様式３

論　文　内　容　の　要　旨

氏　　名　（広兼　浩二朗）	
論文題名	Striatal neurons encode rhythm parameters subserving the coordination of body parts in complex movements. (複雑な運動における体部位間協調を司るリズムパラメターをコードする線条体神経細胞)

Our movements, such as playing musical instruments, participating in sports, walking and running, often entail continuous execution of multiple body parts. The coordination of movement elements that allow for the seamless and graceful performance of continuous movements is an intriguing phenomenon. Take, for instance, the playing of a piano, where the fingers move in a repetitive and rhythmic manner, alternating or moving simultaneously, yet in temporal coordination as if linked. However, the underlying control and neural mechanisms that facilitate these movements remain elusive. To shed light on these issues, I have employed two experimental approaches: behavioral analysis and electrophysiology, which clarified the aforementioned phenomena.

I first performed movement analysis of mice using an original system that was capable of producing complex movement, revealing that mice execute complex movement by creating a chunk of motion sequences through a rhythm I term "Rhythm Chunk." In prior studies, a complex stepping task named the "step-wheel task" was developed to investigate the coordination of multiple body parts in continuous running of mice. The step-wheel is a motor-driven vertical wheel and mice were trained to step on complexly arranged ladder-like pegs (peg-patterns) to obtain water. To comprehend the coordination of multiple body parts in continuous movements, I measured the timing of stepping and licking and elucidated that mice formed stable (chunks) and unstable (non-chunk) running segments in their complex stepping sequences. I found that the parameters of rhythms, such as the interval and phase of repetitive movements of body parts, were more firmly locked inside the stable running segments, indicating that the mice formed a motor chunk through rhythms (rhythm chunk) which contributes to the coordination of multiple body parts in a timely manner.

I next identified a group of neurons in the dorsolateral striatum that encoded the rhythm parameters of movements during the complex stepping task. Multi-unit recordings were performed during the step-wheel running and neurons were found to respond to events, including the approach to and leave from reward, licking of the spout, and touches of forelimb paws to pegs. To gain a deeper understanding of those neurons, I used specific peg-patterns that only changed the interval and phase of the left and right peg timing. Through the use of these two patterns and a complex peg-pattern, I found that a considerable number of striatal neurons demonstrated modulation of firing rates by the interval and/or phase. Interestingly, the firing rate of those neurons tends to increase as the touch of pegs is repeated, indicating a responsiveness to repetition, which is considered a parameter of rhythm. I have thus identified these neurons as rhythm neurons. Furthermore, rhythm neurons were found to be responsive to specific phases within each touch and lick movement cycle, indicating that the activity of these neurons also reflects the state of multiple body parts coordination.

In conclusion, I found that complex and continuous movements are successfully executed by incorporating rhythm chunks and that rhythm neurons may serve as the underlying neural mechanism that coordinates the rhythms of multiple body parts and enables fluent movement. Although the number of neurons is limited, some were found to change their firing rate between inside and outside of rhythm chunks, suggesting a role in the formation or execution of rhythm chunks. I hypothesize that rhythm neurons may convey rhythm information throughout the brain via projections to the spinal cord, cerebellum, or cerebral cortex through the basal ganglia loop and may be involved in the rhythmic regulation of overall movement. Understanding the contributions of these neurons are expected to lead to advancements in treatments for Parkinson's patients and rehabilitation techniques.

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論文審査の結果の要旨及び担当者

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論文審査の結果の要旨

申請者は新規の実験系を用いたマウスの連続運動の解析、および線条体からの神経細胞記録を通し、複雑な運動を処理する神経機構についての考察を行った。申請者は、複数の体部位間協調を必要とする複雑な連続運動を、どのようにして滑らかかつリズミカルに行うことができるのかについて明らかにしたいと考えた。そこで、複雑なペグパターン上をマウスに走らせることによって、複雑な連続運動をマウスに行わることに成功した。運動解析の結果から、マウスは複雑で長い系列の運動を、短い単純な運動の塊(運動チャンク)に切り分けて実行しており、その運動チャンクの内部ではリズムが保存されていることを明らかにした。次に、複雑な運動を実行する際に関連する神経機構を明らかにするために、運動シーケンスの学習や実行に必要と考えられてきた線条体から記録実験を行い、運動リズムのパラメター(周期・位相・反復)に反応する神経細胞群を見出した。これらの結果により、本論文では、複雑な運動系列の実行時にはリズムが重要となり、そのリズムは線条体によってエンコードされているとする新たな仮説を提唱している。以上の論文を、博士の学位を授与するに値するものと認める。なお、チェックツール“iThenticate”を使用し、剽窃、引用漏れ、二重投稿等のチェックを終えていることを申し添えます。