MATERIALS AND METHODS: Term encephalopathic neonates meeting criteria for hypothermia between June 2011 and January 2012 were enrolled in this prospective observational study. MR imaging-ASL was performed in the second week of life. Comparisons were made with data from neonate controls who underwent the same imaging protocol. NIRS measures of cerebral oxygenation during and immediately after hypothermia were also evaluated in a subset of patients. Secondary analyses were performed to assess cerebral perfusion and oxygenation differences by pattern of injury on qualitative MR imaging interpretation. RESULTS: We enrolled 18 infants with HIE and 18 control infants. Mean global CBF and regional CBF in the basal ganglia, thalamus, and anterior white matter were higher in cases compared with controls. Infants with HIE with injury on MR imaging, however, had lower CBF (significant in the thalamus) compared with those with normal MR imaging. Decreased FTOE by NIRS further differentiated patients with HIE with injury on MR imaging. CONCLUSIONS: Disturbed cerebral perfusion is observed in the second week of life in some babies with HIE despite treatment with hypothermia. Infants with HIE with injury on MR imaging have lower regional CBF in the thalamus compared with those without injury, possibly representing pseudonormalization of CBF and low metabolic demand after progression to irreversible brain injury.

31. Demir et al. (2013). **Near-Infrared Spectroscopy Monitoring of the Spinal Cord During Type B Aortic Dissection Surgery**

Abstract: Near-infrared spectroscopy (NIRS) is a noninvasive continuous monitoring method for measuring the oxyhemoglobin saturation of the brain tissue. NIRS monitoring can suggest neuronal hypoxia in the frontal-brain before irreversible impairment of cellular metabolism. We report two cases of Type B aortic dissection surgery in which spinal regional perfusion monitoring was performed by placing two NIRS sensors on the back-skin through T6–T8 and T9–T11 vertebraes.

32. Baerts et al. (2013). **Tocolytic indomethacin: effects on neonatal haemodynamics and cerebral autoregulation in the preterm newborn**

Abstract: Background Indomethacin has vasoactive properties in cerebral and systemic vascular beds, and it improves cerebral autoregulatory ability. We speculated that tocolytic indomethacin will improve cerebral autoregulatory ability in the very preterm infant in early postnatal life. Methods Eighteen stable preterm infants gestational age (GA) 25.3–29.6 weeks, birth weight (BW) 660–1430 grams), whose mothers had received 50–150 mg of tocolytic indomethacin within 24 h before birth, and 18 individually matched controls (GA 25.0–29.7 weeks, BW 700–1390 grams) were studied four times for 15 min in the first 24 h of life. Autoregulation was assessed by determining correlations between mean arterial blood pressure (MABP (mm Hg)) and near-infrared spectroscopy-monitored cerebral oxygenation (rScO2). Results MABPs were significantly higher in the indomethacin infants than in the control infants (p=0.03). A decreased ability to autoregulate was found in four of the indomethacin infants, and in six of the control infants, which is not significantly different. Conclusions Prenatally administered indomethacin, given as a tocolytic in doses of 50–150 mg per day, improved transitional circulation in very preterm infants by significantly raising the MABP. It did not have an effect on the ability to autoregulate the cerebral circulation. In this study, no differences in short-term outcomes, like haemorrhagic or ischaemic cerebral lesions, were observed.

33. Drury et al. (2013). **Deep hypothermic circulatory arrest during the arterial switch operation is associated with reduction in cerebral oxygen extraction but no increase in white matter injury**

Abstract: Objective: Deep hypothermic circulatory arrest may be associated with increased neural injury. We investigated whether short periods of deep hypothermic circulatory arrest are associated with altered neurophysiologic recovery or greater risk of injury. Methods: Eighteen term infants with transposition of the great arteries undergoing the arterial switch operation were enrolled. Deep hypothermic circulatory arrest was used in 11, and bypass alone in 7. Near-infrared spectroscopy and amplitude-integrated electroencephalography were recorded with standard monitoring during and from 4 to 16 h after surgery. Fractional tissue oxygen extraction was determined from arterial oxygen saturation and venous weighted intracerebral oxygenation. Magnetic resonance imaging was performed before and 5 to 7 days after surgery. Results: There were no significant differences between patients requiring deep hypothermic circulatory arrest (median, 5 min; range, 3-6 min) or cardiopulmonary bypass only at the beginning of surgery. At the end of surgery, amplitude-integrated electroencephalography minimum amplitude was significantly lower in the deep hypothermic circulatory arrest group ($P < .05$), and fractional tissue oxygen extraction tended to be lower ($P = .068$). After surgery, deep hypothermic circulatory arrest was associated with significantly higher tissue oxygenation index, lower fractional tissue oxygen extraction, and lower core temperature ($P < .05$). Magnetic resonance imaging–defined white matter injuries before and after surgery were similar between groups. Conclusions: In this prospective, observational study, brief deep hypothermic circulatory arrest during arterial switch was associated with reduced cerebral oxygen uptake during recovery, with transient electroencephalographic suppression but no increase in risk of white matter injury.

34. Hervey et al. (2013). **Motion tracking and electromyography assist the removal of mirror hand contributions to fNIRS images acquired during a finger tapping task performed by children with cerebral palsy**

Abstract: Functional neurological imaging has been shown to be valuable in evaluating brain plasticity in children with cerebral palsy (CP). In recent studies it has been demonstrated that functional near-infrared spectroscopy (fNIRS) is a viable and sensitive method for imaging motor cortex activities in children with CP. However, during unilateral finger tapping tasks children with CP often exhibit mirror motions (unintended motions in the non-tapping hand), and current fNIRS image formation techniques do not account for this. Therefore, the resulting fNIRS images contain activation from intended and unintended motions. In this study, cortical activity was mapped with fNIRS on four children with CP and five controls during a finger tapping task. Finger motion and arm muscle activation were concurrently measured using motion tracking cameras and electromyography (EMG). Subject-specific regressors were created from motion capture and EMG data and used in a general linear model (GLM) analysis in an attempt to create fNIRS images representative of different motions. The analysis provided an fNIRS image representing activation due to motion and muscle activity for each hand. This method could prove to be valuable in monitoring brain plasticity in children with CP by providing more consistent images between measurements. Additionally, muscle effort versus cortical effort was compared between control and CP subjects. More cortical effort was required to produce similar muscle effort in children with CP. It is possible this metric could be a valuable diagnostic tool in determining response to treatment.

35. Lin et al. (2013). **Monitoring of human brain functions in risk decision-making task by diffuse optical tomography using voxel-wise general linear model**

Abstract: Functional near-infrared spectroscopy (fNIRS) is a non-invasive imaging technique which measures the hemodynamic changes that reflect the brain activity. Diffuse optical tomography (DOT), a variant of fNIRS with multi-channel NIRS measurements, has demonstrated capability of three dimensional (3D) reconstructions of hemodynamic changes due to the brain activity. Conventional method of DOT image analysis to define the brain activation is based upon the paired t-test between two different states, such as resting-state versus task-state. However, it has limitation because the selection of activation and post-activation period is relatively subjective. General linear model (GLM) based analysis can overcome this limitation. In this study, we combine the 3D DOT image reconstruction with GLM-based analysis (i.e., voxel-wise GLM analysis) to investigate the brain activity that is associated with the risk-decision making process. Risk decision-making is an important cognitive process and thus is an essential topic in the field of neuroscience. The balloon analogue risk task (BART) is a valid experimental model and has been commonly used in behavioral measures to assess human risk taking action and tendency while facing risks. We have utilized the BART paradigm with a blocked design to investigate brain activations in the prefrontal and frontal cortical areas during decision-making. Voxel-wise GLM analysis was performed on 18human participants (10 males and 8females).In this work, we wish to demonstrate the feasibility of using voxel-wise GLM analysis to image and study cognitive functions in response to risk decision making by DOT. Results have shown significant changes in the dorsal lateral prefrontal cortex (DLPFC) during the active choice mode and a different hemodynamic pattern between genders, which are in good agreements with published literatures in functional magnetic resonance imaging (fMRI) and fNIRS studies.

36. Li et al. (2013). **Test-retest assessment of functional near-infrared spectroscopy to measure risk decision making in young adults**

Abstract: Investigation of the reliability and reproducibility of the hemodynamic response is important for interpretation and understanding of the results of functional near-infrared spectroscopy (fNIRS). It measures optical signals absorbed by the brain tissue and reflects the neuronal activities indirectly. Here we described an fNIRS study measured in the prefrontal region (Brodman area 9, 10, part of 46) to examine the risk decision-

making behavior in nine young adults. The Balloon Analog Risk Task (BART) is widely used to test the level of risk taking ability in the field of psychology. BART was a protocol utilized in this study to evoke a risk-taking environment with a gambling-like balloon game in each subject. Specifically, we recorded the brain oxygenated-hemoglobin (HbO) and deoxygenated-hemoglobin (HHb) changes during the two repeated measurements within a time interval of 3 weeks. The results demonstrate that the changes in HbO2 amplitudes have high reliability at the group level, and that the spatial patterns of the tomographic images have high reproducibility in size and a moderate degree of overlap. Overall, this study confirms that the hemodynamic response to risk decision-making (i.e., BART) seen by fNIRS is highly reliable and reproducible.

37. Grossmann (2013). **Mapping Prefrontal Cortex Functions in Human Infancy**

Abstract: It has long been thought that the prefrontal cortex, as the seat of most higher brain functions, is functionally silent during most of infancy. This review highlights recent work concerned with the precise mapping (localization) of brain activation in human infants, providing evidence that prefrontal cortex exhibits functional activation much earlier than previously thought. A systematic evaluation of the activation patterns in these neuroimaging studies mainly based on functional near-infrared spectroscopy reveals that prefrontal cortex function can be broadly divided into two distinct anatomical clusters with different functional properties. One cluster of activations falls within the region of the medial prefrontal cortex and is mainly involved in affective processes; another cluster is located in lateral aspects of the prefrontal cortex and shows sensitivity to cognitive processes such as memory and attention. This distinction is in line with adult data and evolutionary models and may represent a developmentally continuous organization principle of prefrontal cortex function. All in all, this review is aimed at providing a synthesis of new findings that are emerging from the use of neuroimaging techniques with infants as well as at encouraging further theory-driven research to understand the developmental origins of prefrontal cortex function.

