平成18年度生理研研究会

2006 Seiriken Kenkyu-kai

「神経科学の道具としてのfMRI研究会」

“fMRI - a tool for neuroscience research”

開催日：平成18年11月16-17日（2006.11.16~17）

場所：自然科学研究機構生理学研究所１階会議室

（First floor Conference room at NIPS）

日程 (Schedule)

11月16日（木）(Nov.16)

13:30 ~ 13:35	開会の辞 (Welcome remarks)	
13:35 ~ 14:10	1. 郷田直一 (GODA, Naokazu)	生理研 (NIPS)
14:10 ~ 14:45	2. 杉浦元亮 (SUGIURA, Motoaki)	生理研 (NIPS)
14:45 ~ 15:20	3. BOSCH, Jorge	統数研 (ISM)
15:20 ~ 15:55	4. COSTAGLI, Mauro	理研 (RIKEN)
15:55 ~ 16:15	コーヒーブレイク (Coffee beak)	
16:15 ~ 16:50	5. 万小紅 (WANG, Xiaohong)	理研 (RIKEN)
16:50 ~ 17:25	6. 森健之 (MORI, Takeyuki)	精神神経セ (NCNP)
17:25 ~ 18:00	7. 土岐茂 (TOKI, Shigeru)	広島大 (Hiroshima U.)
18:30 ~	懇親会 (Get-together)	

11月17日（金）(Nov.17)

09:00 ~ 09:35	8. 吉岡芳親 (YOSHIOKA, Yoshichika)	岩手医大 (Iwate Med. U.)
09:35 ~ 10:10	9. 駒井豊 (KOMAI, Yutaka)	国循セ (NCVC)
10:10 ~ 10:30	コーヒーブレイク (Coffee beak)	
10:30 ~ 11:05	10. 神作憲司 (KANSAKU, Kenji)	国リハ (NRCPD)
11:05 ~ 11:40	11. 花川隆 (HANAKAWA, Takashi)	精神神経セ (NCNP)
11:40 ~ 11:50	閉会の辞 (Concluding remarks)	

1. Mapping cortical activity using fMRI in awake behaving monkeys

Naokazu Goda1, Takuya Harada1, Tadashi Ogawa2, Minami Ito1, Hiroshi Toyoda1, Norihiro Sadato1 Hidehiko Komatsu1

1. NIPS 2. Kyoto Univ.

FMRI study in awake behaving monkey is expected to be a new valuable experimental approach for investigating large-scale brain function, which is complementary to electrophysiological recordings from relatively small number of neurons. Here, we report the results of preliminary fMRI in the awake monkeys aimed to map retinotopy and motion- as well as form-selective regions in the visual cortex, with our experimental setups developed for fMRI in the awake monkeys.

Two monkeys were trained to fixate for 1-4s at a central fixation spot. The monkey viewed a screen in the 'sphinx' position inside a custom monkey chair. The head was fixed rigidly with the chair. Eye position was measured by tracking the pupil with an IR video camera. We presented stimuli of the different conditions (checkerboard wedges for retinotopic mapping, moving/stationary dots and object/noise pictures for measuring motion- and form-selective activities, respectively) in a block-design; each block consisted of 4 trials, in each of which the stimulus was presented for 0.5-3.5s during the fixation. BOLD responses during the blocks were measured using a 3T scanner and a surface coil with EPI sequences optimized to reduce susceptibility artifact. The data with large head/body motion were excluded from the analysis.

We obtained the retinotopic maps in areas V1/V2/V3/V3A/V4 in good agreement with the maps reported by previous electrophysiological studies. We found robust motion-selective activities within superior temporal sulcus (STS) including area MT, and form-selective activities as patches within STS and gyrus in the inferior temporal cortex, largely consistent with previous electrophysiological studies. Interestingly, some of these were observed in the regions where electrophysiological recordings were not explored. These results demonstrate the feasibility and the utility of fMRI for functional mapping in the monkey visual cortex.

