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Research Article

Demonstration of Central Nervous System Regeneration with Functional Magnetic Resonance Imaging (fMRI) in Multiple Sclerosis

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Abstract

Objectives: This scientific study aimed to showcase central nervous system (CNS) regeneration in multiple sclerosis (MS) patients by quantifying neural activities using functional Magnetic Resonance Imaging (fMRI). The objectives were to investigate regeneration patterns and correlations with disease parameters.

Methods: Twelve MS patients with an expanded disability status scale (EDSS) less than four, and an age and sex-matched control group, were examined using fMRI during finger-counting tasks. Cortical activation patterns were compared, and correlations with disease parameters were assessed. Blood oxygenation level-dependent (BOLD) contrast was employed, and motor activation was illustrated through imaging.

Results: Statistical analysis revealed significant differences in cortical activation during motor tasks between MS patients and controls. The number of activated cortical regions was higher in MS patients. Negative correlation was observed between EDSS scores and activated areas, indicating reduced activation with higher disability. Cortical activation patterns differed between patient and control groups, particularly in sensory motor cortex (SMC) areas.

Conclusion: The study demonstrated CNS regeneration through quantification of neural activities using fMRI in MS patients. Cortical activation differences and correlations with disease parameters suggest potential insights into the regenerative process. Further research is warranted to explore the implications of these findings for understanding and treating multiple sclerosis.

Keywords: Multiple sclerosis, Functional MRI, regeneration

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Since the early observations by Marburg in 1906, regeneration and remyelination in multiple sclerosis (MS) have been subjects of investigation.[1] While spontaneous remyelination is a common physiological response after demyelinating conditions,[2] its extent varies significantly, with approximately 20-30% of MS patients experiencing such regeneration. Recent research has unveiled regeneration patterns within and around MS plaques, indicating a cessation of destructive activity in new lesions, often followed by remyelination upon repopulation by oligodendrocytes. Notably, regeneration is particularly prominent during the 3-10 month phase of the disease. This study aimed to showcase CNS regeneration through neural activity quantification using functional MRI.

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Table 1. Summery of fMRI activated areas of SMC during bouth hand motor tasking

	Contralateral activation area	Ipsilalateral activation area	Total activation of area
Patients (n=12)			
Tasking Right hand	7-22 (mean=12.9)	2-15 (mean=8.5)	13-61 (mean=47.5)
Tasking left hand	1-34 (mean 13.7)	0-37 (mean=9.8)	
Control (n=11)			
Tasking right hand	4-19 (mean=9.5)	0-8 (mean=5.0)	9-51 (mean=28.4)
Tasking left hand	2-14 (mean=7.5)	0-10 (mean=4.3)	

Methods

A total of 12 multiple sclerosis patients were evaluated, all with an expanded disability status scale (EDSS) less than four. The mean age of the subjects was 31.5 years, with a disease duration of 4.12 years (Table 1). Additionally, a control group of 11 right-handed individuals matched for age and sex was included. Functional MRI examinations were performed during finger-counting tasks, with a rest-tasking paradigm comprising 8 periods, each lasting 30 seconds. A 1.5 Tesla MRI system (Signa Horizon, GE Medical Systems) was used. The data analysis included comparisons of cortical activation between patient and control groups, as well as correlations with disease parameters. Functional magnetic resonance imaging (f MRI) relies on blood oxygenation level-dependent (BOLD) contrast: a change in the signal strength of brain water protons produced by the paramagnetic effects of venous blood deoxyhemoglobin.[3] In the Figure 1, Figure 2 and Figure 3 is illustrated sample of motor activation.

Analysis of the data showed that after motor tasking without demonstrating specific area or localization in cortical area, there was a significant difference between cortical activation on the ipsilateral side in patients and controls ($p<0.05$). When the findings of the patients where evaluated, the number of ipsilateral cortical activated fields was higher than the controls. When the patients' disability and fMRI examinations were compared from the clinical parameters, the disease was negatively correlated with the total num-

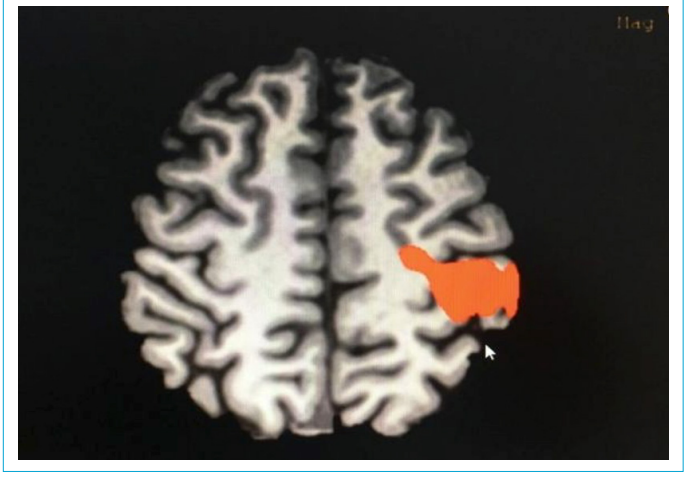

Figure 2. Axial plane fMRI in MS patient left side SMC activated area during right-hand motor tasking.

