Fribourg Day of Cognition 02

2 octobre 2013

Pérolles II

09:00 – 12:00 Salle 002 Joseph Deiss

13:30 – 17:00 Salle A140

Fribourg Centre for Cognition

Program

9 :00	*Welcome*
9 :15	Isabel De Araujo Salgado
9 :30	Anne-Dominique Gindrat
9 :45	Loïc Chareyron
10 :00	Jayakrishnan Nair
10 :15	*Pause*
10 :45	Katharina Ledermann
11 :00	Vanessa Loaiza
11 :15	Sébastien Miellet
11 :30	Anne-Laure Oftinger
11 :45	Benoît Perriard
12 :00	*Repas*
13 :00	Posters
13 :30	N.N.
13 :45	Prof. Rasch
14 :00	Narges Radman
14 :15	Farfalla Ribordy
14 :30	Anne-Raphaëlle Richoz
14 :45	Helen Rodger
15 :00	Réunion

Posters

S Badoud, D Nguyen, I Barnaure, M-L Montandon, K-O Lovblad, PR Burkhard, S Haller

Differentiation between Parkinson disease and other forms of Parkinsonism using support vector machine analysis of susceptibility-weighted imaging (SWI): initial results

To diagnose Parkinson disease (PD) at the individual level using pattern recognition of brain susceptibility-weighted imaging (SWI).

Methods
We analysed brain SWI in 36 consecutive patients with Parkinsonism suggestive of PD who had (1) SWI at 3 T, (2) brain ^{123}I-ioflupane SPECT and (3) extensive neurological testing including follow-up (16 PD, 67.4 ± 6.2 years, 11 female; 20 OTHER, a heterogeneous group of atypical Parkinsonism syndromes 65.2 ± 12.5 years, 6 female). Analysis included group-level comparison of SWI values and individual-level support vector machine (SVM) analysis.

Results
At the group level, simple visual analysis yielded no differences between groups. However, the group-level analyses demonstrated increased SWI in the bilateral thalamus and left substantia nigra in PD patients versus other Parkinsonism. The inverse comparison yielded no supra-threshold clusters. At the individual level, SVM correctly classified PD patients with an accuracy above 86 %.

Conclusions
SVM pattern recognition of SWI data provides accurate discrimination of PD among patients with various forms of Parkinsonism at an individual level, despite the absence of visually detectable alterations. This pilot study warrants further confirmation in a larger cohort of PD patients and with different MR machines and MR parameters.

D. de León Rodríguez, K. Butler, N. Eggenberger, B. Preisig, R. Schumacher, L. Sprierer, M. Laganaro, T. Nyffeler, J -M. Annoni, and R. Müri

Reading strategies across languages in early bilinguals: An eye-movement study

Reading strategies vary across languages; Eye-movement patterns during reading indeed differ between transparent and opaque languages with respectively direct or complex grapheme/phoneme conversions. However, the literature so far investigated this question using between-subject factors designs which were potentially confounded by differences across groups unrelated to reading per se. To circumvent this issue, we examined reading strategies between a transparent (German) and an opaque (French) language in the same early bilingual individuals. We recruited 26 participants who learned French and German before the age of 7 and reached a high proficiency in both languages. They were instructed to read aloud isolated words and pseudowords presented in a French or German context while the landing position of the First Fixation Location (FFL) was measured. Because the transparent context would preferentially involve a direct grapheme/phoneme conversion, German reading should consist of a more local word processing strategy than French. In turn, the FFL should be closer to the beginning of the words and pseudowords in the German than in the opaque French context. Our results confirm this hypothesis for words but not for pseudowords, suggesting that semantic processing may also play a role in selecting a local reading strategy. Our data provide the first evidence for different reading strategies as a function of language opacities in the same population.

