LA FATICA NELLA SCLEROSI MULTIPLA

Valutazione neurofisiologica

Prof. Vincenzo Rizzo

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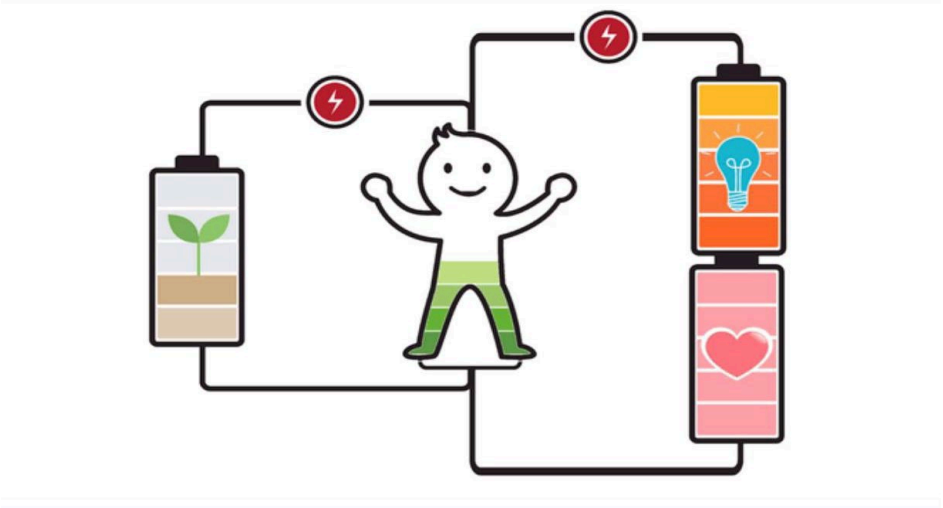
… motor and cognitive impairment with reduced motivation and desire to rest, either appearing spontaneously or brought on by mental or physical activity, humidity, acute infection and food ingestion.

It can occur at any time but is usually worse in the afternoon.

In MS, fatigue can be daily, has usually been present for years and has greater severity than any premorbid fatigue.



Mills and Young 2007

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Motor fatigue can be classified as central or peripheral.

Peripheral fatigue is the inability to generate force at the muscle level, while central fatigue refers to changes arising from the neural networks in the brain and the spinal cord, causing a lack of drive to the muscles.

Capone F. et al 2019

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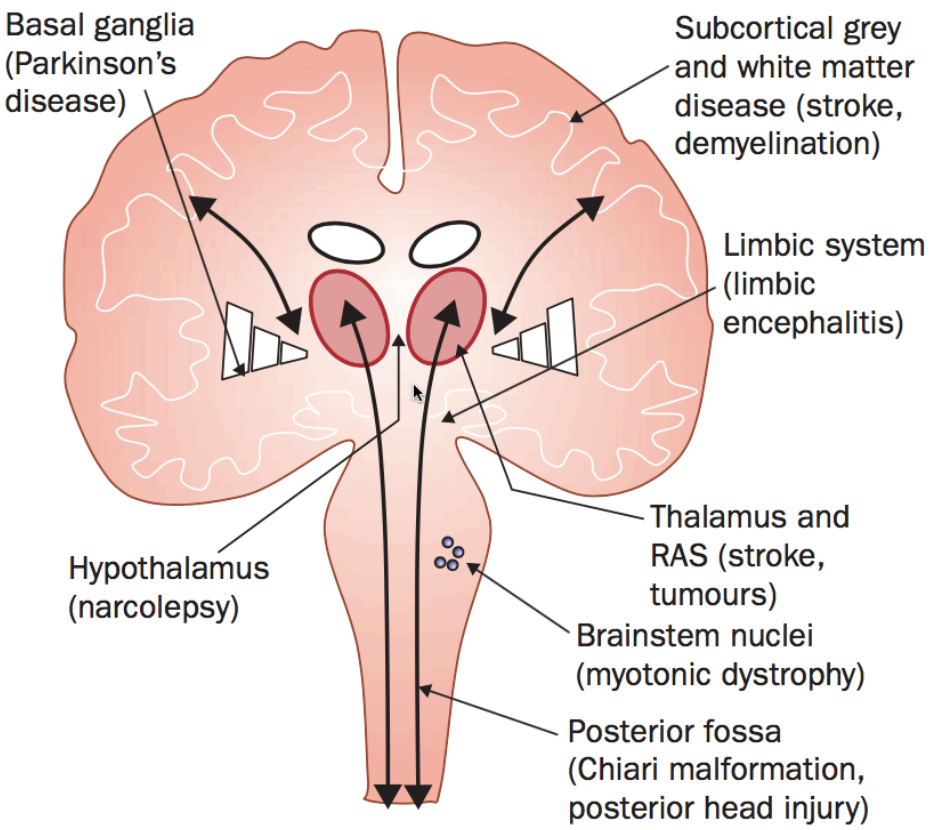

Central fatigue seems to arise from the disruption of a complex neural network involving the cerebral cortex, the thalamus, and the basal ganglia

