氏　　名	高浦　加奈
学位（専攻分野）	博士（理学）
学位記番号	総研大 1297 号
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論文審査委員	主　査　教授　南部　篤 教授　定藤　規弘 准教授　田中　真樹（北海道大学） 教授　伊佐　正

論文内容の要旨

'Blindsight' is a phenomenon in which patients with damage to their primary visual cortex (V1) exhibited residual visual function without visual awareness in their visual field affected by the damage. Patients deny any visual awareness in the affected visual field, but when they are forced, they can orient to visual stimuli in the affected visual field by pointing or saccades. The residual functions are attributed to the visual pathways bypassing the V1, including the extrageniculate pathway mediated by the superior colliculus (SC). Visual awareness seems to support our flexible use of visual information in daily life. Once we become aware of something in our vision, we can use them for thinking or imaging even after it disappears from the view. Such mental processes are supposed to depend on the ability to retain visual information available, which is often discussed with the term of 'working memory'. Thus, the relationship between visual awareness and working memory has often become a topic in theoretical or experimental studies, and it is commonly accepted that they are tightly linked to each other. Thus, it is intriguing to examine whether visual information in the affected visual field after V1 damage is available for the tasks which require working memory. In this study, the authors investigated spatial working memory after V1 lesion by using the monkeys with unilateral V1 lesion. It was previously reported that monkeys with unilateral V1 lesion could make saccades or reach to visual stimuli in the affected visual field when they were forced to respond. However, when they were required to report whether the visual stimulus was presented or not, they failed to detect them. They behaved as if there was no stimulus. This phenomenon seems parallel to the dissociation between the visual awareness and the residual visual function observed in the patients. Thus, the monkeys with unilateral V1 lesion have been used as an animal model of blindsight.

The authors examined the monkeys' capability for the memory-guided saccade task, which is commonly used as a task requiring spatial working memory. In this task, subjects have to retain the position of the briefly flashed visual stimulus (cue) in their memory. Two Japanese monkeys were used. Their left V1 was removed by suction. During the postoperative period, their recovery process and the area affected by the lesion were investigated with visually guided saccade task.

After their performance in this task reached the steady state, their performance in the memory-guided saccade task was examined.

It is found that both monkeys could retain spatial memory of the cues presented in the affected visual field as long as 2 seconds. The success ratios were 91.7 % and 93.8 %, respectively in each monkey. This means that the visual information in the affected visual field is available for spatial working memory.

To examine the neural mechanisms underlying the memory-guided behavior in the affected visual field, neuronal activity in the deeper layer of the SC was recorded. The deeper layer of the SC interacts with various regions of the cerebral cortex and is one of the key regions for control of saccades. Furthermore, because of the projection from the superficial layer of the SC which directly receives visual inputs from retina, its functional role is likely to become larger after V1 lesion. While the monkeys were performing the task in the affected visual field, activities of the 72 neurons in the ipsilesional SC (ipsi SC) were recorded. Responses to the visual stimuli presented in the affected visual field were observed in 58 neurons. Based on the activities during the visually-guided delayed saccade task, the neurons were classified into the 2 groups: visual and visuomotor neurons. In the ipsi SC, 12 visual and 46 visuomotor neurons were recorded. As a control, activities of 16 visual and 50 visuomotor neurons in the contralesional SC (contra SC) of the same monkeys were recorded while the monkeys were performing the task in the normal visual field. The magnitudes of the visual responses and those of the saccadic bursts were not significantly different between the contra and the ipsi SC.

Clear difference in the neuronal activity between the contra and ipsi SC was found during the retention interval in the memory-guided saccade task. The majority of the neurons in the ipsi SC kept discharging throughout the temporal interval from the offset of the cue until the go-signal (delay period), in case the cue was presented inside the receptive field (RF). In correct trials, the persistent activities during the delay period discriminated whether the cue was presented inside the RF or outside the RF with high probabilities. It is noteworthy that the persistent activities during the delay period were observed not only in the visuomotor neurons but also in the visual neurons, which were supposed to play a minor role for saccade execution. In the contra SC, such persistent activities were observed only in a part of the neurons, and the magnitudes of

them were significantly smaller than those in the ipsi SC. Analysis of error trials revealed that the persistent activities in the ipsi SC were correlated with the monkeys' behavioral outcome. When the monkeys made error saccades toward the outside RF, the persistent activities decayed before the go-signals. In contrast, when the monkeys made error saccades toward the inside RF, the neurons discharged during the delay period.