Camille Roux, Michela Fregosi, Mélanie Kaeser, Julie Savidan,

Lucas Spierer, Michael Mouthon, Eric Rouiller and Eric Schmidlin

Consequences of a transient inactivation of primary motor cortex on the activity of arm and hand muscles

The primary motor cortex (M1) plays an important role in the performance of complex behavioral tasks requiring coordinated movements of arm and hand muscles. The aim of the present study is to assess the role played by M1 hand area in the performance of a manual dexterity task involving a synergic action of proximal and distal muscles called the "reach and grasp" drawer task, before and after a transient inactivation of M1 using repetitive transcranial magnetic stimulation (rTMS).
Three categories of motor parameters were taken into consideration: first, the temporal unfolding of the task, second, the continuous recordings of the force needed to grasp the button of the drawer (grip force) and the force needed to open the drawer against adjustable levels of resistance (load force), and third, the electromyographic (EMG) activity of six to eight arm and hand muscles. To specifically inactivate the area of M1 involved in hand movements, we defined M1 hand region where single pulse of TMS stimulation elicited motor evoked potentials (MEP) with the largest amplitude and the highest probability, and we applied series of burst (3 pulses with 33.3 ms time interval) during 33.3 seconds.
Preliminary results show a pronounced decrease of EMG activity of hand and arm muscles associated with a decrease of grip and load forces needed to perform the "reach and grasp" drawer task at larger.
In future studies, the inactivation of other premotor areas also involved in the control of manual dexterity, such as the premotor cortex and the supplementary motor area should assess the exact implication of those areas in manual dexterity.

Talks

Isabel De Araujo Salgado & Christophe Lamy

Cortical circuits matching body metabolic signals and behavior.

The insular cortex (IC) monitors the homeostatic state of the body and responds to peripheral metabolic challenges, such as fasting. Studies in humans and animal models have shown that it also plays a key role in complex behaviors, such as decision making and emotions. However, the neuronal circuits involved in these integrative functions of IC are poorly understood. We aim to investigate the cellular mechanisms implicated in the monitoring of body metabolic states by IC and to identify the cortical microcircuits that link these mechanisms with complexes behaviors. We use whole-cell electrophysiological recordings from acute slices of mouse IC combined with histological techniques to characterize the biophysical, morphological, and molecular identity of IC neurons and their patterns of responses to metabolic signals. A subpopulation of IC neurons was sensitive to changes in extracellular glucose concentrations with either a glucose-inhibited or a glucose-excited phenotype. We further showed that glucose responsiveness is an intrinsic property of some of these cells. We are now looking at the cellular mechanisms involved in these responses.

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Gindrat Anne-Dominique, Quairiaux Charles, Britz Juliane, Lanz Florian, Brunet Denis, Leuthard C; Kaeser M; Hamadjida A; Wyss A, Michel Christoph M. and Rouiller Eric M.

The sensorimotor system in macaque monkeys following a motor cortex lesion: study from whole-scalp EEG mapping of somatosensory evoked potentials and from the Brinkman box task

Motor areas and somatosensory areas are densely interconnected and participate together to the motor control, forming the functional sensorimotor system. The primary somatosensory cortex (S1) sends corticospinal projections and somatosensory corticocortical inputs to the primary motor cortex (M1),

contributing to the control of voluntary movements. It is therefore expected that, after a lesion in M1, S1 will be affected in parallel with the motor control itself.

We present a method for long-term investigation of the brain activity in anaesthetised *Macaca fascicularis* using high-density EEG recordings of somatosensory evoked potentials (SSEPs). This electrophysiological approach was designed to allow repeated assessments of the cortical activity during the functional recovery following a unilateral permanent cortical lesion of the hand representation of M1. SSEPs are expected to allow monitoring the post-lesion rearrangement of connections, including also remote areas from the lesion. We show that pre-lesion SSEPs obtained after median nerve stimulations in macaque monkeys are characterised by a progression of quasi-stable brain component maps. The main generators of the surface topographies are successively localised to the contralateral brainstem and to the lateral parts of the parietal and frontal cortices close to the expected localisations of the sensory and motor representations of the hand. In addition, we demonstrate that a unilateral craniotomy of 300 mm^2 over the sensorimotor cortex followed by bone flap repositioning, suture and gap plugging with calcium phosphate cement, does not induce major changes or artefacts in SSEPs.