Chaudhuri A. et al 2004

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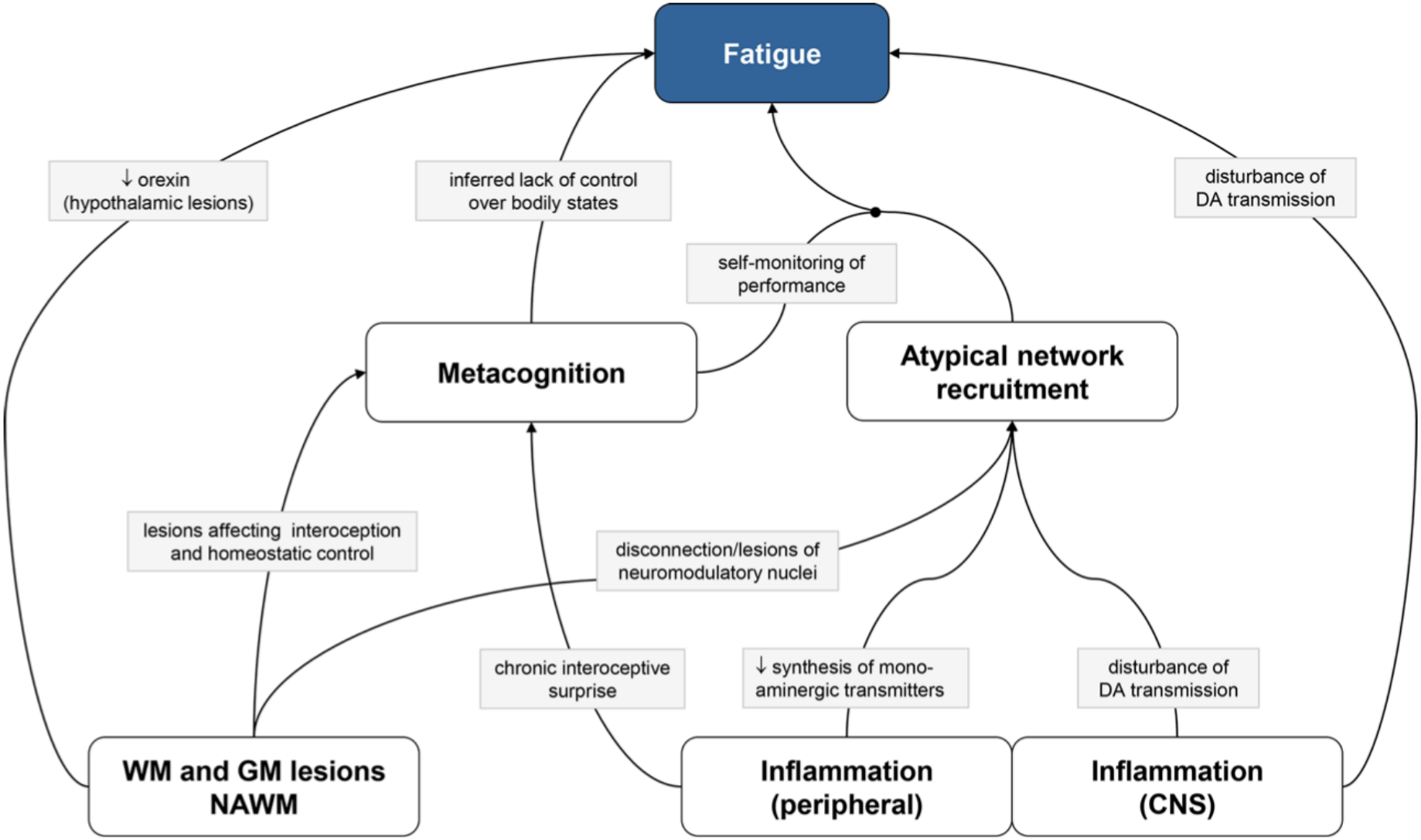

Manjaly ZM et al 2019

64° CONGRESSO SINC
29 MAGGIO – 1 GIUGNO 2019
ROMA

Sclerosi Multipla: le tecniche neurofisiologiche nella valutazione della storia naturale e degli interventi terapeutici
Moderatori: G. Comi *(Milano)* - G.L. Mancardi *(Genova)*

Assessment della neurite ottica
V. Parisi *(Roma)*

Neuroprotezione e rimielinizzazione: evidenze neurofisiologiche
L. Leocani *(Milano)*

Valutazione neurofisiologica della spasticità nella sclerosi multipla
C. Trompetto (*Genova)*

Basi neurofisiologiche del recupero - ruolo della plasticità
V. Rizzo *(Messina)*

The advent of magnetic resonance imaging (MRI) significantly changed the overall management of MS. The role of neurophysiology remains of great importance in the functional evaluation of specific pathways such as visual, somatosensory, auditory, and motor systems and in the study of the central and the peripheral mechanisms of sensorimotor integration.

