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論　文　要　旨

論文題目

Cerebral hemodynamic responses to the sensory conflict between visual and rotary stimulus: Analysis with a multichannel Near-Infrared Spectroscopy (NIRS) system.

（　視覚刺激と回転性前庭刺激との不一致が大脳皮質血流応答に及ぼす影響- fNIRS による研究）

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Background.

The postural instability or vertiginous sensation was formed by the sensory conflict and it was originated from differences between the input information received by the visual and vestibular receptors. In humans, the cortical activations related to the visual or vestibular information processing have been investigated separately using functional MRI (fMRI). The results showed that the vestibular inputs elicited the activation of the regions related to visual flow processing including the medial superior temporal area (MST) and the ventral intra-parietal area (VIP), including temporoparietal junction (TPJ), posterior parietal cortex (PPC), somatosensory cortex and hippocampus. Because of movement restrictiveness for head rotation, fMRI is not suitable for the experiment of head rotatory (vestibular) stimulation. So, it is still unclear how these regions work during sensory conflict between visual and vestibular inputs in humans. To circumvent these limitations, we evaluate the cortical hemodynamic responses in the sensory conflict between visual and horizontal rotatory stimulation using functional near-infrared spectroscopy (fNIRS). It is the functional, non-invasive neuroimaging technique, suitable to analyze task-related cortical activity during motion. We would expect the changes in cortical activities in and around the TPJ including bilateral upper parts of the temporal lobe, the parietal lobe, posterior parts of the frontal lobe.

Methods.

There were 14 healthy men (aged 25.8±8.2 years, all right-handed) were enrolled in this study who had no medical history of ear disease, vertigo, and head injury. The visual-vestibular stimulator (OKN/VOR stimulator; First Medicals Co. Ltd, Tokyo, Japan) consisted of a rotatory chair, cylindrical screen and projector were used. We could control the speed of the rotatory chair and select the direction of horizontal movement of visual stimulation (black and white stripes) which were identical or opposite to that of rotatory chair. Two kinds of the rotatory direction of the chair ("Right to Left" or opposite) and two kinds of visual stimulations (“Congruent” and “Incongruent”) were combined. In “Right to Left” vestibular stimulation, the chair was accelerated to rotate to the right side in 3 degree/sec^2 for 20 sec and then rotated in the same velocity for 80sec. After that, the chair was decelerated to rotate in 3 degree/sec^2 for 20sec. Then, the rotatory chair accelerated to the opposite side in 3 degree/sec for 20 sec, rotated in a constant angular velocity (60 degree/sec) for 80 sec, decelerated in 3 degree/sec^2 for 20 sec, and stopped for 80 sec. In “Congruent” visual stimulation, the strips were accelerated or decelerated in the opposite rotatory direction of the rotatory chair. In “Incongruent” visual stimulation, the stripes were accelerated or decelerated in the same rotatory direction of the rotatory chair. Four conditions were made from the combination of the direction of rotatory chair and visual stimulation (i.e. Condition 1:”Right” vestibular and “Congruent” visual stimulation; Condition 2:“Left” vestibular and “Congruent” visual stimulation; Condition 3:“Right” vestibular and “Incongruent” visual stimulation; Condition 4:“Left” vestibular and “Incongruent” visual stimulation). Self-assessment of the strength of vertiginous uncomfortable sensation during the acceleration phase was performed after each task (Visual Analog Scale: VAS).

Two portable fNIRS imaging systems (LIGHTNIRS; Shimadzu Co., Ltd, Kyoto, Japan) were used to measure cerebral hemodynamics and we recorded a total of 46 channels (“NIRS channel”). The recording areas were composed to the bilateral ventral part of supra parietal lobule (vSPL), infraparietal sulcus (IPS), supramarginal gyrus (SMG), anglar gyrus(AG), posterior supratemporal gyrus(pSTG), parietal operculum(p-OP), frontal operculum (f-Op), ventral part of pre- and postcentral gyrus (PrG and PoG), posterior middle temporal gyrus (pMTG) and ventral third visual association area (V3).