Moreover, to assess the integrity of the sensorimotor system from a behavioural point of view, the Brinkman box task was developed, specifically designed to assess the precision grip in macaque monkeys with or without visual feedback. It consists in retrieving food pellets from vertically and horizontally oriented wells on a board located in a box whose top can be opened or closed. The task can consequently be performed unimanually with or without visual feedback. We present preliminary data for the contralesional hand in monkeys performing the Brinkman box task without vision before and after unilateral permanent cortical lesion of the hand representation of M1.

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Loïc J. Chareyron, Pierre Lavenex

Functional reorganization of the medial temporal lobe memory system following neonatal hippocampal damage in monkeys.

In humans, the hippocampal formation is essential for the processing of declarative memory and damage to this structure in adult subjects results in amnesia. However, semantic memory is largely preserved in patients who sustained hippocampal damage early in life, suggesting that the medial temporal lobe memory system might undergo structural and functional reorganization after neonatal hippocampal lesion. Similarly, we have previously shown that spatial relational learning is impaired in monkeys who sustained hippocampal lesions during adulthood, whereas spatial relational learning persists in monkeys who sustained hippocampal lesions shortly after birth. Here, we aimed to characterize the structural and functional reorganization of the medial temporal lobe memory system in macaque monkeys (*Macaca mulatta*) following neonatal hippocampal lesion. Shortly before killing, animals explored a novel open-field environment in order to activate brain structures involved in spatial learning and memory. Quantitative analyses of expression of the immediate-early gene *c-fos*, a marker of neuronal activation, were performed to determine the brain structures that might enable spatial relational learning following early hippocampal lesions. Preliminary evidence suggests that the entorhinal, perirhinal and parahippocampal cortices are differentially activated by spatial learning after early hippocampal lesions, as compared to what is observed in control monkeys, and may thus contribute to the preservation of spatial memory function. Our findings support the hypothesis that the functional reorganization of the medial temporal memory system contributes to the partial recovery of memory function following early hippocampal lesion.

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Jayakrishnan Nair, Abbas Khani, Manuela Isenschmid, Gregor Rainer

Behavioral investigation of the dynamics of spatial memory formation in the tree shrew

Exploration is closely linked to memory formation in mammals. When first exposed to a novel environment, animals typically show initial signs of stress and subsequently generally shift to exploratory behavior, for example examining objects in the environment. With repeated exposure, explorative behaviors decrease or habituate. This habituation reflects memory formation underlying scene recognition and is typically accompanied by reductions in stimulus-evoked neural activity in relevant brain areas. Explorative behaviors typically rebound when an element of the familiar environment is modified, for example a new object might be introduced or the spatial configuration of the environment changed. There are substantial variations between mammalian species related to the temporal dynamics of explorative behaviors and manifestations of stress.

Here we used a spatial recognition paradigm to study temporal aspects of exploration behavior in the tree shrew, a mammalian species that is a close relative of primates. Tree shrews were initially accustomed to an empty arena during 10 minute periods for three days, and then allowed to explore three objects placed inside this arena for several days. On the test day, the spatial configuration of the objects was modified. Behavior was monitored using video tracking and scoring during all experiment phases. Depending on the temporal structure of the training period, animals exhibited signs of memory formation for the scene configuration as well as location of individual objects. We describe general behavioral characteristics during the habituation and object exploration phases, and relate these to the fidelity of memory formation. Our findings show that tree shrews form memories during spontaneous behavioral exploration of the environment in the absence of external reinforcers during a spatial memory paradigm.

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Ledermann, K., Jenewein, J., Sprott, H., Hasler, G., Schnyder, U., Burger, C., Johayem, A., Cservenyak, T., Kollias, S., Buck, A., Martin-Soelch

A common neurobiology for pain and reward?