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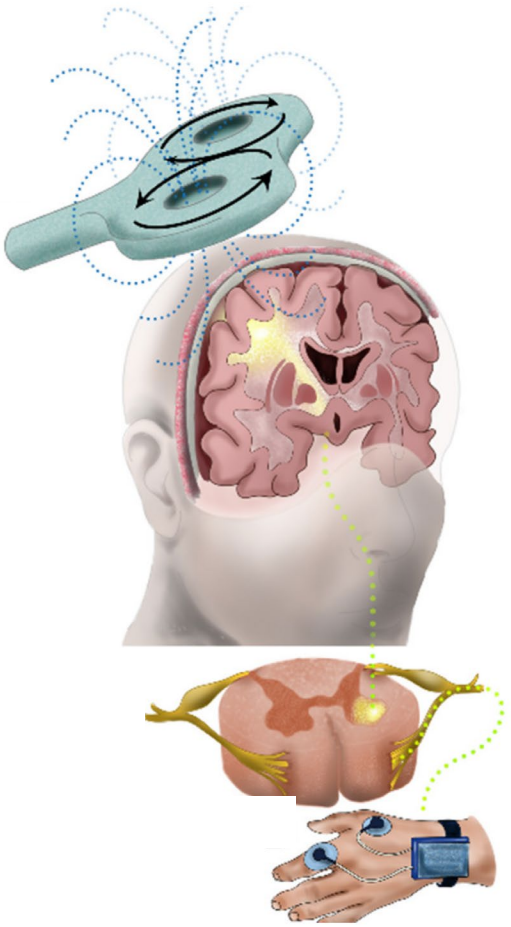
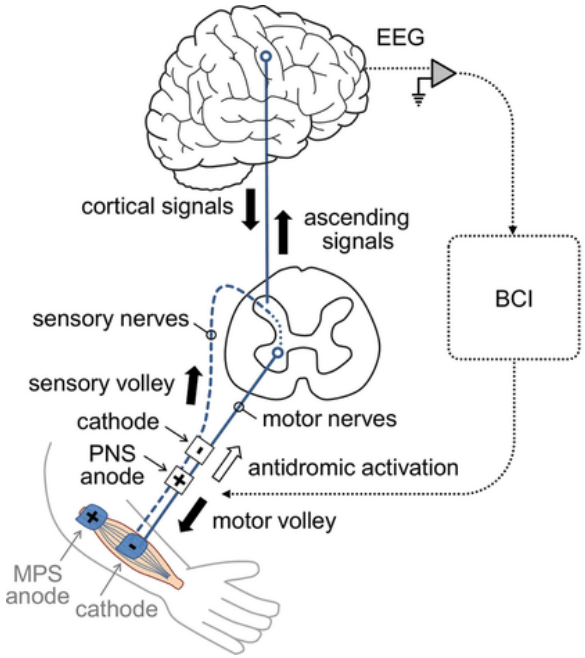
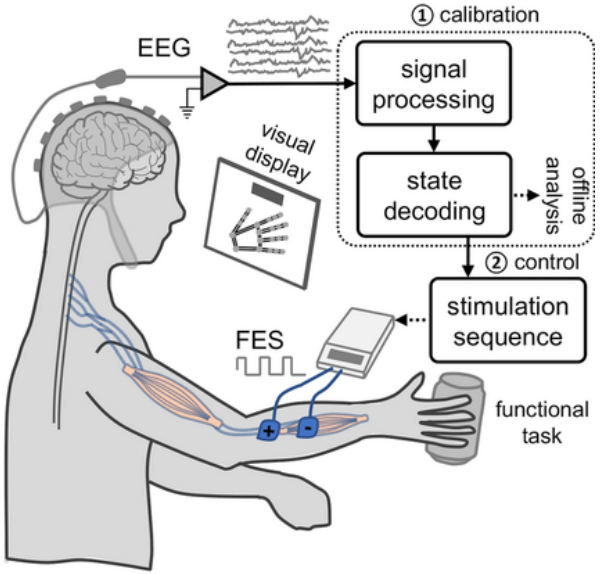
Valutazione neurofisiologica







The neurophysiological techniques can play a decisive role in the assessment of the pathophysiology of MS-related fatigue, thanks to their ability to provide objective measures and to explore the peripheral and the central structures of the nervous system,

with excellent time resolution.

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Valutazione neurofisiologica

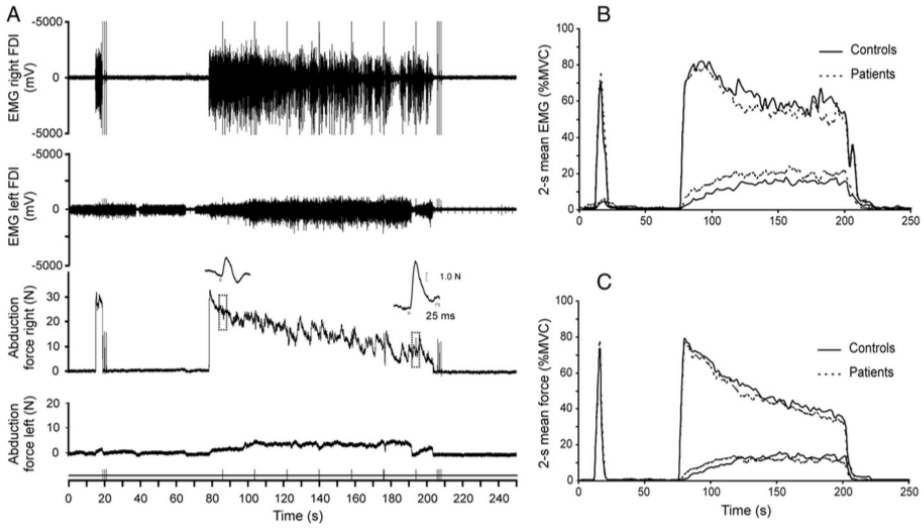
OUTLINE

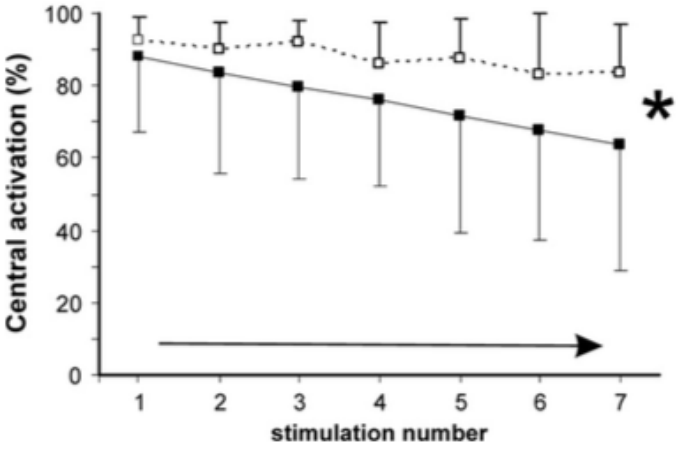
- application of neurophysiological techniques for exploring the pathogenic mechanisms of fatigue.

