



Title	Relationship between repetitive transcranial magnetic stimulation and microstructural property in the human brain
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Citation	大阪大学, 2023, 博士論文
Version Type	
URL	https://doi.org/10.18910/92126
rights	
Note	

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論文内容の要旨

氏 名 (木村 一皓)	
論文題名	Relationship between repetitive transcranial magnetic stimulation and microstructural property in the human brain (反復経頭蓋磁気刺激と脳の微細構造の関係)
論文内容の要旨	
Repetitive transcranial magnetic stimulation (rTMS) can noninvasively modulate human brain activity. Since its development in the late 20th century, rTMS has been widely applied to reveal the contribution of each brain area to certain behavior and to treat neurological or psychiatric diseases. However, the substantial inter-individual variability in the after-effect of rTMS has been a major concern in applying rTMS for neuroscientific research and clinical practice for over the past ten years. For these backgrounds, the studies in this thesis investigate the relationship between the after-effect of rTMS and the microstructural property in the human brain, which can be non-invasively assessed with diffusion magnetic resonance imaging (dMRI). In the first study, I investigated whether the microstructural property assessed with dMRI can predict the magnitude of the after-effect of intermittent theta burst stimulations (iTBS), which is one of the patterned rTMS protocols. iTBS has an advantage for relatively short stimulation duration compared to other rTMS protocols and is widely applied for both neuroscientific and clinical purposes. Here, I evaluated the after-effect of iTBS over the right primary motor cortex (M1) in every individual by assessing the change in amplitude of motor-evoked potential (MEP). Then, I explored the correlation between the MEP change and the fractional anisotropy (FA) values in the gray and white matter, evaluated by dMRI scans obtained in the previous day of iTBS experiment. As a result, the early-phase (5–10 min post-iTBS) of the MEP change was significantly correlated with the FA values in the white matter. To the contrary, the late phase (15–30 min post-iTBS) of the MEP change was correlated with the FA values on the right cerebral cortex. This study will be useful for creating the predictive indicator of rTMS after-effect by pre-measured MRI data. In the second study, I examined whether rTMS can, in turn, induce the microstructural changes after the stimulation. Previous studies have reported contradictory results regarding the microstructural change in the human brain right after rTMS. Moreover, the change of this property has not been directly compared between the excitatory and inhibitory protocols of rTMS. Thus, by using quadri-pulse stimulation (QPS), whose after-effect is relatively strong and robust compared to other rTMS protocols, I compared the FA or mean diffusivity (MD) values in the white matter, cerebral cortex, and subcortical structures before and after the excitatory (QPS5) and inhibitory (QPS50) protocols of QPS. As a result, I found that the FA and MD values in the cerebral cortex and white matter were not significantly changed either after QPS5 or QPS50. In contrast, the MD values in the bilateral cerebellum were decreased both after QPS5 and QPS50. These results suggest that microstructural alteration might not be observed right after QPS in most of the areas in the human brain. The results of these two studies will be an important basis for future studies in creating the predictive-indicator for the rTMS after-effect and in clarifying the mechanisms evoked by rTMS throughout the brain.	

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

木村氏は非侵襲的なニューロモジュレーション手法の一つである反復経頭蓋磁気刺激（rTMS）と脳の微細構造の関連性を調べる研究に従事して2つの成果を挙げた。まず、rTMSの一種である間欠的シータバースト刺激（iTBS）の大きな個人差に着目し、iTBSの事後効果の個人差を、拡散MRIから算出される拡散異方性（FA）に基づく脳の微細構造から予測出来ることを示した。次いで、rTMSの中でも刺激部位への効果が強いことが知られる四連発磁気刺激（QPS）の再現性を検証した。さらに、QPS前後で拡散強調MRIを測定し、脳の微細構造が変化しないことを示した。rTMSが脳の微細構造に影響を与えるかどうかの問題となっていることから、本研究で得られた成果はQPSの臨床応用に向けた検討にも役立つ重要な成果である。以上の理由から、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。