Emerging evidence points to a role of mesolimbic dopamine (DA) in processing of pain and reward. In Fibromyalgia (FMS) first indication of DA dysfunction was evidenced. FMS is frequently associated with depression: Reduced DA function and reduced responses to reward were also evidenced in depression. Therefore reduced DA reaction to reward could be involved in depressive or pain symptoms observed in FMS. We measured DA receptor binding potential (BP) between FMS patients with and without comorbid depression (MDD) and controls in response to unpredictable monetary rewards using the [11C]Raclopride PET method. We expected FMS patients to show a reduced endogenous DA release compared to controls and an even stronger reduction in FMS patients with MDD compared to those without MDD that will be expressed by a greater binding of raclopride. Twenty four female FMS patients (11 with MDD) and 17 controls were measured while performing a slot-machine task where they could or receive monetary rewards in an unpredictable fashion or receive no feedback (control condition). PET measures were acquired in MRI-based striatal regions of interest and compared between FMS with and without co-morbid MDD and healthy controls. We found a significantly greater raclopride binding in the right Caudate Nucleus in FMS patients with comorbid MDD compared to FMS patients without comorbid MDD ($p=0.022$) and a greater raclopride binding in the right nucleus accumbens in FMS patients with comorbid MDD compared to healthy controls ($p=0.006$). These results show involvement of DA in the pathophysiology of FMS and suggest differences in the modulation of pain perception in FMS patients with and without MDD.

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Vanessa Loaiza & Valérie Camos

Words: 198

The following project investigated the effectiveness of semantic and phonological cues during immediate recall from working memory (WM) in order to elucidate underlying encoding mechanisms during WM tasks. In both experiments, participants completed two blocks of location judgment span task. During recall in both blocks, participants were given the opportunity to ask for a help word that would cue them to the word that was presented in that serial position (e.g., "lapin"). In one block, the cue word was semantically related to the target (e.g., "carotte"), while in the other block, the cue word rhymed with the target (e.g., "copain"). In the second experiment, participants were asked to either use rehearsal-based or refreshing-based maintenance strategies (cf. Camos, Mora, & Oberauer, 2011). The results suggested that use of the cues was similar between cue types (Experiment 1), but the effectiveness of the cues for recall depended on the strategy (Experiment 2). Specifically, phonological cues were more effective for the rehearsal-based strategy group, while semantic cues were more effective for the refreshing-based strategy group. This extends current research showing that rehearsal and refreshing are distinguishable maintenance mechanisms such that these mechanisms differentially support underlying levels of processing during WM encoding.

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Sébastien Miellet

Mapping information use with gaze-contingent techniques

In the past few years we have developed various gaze-contingent and data processing techniques in order to investigate eye movements in reading, face and scene processing.
In this talk, I will review these findings and focus particularly on the use of gaze-contingent techniques to precisely isolate facial diagnostic information and the influence of the culture of the observer, the task and various visual constraints. I will also

illustrate why, to our view, it is crucial to use data-driven, robust, statistical methods for mapping fixation densities.
I will then face the sensitive issue of concluding on the nature of representations involved in visual cognition from eye movement patterns. This will lead to the presentation of recent results aiming to clarify this issue and characterize the perceptual span for faces.
Overall our approach allows the precise isolation of the visual information sampled during active vision. Thus, our findings provide empirical constraints for face processing models and a benchmark to study visual perception across distinct populations.

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Anne-Laure Oftinger & Valérie Camos

Developmental interplay of articulatory rehearsal and attentional refreshing in children aged 6 to 9 in working memory

In adults, two mechanisms allow the maintenance of verbal information in working memory: articulatory rehearsal and attentional refreshing. Both are already in use at 7. This study evaluated the interplay between these mechanisms from 6 to 9 in 2 experiments. The opportunity for refreshing was manipulated either by introducing a concurrent task or by varying its attentional demand. Moreover, we impeded the subvocal rehearsal either by asking children to perform the concurrent task aloud, or by concurrently repeating “oui”. As expected, recall performance increased with age, and decreased with articulatory suppression regardless age.

Moreover, impeding the refreshing by varying the attention demand of the concurrent task reduced recall. However, this effect did not interact with the age. Finally, the interaction between rehearsal and refreshing depended on the manipulation of the attentional demand, without interacting with age. To conclude, the efficiency of mechanisms improves from 6 to 9, refreshing and rehearsal being independent in children, as in adults.