2. Network extraction using exploratory multivariate analysis of intersubject variability in task-related activation

Motoaki Sugiura
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In complex environment in the daily life, perception and behavior differ among individuals. Each brain may respond incidentally or engage complementary processes to different extents for a single behavioral goal. This entails intersubject variability in activation and reduces the sensitivity of the conventional intersubject analysis of the functional imaging study, which tests the average between-condition difference in activation, treating the between-subject effect as noise. A novel approach to identification of brain networks using this intersubject variably has been recently proposed (Sugiura et al., Human Brain Mapping 2006, in press). The assumption is simply that a network for a specific cognitive mechanism will be activated differently in different subjects and that this will be expressed as a systematic pattern of intersubject variability. A principal component analysis (PCA) is used to summarize patterns of variability, over subjects, in regions of interest (ROIs) showing task-specific effects. Inclusion of multiple ROIs and task conditions enables to extract patterns of intersubject variability in distributed networks induced by different conditions. The principal component scores enters a voxel-by-voxel multiple regression analysis of subject-specific activations (i.e., contrast images). The resulting statistical parametric maps identify cortical networks that participate in the principal modes of intersubject variability. The functional attribution of these principal components is based on the functional selectivity of the ROIs used in the PCA. Examples of the successful applications of this approach will be presented and the limitation of the technique will be discussed.

3. A Toolbox for NN-ARX Modeling of fMRI Time Series

Bosch,J., Riera,J., Biscay,R., Galka,A., Valdes,P., Sadato,N. and Ozaki,T.
情報システム研究機構、統計数理研究所

A Matlab software is presented to analyze fMRI data on the basis of the NN-ARX approach [1]. NN-ARX is a voxel-wise methodology for estimating both the brain responses to stimuli contained in fMRI data, as well as gathering areas of the brain highly correlated. In contrast with other models, NN-ARX takes also into consideration dynamic aspects of consecutive fMRI scans interpreted as a multiple time series. The software includes facilities for data preprocessing (SPM like) but can also accepts the output from SPM preprocessing. Automated brain segmentations as well as coregistration to Talairach space are provided. The software offers options for the estimation of the optimal model parameters. To estimate the correlated areas, interesting voxels are selected as reference. The voxels of interest can be taken either from the voxels that show higher stimulus activation values or the voxels with higher innovations (the residual after model estimation). The HRF is also estimated for each experimental condition and shown as a 3D spatial map. A Hotelling T2 is used to assess the significance of the stimuli related activations as well as to assess differences between conditions. By pinpointing with the mouse over the spatial maps, a specific voxel can be picked up and its specific HRF is displayed for each condition. Information about the reference voxels is provided and the user can study them separately. Also, for a selected voxel, the optimal model selection, the parameters, the original and the estimated signals are shown, as well as the HRF for each condition, the residuals and some statistical tests about the residuals. [1]fMRI activation maps based on the NN-ARx model, Riera-Diaz, J.J.; Bosch-Bayard, J.; Yamashita, O.; Kawashima, R.; Sadato, N.; Okada, T.; Ozaki, T. Neuroimage, 23(2), (2004), 680-697

4. Motion correction in k-space for fMRI

Costagli M, Waggoner RA, Ueno K, Tanaka K, Cheng K
RIKEN Brain Science Institute

Unlike the most widely used applications such as AFNI and SPM that operate in image domain, the algorithm presented here corrects 3D rigid-body motion by operating in k-space, thus decoupling and independently correcting rotation and translation effects. Rotations between two volumes to be aligned are visible in their 3D-FFT magnitude data, where no contribution from translational effects is present. Since rotations in k-space are always about the origin of the spatial frequency axes, we estimate them by aligning spherical shells of equal radius, centered at the origin, encoding magnitude Fourier data of the volumes to be registered. After correcting rotations, we exploit the Fourier shift theorem for treating translations: a shift along any spatial axis introduces a linear phase change along the corresponding frequency axis, which is estimated by considering the cross power spectrum (CPS) of the original and the translated volumes. Translation correction is achieved by fitting a linear function (a hyperplane in 3D) to the phase of the CPS, adding it to the Fourier transform of the test volume, and finally inverse Fourier-transform the result. The method is non-iterative, and can accurately detect subvoxel translations.

The algorithm was tested on both synthetic and real EPI time series, and compared to the registered data obtained with AFNI and SPM2. Better volume registration was achieved by serial application of motion correction in k-space and then in image-space, the former step being more robust to local minima and correcting for larger motions, and the latter seeming more suitable for fine corrections.