38. Khan et al. (2013). **Use of functional near-infrared spectroscopy to monitor cortical plasticity induced by transcranial direct current stimulation**

Abstract: Electrical stimulation of the human cortex in conjunction with physical rehabilitation has been a valuable approach in facilitating the plasticity of the injured brain. One such method is transcranial direct current stimulation (tDCS) which is a non-invasive method to elicit neural stimulation by delivering current through electrodes placed on the scalp. In order to better understand the effects tDCS has on cortical plasticity, neuroimaging techniques have been used pre and post tDCS stimulation. Recently, neuroimaging methods have discovered changes in resting state cortical hemodynamics after the application of tDCS on human subjects. However, analysis of the cortical hemodynamic activity for a physical task during and post tDCS stimulation has not been studied to our knowledge. A viable and sensitive neuroimaging method to map changes in cortical hemodynamics during activation is functional near-infrared spectroscopy (fNIRS). In this study, the cortical activity during an event-related, left wrist curl task was mapped with fNIRS before, during, and after tDCS stimulation on eight healthy adults. Along with the fNIRS optodes, two electrodes were placed over the sensorimotor hand areas of both brain hemispheres to apply tDCS. Changes were found in both resting state cortical connectivity and cortical activation patterns that occurred during and after tDCS. Additionally, changes to surface electromyography (sEMG) measurements of the wrist flexor and extensor of both arms during the wrist curl movement, acquired concurrently with fNIRS, were analyzed and related to the transient cortical plastic changes induced by tDCS.

39. Chou et al. (2013). **The role of near-infrared spectroscopy in Alzheimer's disease**

Abstract: Near-infrared spectroscopy (NIRS) is a noninvasive neuroimaging tool used to measure activation-induced changes in cerebral hemoglobin concentration. By this technique, changes in the optical absorption of

light are recorded over time and are used to estimate the functionally evoked changes in cerebral oxyhemoglobin and deoxyhemoglobin concentrations that result from local cerebral vascular and oxygen metabolic effects during brain activities. Over the past decades, it has become a frequently used technique in psychiatry studies such as depression, schizophrenia, and Alzheimer's disease. Compared to positron emission tomography or magnetic resonance imaging, NIRS has the advantages of having higher temporal resolution, being easier to perform, and the ability to use portable equipment. Because of its growing popularity and promising perspectives in clinical applications, we review Alzheimer's disease-related studies using NIRS methodology in this article. The existing evidence shows that NIRS might have the potential to become either a disease- or syndrome-specific diagnostic tool in the future. However, larger studies with more study participants are needed to establish disease-specific sensitivity and specificity.

40. Toronov & Schelkanova (2013). **Hyperspectral functional imaging of the human brain**

Abstract: We performed the independent component analysis of the hyperspectral functional near-infrared data acquired on humans during exercise and rest. We found that the hyperspectral functional data acquired on the human brain requires only two physiologically meaningful components to cover more than 50% of the temporal variance in hundreds of wavelengths. The analysis of the spectra of independent components showed that these components could be interpreted as results of changes in the cerebral blood volume and blood flow. Also, we found significant contributions of water and cytochrome c oxydase into changes associated with the independent components. Another remarkable effect of ICA was its good performance in terms of the filtering of the data noise.

41. Poulet et al. (2013). **A time-gated near-infrared spectroscopic imaging device for clinical applications**

Abstract: A time-resolved, spectroscopic, diffuse optical tomography device was assembled for clinical applications like brain functional imaging. The entire instrument lies in a unique setup that includes a light source, an ultrafast time-gated intensified camera and all the electronic control units. The light source is composed of four near infrared laser diodes driven by a nanosecond electrical pulse generator working in a sequential mode at a repetition rate of 100 MHz. The light pulses are less than 80 ps FWHM. They are injected in a four-furcated optical fiber ended with a frontal light distributor to obtain a uniform illumination spot directed towards the head of the patient. Photons back-scattered by the subject are detected by the intensified CCD camera. There are resolved according to their time of flight inside the head. The photocathode is powered by an ultrafast generator producing 50 V pulses, at 100 MHz and a width corresponding to a 200 ps FWHM gate. The intensifier has been specially designed for this application. The whole instrument is controlled by an FPGA based module. All the acquisition parameters are configurable via software through an USB plug and the image data are transferred to a PC via an Ethernet link. The compactness of the device makes it a perfect device for bedside clinical applications. The instrument will be described and characterized. Preliminary data recorded on test samples will be presented.

42. Chaudhary et al. (2013). **Simultaneous NIRS and kinematics study of planning and execution of motor skill task: towards cerebral palsy rehabilitation**

Abstract: Cerebral palsy (CP) is a term that describes a group of motor impairment syndromes secondary to genetic and/or acquired disorders of the developing brain. In the current study, NIRS and motion capture were used simultaneously to correlate the brain's planning and execution activity during and with arm movement in healthy individual. The prefrontal region of the brain is non-invasively imaged using a custom built continuous-wave based near infrared spectroscopy (NIRS) system. The kinematics of the arm movement during the studies is recorded using an infrared based motion capture system, Qualisys. During the study, the subjects (over 18

years) performed 30 sec of arm movement followed by 30 sec rest for 5 times, both with their dominant and non-dominant arm. The optical signal acquired from NIRS system was processed to elucidate the activation and lateralization in the prefrontal region of participants. The preliminary results show difference, in terms of change in optical response, between task and rest in healthy adults. Currently simultaneous NIRS imaging and kinematics data are acquired in healthy individual and individual with CP in order to correlate brain activity to arm movement in real-time. The study has significant implication in elucidating the evolution in the functional activity of the brain as the physical movement of the arm evolves using NIRS. Hence the study has potential in augmenting the designing of training and hence rehabilitation regime for individuals with CP via kinematic monitoring and imaging brain activity.

43. Schmid et al. (2013). **Cerebral desaturations in preterm infants: a crossover trial on influence of oxygen saturation target range**

Abstract: Objective To test the hypothesis that a higher pulsoximetric arterial oxygen saturation (SpO2) target range is associated with reduced cerebral tissue oxygen desaturations from baseline during events of hypoxaemia or bradycardia. Design: Randomised crossover trial. Setting: Single tertiary care neonatal intensive care unit. Patients: Sixteen preterm infants with severe intermittent hypoxaemia or bradycardia. Interventions: SpO2 target was set to 80–92% and 85–96% for 4 h each in random sequence. On a subsequent day, the target sequence was reversed and the study was repeated. Main outcome measures: We simultaneously recorded cerebral tissue oxygen saturation (cerebral StO2), SpO2 and heart rate. Cerebral StO2 was measured by near infrared spectroscopy. The primary outcome was the cumulative cerebral StO2 desaturation score representing the area below a cerebral StO2 baseline value before onset of each hypoxaemic or bradycardic event. Results: During low SpO2 target range the median (IQR) cumulative cerebral StO2 desaturation score was higher (27384 (15825–37396) vs 18103 (6964–32946), p=0.011) and the mean (±SD) number of events was higher (29.1 (±15.3) vs 21.1 (±11.4), p=0.001). More time was spent with SpO2 below 80% (57.2 (±24.8) min vs 34.0 (±29.6) min, p=0.006). Total time of hyperoxaemia (defined as SpO2 ≥97% and ≥99%, respectively) and total time with cerebral StO2 <60% and <55% were similar. Conclusions: A lower SpO2 target range was associated with a greater cumulative cerebral StO2 desaturation score, caused by more frequent SpO2 desaturations. However, time at very low cerebral StO2 was not affected. Episodes of hyperoxaemia were not reduced.

44. Garett et al. (2013). **Moment-to-moment brain signal variability: A next frontier in human brain mapping?**

Abstract: Neuroscientists have long observed that brain activity is naturally variable from moment-to-moment, but neuroimaging research has largely ignored the potential importance of this phenomenon. An emerging research focus on within-person brain signal variability is providing novel insights, and offering highly predictive, complementary, and even orthogonal views of brain function in relation to human lifespan development, cognitive performance, and various clinical conditions. As a result, brain signal variability is evolving as a bona fide signal of interest, and should no longer be dismissed as meaningless noise when mapping the human brain.

45. Takizawa et al. (2013). **Anxiety and Performance: The Disparate Roles of Prefrontal Subregions Under Maintained Psychological Stress**

Abstract: Despite increasing interest in anxiety and psychological stress in daily life, little is known about neural correlates that underlie maintained psychological stress and their relationship with anxiety. In particular, the activation characteristics of lateral prefrontal subregions and their relationship with anxiety and cognitive performance under maintained psychological stress remain unknown. This study used near-infrared spectroscopy (NIRS), a noninvasive and "real-world" functional neuroimaging method, to investigate the

hemodynamic responses in wide areas of the prefrontal cortex (PFC) and the influence of anxiety under conditions of maintained stress induced by a continuous arithmetic task (2 sets, 15 min each) performed in a natural sitting posture. Although anxiety and performance are not directly correlated, the hemodynamic response in the medial portion of the lateral PFC (dorsolateral and frontopolar PFC) was significantly associated with anxiety, while hemodynamic responses in the ventrolateral PFC were associated with performance. Additionally, in the same medial region of the lateral PFC, trait and state anxieties were related to changes in deoxy- and oxy-hemoglobin concentrations, respectively. This NIRS finding suggests disparate roles for prefrontal subregions in anxiety and performance under psychological stress and may lead to a better understanding of neural correlates for anxiety in everyday life.

46. Kozberg et al. (2013). **Resolving the transition from negative to positive blood oxygen level-dependent responses in the developing brain**

Abstract: The adult brain exhibits a local increase in cortical blood flow in response to external stimulus. However, broadly varying hemodynamic responses in the brains of newborn and young infants have been reported. Particular controversy exists over whether the “true” neonatal response to stimulation consists of a decrease or an increase in local deoxyhemoglobin, corresponding to a positive (adult-like) or negative blood oxygen level-dependent (BOLD) signal in functional magnetic resonance imaging (fMRI), respectively. A major difficulty with previous studies has been the variability in human subjects and measurement paradigms. Here, we present a systematic study in neonatal rats that charts the evolution of the cortical blood flow response during postnatal development using exposed-cortex multispectral optical imaging. We demonstrate that postnatal-day-12–13 rats (equivalent to human newborns) exhibit an “inverted” hemodynamic response (increasing deoxyhemoglobin, negative BOLD) with early signs of oxygen consumption followed by delayed, active constriction of pial arteries. We observed that the hemodynamic response then matures via development of an initial hyperemic (positive BOLD) phase that eventually masks oxygen consumption and balances vasoconstriction toward adulthood. We also observed that neonatal responses are particularly susceptible to stimulus-evoked systemic blood pressure increases, leading to cortical hyperemia that resembles adult positive BOLD responses. We propose that this confound may account for much of the variability in prior studies of neonatal cortical hemodynamics. Our results suggest that functional magnetic resonance imaging studies of infant and child development may be profoundly influenced by the maturing neurovascular and autoregulatory systems of the neonatal brain.