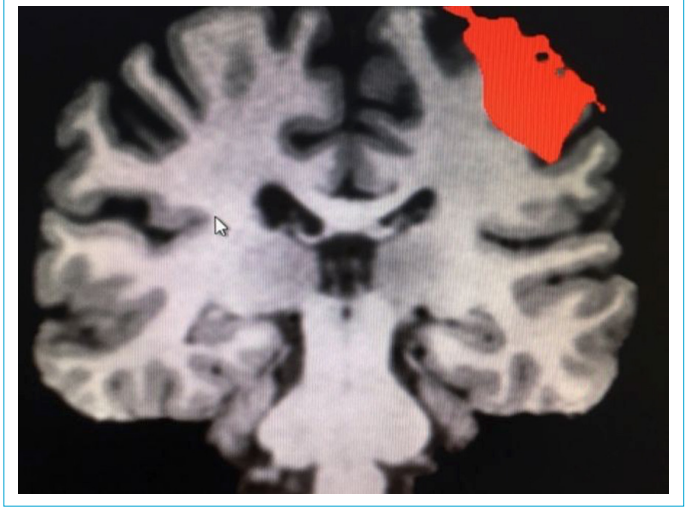

Figure 1. Coronal plain fMRI of MS patient activated area during right-hand motor tasking.

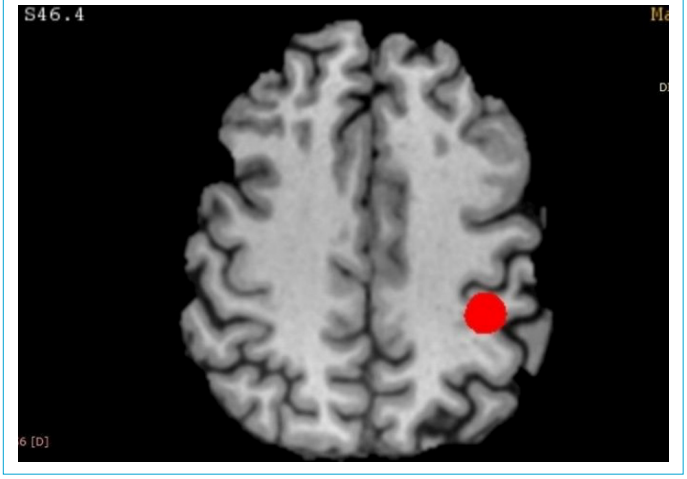

Figure 3. Axial plane fMRI in control subject left side SMC activated area during right-hand motor tasking. Same protocol but the significant smaller area.

ber of cortical areas activated by EDSS (p<0.0005 r-0.1482). The number of activated areas was low in patients with high EDSS. There were no significant differences between the duration of disease and the total number of activated areas. Activation sites observed in the sensory motor cortec SMC areas in MS cases were more irregular and did not show continuity with each other. In the control group activation sites were regular and consistent with each other. fMRI activation localizations inpatient and controls during tasking were sensory motor cortex (SMC) ,supplementary cortex , and (SMC) posterior areas. The number of SMC posterior activation sites was compared between controls and patient groups and no statistical significance was detected. The number of cortical activation areas in the control group was observed to shift in the posterior region of SMC.

Results

Statistical analysis revealed a significant difference in cortical activation between the patient and control groups during motor tasks. Notably, the number of activated cortical regions was higher in MS patients. A negative correlation was established between EDSS scores and the total number of activated areas, signifying decreased activation in patients with higher disability. However, disease duration did not correlate significantly with the number of activated areas. Cortical activation patterns differed between patient and control groups, particularly in the sensory motor cortex (SMC) areas.