- potential use of neurophysiology for measuring fatigue and monitoring the response to symptomatic therapies.

- potential application of neuromodulation as an innovative treatment for fatigue.

Neurophysiological techniques for exploring the pathogenic mechanisms of fatigue

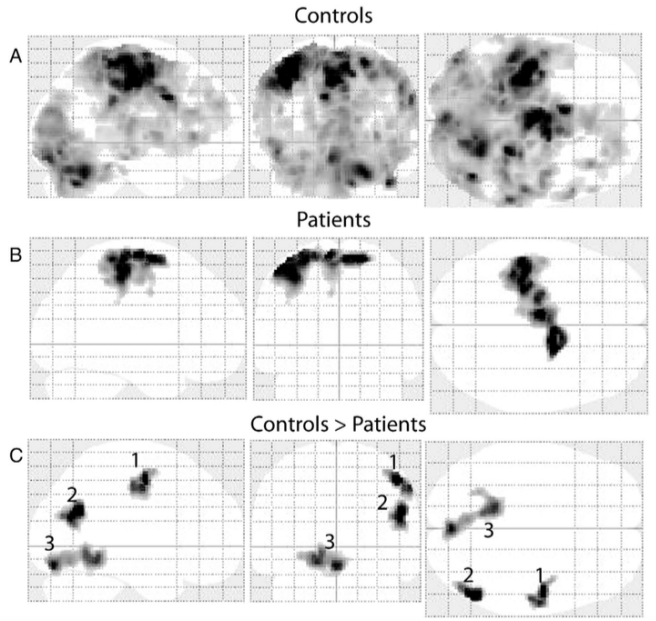




- changes in cortical activation (BOLD), voluntary activation (twitch interpolation) and muscle force during a sustained maximal voluntary contraction (MVC) in twenty MS patients and twenty healthy controls.

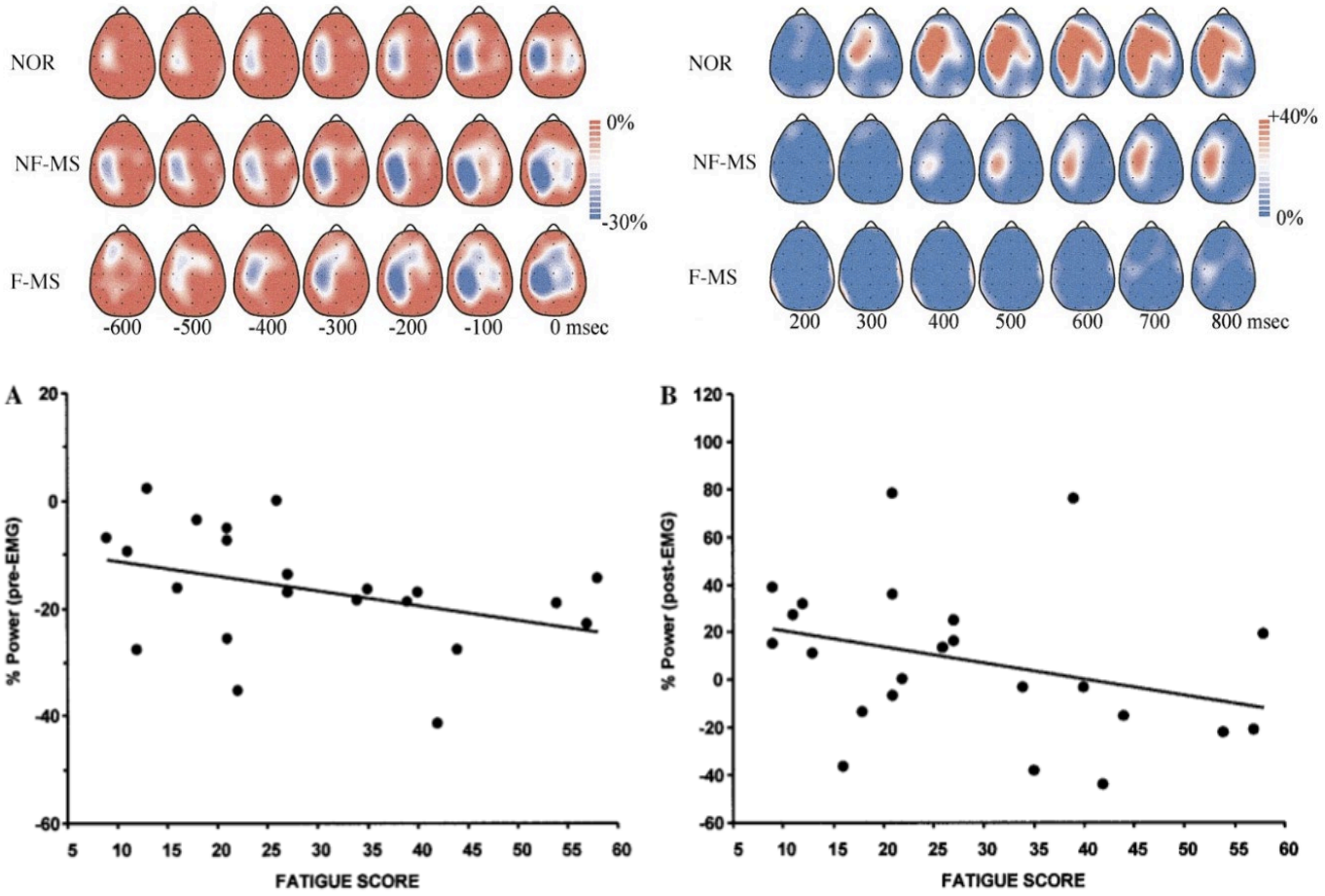
- in MS patients, the differences in the decline in force were significantly associated with a decline in voluntary activation and not with maximal force or decline in rest twitch.