47. Macnab et al. (2013). **Ambulant monitoring of bladder oxygenation and hemodynamics using wireless near-infrared spectroscopy**

Abstract: I NTRODUCTION: Near-infrared spectroscopy (NIRS) non-invasively detects changes in the concentration of the chromophores oxygenated (ΔO(2)Hb) and deoxygenated hemoglobin (ΔHHb) as the bladder detrusor muscle contracts during voiding. Such data provide novel information on bladder oxygenation and hemodynamics. We evaluated the feasibility of monitoring ambulant subjects using a wireless NIRS device. METHODS: The wireless device uses paired light-emitting diodes (wavelengths 760 and 850 nm) and a silicon photodiode detector. We monitored 14 asymptomatic subjects (10 adults, 4 children) and 6 symptomatic children with non-neurogenic lower urinary tract dysfunction (NLUTD) during spontaneous voiding after natural filling. The device was taped to the abdominal skin 2 cm above the symphysis pubis across the midline. The wireless NIRS data (patterns of change in chromophore concentration) were compared between subjects and to the data obtained using a laser-powered instrument. RESULTS: Graphs of ΔO(2)Hb, ΔHHb and total hemoglobin (ΔtHb) were obtained from all 20 patients. Data during uroflow showed reproducible patterns of bladder chromophore change between asymptomatic subjects (rise in ΔtHb/ΔO (2)Hb), consistent with laser instrument data. In contrast, all 6 symptomatic children had a negative trend in ΔtHb, with falls in ΔO(2)Hb. One adult experienced "shy" bladder and changes in hemodynamics/oxygenation occurred while bladder volume was unchanged.

CONCLUSIONS: Wireless NIRS bladder monitoring is feasible in ambulant adults and children; wireless and laser-derived data in asymptomatic subjects are comparable. Pilot data suggest that subjects with symptomatic NLUTD have impaired bladder oxygenation/ hemodynamics. The fact that chromophore changes occur when bladder volume remains constant supports the concept that NIRS data are a physiologic measure.

48. Binder et al. (2013). **Cerebral and Peripheral Regional Oxygen Saturation during Postnatal Transition in Preterm Neonates**

Abstract: Objective: To evaluate peripheral regional oxygen saturation (rpSO2) and cerebral regional oxygen saturation (rcSO2) during the immediate postnatal transition in late preterm infants with and without the need for respiratory support. Study design: This was a prospective observational study using near-infrared spectroscopy to evaluate changes in rpSO2 and rcSO2. These variables were measured during the first 15 minutes of life after elective cesarean delivery. Peripheral oxygen saturation (SpO2) and heart rate were measured continuously by pulse oximetry, and cerebral fractional tissue oxygen extraction (cFTOE) was calculated. Two groups were compared based on their need for respiratory support: a respiratory support group and a normal transition group. Positive-pressure ventilation was delivered with a T-piece resuscitator, and oxygen was adjusted based on SpO2 values. A Florian respiratory function monitor was used to record the ventilation variables. Results: There were 21 infants in the normal transition group and 21 infants in the respiratory support group. Changes in heart rate over time were similar in the 2 groups. SpO2, rcSO2, and rpSO2 values were consistently higher in the normal transition group. In the respiratory support group, cFTOE values remained significantly elevated for a longer period. Conclusion: This systematic analysis of rpSO2, rcSO2, and cFTOE in late preterm infants found significantly lower oxygen saturation values in infants who received respiratory support compared with a normal transition group. We hypothesize that the elevated cFTOE values in the respiratory support group represent compensation for lower oxygen delivery.

49. Karim et al. (2013). **Functional brain imaging of multi-sensory vestibular processing during computerized dynamic posturography using near-infrared spectroscopy**

Abstract: Functional near-infrared spectroscopy (fNIRS) is a non-invasive brain imaging method that uses light to record regional changes in cerebral blood flow in the cortex during activation. fNIRS uses portable wearable sensors to allow measurements of brain activation during tasking. In this study, fNIRS was used to investigate how the brain processes information from multiple sensory modalities during dynamic posturography. Fifteen healthy volunteers (9M/6F; ages 28 +/− 9 yrs) participated in the posturography study while undergoing fNIRS brain imaging. Four standard conditions from the sensory organization test (SOT) were performed and a bilateral fNIRS probe was used to examine the cortical brain responses from the frontal, temporal, and parietal brain regions. We found that there was bilateral activation in the temporal–parietal areas (superior temporal gyrus, STG, and supramarginal gyrus, SMG) when both vision and proprioceptive information were degraded; forcing reliance on primarily vestibular information in the control of balance. This is consistent with previous reports of the role of these regions in vestibular control and demonstrates the potential utility of fNIRS in the study of cortical control of vestibular function during standing balance tasks.

50. Costantini et al. (2013). **Studying social cognition using near-infrared spectroscopy: the case of social Simon effect**

Abstract: In order to understand the so-called "social brain," we need to monitor social interactions in face-to-face paradigms. Near-infrared spectroscopy (NIRS) is a promising technique to achieve this goal. We investigate the neuronal underpinnings of sharing a task in a proper social context. We record cortical activity by means of NIRS, while participants perform a joint Simon task. Different from other hemodynamic techniques, NIRS allows us to have both participants sit comfortably close to each other in a realistic and ecological environment.

We found higher activation in the sensorimotor cortex while processing compatible trials as compared to incompatible ones referring to one's own action alternative. Strikingly, when the participant was not responding because it was the turn of the other member of the pair, the inferior parietal was activated. This study provides twofold findings: first, they suggest that the joint Simon effect relies more on shared attentional mechanisms than a proper mapping of the other's motor response. Second, they highlight the invaluable contribution NIRS can afford to social neuroscience in order to preserve ecological and naturalistic settings.

51. Diop & Lawrence (2013). **Improving the depth sensitivity of time-resolved measurements by extracting the distribution of times-of-flight**

Abstract: Time-resolved (TR) techniques provide a means of discriminating photons based on their time-of-flight. Since early arriving photons have a lower probability of probing deeper tissue than photons with long time-of-flight, time-windowing has been suggested as a method for improving depth sensitivity. However, TR measurements also contain instrument contributions (instrument-response-function, IRF), which cause temporal broadening of the measured temporal point-spread function (TPSF) compared to the true distribution of times-of-flight (DTOF). The purpose of this study was to investigate the influence of the IRF on the depth sensitivity of TR measurements. TPSFs were acquired on homogeneous and two-layer tissue-mimicking phantoms with varying optical properties. The measured IRF and TPSFs were deconvolved using a stable algorithm to recover the DTOFs. The microscopic Beer-Lambert law was applied to the TPSFs and DTOFs to obtain depth-resolved absorption changes. In contrast to the DTOF, the latest part of the TPSF was not the most sensitive to absorption changes in the lower layer, which was confirmed by computer simulations. The improved depth sensitivity of the DTOF was illustrated in a pig model of the adult human head. Specifically, it was shown that dynamic absorption changes obtained from the late part of the DTOFs recovered from TPSFs acquired by probes positioned on the scalp were similar to absorption changes measured directly on the brain. These results collectively demonstrate that this method improves the depth sensitivity of TR measurements by removing the effects of the IRF.

52. Mihara et al. (2013). **Near-infrared Spectroscopy–mediated Neurofeedback Enhances Efficacy of Motor Imagery–based Training in Poststroke Victims**

Abstract: Background and Purpose—Despite the findings that motor imagery and execution are supposed to share common neural networks, previous studies using imagery-based rehabilitation have revealed inconsistent results. In the present study, we investigated whether feedback of cortical activities (neurofeedback) using near-infrared spectroscopy could enhance the efficacy of imagery-based rehabilitation in stroke patients. Methods—Twenty hemiplegic patients with subcortical stroke received 6 sessions of mental practice with motor imagery of the distal upper limb in addition to standard rehabilitation. Subjects were randomly allocated to REAL and SHAM groups. In the REAL group, cortical hemoglobin signals detected by near-infrared spectroscopy were fed back during imagery. In the SHAM group, irrelevant randomized signals were fed back. Upper limb function was assessed using the finger and arm subscales of the Fugl-Meyer assessment and the Action Research Arm Test. Results—The hand/finger subscale of the Fugl-Meyer assessment showed greater functional gain in the REAL group, with a significant interaction between time and group ($F_{2,36}=15.5$; $P<0.001$). A significant effect of neurofeedback was revealed even in severely impaired subjects. Imagery-related cortical activation in the premotor area was significantly greater in the REAL group than in the SHAM group ($T_{58}=2.4$; $P<0.05$). Conclusions—Our results suggest that near-infrared spectroscopy–mediated neurofeedback may enhance the efficacy of mental practice with motor imagery and augment motor recovery in poststroke patients with severe hemiparesis.

53. Näsi et al. (2013). **Effect of task-related extracerebral circulation on diffuse optical tomography: experimental data and simulations on the forehead**

Abstract: The effect of task-related extracerebral circulatory changes on diffuse optical tomography (DOT) of brain activation was evaluated using experimental data from 14 healthy human subjects and computer simulations. Total hemoglobin responses to weekday-recitation, verbal-fluency, and hand-motor tasks were measured with a high-density optode grid placed on the forehead. The tasks caused varying levels of mental and physical stress, eliciting extracerebral circulatory changes that the reconstruction algorithm was unable to fully distinguish from cerebral hemodynamic changes, resulting in artifacts in the brain activation images. Crosstalk between intra- and extracranial layers was confirmed by the simulations. The extracerebral effects were attenuated by superficial signal regression and depended to some extent on the heart rate, thus allowing identification of hemodynamic changes related to brain activation during the verbal-fluency task. During the hand-motor task, the extracerebral component was stronger, making the separation less clear. DOT provides a tool for distinguishing extracerebral components from signals of cerebral origin. Especially in the case of strong task-related extracerebral circulatory changes, however, sophisticated reconstruction methods are needed to eliminate crosstalk artifacts.

54. Peck et al. (2013). **Investigation of fNIRS Brain Sensing as Input to Information Filtering Systems**

Abstract: Today's users interact with an increasing amount of information, demanding a similar increase in attention and cognition. To help cope with information overload, recommendation engines direct users' attention to content that is most relevant to them. We suggest that functional near-infrared spectroscopy (fNIRS) brain measures can be used as an additional channel to information filtering systems. Using fNIRS, we acquire an implicit measure that correlates with user preference, thus avoiding the cognitive interruption that accompanies explicit preference ratings. We explore the use of fNIRS in information filtering systems by building and evaluating a brain-computer movie recommender. We find that our system recommends movies that are rated higher than in a control condition, improves recommendations with increased interaction with the system, and provides recommendations that are unique to each individual.