Discussion

This experimental study demonstrated a notable increase in the number of activated cortical areas in MS patients compared to healthy controls, particularly after simple motor cortical activation. Notably, the activation of the SMC posterior area remained consistent across both groups (p<0.05) Table 2 and Figure 4 ilustrates these findings. Axonal damage in the early stages of MS, often irreversible, is a well-established phenomenon.[4]

Functional recovery in MS patients is attributed to diverse mechanisms, with fMRI emerging as a tool to assess func-

Table 2. Ipsilaterally and contralateral activated signals after simple motor tasking

Patient Group				**Control Group**			
Patient (n=12) Contralateral Active signals	**Ipsilaterala ctive signal**	**SMC and posterior SMC**	**Total**	**Patient (n=11) Contralateral Active signals**	**Ipsilaterala ctive signal**	**SMC and posterior SMC**	**Total**
1) Right and 14	3	0/3	40	1) Right and 14	6	8/12	37
Left hand 15	8	12/11		Left hand 8	9	7/12	
2) Right hand 15	13	11/17	54	2) Right hand 17	8	14/11	36
Left hand 17	9	0/26		Left hand 5	6	5/6	
3) Right hand 10	5	8/7	39	3)Right hand 14	6	13/7	30
Left hand 11	13	11/13		Left hand 10	-	4/6	
4) Rigt hand 22	15	20/27	58	4) Rigt hand 9	3	4/7	20
Left hand 15	6	12/9		Left hand 7	1	6/2	
5) Right hand 11	10	9/12	45	5) Right hand 9	3	10/2	18
Left hand 15	9	14/10		Left hand 4	-	0/4	
6) Right hand 9	6	7/8	42	6 Right hand 10	10	13/7	51
Left hand 14	13	16/11		Left hand 19	12	16/15	
7) Right hand 13	11	17/7	61	7) Right hand 7	3	4/6	29
Left hand 21	16	22/15		Left hand 9	10	7/12	
8) Right hand 15	9	20/4	95	8) Right hand 10	5	2/13	28
Left hand 34	37	47/24		Left hand 9	4	2/11	
9) Right hand 10	0	17/7	61	9) Right hand 4	6	6/4	14
Left hand 2	2	4/0		Left hand 2	2	1/3	
10) Right hand 14	3	17/10	40	10) Right hand 3	-	0/3	9
Left hand 15	8	12/11		Left hand 5	-	0/5	
11) Righ hand 9	2	7/4	13	11) Righ hand 17	4	14/7	41
Left hand 1	2	1/1		Left hand 14	6	0/20	
12) Right hand 20	8	20/8	42				
Left hand 10	4	5/9					

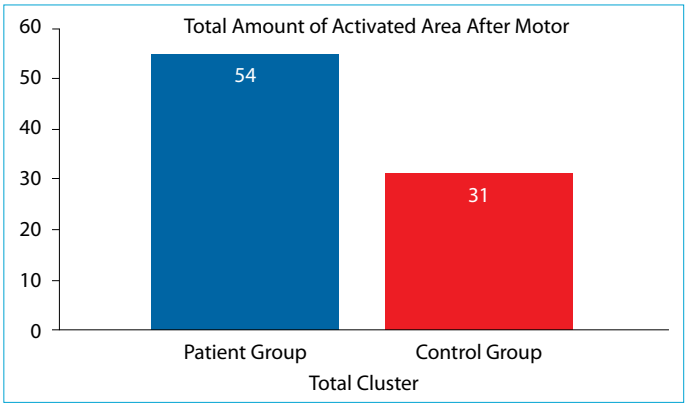

Figure 4. Ilustrate the total fields activated after motor tasking and shows the difference between the two groups.

tional adaptations after clinical attacks. Unlike conventional MRI, fMRI can unveil disease-induced abnormal brain activation patterns and provide insights into neural mechanisms. The detection of distinct cortical activation patterns,[5] including heightened activation in specific regions, offers valuable information regarding the pathophysiology of MS. One of the different cortical activation patterns detected in MS patients is an increase in contralateral activation.[6] Achieved results are obtained using the "Lateralization Index"[7] and measurements of a pixel threshold value.

Conclusion

In summary, this study successfully demonstrated an increase in the number of activated cortical areas in MS patients during motor tasks, signifying potential regeneration and adaptive processes. The utilization of functional MRI highlighted significant differences in neural activity between MS patients and controls, enhancing our understanding of the regenerative potential within the central nervous system in the context of multiple sclerosis.

Disclosures

Ethics Committee Approval: This retrospective study was conducted in the Neurology clinic of Marmara University Faculty of Medicine.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Concept – D.I.G.; Design – H.Ş.; Supervision – D.I.G.; Materials – H.Ş.; Data collection &/or processing – H.Ş.; Analysis and/or interpretation – D.I.G.; Literature search – H.Ş., D.I.G.; Writing – H.Ş.; Critical review – D.I.G.

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