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Benoît Perriard & Valerie Camos

Language switching in a complex span task in bilinguals

Most models of working memory propose that its two functions, i.e., processing and storage of information, both require a limited attentional resource (e.g. Cowan, 2005). The Time-Based Resource-Sharing model (Barrouillet & Camos, 2010) suggests that information is maintained by a fast switching of attention between processing and storage, allowing the attentional refreshment of memory traces. Thus, the amount of time attention is occupied by a concurrent task (that is its cognitive load) is the determinant factor of recall performance.

In the present study, we investigated how language switching among early and late bilingual adults increased the cognitive load in a working memory span task. Participants completed a complex span task. Participants completed four conditions. In the two same-language conditions, the two tasks were in their dominant language (L1) or their secondary language (L2). In mixed conditions, naming and memorizing digits were in L1 while performing the concurrent shape task in L2, and vice versa. Our hypothesis was that recall performance would be higher in the L1/L1 condition than in the L2/L2 condition. Also, if language switching increased cognitive load, recall performance would be lower in mixed conditions than in the two same-language conditions.

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Narges Radman, Stephanie Cacioppo, Lucas Spierer, Eric Schmidlin, Eugène Mayer & Jean-Marie Annoni

Posterior SMA Syndrome following subcortical stroke: contralateral akinesia reversed by visual feedback

BACKGROUND: The Supplementary Motor Area (SMA) plays a key role in motor programming and production and is involved in internally-cued movements. In neurological populations, SMA syndrome following a lesion to the "SMA proper" is characterized by transient impairment of voluntary movements and motor sequences. This syndrome is assumed to follow on

from an interruption of the motor cortico-subcortical loop, and some case reports indicate that such a syndrome could occur after a brain lesion isolating the SMA from subcortical structures.

AIM: To characterize the pattern of motor impairments in a patient whose stroke disconnects the SMA from the subcortical motor loop.

METHOD**:** A patient developed a moderate transient left hemiparesis following a subcortical stroke in the right anterior cerebral artery area, which disconnected the SMA from basal ganglia. Eight days after the stroke, when the hemiparesis had regressed, the patient presented a specific SMA motor disorder of the left hand which manifested as an akinesia and was exacerbated when his visual attention was not directed towards his hand. We assessed finger tapping with left and right hands, eyes closed and open, in the left and right hemispace. We indexed movement speed as the number of taps filmed over five-second periods.

RESULTS**:** Left motor weakness (grasping strength of right hand: 49 kg and left hand: 41 kg) was resolved in a week. Ideomotor and ideational gestures and motor sequences were preserved. On the tapping task, left-hand tapping was slower than right-hand tapping. Critically, visual feedback improved tapping speed for the left, but not for the right, hand. The hemispace of the task execution had no effect on tapping performance.

CONCLUSION: Our results suggest that SMA-basal ganglia disconnection decreases contralateral movement initiation and maintenance and this effect is partly compensated by visual cues.
Keywords**:** Supplementary motor area, akinesia, visual feedback, SMA syndrome

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Björn Rasch

Memory reactivation and sleep

According to a widely held concept, the formation of long-term memories relies on a reactivation and redistribution of newly acquired memory representations from temporary storage to neuronal networks supporting long-term storage. This process of system consolidation takes place preferentially during sleep as an "off-line" period during which memories are spontaneously reactivated and redistributed in the absence of interfering external inputs. I will present recent evidence supporting the notion that memories are spontaneously reactivated during sleep and that induced reactivation during sleep by cueing improves memory consolidation during sleep, but not during wakefulness.