We analyzed changes in Oxy-Hb concentration as cerebral hemodynamic activity. The NIRS-statistical parametric mapping (SPM) software was used to perform the group statistical analysis of the activated cortical regions in each test condition. We also analyzed the correlation between hemodynamic activity and the strength of subjective vertiginous sensation (VAS score) in each condition.

Results.

Subjective vertiginous sensation: The result of the statistical analysis indicated that the strength of subjective vertiginous sensation in the incongruent condition was significantly larger than that in the congruent condition (P=0.032, paired t-test). Furthermore, both VAS scores in congruent and incongruent conditions have positively significant correlation (R=0.86342, Pearson correlation coefficient), suggesting that subjects had different sensitivity of vertigo for visual and vestibular stimulation.

Analyses of the NIRS data: As for the results of the group statistical analysis of NIRS Oxy-Hb, the topographical maps indicated significant activation in the left ventral primary somatosensory area (S1) and the right ventral part of SMG (vSMG) in Condition 1. Small part of the left vSMG was activated in condition 2. Bilateral vSMG, ventral part of AG and right pMTG were activated significantly in Condition 3. Bilateral vSMG, pSTG, pMTG, right AG were activated significantly in Condition4.

Correlation analysis between vertical activation and subjective vertiginous sensation: Negative correlation between T-value and subjective vertiginous sensation was shown in the results based on Spearman's rank coefficient test. In dorsal part of left SMG, negative correlation was found in Condition 1 (p=0.0033) and Condition 3 (p=0.0033). In dorsal part of right SMG (p=0.0046) and left pSTG (p=0.0244), negative correlation was found in Condition 4. There was no significant correlation in condition 2.

Discussion and Conclusions.

Incongruent visual stimulation strongly enhanced hemodynamic activity in the posterior part of the MTG (pMTG). This area may be homologous to the middle temporal area (MT) and the medial superior temporal area (MST) in monkey. Dorsal MST neurons respond to both optic flow and translational movement. In addition, these neurons respond to rotation with incongruent visual and vestibular inputs. These results suggest that the pMTG activated in this study might be involved in detection of sensory conflict between visual and vestibular stimulation in human MST.

Bilateral ventral SMG (vSMG) and the posterior STG (pSTG) around the limb of the Sylvian fissure was activated in incongruent visual stimulation (Conditions 3 and 4). These areas correspond to the PIVC which receives multimodal information including vestibular, visual and proprioceptive inputs in monkey. In addition, the PIVC is strongly interconnected with other vestibular cortical areas. These results suggested that bilateral human TPJ activation in the present study might reflect altered perception of head position and movements in incongruent visual-vestibular conditions.

Negative correlation was found between the hemodynamic activity in bilateral dorsal part of the SMG (dSMG) in and around the infraparietal sulcus (IPS) and subjective vertiginous sensation in the incongruent visual stimulation (Condition 3 and 4). Greater activities in the dSMG induces weaker subjective vertiginous sensation during visual-vestibular sensory conflict. In monkeys, the ventral intraparietal area (VIP), located in the fundus of the IPS, receives multimodal information: (1) vestibular information from the PIVC, (2) vestibular and somatosensory information from the vestibular neck subregions in areas 3a and 2, (3) visual information from the MT and MST complex, and (4) somatosensory information from the S1 area. In addition, the monkey VIP neurons represented vestibular heading in an egocentric (body-centered) reference frame in a body-fixed gaze condition that corresponds to the present experimental situation, which might result in flexible transformation of the spatial reference frame to egocentric. The subjects, who could not flexibly switch reference frames during sensory conflict, might feel vertiginous sensation.