55. Heinzel et al. (2013). **Variability of (functional) hemodynamics as measured with simultaneous fNIRS and fMRI during intertemporal choice.**

Abstract: Neural processing inferred from hemodynamic responses measured with functional near infrared spectroscopy (fNIRS) may be confounded with individual anatomical or systemic physiological sources of variance. This may hamper the validity of fNIRS signal interpretations and associations between individual traits and brain activation, such as the link between impulsivity-related personality traits and decreased prefrontal cognitive control during reward-based decision making. Hemodynamic responses elicited by an intertemporal choice reward task in 20 healthy subjects were investigated for multimodal correlations of simultaneous fNIRS-fMRI and for an impact of anatomy and scalp fMRI signal fluctuations on fNIRS signals. Moreover, correlations of prefrontal activation with trait "sensitivity to reward" (SR) were investigated for differences between methods. While showing substantial individual variability, temporal fNIRS-fMRI correlations increased with the activation, which both methods consistently detected within right inferior/middle frontal gyrus. Here, up to 41% of fNIRS channel activation variance was explained by individual gray matter volume simulated to be reached by near-infrared light, and up to 20% by scalp-cortex distance. Extracranial fMRI and fNIRS time series showed significant temporal correlations in the temple region. SR was negatively correlated with fMRI but not fNIRS activation elicited by immediate rewards of choice within right inferior/middle frontal gyrus. Higher SR increased the correlation between extracranial fMRI and fNIRS signals and decreased fNIRS-fMRI correlations. Task-related fNIRS signals might be impacted by regionally and individually weighted sources of anatomical and systemic physiological error variance. Trait-activation

correlations might be affected or biased by systemic physiological responses, which should be accounted for in future fNIRS studies of interindividual differences.

56. Lindkvist et al. (2013). **Coherent Derivation of Equations for Differential Spectroscopy and Spatially Resolved Spectroscopy: An Undergraduate Tutorial**

Abstract: Near-infrared spectroscopy (NIRS) is a spectroscopic method that is frequently used in health care and sports medicine to monitor oxygenation parameters in biological tissue. This tutorial provides a coherent derivation of equations for differential spectroscopy and spatially resolved spectroscopy, from basic theories to implementable equations. The basic theories are applicable to any kind of tissue oximeter but mainly focus on continuous-wave instruments.

57. Schneider et al. (2013). **Changes in cerebral oxygenation during parabolic flight**

Abstract: Assessing changes in brain activity under extreme conditions like weightlessness is a desirable, but difficult undertaking. Results from previous studies report specific changes in brain activity connected to an increase or decrease in gravity forces. Nevertheless, so far it remains unclear (1) whether this is connected to a redistribution of blood volume during micro- or hypergravity and (2) whether this redistribution might account for neurocognitive alterations. This study aimed to display changes in brain oxygenation caused by altered gravity conditions during parabolic flight. It was hypothesized that an increase in gravity would be accompanied by a decrease in brain oxygenation, whereas microgravity would lead to an increase in brain oxygenation. Oxygenized and deoxygenized haemoglobin were measured using two near infrared spectroscopy (NIRS) probes on the left and right prefrontal cortex throughout ten parabolas in nine subjects. Results show a decrease of 1.44 µmol/l in oxygenized haemoglobin with the onset of hypergravity, followed by a considerable increase during microgravity (up to 5.34 µmol/l). In contrast, deoxygenized haemoglobin was not altered during the first but only during the second hypergravity phase and showed only minor changes during microgravity. Changes in oxygenized and deoxygenized haemoglobin indicate an increase in arterial flow to the brain and a decrease in venous outflow during microgravity.

58. Ding et al. (2013). **Neural correlates of spontaneous deception: A functional near-infrared spectroscopy (fNIRS) study**

Abstract: Deception is commonly seen in everyday social interactions. However, most of the knowledge about the underlying neural mechanism of deception comes from studies where participants were instructed when and how to lie. To study spontaneous deception, we designed a guessing game modeled after Greene and Paxton (2009) "Proceedings of the National Academy of Sciences, 106(30), 12506-12511", in which lying is the only way to achieve the performance level needed to end the game. We recorded neural responses during the game using near-infrared spectroscopy (NIRS). We found that when compared to truth-telling, spontaneous deception, like instructed deception, engenders greater involvement of such prefrontal regions as the left superior frontal gyrus. We also found that the correct-truth trials produced greater neural activities in the left middle frontal gyrus and right superior frontal gyrus than the incorrect-truth trials, suggesting the involvement of the reward system. Furthermore, the present study confirmed the feasibility of using NIRS to study spontaneous deception.

59. Yadev et al. (2013). **In vivo detection of epileptic brain tissue using static fluorescence and diffuse reflectance spectroscopy**

Abstract: Diffuse reflectance and fluorescence spectroscopy are used to detect histopathological abnormalities of an epileptic brain in a human subject study. Static diffuse reflectance and fluorescence spectra are acquired

from normal and epileptic brain areas, defined by electrocorticography (ECoG), from pediatric patients undergoing epilepsy surgery. Biopsy specimens are taken from the investigated sites within an abnormal brain. Spectral analysis reveals significant differences in diffuse reflectance spectra and the ratio of fluorescence and diffuse reflectance spectra from normal and epileptic brain areas defined by ECoG and histology. Using these spectral differences, tissue classification models with accuracy above 80% are developed based on linear discriminant analysis. The differences between the diffuse reflectance spectra from the normal and epileptic brain areas observed in this study are attributed to alterations in the static hemodynamic characteristics of an epileptic brain, suggesting a unique association between the histopathological and the hemodynamic abnormalities in an epileptic brain.

60. Gagnon et al. (2013). **Further improvement in reducing superficial contamination in NIRS using double short separation measurements**

Abstract: Near-Infrared Spectroscopy (NIRS) allows the recovery of the evoked hemodynamic response to brain activation. In adult human populations, the NIRS signal is strongly contaminated by systemic interference occurring in the superficial layers of the head. An approach to overcome this difficulty is to use additional NIRS measurements with short optode separations to measure the systemic hemodynamic fluctuations occurring in the superficial layers. These measurements can then be used as regressors in the post-experiment analysis to remove the systemic contamination and isolate the brain signal. In our previous work, we showed that the systemic interference measured in NIRS is heterogeneous across the surface of the scalp. As a consequence, the short separation measurement used in the regression procedure must be located close to the standard NIRS channel from which the evoked hemodynamic response of the brain is to be recovered. Here, we demonstrate that using two short separation measurements, one at the source optode and one at the detector optode, further increases the performance of the short separation regression method compared to using a single short separation measurement. While a single short separation channel produces an average reduction in noise of 33% for HbO, using a short separation channel at both source and detector reduces noise by 59% compared to the standard method using a general linear model (GLM) without short separation. For HbR, noise reduction of 3% is achieved using a single short separation and this number goes to 47% when two short separations are used. Our work emphasizes the importance of integrating short separation measurements both at the source and at the detector optode of the standard channels from which the hemodynamic response is to be recovered. While the implementation of short separation sources presents some difficulties experimentally, the improvement in noise reduction is significant enough to justify the practical challenges.

61. Fazel Bakhsheshi et al. (2013). **Effects of combined xenon and hypothermia on cerebral blood flow and oxygen consumption in newborn piglets measured with a time-resolved near-infrared technique**

Abstract: Mild hypothermia (HT), in which the brain is cooled to 32-33°C, has been shown to be neuroprotective for neurological emergencies such as head trauma and neonatal asphyxia. Xenon (Xe), a scarce and expensive anesthetic gas, has also shown great promise as a neuroprotectant, particularly when combined with HT. The purpose of the present study was to investigate the combined effect of Xe and HT on the cerebral metabolic rate of oxygen (CMRO2) and cerebral blood flow (CBF). A closed circuit re-breathing system was used to deliver the Xe in order to make the treatment efficient and economical. A bolus-tracking method using indocyanine green (ICG) as a flow tracer with time-resolved near-infrared (TR-NIR) technique was used to measure CBF and CMRO2 in newborn piglets.

62. Yasumara et al. (2013). **Neurobehavioral and hemodynamic evaluation of Stroop and reverse Stroop interference in children with attention-deficit/hyperactivity disorder**

Abstract: Failure of executive function (EF) is a core symptom of attention-deficit/hyperactivity disorder (ADHD). However, various results have been reported and sufficient evidence is lacking. In the present study, we evaluated the characteristics of children with ADHD using the Stroop task (ST) and reverse Stroop task (RST) that reflects the inhibition function of EF. We compared children with ADHD, typically developing children (TDC), and children with autism spectrum disorder (ASD), which is more difficult to discriminate from ADHD. A total of 10 children diagnosed with ADHD, 15 TDC, and 11 children diagnosed with ASD, all matched by age, sex, language ability, and intelligence quotient, participated in this study. While each subject performed computer-based ST and RST with a touch panel, changes in oxygenated hemoglobin (oxy-Hb) were measured in the prefrontal cortex (PFC) by near-infrared spectroscopy (NIRS) to correlate test performance with neural activity. Behavioral performance significantly differed among 3 groups during RST but not during ST. The ADHD group showed greater color interference than the TDC group. In addition, there was a negative correlation between right lateral PFC (LPFC) activity and the severity of attention deficit. Children with ADHD exhibit several problems associated with inhibition of color, and this symptom is affected by low activities of the right LPFC. In addition, it is suggested that low hemodynamic activities in this area are correlated with ADHD.

63. Kikushi et al. (2013). **Anterior Prefrontal Hemodynamic Connectivity in Conscious 3- to 7-Year-Old Children with Typical Development and Autism Spectrum Disorder**

Abstract: Socio-communicative impairments are salient features of autism spectrum disorder (ASD) from a young age. The anterior prefrontal cortex (aPFC), or Brodmann area 10, is a key processing area for social function, and atypical development of this area is thought to play a role in the social deficits in ASD. It is important to understand these brain functions in developing children with ASD. However, these brain functions have not yet been well described under conscious conditions in young children with ASD. In the present study, we focused on the brain hemodynamic functional connectivity between the right and the left aPFC in children with ASD and typically developing (TD) children and investigated whether there was a correlation between this connectivity and social ability. Brain hemodynamic fluctuations were measured non-invasively by near-infrared spectroscopy (NIRS) in 3- to 7-year-old children with ASD (n = 15) and gender- and age-matched TD children (n = 15). The functional connectivity between the right and the left aPFC was assessed by measuring the coherence for low-frequency spontaneous fluctuations (0.01 – 0.10 Hz) during a narrated picture-card show. Coherence analysis demonstrated that children with ASD had a significantly higher inter-hemispheric connectivity with 0.02-Hz fluctuations, whereas a power analysis did not demonstrate significant differences between the two groups in terms of low frequency fluctuations (0.01 – 0.10 Hz). This aberrant higher connectivity in children with ASD was positively correlated with the severity of social deficit, as scored with the Autism Diagnostic Observation Schedule. This is the first study to demonstrate aberrant brain functional connectivity between the right and the left aPFC under conscious conditions in young children with ASD.