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Farfalla Ribordy, Pierre Lavenex et Pamela Banta Lavenex

Increased resolution of allocentric spatial memory in children form 2 to 4 years of age

Episodic memories for events that happen in unique spatiotemporal contexts are central to defining who we are. Yet, before 2 years of age, children are unable to form or store episodic memories for recall later in life; from 2 to 7 years of age, there are fewer memories than predicted based on a forgetting function alone. Here, we studied the development of allocentric spatial memory, a fundamental component of episodic memory. Children were tested in a real-world spatial memory task, in which they searched for rewards hidden beneath cups distributed in an open-field arena. Experiment 1 confirmed our previous results showing that the ability to form basic allocentric spatial representations emerges around 2 years of age. Experiment 2 revealed that the resolution of allocentric spatial memories improves gradually from 2 to 4 years of age, when children's ability to form elaborate allocentric memories over repeated trials is similar to that of young adults. The ability to form basic allocentric spatial representations appears to depend on the ability to represent the topological relations between objects, which

might depend on the functional maturation of the CA1 region of the hippocampus. The ability to form elaborate allocentric spatial representations might depend on the ability to encode metric information (distances and angles) between objects, which might depend on the functional maturation of the dentate gyrus and CA3 region of the hippocampus. These findings are consistent with the hypothesis that the gradual maturation of hippocampal circuits contributes to the development of episodic memories in childhood.

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Anne-Raphaëlle Richoz

Reconstructing Emotions in Motion Abolishes Facial Expression Categorization Impairment in Prosopagnosia

The human face transmits a wealth of nonverbal signals that readily provide crucial information for social interactions, such as face identification and emotional expression. Yet, a fundamental question remains unresolved: does the face information of identity and emotional expression categorization tap into a unique or separate representational system? To address this question we tested PS, a pure case of acquired impaired face identification – prosopagnosia – with occipitotemporal lesions sparing the neural substrates dedicated to emotional expression decoding. We previously demonstrated that PS does not use the eyes to identify faces but the mouth, revealing defective neural processes to recover identity. Thus, PS' functional dissociation represents a unique opportunity to test whether the face system relies on unique face representations.

Here, we used a FACS-based random facial expression generator coupled with a reverse correlation technique to reconstruct 3D dynamic mental models of the six basic facial expressions of emotion, in PS and age-matched healthy observers. Although PS shows categorization impairment for many expressions of the static Ekman faces, her dynamic mental models of facial expressions were comparable to controls. Subsequent verification tasks revealed that PS normally categorized *dynamic*

reconstructed mental models, but not the *static* version of the very same dynamic models. Evidence that PS identified dynamic facial expressions by using all facial features demonstrates that the face system relies on distinct representations for identity and emotion, flexibly adapting to categorization constraints. Our data also question evidence of deficits obtained from patients with static images, and offer novel routes for patient rehabilitation.

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Helen Rodger

Mapping the ontogenesis of facial expression recognitionReading
Reading the non-verbal cues from faces to infer the emotional states of others is central to our daily social interactions from very early life. Despite the relatively well-documented ontogeny of emotion recognition in infancy, our understanding of the development of this important biological skill throughout childhood remains limited. Therefore, for the first time, we aimed to map in a uniform way the developmental trajectory of all 6 basic emotions throughout middle childhood into adulthood. Using a novel psychophysical approach, we investigated the development of facial expression recognition in healthy school-aged children from 5 years-old up to adulthood. We implemented the QUEST threshold-seeking algorithm to parametrically manipulate the quantity of face signals and determine an observer's perceptual threshold for effective discrimination of each of the 6 emotional expressions, plus neutral. Essentially, all images were normalized for contrast and luminance. Overall, recognition accuracy improved with age for all emotions except happiness, for which all age groups including the youngest remained within the adult range. Fundamentally, the ontogenesis of each expression was unique but fell into two broad groupings: emotional expressions that showed a steep improvement in recognition with age - neutral, disgust, and anger; and those that showed a more gradual improvement with age - happiness, sadness, fear, and surprise. Consistent with previous studies, happiness was correctly recognized with minimum signals,

whereas fear required the maximum signals across groups. Our data provide for the first time a fine-grained mapping of the ontogenesis of facial expression recognition. This approach significantly increases our understanding of the decoding of emotions across development and offers a novel tool to measure impairments to specific facial expressions in developmental clinical populations.