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科学研究費助成事業　　研究成果報告書

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研究課題名（和文）Brain-controlled neuroprosthetic for restoration of upper-limb function

研究課題名（英文）Brain-controlled neuroprosthetic for restoration of upper-limb function

研究代表者
ＭＩＬＯＳＥＶＩＣ　ＭＡＴＩＪＡ（Milosevic, Matija）

大阪大学・基礎工学研究科・助教

研究者番号：５０８４０１８８

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研究成果の概要（和文）：我々は、ヘブ型学習を用いた上肢運動回復の基礎的なメカニズムを明らかにするために、脳制御型機能的電気刺激（FES）システムを開発した。まず、脳制御型FESシステムの実験を行い、FESが皮質脊髄の興奮性変調を速やかに誘導することを示した。 次に、一次運動野（M1）を用いた脳制御型FESと運動前野を用いたFESを比較した。その結果、M1を用いた介入は皮質脊髄の調節を誘発する上で優れていることが示された。以上のことから、閾値法と機械学習法を用いて85%以上の精度を持つ脳内FESシステムを開発し、テストを行った。この結果は、脳制御FESが中枢神経系の興奮性を迅速に神経調節できることを示すものである。

研究成果の学術的意義や社会的意義
Our research findings elucidated the underlying mechanisms implemented through brain-controlled FES. This can be used in neurorehabilitation practice to rapidly neuromodulate the central nervous system excitability, which could improve motor function after neurological injuries.

研究成果の概要（英文）：We developed a brain-controlled functional electrical stimulation (FES) system to elucidate the underlying mechanisms of upper limb motor recovery using Hebbian learning. We first tested the brain-controlled FES system and demonstrated that FES rapidly induced corticospinal excitability modulation. We then compared brain-controlled FES using primary motor cortex (M1) with FES using premotor cortex. Our results showed that the M1-based intervention was superior in eliciting corticospinal modulation. In summary, we developed a brain FES system with an accuracy of over 85% using threshold and machine learning methods and tested it. Our results demonstrate that brain control FES can rapidly neuromodulate the excitability of the central nervous system.

研究分野：neuroprosthetics

キーワード：brain-computer interface　neuroprosthetics　upper-limb　rehabilitation　neuroplasticity　neuromodulation

１．研究開始当初の背景

Declined upper-limb function is one of the most devastating consequences of SCI, which is accompanied by maladaptive reorganization within the central nervous system, including increased spasticity, decreased corticospinal excitability, as well as displacement of cortical representations. Functional electrical stimulation (FES) can be used to artificially contract muscles by applying short electric impulses on the surface of the skin over the muscle nerves. By sequencing the contractions temporally, it is possible to generate upper-limb movements (i.e., a neuroprosthesis for grasping). Brain-computer interface (BCI) can be used to detect descending motor commands to trigger FES and facilitate movement completion when individuals are unable to do so voluntarily. Importantly, this can also ensure temporal synchronization of motor tasks at the precise time when the users attempt to perform movements. The ability to effectively engage the spinal interneuronal networks is essential for inducing neuroplastic changes. The nervous system's ability to reorganize itself also requires precise temporal synchronization of residual voluntary commands and successful execution of the intended task with help of BCI and FES technologies. Such positive reinforcement, known as Hebbian learning, can be realized using a BCI system. However, it is not clear now FES and BCI-controlled FES affect the central nervous system excitability. To this end, this project aimed to develop a BCI system for detection of hand wrist movement and a real-time system for BCI-FES.

２．研究の目的

The objectives of this research project were to: (1) develop a BCI system that can detect hand movements using non-invasive cortical (brain) signal recordings from human participants during motor imagery; (2) evaluate a neuroprosthetic technology that can activate upper-limb muscles through FES; and (3) test the feasibility of using BCI-controlled FES neuroprosthetic to examine how it can contribute to central nervous system neuromodulation.