64. Derosière et al. (2013). **Similar scaling of contralateral and ipsilateral cortical responses during graded unimanual force generation**

Abstract: Hemibody movements are strongly considered as being under the control of the contralateral hemisphere of the cerebral cortex. However, some neuroimaging studies have found a bilateral activation of either the primary sensori-motor (SM1) areas or the rostral prefrontal cortex (PFC), during unimanual tasks. More than just bilateral, the activation of these areas was found to be symmetrical in some studies. However, the symmetrical response remains strongly controversial notably for handgrip force generations. We therefore aimed to examine the bilateral SM1 and rostral PFC area activations in response to graded submaximal force generation during a unilateral handgrip task. Fifteen healthy subjects performed 6 levels of force (ranging from 5 to 50% of MVC) during a handgrip task. We concomitantly measured the activation of bilateral SM1 and

rostral PFC areas through near-infrared spectroscopy (NIRS) and the electromyographic (EMG) activity of the bilateral flexor digitorum superficialis (FDS) muscles. Symmetrical activation was found over the SM1 areas for all the investigated levels of force. At the highest level of force (i.e., 50% of MVC), the EMG of the passive FDS increased significantly and the ipsilateral rostral PFC activation was found more intense than the corresponding contralateral rostral PFC activation. We suggest that the visuo-guided control of force levels during a handgrip task requires the cross-talk from ipsi- to contralateral SM1 to cope for the relative complexity of the task, similar to that which occurs during complex sequential finger movement. We also propose alternative explanations for the observed symmetrical SM1 activation including (i) the ipsilateral corticospinal tract and (ii) interhemispheric inhibition (IHI) mechanism. The increase in EMG activity over the passive FDS could be associated with a release of IHI at 50% of MVC. Finally, our results suggest that the greater ipsilateral (right) rostral PFC activation may reflect the greater demand of attention required to control the motor output at high levels of force.

65. Scarpa et al. (2013). **A reference-channel based methodology to improve estimation of event-related hemodynamic response from fNIRS measurements**

Abstract: Functional near-infrared spectroscopy (fNIRS) uses near-infrared light to measure cortical concentration changes in oxygenated (HbO) and deoxygenated hemoglobin (HbR) held to be correlated with cognitive activity. Providing a parametric depiction of such changes in the classic form of stimulus-evoked hemodynamic responses (HRs) can be attained with this technique only by solving two problems. One problem concerns the separation of informative optical signal from structurally analogous noise generated by a variety of spurious sources, such as heart beat, respiration, and vasomotor waves. Another problem pertains to the inherent variability of HRs, which is notoriously contingent on the type of experiment, brain region monitored, and human phenotype. A novel method was devised in the present context to solve both problems based on a two-step algorithm combining the treatment of noise-only data extrapolated from a reference-channel and a Bayesian filter applied on a per-trial basis. The present method was compared to two current methods based on conventional averaging, namely, a typical averaging method and an averaging method implementing the use of a reference-channel. The result of the comparison, carried out both on artificial and real data, revealed a sensitive accuracy improvement in HR estimation using the present method relative to each of the other methods.

66. Bennett et al. (2013). **fNIRS detects temporal lobe response to affective touch**

Abstract: Touch plays a crucial role in social-emotional development. Slow, gentle touch applied to hairy skin is processed by C-tactile (CT) nerve fibers. Further, 'social brain' regions such as the posterior superior temporal sulcus (pSTS) have been shown to process CT-targeted touch. Research on the development of these neural mechanisms is scant, yet such knowledge may inform our understanding of the critical role of touch in development and its dysfunction in disorders involving sensory issues, such as autism. The aim of the current study was to validate the ability of functional near-infrared spectroscopy (fNIRS), an imaging technique well suited for use with infants, to measure temporal lobe responses to CT-targeted touch. Healthy adults received brushing to the right forearm (CT) and palm (non-CT) separately, in a block design procedure. We found significant activation in right pSTSand dorsolateral prefrontal cortex to arm > palm touch. Additionally, individual differences in autistic traits were related to the magnitude of peak activation within pSTS. These findings demonstrate that fNIRS can detect brain responses to CT-targeted touch and lay the foundation for future work with infant populations that will characterize the development of brain mechanisms for processing CT-targeted touch in typical and atypical populations.

67. Nguyen et al. (2013). **Wavelet Coefficient Average Value for Prediction of Motor Control Area of Human Brain Using fNIRS**

Abstract: This paper proposed a average threshold algorithm for predicting motor control area of human brain using fNIRS technique. Firstly, data obtained from human brain were pre-processed to reduce noise and artifacts. Thus, the data were analyzed using a decomposition wavelet algorithm with a Bior 5.5 function to produce wavelet coefficients. From these coefficients, one can create a coefficient threshold to determine motor control area as well as to distinguish two brain hemispheres based on oxy hemoglobin (oxy-Hb) concentration. Experimental results for predicting motor control area confirmed the feasibility of the proposed method.

68. Ngo et al. (2013). **Linear Regression Algorithm for Hand Tapping Recognition Using Functional Near Infrared Spectroscopy**

Abstract: This paper proposed a linear regression (LR) algorithm for hand tapping recognition using functional Near Infrared Spectroscopy (fNIRS). Brain data with noise and artifacts were re-processed to obtain data smoothy using a Savitzky-Golay filter. The smoothy data were calculated using the proposed LR algorithm in order to produce the angular coefficients of the straight lines which correspond to oxygen-Hemoglobin (Oxy-Hb) concentration. Therefore, one can distinguish the right and left hand tapping tasks based on the different angular coefficients of the lines corresponding to the difference of the right and left brain Oxy-Hb. In addition, the difference of the left and right brain activities were determined based on comparing the angular coefficients. Experimental results showed to illustrate the effectiveness of the proposed method.

69. Helton et al. (2013). **Post-disaster depression and vigilance: a functional near-infrared spectroscopy study**

Abstract: The present study was designed to explore the relationships between post-disaster self-reports of depression, vigilance task performance, and frontal cerebral oxygenation. Forty participants (20 women) performed vigilance tasks following a magnitude 7.1 earthquake in Christchurch, New Zealand. In addition to performance, we measured self-reports of depression, anxiety, and stress anchored to the initial earthquake event, and frontal cerebral activity with functional near-infrared spectroscopy. Among the participants, one case may have been an outlier with extremely elevated levels of self-reported depressivity. Excluding the extreme case, there was a correlation between change in response time (response slowing) and depressivity. Including the case there was a correlation between depressivity and right hemisphere oxygenation. These results provide some support for a relationship between moderate depressivity and sustained attention difficulties.

70. Hu et al. (2013). **Reduction of trial-to-trial variability in functional near-infrared spectroscopy signals by accounting for resting-state functional connectivity**

Abstract: The reduction of trial-to-trial variability (TTV) in task-evoked functional near-infrared spectroscopy signals by considering the correlated low-frequency spontaneous fluctuations that account for the resting-state functional connectivity in the brain is investigated. A resting-state session followed by a task-state session of a right hand finger-tapping task has been performed on five subjects. Significant ipsilateral and bilateral resting-state functional connectivity has been detected at the subjects' motor cortex using the seed correlation method. The correlation coefficients obtained during the resting-state are used to reduce the TTV in the signals measured during the task sessions. The results suggest that correlated spontaneous low-frequency fluctuations contribute significantly to the TTV in the task evoked fNIRS signals.

71. Fox et al. (2013). **Neural processing of facial identity and emotion in infants at high risk for autism spectrum disorders**

Abstract: Deficits in face processing and social impairment are core characteristics of autism spectrum disorder. The present work examined 7 month-old infants at high risk for developing autism and typically developing controls at low risk, using a face perception task designed to differentiate between the effects of face identity and facial emotions on neural response using functional Near Infrared Spectroscopy (fNIRS). In addition, we employed independent component analysis (ICA), as well as a novel method of condition-related component selection and classification to identify group differences in hemodynamic waveforms and response distributions associated with face and emotion processing. The results indicate similarities of waveforms, but differences in the magnitude, spatial distribution, and timing of responses between groups. These early differences in local cortical regions and the hemodynamic response may, in turn, contribute to differences in patterns of functional connectivity.

72. Girouard et al. (2013). **Designing a passive brain computer interface using real time classification of functional near–infrared spectroscopy**

Abstract: Passive brain–computer interfaces consider brain activity as an additional source of information, to augment and adapt the interface instead of controlling it. We have developed a software system that allows for real time brain signal analysis and machine learning classification of affective and workload states measured with functional near–infrared spectroscopy (fNIRS) called the online fNIRS analysis and classification (OFAC). Our system reproduces successful offline procedures, adapting them for real–time input to a user interface. Our first evaluation compares a previous offline analysis with our online analysis. While results show an accuracy decrease, they are outweighed by the new ability of interface adaptation. The second study demonstrates OFAC's online features through real–time classification of two tasks, and interface adaptation according to the predicted task. Accuracy averaged over 85%. We have created the first working real time passive BCI using fNIRS, opening the door to build adaptive user interfaces.

73. Niu et al. (2013). **Reduced Frontal Activation during a Working Memory Task in Mild Cognitive Impairment: a Non-Invasive Near-Infrared Spectroscopy Study**

Abstract: Aims: Working memory (WM) impairments are considered to be a main feature of mild cognitive impairment (MCI). Functional brain imaging studies have revealed evidence of alterations in the frontal and temporal cortices associated with WM in MCI patients. However, some imaging methods are too expensive for routine clinical use and have a low temporal resolution. Methods: Using a newly developed near-infrared spectroscopy (NIRS) system, we studied the spatiotemporal dynamics of oxygenated hemoglobin (oxy-Hb) during a WM task in eight patients with mild cognitive impairment (MCI) and 16 age- and gender-matched healthy controls. Results: We performed temporal and spatial correlation analyses on each group during their WM tasks. These results consistently demonstrated that, when compared with the healthy controls, the MCI patients exhibited significantly decreased activation in the left frontal, right superior frontal and left temporal lobes. We found evidence of altered frontal and temporal processing during WM tasks in the MCI patients.
Conclusions: These results confirm the functional deficits in the frontal and temporal cortices and the impairment of WM and cognitive abilities in MCI patients and suggest that fNIRS may be a useful tool for evaluating brain activation in cognitive disorders.

74. Barati et al. (2013). **Hemodynamic Response to Repeated Noxious Cold Pressor Tests Measured by Functional Near Infrared Spectroscopy on Forehead**

Abstract: The objective of this research was to assess the utility of a simple near infrared spectroscopy (NIRS) technology for objective assessment of the hemodynamic response to acute pain. For this exploration, we used functional near infrared spectroscopy (fNIRS) to measure the hemodynamic response on the forehead during three trials of a cold pressor test (CPT) in 20 adults. To measure hemodynamic changes at the superficial tissues as well as the intracranial tissues, two configurations of 'far' and 'near' source-detector separations were used. We identified two features that were found to be fairly consistent across all subjects. The first feature was the change of total hemoglobin (THb) concentration in a given condition divided by the duration of that condition THb′ . Statistical analyses revealed that during the first CPT trial THb′ significantly changed from its baseline value in all channels. Also, adaptation to repeated CPTs was observed in both THb′ parameter and the reported post-stimulus pain rating scores. The second feature was the difference between the maximum and the minimum of the evoked changes in the THb concentration (ΔTHb). A significant correlation was observed between the post-stimulus pain rating score and ΔTHb at all channels. An asymmetrical activity was observed only at the 'far' channels. These results suggest that fNIRS can potentially be used as a reliable technique for the assessment of the hemodynamic response to tonic pain induced by the CPT.