- muscle fatigue during a sustained contraction in MS patients is associated with changes in the voluntary activation that are not sufficiently compensated by increased cortical activation.



Steens A. et al 2012

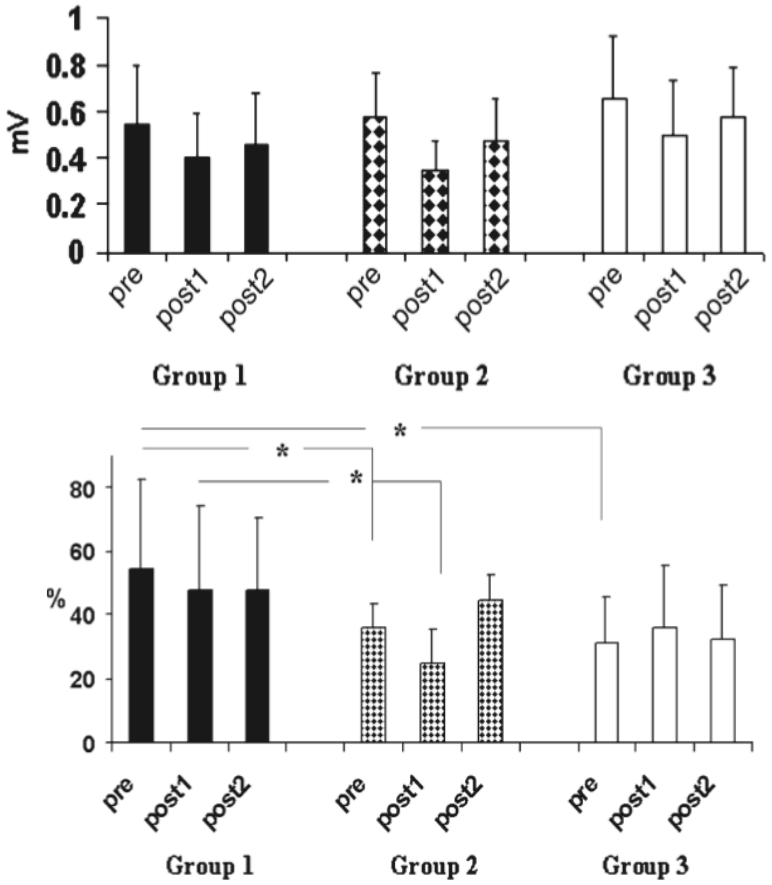
Neurophysiological techniques for exploring the pathogenic mechanisms of fatigue



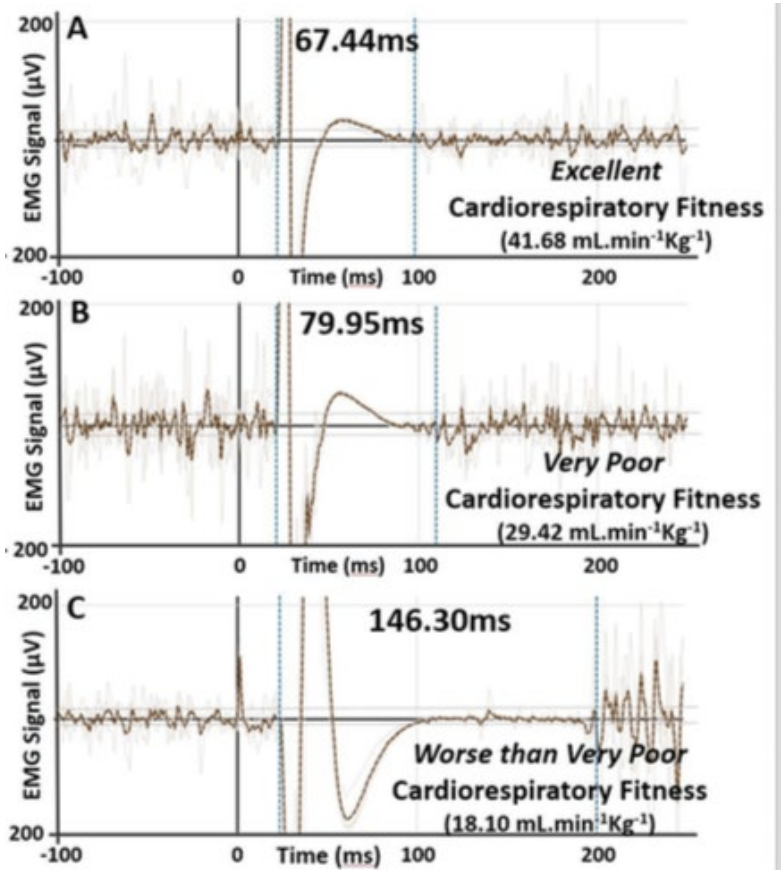
In PwMS compared to healthy controls, FSS correlated positively with ERD over midline frontal structures during movement and inversely with contralateral sensorimotor ERS after movement.
These findings suggest an overactivation of the frontal regions in fatigued patients, a possible expression of a compensatory mechanism for the subcortical dysfunction causing fatigue.