３．研究の方法

Based on these objectives, we developed and tested a BCI-controlled FES system and demonstrated the underlying mechanisms for recovery of upper-limb motor function that can be elicited via Hebbian-type neuroplasticity. Specifically, we first compared a BCI-controlled FES intervention and demonstrated that it can elicit rapid corticospinal excitability modulation of the stimulated muscles, while FES alone was ineffective. We then compared primary motor cortex (M1) BCI-controlled FES to that when premotor cortical areas were used for BCI operation. Our results demonstrated that M1-based BCI-controlled FES intervention was superior to elicit corticospinal modulation. In summary, a BCI-FES system with an accuracy of ~85% was developed and tested both offline and in real-time operation using threshold-based and machine learning approaches. Our results demonstrated that a motor imagery-based motor cortical BCI-controlled FES system, which we developed in this project, could rapidly neuromodulate central nervous system excitability.

４．研究成果

Related to the specific project objectives, the following achievements were realized:

(1) "Develop a BCI system to detect hand movements" – We implemented and tested the BCI system for controlling FES. Specifically, we showed that a motor imagery-based cortical signal power threshold BCI algorithm can detect movement intentions with an accuracy of approximately 85% (see Suzuki et al. 2022 [J5] and Fadli et al. unpublished). A machine learning algorithm using a support-vector machine classifier a had a comparable detection accuracy for a one degree of freedom BCI classification (Yamanouchi et al. unpublished). While hand wrist rest-flexion-extension detection was less accurate overall compared to rest-active detection, both performed above the chance level, implying the suitability for controlling FES (Yamanouchi et al. unpublished). (Figure 1).

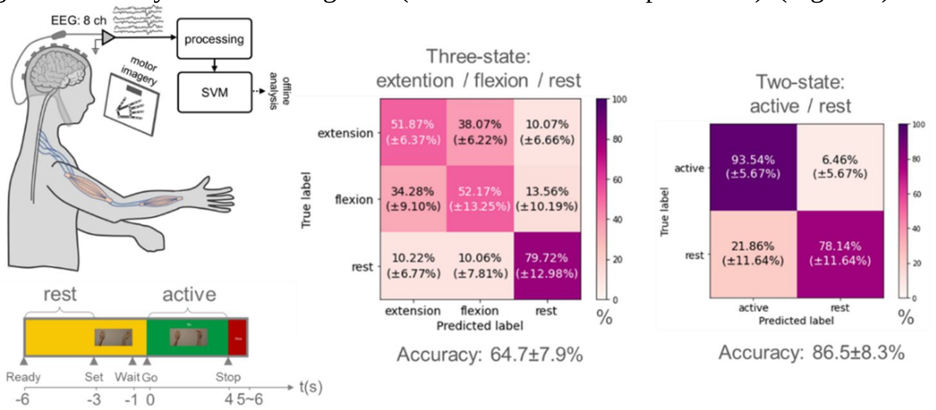

Figure 1: BCI detection based on support vector machine (SVM) classification.

(2) "Evaluate a neuroprosthetic technology for activating upper-limb muscles" – We demonstrated that activity dependent FES can elicit long-term cortical reorganization to improve motor function after an intervention consisting of 36 training session (see Milosevic et al. 2021 [J9]). For a summary, also see Figure 2. We also tested how FES activates muscles and the central nervous system by showing voluntary input contributions during FES for exciting somatosensory networks (see Kato et al. 2022 [J6]). Finally, we proposed a novel method using direct electrical stimulation of the spinal cord and demonstrated that non-invasive stimulation can selectively activate dorsal root sensory fibers at different spinal segments (see de Freitas et al. 2021 [J10]), although muscle-level FES is more effective for generating functional movements.