75. Ward (2013). **Hybrid Optical–Electrical Brain Computer Interfaces, Practices and Possibilities**

Abstract: Noninvasive brain computer interfaces (BCI) rely on measurements taken from the scalp in order to directly infer changes in brain activation associated with volitional thought. There is limited scalp over brain regions of interest from which to take such measurements therefore efficient utilisation of the measurement area is important. Hybrid optical–electrical sensors represent one method through which this improvement in measurement area utilization is achievable. In particular, optical measurements of brain activity through techniques such as near infrared spectroscopy (NIRS) rely on geometrical arrangements of optodes which do not constrain the placements of electrodes associated with electroencephalography. Consequently a BCI making use of such a hybrid sensor arrangement is capable of extracting more information during brain activation. In addition, the different aspects of brain physiology under measurement lead to a compound signal which more completely characterises the active brain area. This chapter provides an introduction to such hybrid systems with an emphasis on the less well-known optical measurement technology embodied in NIRS systems. Topics covered include the physics of the measurement, description of the physiological dynamics, an overview of sensor technology, signal characteristics, processing and analysis in a BCI context. The chapter concludes with a discussion on current practise in this emerging field with some commentary on future directions and possibilities.

76. Tsujimoto et al. (2013). **Increased Prefrontal Oxygenation Related to Distractor-Resistant Working Memory in Children with Attention-Deficit/Hyperactivity Disorder (ADHD)**

Abstract: This study aimed at investigating the effect of distraction on working memory and its underlying neural mechanisms in children with attention-deficit/hyperactivity disorder (ADHD). To this end, we studied hemodynamic activity in the prefrontal cortex using near-infrared spectroscopy while 16 children with ADHD and 10 typically developing (TD) children performed a working memory task. This task had two conditions: one involved a distraction during the memory delay interval, whereas the other had no systematic distraction. The ADHD patients showed significantly poorer behavioral performance compared with the TD group, particularly under the distraction. The ADHD group exhibited significantly higher level of prefrontal activation than did TD children. The activity level was positively correlated with the severity of ADHD symptoms. These results suggest that the impairment in the inhibition of distraction is responsible for the working memory deficits observed in ADHD children. Inefficient processing in the prefrontal cortex appears to underlie such deficits.

77. Huppert (2013). **History of Diffuse Optical Spectroscopy of Human Tissue**

Abstract: Diffuse optical spectroscopy is a noninvasive method that uses low levels of near-infrared light to measure blood oxygenation in the brain. Over the last 35 years, the number of diffuse optical studies and the range of clinical and research applications have grown steadily. Compared to other neuroimaging methods to measure cerebral blood oxygenation, such as magnetic resonance imaging or positron emission tomography, diffuse optical imaging (DOI) is more cost effective and often uses small portable instrumentation. Wireless and bedside optical systems are currently produced commercially. The portability of these instruments has extended the use of optical methods into several unique applications including brain imaging in infants and children, studies of the brain during ambulatory tasks such as walking or balance, and interoperative brain assessments. This chapter will introduce the history and basic principles of DOI including discussion of the factors contributing to the optical properties of tissue, instrumentation, and an overview of applications of the technology.

78. Tokamoto et al. (2013). **Thermotherapy to the facial region in and around the eyelids altered prefrontal hemodynamic responses and autonomic nervous activity during mental arithmetic**

Abstract: To investigate neural mechanisms of local thermotherapy to reduce mental stress, participants were required to perform mental arithmetic after treatment by a heat- and steam-generating sheet on the facial eyelid region while hemodynamic activity and ECGs were monitored. The results indicated that thermotherapy decreased hemodynamic activity in the anterior dorsomedial prefrontal cortex (aDMPFC) involved in sympathetic activity. Consistently, thermotherapy increased parasympathetic activity while it decreased sympathetic activity. Furthermore, thermotherapy increased hemodynamic activity in the dorsolateral prefrontal cortex (DLPFC) during mental arithmetic. These hemodynamic responses in the DLPFC during mental arithmetic were negatively correlated with that in the aDMPFC during thermotherapy. The results suggest that thermotherapy in the facial eyelid region is useful to ameliorate mental fatigue through its effects on the prefrontal cortex. Working memory, defined as the ability to transiently hold and manipulate information "on line" and to use it to guide behaviors (Goldman-Rakic, 1995), is considered a distinctive function of the prefrontal cortex (PFC). Acute stress impairs high-order cognitive functions including working memory (Arnsten & Goldman-Rakic, 1998; de Kloet, Joëls, & Holsboer, 2005; Elzinga & Roelofs, 2005; Schoofs, Preuss, & Wolf, 2008). Recently, neuroimaging studies reported that acute stress significantly reduced working memory–related activity in the dorsolateral PFC (DLPFC) in healthy participants (Qin, Hermans, van Marle, Luo, & Fernandez, 2009). Similar impairments in working memory are observed in various psychiatric disorders that are associated with higher susceptibility to stress and prefrontal dysfunction (Arnsten, 2007; Arnsten & Li, 2005; Driesen et al., 2008; Hammen & Gitlin, 1997). These findings suggest that acute stress is a potential factor inducing higher-order cognitive dysfunctions. Prolonged stress, both physical and emotional, is postulated to cause fatigue (Aistars, 1987) and also impairs working memory (Cerqueira, Mailliet, Almeida, Jay, & Sousa, 2007). Self-reported depression, anxiety, and emotional stress are highly associated with fatigue and are independently predictive of it (Chen, 1986). These findings suggest that chronic mental stress induces fatigue, which impairs working memory. More than half of the general adult population complains of fatigue, and more than one third of the population suffers from chronic fatigue lasting longer than 6 months (Watanabe, 2007). Thus, fatigue is a common problem that adversely affects quality of life and work productivity. These impairments might be also related to PFC dysfunction. Chronic fatigue syndrome (CFS) displays impairments in concentration and short-term memory (Fukuda et al., 1994) and reduced activation in working memory–related brain regions (DLPFC and parietal cortices) (Caseras et al., 2006). Taken together, these results indicate that the PFC is one of the critical sites that are affected by various acute and chronic stresses as well as in the pathological conditions including CFS (Arnsten, 2009; Okada, Tanida, Watanabe, & Sadato, 2004). Since the PFC is implicated in regulation of fatigue sensations (Okada et al., 2004), fatigue is strongly associated with PFC dysfunction not only in pathological conditions such as CFS but also in healthy individuals when acute or chronic stress is induced. Thermotherapy is one of the physical therapies that have been used to ameliorate mental stress and fatigue.

Local thermotherapy (with hot packs or paraffin) is reported to improve quality of sleep and life in general (Greenberg, 1972; Tei et al., 1995) and to ameliorate chronic fatigue (Masuda, Koga, Hattanmaru, Minagoe, & Tei, 2005; Masuda, Kihara et al., 2005). Recently, it has been reported that application of a heat- and steam-generating (HSG) sheet to the neck region significantly ameliorated both fatigue perception and neck stiffness (Yasui et al., 2010). However, neural mechanisms of fatigue reduction by thermotherapy are still unclear. HSG sheets at least deactivated the anterior dorsomedial PFC (aDMPFC) with concomitant increase in parasympathetic nervous activity and decrease in sympathetic nervous activity (Yasui et al., 2010). We hypothesized that deactivation of the aDMPFC by thermotherapy would enhance DLPFC activity during mental load such as mental arithmetic in healthy individuals. In the present study, to elucidate the neural mechanisms of fatigue reduction by thermotherapy, we investigated relationships among aDMPFC deactivation during HSG sheet application to the facial region in and around the eyelids, autonomic nervous activity, and DLPFC activity during mental arithmetic by means of near-infrared spectroscopy (NIRS) and spectral analysis of heart rate variability. Since various symptoms around the eyes such as blepharospasm are induced by stress and fatigue (Diamond, Trobe, & Belar, 1984; Johnson et al., 2007), application of HSG sheets to the facial region in and around the eyelids might be also effective to reduce fatigue and mental stress. It has been reported that increased sympathetic activity and decreased parasympathetic activity are characteristics of both acute and daily levels of fatigue (Tanaka et al., 2011), while task performance is not a good index of mental fatigue (Tanaka, Mizuno, Tajima, Sasabe, & Watanabe, 2009). Therefore, effects of thermotherapy on fatigue were assessed by autonomic nervous activity in the present study.

79. Madsen (2013). **Optical Properties of Brain Tissue**

Abstract: Accurate assessment of light distributions in the brain is vital for both diagnostic and therapeutic applications. This, in turn, requires knowledge of the optical properties of brain tissues. The optical properties of a variety of mammalian brain tissues are summarized in this review. Both ex vivo and in vivo measurement techniques are reviewed as are solutions to the radiation transport equation which are required for calculating light distributions in the brain.

80. Pifferi et al. (2013). **Realistic phantoms for diffuse optical imaging using totally absorbing objects**

Abstract: We propose and validate the design of inhomogeneous phantoms for diffuse optical imaging purposes using totally absorbing objects embedded in a diffusive medium. From Monte Carlo simulations, we show that a given or desired perturbation strength caused by an realistic absorbing inhomogeneity of a certain absorption and volume can be approximately mimicked by a small totally absorbing object of a so-called Equivalent Black Volume (Equivalence Relation). This concept can be useful to design realistic inhomogeneous phantoms using a set of black objects with different volumes. Further, it permits to grade physiological or pathological changes on a reproducible scale of equivalent black volumes, thus facilitating the performance assessment of clinical instruments. We have also provided a plot to derive the Equivalent Black Volume yielding the same effect of a realistic absorption object.

81. Gurden et al. (2013). **Astrocytes: can they be the missing stars linking neuronal activity to neurofunctional imaging signals?**

Abstract: Functional neuroimaging techniques are currently used in fundamental neuroscience as well as in cognitive neuroscience and clinics to study brain function at large spatial scales. They include Blood Oxygenation Level Dependent-functional Magnetic Resonance Imaging (BOLD-fMRI, Kim and Ogawa, 2012), the gold standard of functional neuroimaging techniques, and many optical techniques including functional Near InfraRed Spectroscopy (fNIRS) in human research or intrinsic/spectroscopic optical signal (IOS) imaging in

animal research (Devor et al., 2012). These techniques rely on vascular signals [cerebral blood flow (CBF) and volume and metabolic rate of oxygen consumption] that constitute a proxy for neuronal activity because of the existence of functional hyperemia, a mechanism defined as the matching of vascular changes to the activity level in a given brain area (Iadecola and Nedergaard, 2007). To date, some crucial open questions remain concerning these functional signals, including: what kind of brain activity are they related to? What are their cellular/molecular sources? Can astrocytes, in addition to roles in translating neuronal into vascular activity, also be capable of generating functional neuroimaging signals on their own?