Leocani L. et al 2001

Neurophysiological techniques for exploring the pathogenic mechanisms of fatigue



Reduced SICI

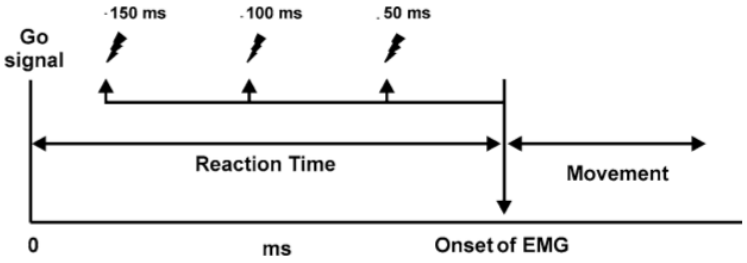


Prolonged CSP

Liepert J. et al 2005

Chaves AR. et al 2019

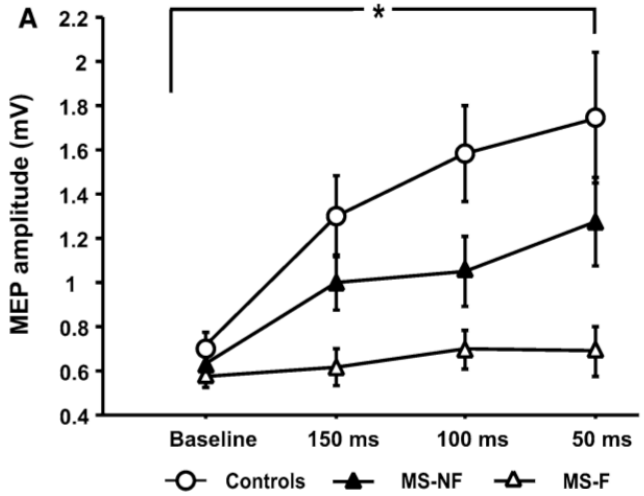
Neurophysiological techniques for exploring the pathogenic mechanisms of fatigue

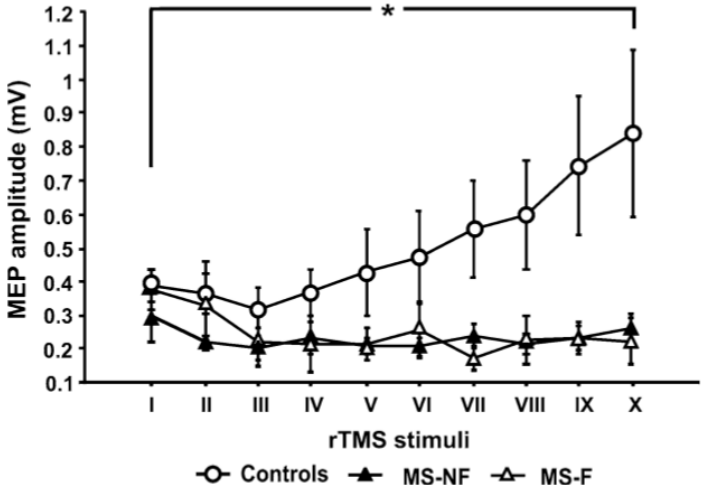


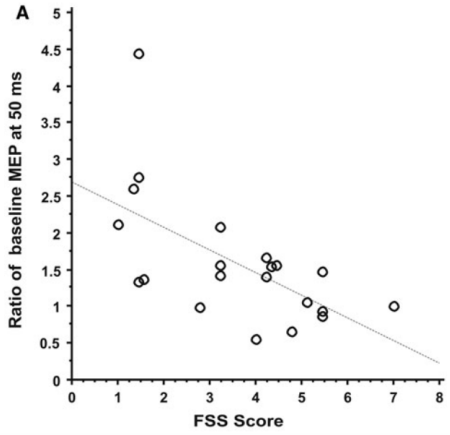
Increase of MEP size produced by 5 Hz rTMS in controls was absent in both MS-NF and MS-F.

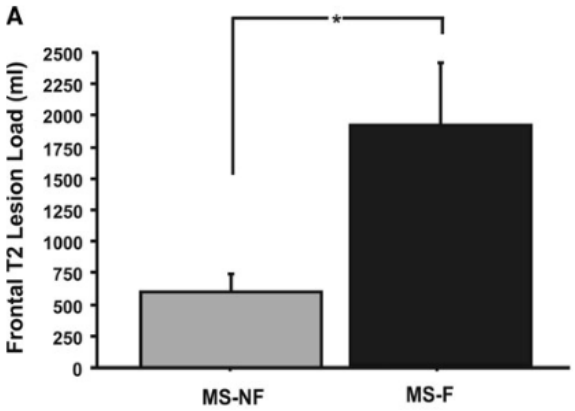
MS-F lacked pre-movement facilitation compared with MS-NF and controls.