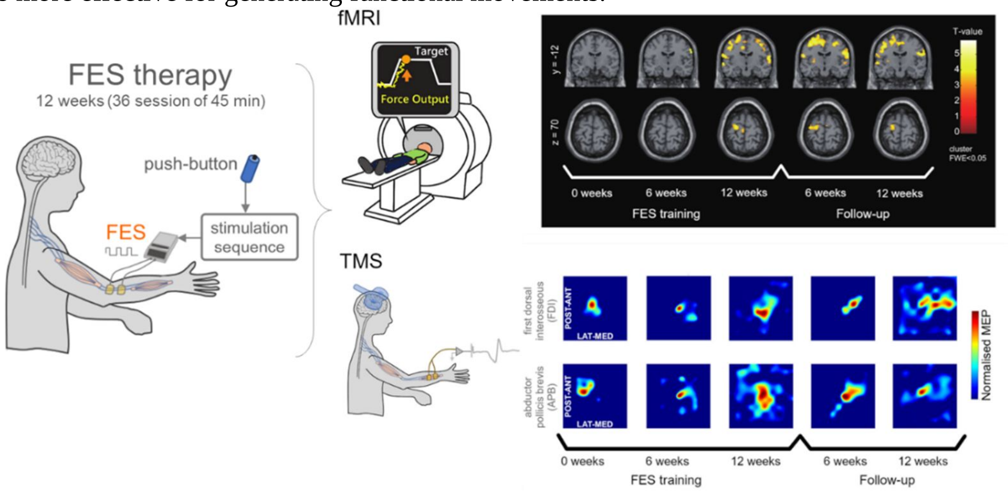

Figure 2: FES system intervention resulting in long term cortical re-organization. See [J9].

(3) "Neuromodulation using BCI-controlled FES" – We implemented and tested a BCI-controlled FES system to prove the underlying mechanisms of associative stimulation for recovery of upper-limb function. Notably, using the BCI-controlled FES system, we first demonstrated that it could elicit rapid corticospinal excitability modulation of the stimulated muscles, while random delivery of FES alone was not effective (see Suzuki et al. 2022 [J5]). For a summary, also see Figure 3. We also compared an intervention using primary motor cortex (M1) BCI to control FES to non-motor area BCI-controlled intervention. Our results demonstrated that M1-based BCI-controlled FES intervention was superior to elicit corticospinal modulation (see Yamanouchi et al. unpublished), likely by focusing motor cortical activations. Therefore, we developed a BCI-controlled FES system and demonstrated that using this system can result in presynaptic cortical facilitation followed by postsynaptic FES sensorimotor activation to elicit rapid corticospinal facilitation through Hebbian learning. These findings are consistent with our results indicating that cortical facilitation before FES is necessary to elicit neural plasticity (see Cao et al. 2022 [J3]). A book chapter a textbook titled Neurorehabilitation Technology edited by Dr. Volker Dietz (see Popovic, Masani and Milosevic, 2022 [B1]) and a review article (see Milosevic et al. 2020 [J14]) are prepared to summarize these proposed neuromodulation mechanisms of BCI-controlled FES in neurorehabilitation.

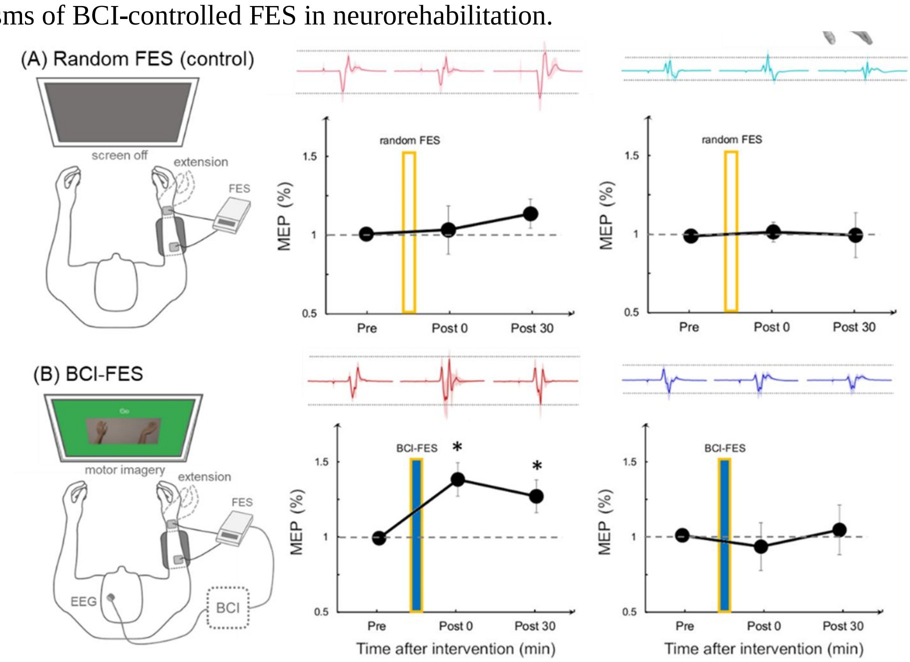

Figure 3: BCI-FES system intervention resulting in rapid corticospinal facilitation. See [J5].