82. Hoang et al. (2013). **Experiments on Synchronous Nonlinear Features for 2-Class NIRS-Based Motor Imagery Problem**

Abstract: This paper aims to experiment several synchronous nonlinear features in the well-known 2-class motor imagery problem in Brain Computer Interface (BCI) systems using Near Infrared Spectroscopy (NIRS) technique. Those features including phase synchronizations and nonlinear interdependences are well known and widely applied on several neural-related problems such as epilepsy prediction. However, only a few publications are related to NIRS-based BCI systems. We conducted several experiments using NIRS technique to analyze how useful those synchronous nonlinear features can be applied on NIRS-based BCI systems. Results show that while the nonlinear interdependences can produce quite good recall and precision ratios, the phase synchronizations are not good for classification because the accuracy is as low as that in random guessing.

83. Hoang et al. (2013). **High Order Moment Features for NIRS-Based Classification Problems**

Abstract: This paper aims to experiment high order moment features in two well-known problems which are motor imagery and person authentication in Brain Computer Interface (BCI) systems using Near Infrared Spectroscopy (NIRS) technique. To improve performance of the systems, we propose a new feature by combining 2nd order and 4th order moments of signal together. Our results show that such the feature not only achieves very high recall and precision ratios but also is practical for online NIRS-based BCI systems. Our systems can achieve recall and precision ratio at 99.2% for the left-hand and right-hand imagery problem, and up to 100% for the person authentication problem.

84. Giacometti & Diamond (2013). **Diffuse Optical Tomography for Brain Imaging: Continuous Wave Instrumentation and Linear Analysis Methods**

Abstract: Diffuse optical tomography (DOT) is a functional brain imaging technique that measures cerebral blood oxygenation and blood volume changes. This technique is particularly useful in human neuroimaging measurements because of the coupling between neural and hemodynamic activity in the brain. DOT is a multichannel imaging extension of near-infrared spectroscopy (NIRS). NIRS uses laser sources and light detectors on the scalp to obtain noninvasive hemodynamic measurements from spectroscopic analysis of the remitted light. This review explains how NIRS data analysis is performed using a combination of the modified Beer–Lambert law (MBLL) and the diffusion approximation to the radiative transport equation (RTE). Laser diodes, photodiode detectors, and optical terminals that contact the scalp are the main components in most NIRS systems. Placing multiple sources and detectors over the surface of the scalp allows for tomographic reconstructions that extend the individual measurements of NIRS into DOT. Mathematically arranging the DOT measurements into a linear system of equations that can be inverted provides a way to obtain tomographic reconstructions of hemodynamics in the brain.

85. Lesage et al. (2013). **Diffuse Optical Tomography and Biophysical Modeling of the Aging Brain**

Abstract: Diffuse optical imaging (DOI) of the brain has emerged as a new neuroimaging technique that is seeing growing applications in brain research. The technique's simplicity, lower cost and applicability to children have contributed to its popularity. However, poor quantification of local hemodynamic changes based on optical signals remains a major hurdle and significant efforts are still being pursued to better understand how to recover accurate images of functional activation, generate statistical maps and recognize the limitations of DOI. In the context of aging, further confounds arise due to anatomical and physiological changes that must be accounted for in the signal modeling. In this work, DOI signals are revisited in this context. In particular we investigate the diffusion path length factor and its modifications with age.

86. Furubayashi et al. (2013). **Cortical hemoglobin concentration changes underneath the coil after single-pulse transcranial magnetic stimulation: a near-infrared spectroscopy study**

Abstract: Using near-infrared spectroscopy (NIRS) and multichannel probes, we studied hemoglobin (Hb) concentration changes when single-pulse transcranial magnetic stimulation (TMS) was applied over the left hemisphere primary motor cortex (M1). Seventeen measurement probes were centered over left M1. Subjects were studied in both active and relaxed conditions, with TMS intensity set at 100%, 120%, and 140% of the active motor threshold. The magnetic coils were placed so as to induce anteromedially directed currents in the brain. Hb concentration changes were more prominent at channels over M1 and posterior to it. Importantly, Hb concentration changes at M1 after TMS differed depending on whether the target muscle was in an active or relaxed condition. In the relaxed condition, Hb concentration increased up to 3–6 s after TMS, peaking at ~6 s, and returned to the baseline. In the active condition, a smaller increase in Hb concentrations continued up to 3–6 s after TMS (early activation), followed by a decrease in Hb concentration from 9 to 12 s after TMS (delayed deactivation). Hb concentration changes in the active condition at higher stimulus intensities were more pronounced at locations posterior to M1 than at M1. We conclude that early activation occurs when M1 is activated transsynaptically. The relatively late deactivation may result from the prolonged inhibition of the cerebral cortex after activation. The posterior-dominant activation at higher intensities in the active condition may result from an additional activation of the sensory cortex due to afferent inputs from muscle contraction evoked by the TMS.

87. Yang et al. (2013). **Handheld miniature probe integrating diffuse optical tomography with photoacoustic imaging through a MEMS scanning mirror**

Abstract: We describe a novel dual-modality imaging approach that integrates diffuse optical tomography (DOT) and photoacoustic imaging (PAI) through a miniaturized handheld probe based on microelectromechanical systems (MEMS) scanning mirror. We validate this dual-modal DOT/PAI approach using extensive phantom experiments, and demonstrate its application for tumor imaging using tumor-bearing mice systematically injected with targeted contrast agents.
asd

88. Kawauchi (2013). **Diffuse light reflectance signals as potential indicators of loss of viability in brain tissue due to hypoxia: charge-coupled-device-based imaging and fiber-based measurement**

Abstract: Brain tissue is highly vulnerable to ischemia/hypoxia, and real-time monitoring of its viability is important. By fiber-based measurements for rat brain, we previously observed a unique triphasic reflectance change (TRC) after a certain period of time after hypoxia. After TRC, rats could not be rescued, suggesting that TRC can be used as an indicator of loss of brain tissue viability. In this study, we investigated this diffuse-

reflectance change due to hypoxia in three parts. First, we developed and validated a theoretical method to quantify changes in the absorption and reduced scattering coefficients involved in TRC. Second, we performed charge-coupled-device-based reflectance imaging of the rat brain during hypoxia followed by reoxygenation to examine spatiotemporal characteristics of the reflectance and its correlation with reversibility of brain tissue damage. Third, we made simultaneous imaging and fiber-based measurement of the reflectance for the rat to compare signals obtained by these two modalities. We observed a nontriphasic reflectance change by the imaging, and it was associated with brain tissue viability. We found that TRC measured by the fibers preceded the reflectance-signal change captured by the imaging. This time difference is attributable to the different observation depths in the brain with these two methods.

89. Rehn et al. (2013). **Depth probing of diffuse tissues controlled with elliptically polarized light**

Abstract: Polarization gating is a popular technique in biomedical optics. It is widely used to inspect the surface of the tissues (under colinear or cocircular detection) or instead to probe the volume (cross-linear detection), without information on the probed depth. Elliptical polarization is introduced to explore the possibility of probing diffuse tissues at selective depths. A thorough Monte Carlo simulation study shows complete correlation between the probed depths and the ellipticity of the polarized light, for a medium with known optical properties. Within a wide range of optical parameters, a linear relation between the backscattered intensity and the depth extension of the probed volume was found whatever the polarization used, but with a controlled extension depending on the ellipticity.

90. Sultan et al. (2013). **Accurate optical parameter extraction procedure for broadband near-infrared spectroscopy of brain matter**

Abstract: Modeling behavior of broadband (30 to 1000 MHz) frequency modulated near-infrared (NIR) photons through a phantom is the basis for accurate extraction of optical absorption and scattering parameters of biological turbid media. Photon dynamics in a phantom are predicted using both analytical and numerical simulation and are related to the measured insertion loss (IL) and insertion phase (IP) for a given geometry based on phantom optical parameters. Accuracy of the extracted optical parameters using finite element method (FEM) simulation is compared to baseline analytical calculations from the diffusion equation (DE) for homogenous brain phantoms. NIR spectroscopy is performed using custom-designed, broadband, free-space optical transmitter (Tx) and receiver (Rx) modules that are developed for photon migration at wavelengths of 680, 780, and 820 nm. Differential detection between two optical Rx locations separated by 0.3 cm is employed to eliminate systemic artifacts associated with interfaces of the optical Tx and Rx with the phantoms. Optical parameter extraction is achieved for four solid phantom samples using the least-square-error method in MATLAB (for DE) and COMSOL (for FEM) simulation by fitting data to measured results over broadband and narrowband frequency modulation. Confidence in numerical modeling of the photonic behavior using FEM has been established here by comparing the transmission mode's experimental results with the predictions made by DE and FEM for known commercial solid brain phantoms.

Publications from the BORL, Zurich

91. Holper et al. (2013). **The teaching and the learning brain: A cortical hemodynamic marker of teacher–student interactions in the Socratic dialog**

Abstract: The study aimed to step into two-person (teacher–student) educational neuroscience. We describe a physiological marker of cortical hemodynamic correlates involved in teacher–student interactions during performance of a classical teaching model, the Socratic dialog. We recorded prefrontal brain activity during dialog execution simultaneously in seventeen teacher–student pairs using functional near-infrared spectroscopy (fNIRS). Our main finding is that students, who successfully transferred the knowledge, showed less activity than those who not showed transfer. Correlation analysis between teacher and student activity indicate that in successful educational dialogs student and teachers 'dance at the same pace'. This is the first study measuring simultaneously brain activity of teacher–student interactions and paves future investigations of brain networks involved in complex educational interactions.

92. Marchal-Crespo et al. (2013). **Motor execution detection based on autonomic nervous system responses**

Abstract: Triggered assistance has been shown to be a successful robotic strategy for provoking motor plasticity, probably because it requires neurologic patients' active participation to initiate a movement involving their impaired limb. Triggered assistance, however, requires sufficient residual motor control to activate the trigger and, thus, is not applicable to individuals with severe neurologic injuries. In these situations, brain and body-computer interfaces have emerged as promising solutions to control robotic devices. In this paper, we investigate the feasibility of a body-machine interface to detect motion execution only monitoring the autonomic nervous system (ANS) response. Four physiological signals were measured (blood pressure, breathing rate, skin conductance response and heart rate) during an isometric pinching task and used to train a classifier based on hidden Markov models. We performed an experiment with six healthy subjects to test the effectiveness of the classifier to detect rest and active pinching periods. The results showed that the movement execution can be accurately classified based only on peripheral autonomic signals, with an accuracy level of 84.5%, sensitivity of 83.8% and specificity of 85.2%. These results are encouraging to perform further research on the use of the ANS response in body-machine interfaces.