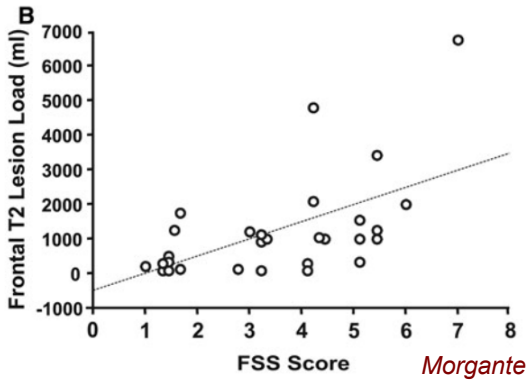
The lack of pre-movement facilitation and the increased frontal lobe lesion load were significantly correlated to the FSS score, suggesting that central fatigue in MS is probably due to a dysfunction of cortical motor areas involved in movement preparation.





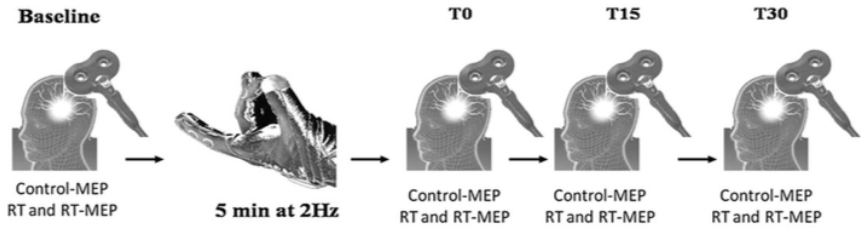


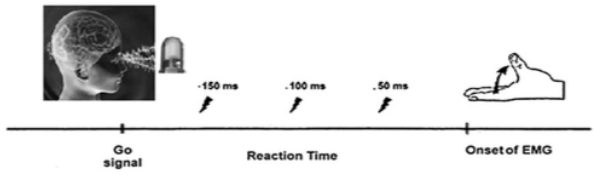




Morgante F et al 2011

Neurophysiological techniques for exploring the pathogenic mechanisms of fatigue

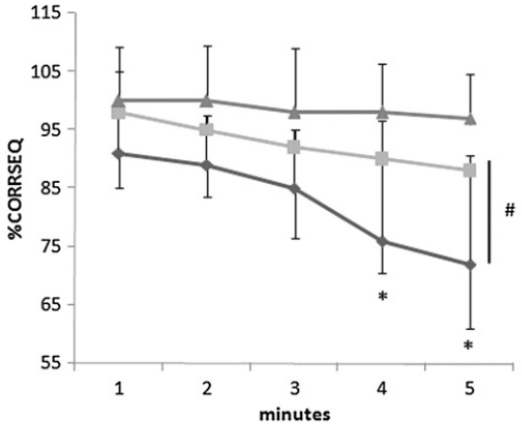


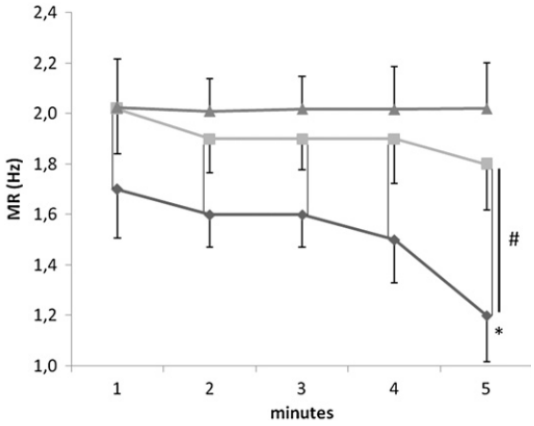


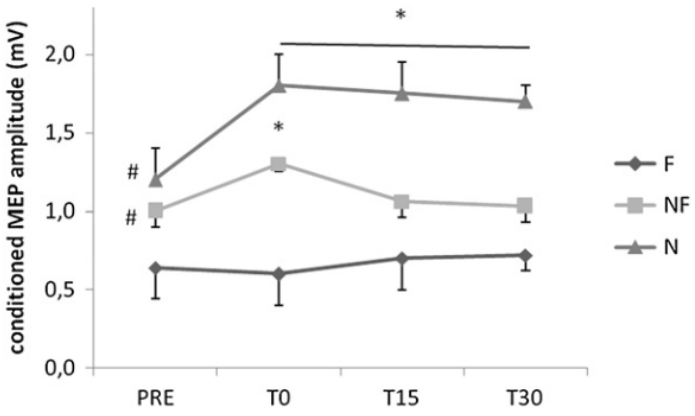
In MS-F patients, the number of correct sequences performed and the ability to keep a fixed movement rate during the 5-min motor task were significantly decreased in comparison to the normal controls and MS-NF patients.

In MS-F patients, post-exercise PMF was significantly decreased. The PMF abnormalities were highly correlated with the performance decay.

PMF may be considered as a kind of servo-mechanism which could play a crucial role during sustained motor task in order to prevent motor performance disruption and to avoid motor exhaustion.