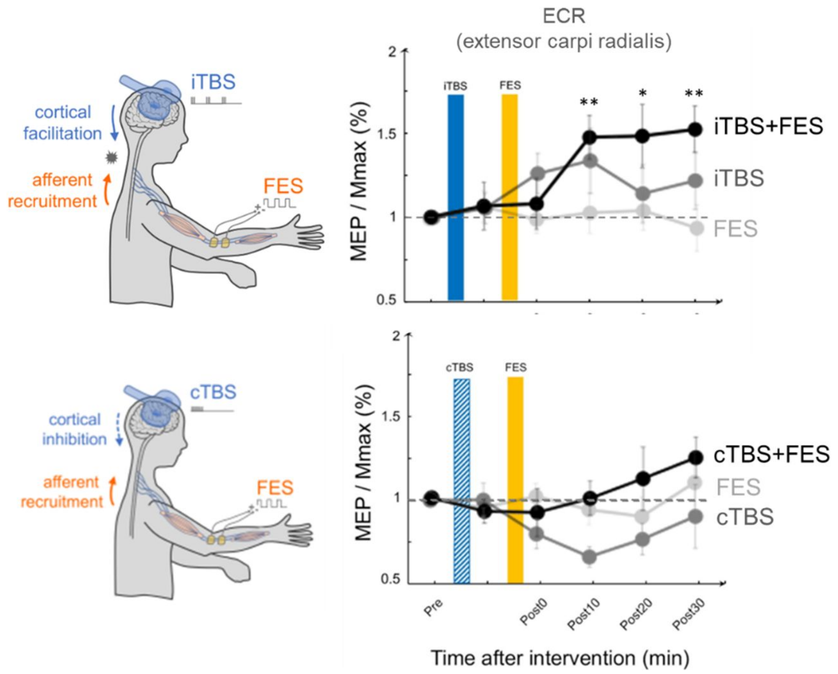

Figure 4: Cortical faciliatory priming (iTBS) followed by FES system intervention resulting in rapid corticospinal facilitation (TOP). Cortical inhibitory priming (cTBS) followed by FES system intervention resulting in rapid corticospinal facilitation (TOP). See [J3].

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5．主な発表論文等

〔雑誌論文〕　計19件（うち査読付論文　19件／うち国際共著　18件／うちオープンアクセス　9件）

1．著者名 de Freitas Roberto M、Capogrosso Marco、Nomura Taishin、Milosevic Matija	4．巻 19
2．論文標題 Preferential activation of proprioceptive and cutaneous sensory fibers compared to motor fibers during cervical transcutaneous spinal cord stimulation: a computational study	5．発行年 2022年
3．雑誌名 Journal of Neural Engineering	6．最初と最後の頁 036012～036012
掲載論文のDOI（デジタルオブジェクト識別子） 10.1088/1741-2552/ac6a7c	査読の有無 有
オープンアクセス オープンアクセスとしている（また、その予定である）	国際共著 該当する