93. Zimmermann et al. (2013). **Detection of motor execution using a hybrid fNIRS-biosignal BCI: a feasibility study**

Abstract: Background; Brain-computer interfaces (BCIs) were recently recognized as a method to promote neuroplastic effects in motor rehabilitation. The core of a BCI is a decoding stage by which signals from the brain are classified into different brain-states. The goal of this paper was to test the feasibility of a single trial classifier to detect motor execution based on signals from cortical motor regions, measured by functional near-infrared spectroscopy (fNIRS), and the response of the autonomic nervous system. An approach that allowed for individually tuned classifier topologies was opted for. This promises to be a first step towards a novel form of active movement therapy that could be operated and controlled by paretic patients. Methods; Seven healthy subjects performed repetitions of an isometric finger pinching task, while changes in oxy- and deoxyhemoglobin concentrations were measured in the contralateral primary motor cortex and ventral premotor cortex using fNIRS. Simultaneously, heart rate, breathing rate, blood pressure and skin conductance response were measured. Hidden Markov models (HMM) were used to classify between active isometric pinching phases and rest. The classification performance (accuracy, sensitivity and specificity) was assessed for two types of input data: (i) fNIRS-signals only and (ii) fNIRS- and biosignals combined. Results; fNIRS data were classified with an average accuracy of 79.4%, which increased significantly to 88.5% when biosignals were also included (p=0.02).

Comparable increases were observed for the sensitivity (from 78.3% to 87.2%, p=0.008) and specificity (from 80.5% to 89.9%, p=0.062).Conclusions; This study showed, for the first time, promising classification results with hemodynamic fNIRS data obtained from motor regions and simultaneously acquired biosignals. Combining fNIRS data with biosignals has a beneficial effect, opening new avenues for the development of brain-body-computer interfaces for rehabilitation applications. Further research is required to identify the contribution of each modality to the decoding capability of the subject's hemodynamic and physiological state.

94. Scholkmann et al. (2013). **The effect of venous and arterial occlusion of the arm on changes in tissue hemodynamics, oxygenation, and ultra-weak photon emission**

Abstract: Ultra-weak photon emission (UPE) is a general feature of living -biological systems. To gain further insights into the origin of UPE and its physiological significance, the aim of the present study was to investigate the connection between hemodynamics (HD), oxygenation (OX), and UPE. Therefore, during venous and arterial occlusion (VO, AO), changes of UPE and surrogates of HD as well as OX were measured simultaneously using two photomultipliers and near-infrared spectroscopy, respectively. We showed that (1) changes in UPE correlate significantly nonlinearly with changes in oxyhemoglobin (Δ[O(2)Hb]), deoxyhemoglobin (Δ[HHb]), and hemoglobin difference (Δ[HbD] = Δ[O(2)Hb]-Δ[HHb]), indicating a complex association between UPE and tissue HD/OX; (2) UPE decreases significantly during AO but not during VO; (3) UPE increases significantly after AO; and (4) the view that ROS are the source of UPE is generally supported by the present study, although some findings remain unexplained in the context of the theory of ROS-mediated UPE generation. In conclusion, the present study revealed new insights into the interplay between HD, OX, and UPE and opens up new questions that have to be addressed by future studies.

95. Scholkmann et al. (2013). **End-tidal CO2: An important parameter for a correct interpretation in functional brain studies using speech tasks**

Abstract: The aim was to investigate the effect of different speech tasks, i.e. recitation of prose (PR), alliteration (AR) and hexameter (HR) verses and a control task (mental arithmetic (MA) with voicing of the result on end-tidal CO2 (PETCO2), cerebral hemodynamics and oxygenation. CO2 levels in the blood are known to strongly affect cerebral blood flow. Speech changes breathing pattern and may affect CO2 levels. Measurements were performed on 24 healthy adult volunteers during the performance of the 4 tasks. Tissue oxygen saturation (StO2) and absolute concentrations of oxyhemoglobin ([O2Hb]), deoxyhemoglobin ([HHb]) and total hemoglobin ([tHb]) were measured by functional near-infrared spectroscopy (fNIRS) and PETCO2 by a gas analyzer. Statistical analysis was applied to the difference between baseline before the task, 2 recitation and 5 baseline periods after the task. The 2 brain hemispheres and 4 tasks were tested separately. A significant decrease in PETCO2 was found during all 4 tasks with the smallest decrease during the MA task. During the recitation tasks (PR, AR and HR) a statistically significant ($p < 0.05$) decrease occurred for StO2 during PR and AR in the right prefrontal cortex (PFC) and during AR and HR in the left PFC. [O2Hb] decreased significantly during PR, AR and HR in both hemispheres. [HHb] increased significantly during the AR task in the right PFC. [tHb] decreased significantly during HR in the right PFC and during PR, AR and HR in the left PFC. During the MA task, StO2 increased and [HHb] decreased significantly during the MA task. We conclude that changes in breathing (hyperventilation) during the tasks led to lower CO2 pressure in the blood (hypocapnia), predominantly responsible for the measured changes in cerebral hemodynamics and oxygenation. In conclusion, our findings demonstrate that PETCO2 should be monitored during functional brain studies investigating speech using neuroimaging modalities, such as fNIRS, fMRI to ensure a correct interpretation of changes in hemodynamics and oxygenation.

96. Baumann et al. (2013). **Tuning the resistance of polycarbonate membranes by plasma-induced graft surface modification**

Abstract: To tune the permeability resistance of porous polycarbonate (PC) membranes for caffeine, their surfaces were plasma modified with different monomers in a grafting from process. These coatings provided characteristic surface hydrophilicities. It was found that membranes with more hydrophilic surfaces have lower resistances to let caffeine pass through than membranes with hydrophobic surfaces. Additionally, it was possible to post-modify a poly(2-aminoethyl methacrylate) (AEMA) coated PC membrane with octanoic acid (Oct) under mild conditions. This post modification allowed transforming a slightly hydrophilic PC-AEMA membrane with a moderate permeability resistance into a hydrophobic PC-AEMA-Oct membrane with a high permeability resistance. Overall, it was possible to tune the PC membrane resistance for caffeine in a range from 5100 up to 15,100 s/cm.

97. Gygax et al. (2013). **Prefrontal cortex activity, sympatho-vagal reaction and behaviour distinguish between situations of feed reward and frustration in dwarf goats**

Abstract: Recent concepts relating to animal welfare accept that animals experience affective states. These are notoriously difficult to measure in non-verbal species, but it is generally agreed that emotional reactions consist of well-coordinated reactions in behaviour, autonomic and brain activation. The aim of the study was to evaluate whether each or a combination of these aspects can differentiate between situations presumed to differ in emotional content. To this end, we repeatedly confronted dwarf goats at short intervals with a covered and an uncovered feed bowl (i.e. presumably frustrating and rewarding situations respectively) whilst simultaneously observing their behaviour, measuring heart-rate and heart-rate variability and haemodynamic changes in the prefrontal cortex using functional near-infrared spectroscopy. When faced with a covered feed bowl, goats occupied themselves at locations away from the bowl and showed increased locomotion, while there was a general increase in prefrontal cortical activity. There was little indication of autonomic changes. In contrast, when feed was accessible, the goats reduced locomotion, focused their behaviour on the feed bowl, showed signs of sympathetically mediated arousal reflecting anticipation and, if any cortical activity at all was present, it was concentrated to the left hemisphere. We thus observed patterns in behaviour, sympathetic reaction and brain activity that distinguished between a situation of frustration and one of reward in dwarf goats. These patterns consisted of a well-coordinated set of reactions appropriate in respect of the emotional content of the stimuli used.

98. Zysset et al. (2013). **Textile integrated sensors and actuators for near-infrared spectroscopy**

Abstract: Being the closest layer to our body, textiles provide an ideal platform for integrating sensors and actuators to monitor physiological signals. We used a woven textile to integrate photodiodes and light emitting diodes. LEDs and photodiodes enable near-infrared spectroscopy (NIRS) systems to monitor arterial oxygen saturation and oxygenated and deoxygenated hemoglobin in human tissue. Photodiodes and LEDs are mounted on flexible plastic strips with widths of 4 mm and 2 mm, respectively. The strips are woven during the textile fabrication process in weft direction and interconnected with copper wires with a diameter of 71 µm in warp direction. The sensor textile is applied to measure the pulse waves in the fingertip and the changes in oxygenated and deoxygenated hemoglobin during a venous occlusion at the calf. The system has a signal-to-noise ratio of more than 70 dB and a system drift of 0.37% ± 0.48%. The presented work demonstrates the feasibility of integrating photodiodes and LEDs into woven textiles, a step towards wearable health monitoring devices.

99. Hyttel-Sørensen et al. (2013). **Clinical use of cerebral oximetry in extremely preterm infants is feasible**

Abstract: INTRODUCTION: The research programme Safeguarding the Brains of our smallest Children (SafeBoosC) aims to test the benefits and harms of cerebral near-infrared spectroscopy (NIRS) oximetry in infants born before 28 weeks of gestation. In a phase II trial, infants will be randomised to visible cerebral NIRS oximetry with pre-specified treatment guidelines compared to standard care with blinded NIRS-monitoring. The primary outcome is duration multiplied with the extent outside the normal range of regional tissue oxygen saturation of haemoglobin (rStO2) of 55 to 85% in percentage hours (burden). This study was a pilot of the Visible -Oximetry Group. MATERIAL AND METHODS: This was an observational study including ten infants. RESULTS: The median gestational age was 26 weeks+three days, and the median start-up time was 133 minutes after delivery. The median recording time was 69.7 hours, mean rStO2 was 64.2±4.5%, median burden of hyper- and hypoxia was 30.3% hours (range 2.8-112.3). Clinical staff responded to an out of range value 29 times--only once to values above 85%. In comparison, there were 83 periods of more than ten minutes with an rStO2 below 55% and four episodes with an rStO2 above 85%. These periods accounted for 72% of the total hypoxia burden. A total of 18 of the 29 interventions were adjustments of FiO2 which in 13 of the 18 times resulted in an out-of-range SpO2. Two infants suffered second-degree burns from the sensor. Five infants died. In all cases, this was unrelated to NIRS monitoring and treatment. CONCLUSION: The intervention of early cerebral NIRS monitoring proved feasible, but prolonged periods of hypoxia went untreated. Thus, a revision of the treatment guideline and an alarm system is required. FUNDING: The Elsass Foundation funded the present study.