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様式８

学　位　論　文　審　査　の　要　旨

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Cerebral hemodynamic responses to the sensory conflict between visual and rotary stimulus: Analysis with a multichannel Near-Infrared Spectroscopy (NIRS) system. （視覚刺激と回転性前庭刺激との不一致が大脳皮質血流応答に及ぼす影響-fNIRS による研究）	（判定） 合格

(論文審査の要旨)

【目的】

めまい感は視覚と回転性前庭覚との感覚不一致、すなわち視覚と前庭覚の受容体によって受容される刺激入力間の差異から生じると考えられる。ヒトにおける視覚あるいは前庭覚情報処理に関連する脳活動は、これまで別々に検討されてきた。前庭覚刺激により内側上側頭野（MST）、腹側頭頂内野（VIP）、側頭頭頂接合部（TPJ）、後部頭頂皮質（PPC）、体性感覚皮質、海馬などが賦活されることが知られているが、視覚と前庭覚との感覚不一致に際して、これらの領域がどのように活動するかは明らかでない。

本研究で、Nguyen Trong Nghia 氏は、視覚と回転性前庭覚との感覚不一致に対する脳活動の変化を明らかにするために、近赤外線スペクトロスコピー（NIRS）を用いて、大脳皮質の血行動態反応について検討した。

【方法】

14 人の健常右利き男性（平均年齢 25.8±8.2 歳）を対象とした。回転椅子と円筒投射スクリーンから成る視覚−前庭覚刺激装置を用いた。回転椅子による前庭刺激は、右方向または左方向に 3 degree/sec^2 で 20 秒間加速し、60 degree/sec で 80 秒間保った後、3 degree/sec^2 で 20 秒間減速した。視覚刺激は、円筒投射スクリーンに白黒の縦縞を投射し、回転椅子の回転に対して動かない“一致（Congruent）”刺激と、回転椅子と同じ速度で同じ方向へ動く“不一致（Incongruent）”刺激とした。回転性前庭刺激と視覚刺激の組み合わせにより、条件 1（右回転、一致）、条件 2（左回転、一致）、条件 3（右回転、不一致）、条件 4（左回転、

不一致）の4条件を設定した。

左右の頭頂部を中心にNIRSのプローブを配置し、合計44チャンネルの記録を行なった。酸素化ヘモグロビン（Oxy-Hb）濃度の変化を指標として、各刺激条件における20秒間の加速期間の脳血行動態を測定し、NIRS-statistical parametric mapping（SPM）により解析した。各条件における主観的めまい感の強さをVASで評価した。

【結果】

1) 主観的めまい感は一致条件に比較して不一致条件で有意に強く（P=0.032）、一致条件と不一致条件における強さは有意に相関した（R=0.86）。

2) 各条件における有意な脳賦活は、条件1では左右の一次体性感覚皮質（S1）と右のTPJ、条件2では左のTPJ、条件3では左右のTPJと右のMST、条件4では左右のTPJとMSTにおいて認められた。不一致条件においてMSTが賦活されること、またTPJの賦活がより大きいことが特徴であった。

3) 主観的めまい感と脳賦活の相関解析では、条件1と条件3では左の縁上回背側部（dSMG）、条件4では右のdSMGと負の相関を示した。条件2では有意な相関はなかった。

【総括】

本研究で、Nguyen Trong Nghia氏は、視覚刺激と回転性前庭刺激の不一致条件ではMSTが賦活されること、また一致条件、不一致条件ともにTPJが賦活されるが不一致条件で賦活がより強いことを明らかにし、MSTとTPJが視覚と前庭覚との感覚不一致の検出に重要な役割を果たすことを示唆した。また、頭頂間溝（IPS）に隣接するdSMGの血行動態反応と主観的めまい感の強さが逆相関することを示し、この領域の活動変化がめまい感の生成に重要であることを示唆した。

本研究は、ヒトにおける視覚および前庭覚情報処理に関連する脳活動を脳画像によって同時に検討し、視覚と前庭覚との感覚不一致に関わる脳血行動態の変化を初めて明らかにしており、新規性が高い。また、視覚、前庭覚、体性感覚の入力が集まり、高次認知機能を司るIPSに隣接するSMGがめまい感の生成に重要であることを示唆した点は、医学における学術的重要性が高い。以上より本審査委員会は、本論文を博士（医学）の学位に十分値すると判断した。