These results suggested that the persistent activities in the ipsi SC during the delay period might serve as a source of the spatial information required for performing memory-guided saccade task in the affected visual field. In normal monkeys, persistent activities in the memory-guided saccade task have been described in the prefrontal and posterior parietal cortex, supporting the key roles of these cerebral regions in spatial working memory. After V1 lesion, the SC might compensate for a part of the functional roles of these cerebral areas.

Thus, the results challenge the currently prevailing idea about the relationship between visual awareness and working memory, and to the view of the working memory as inherent properties to the cerebral cortex.

博士論文の審査結果の要旨

大脳皮質一次視覚野（V1）が損傷されると、対応する視野の欠損がおき視覚的な気付き（awareness）が消失する。しかし、一部の患者では、損傷視野内に視覚刺激を提示し指差しやサッケードなどで定位するように指示すると、口頭では「何も見えない」と報告するにもかかわらず、実際には偶然以上の高い確率で定位することが出来る（盲視）。本現象は、視覚情報を利用するのに必ずしも視覚的なawarenessは必要ではないことを示唆している。一方、ある目的を持った一連の行動の中で必要な情報を一時的に保持するような「作業記憶」の場合、awarenessは必須であると考えられてきた。これまで、V1損傷患者を用い損傷視野内で作業記憶を利用できるかについての報告はあるが、損傷範囲が一定せず一貫した結果が得られていない。

本研究では盲視のモデル動物とされる片側V1を切除したサルに、以下のような記憶誘導性サッケード課題を課すことで、まずこの仮説の検討を行った。サルが注視点（FP）を固視していると、手がかり刺激（cue）が一瞬提示され、その後遅延期間（一約2秒）が続く。この間も、サルはFPを固視し続けなくてはならない。その後、FPが消えたのを合図に記憶に基づいて、cueの提示された位置に向けてサッケードを行う。片側V1を切除した2頭のサルで検討したところ、損傷視野内への記憶誘導性サッケードが可能であること、すなわち損傷視野内でも空間作業記憶は利用可能であることが示された。

次に、その神経基盤を調べるために、記憶誘導性サッケード遂行中のサルの上丘中間層・深層から単一神経細胞記録を行った。サルやヒト患者での先行研究の結果から、上丘は、V1損傷後の残存する視覚情報処理に重要な役割を果たしていることが指摘されている。損傷側の上丘では、損傷視野内にcueを提示した際、遅延期間中に空間選択性を持った持続性の発火活動が計測された。一方、健常側の上丘では、健常視野内にcueを示しても、このような持続性の発火活動はほとんど観察されなかった。さらに、各神経細胞の発火活動が、cueの提示位置について、どの程度情報を保持しているのかROC（receiver operating characteristic）曲線下面積を用いて評価した。健常側の上丘ではcue消灯後、急速に位置情報が失われるのに対し、損傷側の上丘では遅延期間中にcueの位置情報が維持されていた。また、エラー試行を解析してみると、損傷側上丘の持続性発火活動とサッケードの方向との間に相関が見られ、損傷側上丘で維持されている情報が、サルの行動を決定する際に利用されていることを示している。このような持続性発火活動は、これまで前頭前野や後頭頂葉などで報告されているので、V1切除後の損傷側上丘の続性発火活動はこれらの皮質領野の活動の反映かもしれない。

以上、本研究の結果は、空間作業記憶の利用には必ずしも視覚的なawarenessは必要ではない可能性を示しており、現在、広く受け入れられている視覚的なawarenessと作業記憶との関係について、強く再考を促すものである。実験方法は適切に考えられ、導かれている結論も妥当であり、それらは明快かつ平易な英語で記載されている。これらのことから本論文は、学位論文として十分にふさわしい内容であるものと結論された。