1．著者名 Cao Na、Sasaki Atsushi、Yuasa Akiko、Popovic Milos R.、Milosevic Matija、Nakazawa Kimitaka	4．巻 240
2．論文標題 Short-term facilitation effects elicited by cortical priming through theta burst stimulation and functional electrical stimulation of upper-limb muscles	5．発行年 2022年
3．雑誌名 Experimental Brain Research	6．最初と最後の頁 1565～1578
掲載論文のDOI（デジタルオブジェクト識別子） 10.1007/s00221-022-06353-3	査読の有無 有
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1．著者名 Kato Tatsuya、Kaneko Naotsugu、Sasaki Atsushi、Endo Nozomi、Yuasa Akiko、Milosevic Matija、Watanabe Katsumi、Nakazawa Kimitaka	4．巻 55
2．論文標題 Corticospinal excitability and somatosensory information processing of the lower limb muscle during upper limb voluntary or electrically induced muscle contractions	5．発行年 2022年
3．雑誌名 European Journal of Neuroscience	6．最初と最後の頁 1810～1824
掲載論文のDOI（デジタルオブジェクト識別子） 10.1111/ejn.15643	査読の有無 有
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3．雑誌名 Neuromodulation: Technology at the Neural Interface	6．最初と最後の頁 -
掲載論文のDOI（デジタルオブジェクト識別子） 10.1016/j.neurom.2021.12.007	査読の有無 有
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1．著者名	4．巻
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2．論文標題	5．発行年
Task- and Intensity-Dependent Modulation of Arm-Trunk Neural Interactions in the Corticospinal Pathway in Humans	2021年
3．雑誌名	6．最初と最後の頁
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10.1523/ENEURO.0111-21.2021	有
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10.3390/jcm10163633	有
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オープンアクセスとしている（また、その予定である）	該当する

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10.1152/japplphysiol.00132.2021	有
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2．論文標題 Cortical Re-organization After Traumatic Brain Injury Elicited Using Functional Electrical Stimulation Therapy: A Case Report	5．発行年 2021年
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3．雑誌名 Neuroscience Letters	6．最初と最後の頁 -
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オープンアクセス オープンアクセスではない、又はオープンアクセスが困難	国際共著 該当する

1．著者名 Akihiro Nakamura, Yasuyuki Suzuki, Matija Milosevic and Taishin Nomura	4．巻 -
2．論文標題 Long-lasting event-related beta synchronizations of electroencephalographic activity in response to support-surface perturbations during upright stance: A pilot study associating beta rebound and active monitoring in the intermittent postural control	5．発行年 2021年
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1．著者名 Derrick Lim, Mikael Del Castillo, Austin J Bergquist, Matija Milosevic and Kei Masani	4．巻 29
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オープンアクセス オープンアクセスではない、又はオープンアクセスが困難	国際共著 該当する

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掲載論文のDOI（デジタルオブジェクト識別子）	査読の有無
10.1186/s12938-020-00824-w	有
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10.1063/5.0022319	有
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オープンアクセスとしている（また、その予定である）	該当する

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掲載論文のDOI（デジタルオブジェクト識別子）	査読の有無
10.1016/j.neuroscience.2020.10.011	有
オープンアクセス	国際共著
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1．著者名 Akiko Yamaguchi, Atsushi Sasaki, Yohei Masugi, Matija Milosevic and Kimitaka Nakazawa	4．巻 238(9)
2．論文標題 Changes in corticospinal excitability during bilateral and unilateral lower-limb force control tasks	5．発行年 2020年
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掲載論文のDOI（デジタルオブジェクト識別子） 10.1007/s00221-020-05857-0	査読の有無 有
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1．発表者名
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２．出版社 Springer	５．総ページ数 37
３．書名 Functional Electrical Stimulation Therapy: Mechanisms for Recovery of Function Following Spinal Cord Injury and Stroke	

〔産業財産権〕

〔その他〕

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６．研究組織

	氏名 （ローマ字氏名） （研究者番号）	所属研究機関・部局・職 （機関番号）	備考
研究協力者	野村　泰伸 (Nomura Taishin)	大阪大学・Grad School of Engineering Science・Professor	

６．研究組織（つづき）

	氏名 （ローマ字氏名） （研究者番号）	所属研究機関・部局・職 （機関番号）	備考
研究協力者	中澤　公孝 (Nakazawa Kimitaka)	東京大学・Graduate School of Arts and Sciences・Professor	

７．科研費を使用して開催した国際研究集会

〔国際研究集会〕　計0件

８．本研究に関連して実施した国際共同研究の実施状況

共同研究相手国	相手方研究機関			
カナダ	University of Toronto	Toronto Rehabilitation Institute		
韓国	Yeungnam University			
米国	University of Pittsburgh			
米国	Houston Methodist Research Institute			