5. Electromagnetic Source Imaging: Resolution Spread Function-Constrained and Functional MRI-Guided Spatial Filtering

Xiaohong Wan
RIKEN Brain Science Institute

The problem of spatial ambiguity in electromagnetic source imaging has been unresolved. Our heuristic analysis points out the discrepancy between the estimated source and the real source arises from the other sources' interference. We suggest a novel and simple solution based on the principle of spatial filtering combined with the Backus-Gilbert method by minimizing the estimated source power and effectively suppressing the other sources' interference. Within this framework, the functional MRI information can be also effectively integrated into the inverse solution and the source localization is not biased by incompatible knowledge. Our Monte Carlo simulations of EEG system based on a realistic head model show that the resolution spread function-constrained and functional MRI-guided spatial filtering provides precise source localization, even in the cases of multiple simultaneously active sources.

6. Hemodynamic correlates of human sleep spindles: A simultaneous EEG-fMRI study

Takeyuki Mori, Noriko Sato (National Center of Neurology and Psychiatry)
Kimitaka Anami (Takatsuki Hospital)

The EEG-fMRI is being applied to the examinations of the distributed neural networks related to spontaneous neural activities such as awake (alpha rhythms etc.) and sleep (sleep spindles, K complexes etc.) electrophysiological phenomena as well as epileptiform activities. In the present study, we tried to utilize the EEG-fMRI for mapping hemodynamic correlates of sleep spindles.

The sleep spindle is a distinct EEG event observed in non-REM sleep, especially in Stage II of the sleep cycle. Although sleep spindles have been considered to play a role in sleep maintenance, their physiological implication still remains to be clarified. We investigated the hemodynamic correlates of spindles using an EEG-fMRI measurement in 43 normal volunteers. Twelve out of the 43 subjects succeeded in reaching Stage II sleep during fMRI acquisition. We found positive spindle-related BOLD signal changes in the early sensorimotor areas, auditory areas, visual areas, anterior cingulate cortex, posterior cingulate cortex and the thalami. The results indicate that extensive cortical and subcortical areas are involved in the formation of spindles. We suggest that such spindle-related neural substrates play important roles in sensory processing and sleep protection during non-REM sleep.

7. Sex differences in automatic emotion processing: Association with harm avoidance

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2) Department of Social and Clinical Psychology, Faculty of Contemporary Culture, Hijiyama University

Background: Neural science revealed that females appear to be more sensitive and responsive to social, emotional information, including facial expression, than are males. Although subcortical, automatic, face processing has been considered to take an important role in face perception, no neuroimaging studies have been done to elucidate sex differences in subconscious emotion processing and its relationship with personality variables.

Methods: Using fMRI, we investigated the neural responses associated with the subconscious (backwardly-masked) perception of fearful, happy, disgust and neutral faces in 32 healthy volunteers (16 males, 16 females) who varied in harm avoidance, associated with trait anxiety and also threat processing.

Results: When subtracting the activation values of males from those of females, suprathreshold positive signal changes were detected in the right medial frontal gyrus during masked happy presentation, and in the left superior parietal lobule and the right parahippocampal gyrus during masked fear presentation. When subtracting the activation values of females from those of males, suprathreshold positive signal changes were detected in the right anterior cingulated and the right caudate during the masked disgust presentation. While, in females, the harm avoidance positively correlated both, with happy-related neural activation in the right medial frontal gyrus, and with fear-related activation in the right parahippocampal gyrus, in males, there was no such correlation.

Conclusions: Our findings suggest sex-related neural responses to emotional stimuli and could contribute to the understanding of mechanisms underlying sex-related vulnerability of the prevalence and severity of anxiety and mood disorders.

8. 脳機能計測を目指した MRS による非侵襲的脳内温度測定

吉岡芳親 1,5)、高濱祥子 1,5)、及川浩 2,5)、神原芳行 1,5)、松村豊 1,5)、江原茂 1)、関淳二 3,5)、精山明敏 4,5)

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体内温度は生命活動の基盤となる物理量であり、組織の活動度、血流、環境に影響されながら統合的·有機的に制御されていると考えられ、生理的条件下の脳においても部位差があるし活動により変動していると考えられる。安静時の脳は基礎代謝の約 20%を占めており(約 20 ワット)、同等の産熱が行われている。また、活動時には代謝が 10%前後変化すると考えられており、温度は脳活動を評価する一手段となると思われる。しかし、精度の高い非侵襲的な脳内温度計測は容易では無く、脳内温度に関する情報は非常に乏しいのが現状である。温度は定量的に取り扱う事が可能であり、精度良く温度計測ができるようになれば、安静時の脳活動レベル、個体間の比較、脳活動の絶対量を評価できる可能性が有る。私たちは、磁気共鳴法で得られる温度情報を用いた脳機能評価方法を模索しており、これまでに行ってきた磁気共鳴法を用いた脳内温度計測について発表する。

9. 赤外線カメラによるラット神経活動に伴う脳表温度変化の計測

駒井豊*1、大井康浩*2、精山明敏*3、関淳二*1
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　脳機能を可視化する新しい手法として、脳局所温度を計測する方法が提案されている。しかし、その基礎となる生理学的データは限られている。近年、高感度の赤外線カメラ（インジウムアンチモン）が実用化されたことにより、脳の局所的な活動に伴う温度変化を脳表で探知することが可能となった。脳表の温度変化は、脳神経活、及び、それとカップルする脳血流変化によってもたらされると考えられることより、脳神経活動の起きた領域、及び、強度を推測する有効な情報と考えられる。

　本研究では、麻酔下のラットの下肢に電気刺激(3mAx5)を与え、誘起される脳感覚野での温度変化を経頭蓋、及び、頭蓋骨除去後の硬膜表面で計測した。経頭蓋での計測では、最も変化の顕著な部位で、刺激開始から 2.9 秒後に 0.065 度の上昇、頭蓋除去後には 2.0 秒後に 0.087 度の温度上昇が観察され、後者の方がより鋭い空間分布を示した。本計測系は、局所的な温度変化を探知するのに十分な感度と再現性があることが示された。

10. The role of the human left ventral premotor cortex for exact enumeration of successive stimuli

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2. Division of Cerebral Integration, Dept of Cerebral Research, NIPS, Okazaki, Japan
3. Human Motor Control Section, Medical Neurology Branch, NINDS, Bethesda, USA

Adult humans have the ability to count successive stimuli exactly. What brain areas underlie this uniquely human process? To investigate the neural basis, we first used functional magnetic resonance imaging (fMRI) and investigated brain areas involved in counting small numbers of successive stimuli up to 4, and demonstrated activations in the bilateral lateral premotor cortex[1]. We further applied fMRI and found that the upper part of the left ventral premotor cortex was preferentially activated during counting of successive sensory stimuli presented 10 to 22 times, while the area was not activated during small number counting up to 4. We then used transcranial magnetic stimulation (TMS) to assess the necessity of this area, and found that stimulation of this area preferentially disrupted subjects' exact large number enumeration (10-22). Stimulation to the area affected neither subjects' number word perception nor their ability to perform a non-numerical sequential letter task[2]. The results suggest that the left ventral premotor cortex is indispensably involved for exact counting of large numbers of successive stimuli.

1. Kansaku, K. et al. Neural correlates of counting of sequential sensory and motor events in the human brain. *Neuroimage* **31**, 649-60 (2006).
2. Kansaku, K. et al. The role of the human ventral premotor cortex in counting successive stimuli. *Exp Brain Res* (in press).

11. A motor network study by concurrent fMRI and TMS technique

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The concurrent functional MRI and transcranial magnetic stimulation technique can potentially visualize the whole brain networks connected to the stimulated site. However, the quantitative relationship between TMS intensity and BOLD signals in the stimulated and remote areas is yet to be elucidated. To answer this question, fifteen healthy subjects were scanned on a 3-T MRI scanner. An MRI-compatible figure-of-eight TMS coil was attached to the subject's scalp site adequate for eliciting right thumb movement. BOLD measurement was performed with the gradient-echo EPI (TR=2.7 s/TE=30 ms) modified for "stepping-stone" sampling, which enabled online monitoring and recording of motor evoked potentials during scanning. A single TMS pulse was delivered during the delay periods (200 ms) between each volume acquisition. The intensity of TMS pulses was varied from 30% to 95% of machine output (110% with a booster) at a 5% step (mean frequency at ~0.15 Hz). SPM analyses revealed activation of motor and sensory networks as well as auditory areas during TMS stimulation with higher intensities. BOLD signal changes as a function of TMS intensities were assessed in the directly stimulated left primary motor cortex (M1) and other remote areas including supplementary motor areas (SMA). A sharp increase in BOLD signals was observed in M1 only above the 80% stimulation corresponding to the resting motor threshold. The remote motor areas, SMA, for example, showed an increase in signals even below the motor threshold. Further investigation will be necessary to clarify the energy requirement in the direct and remote areas influenced by TMS.