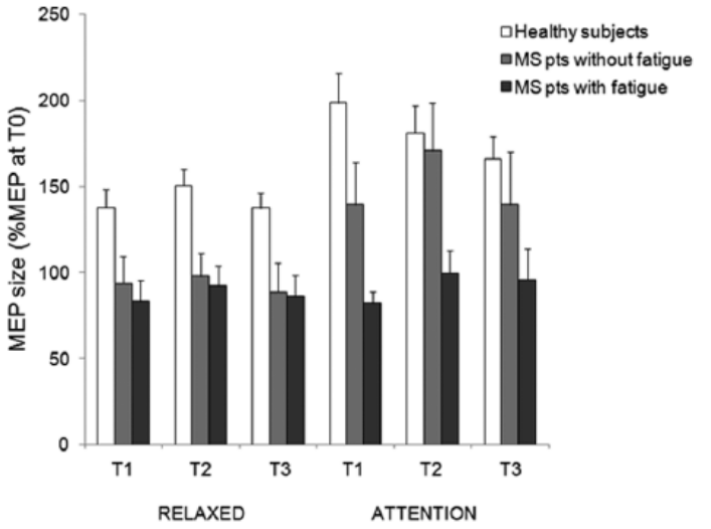






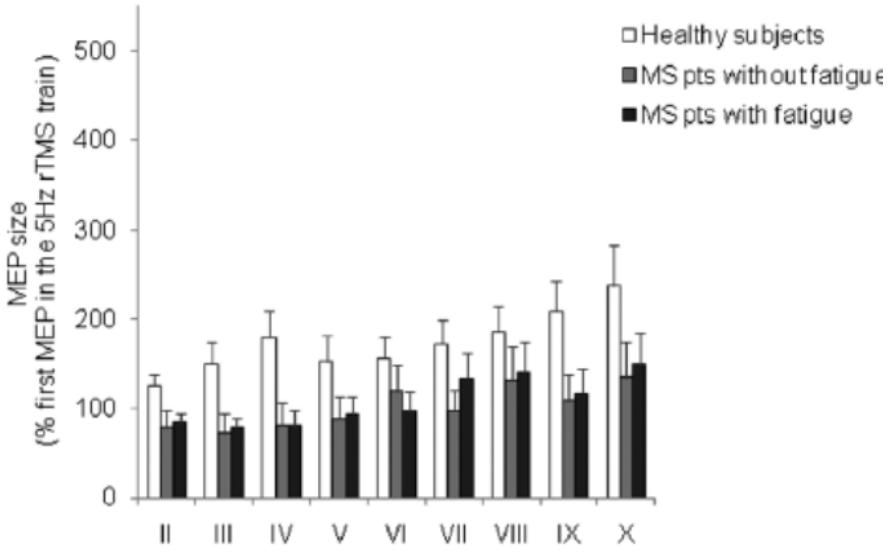
Russo M. et al 2015

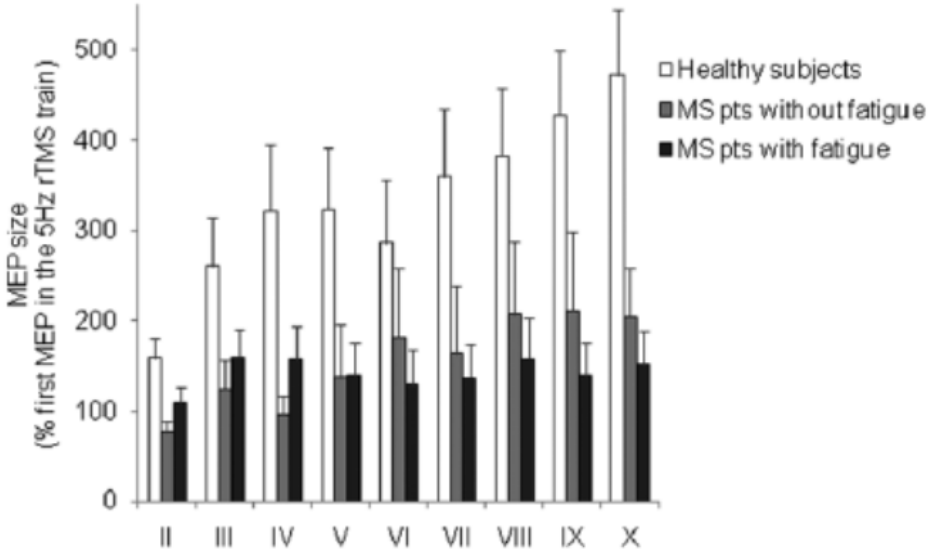
Neurophysiological techniques for exploring the pathogenic mechanisms of fatigue



In fatigued patients both PAS and 5-Hz stimulation did not produce the expected changes in cortical excitability, while in not-fatigued patients they both increased the MEP response, although less efficiently than in healthy subjects.

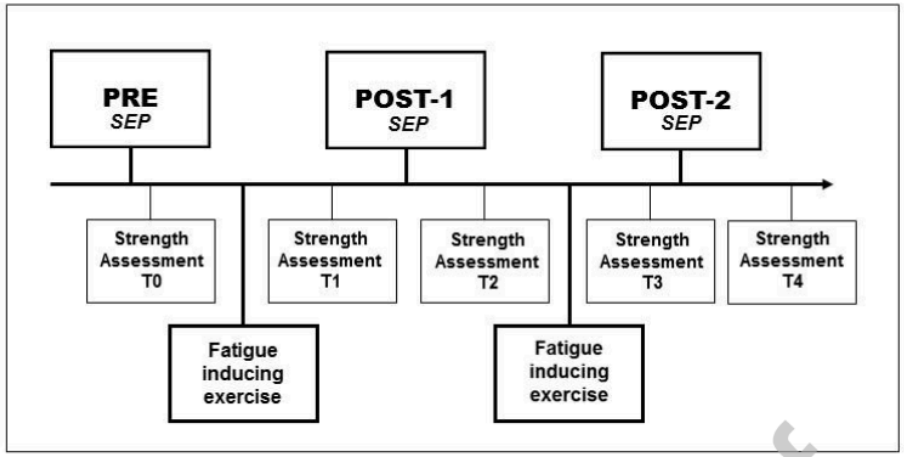
Fatigue in MS reflects disrupted cortical attentional networks related to movement control.

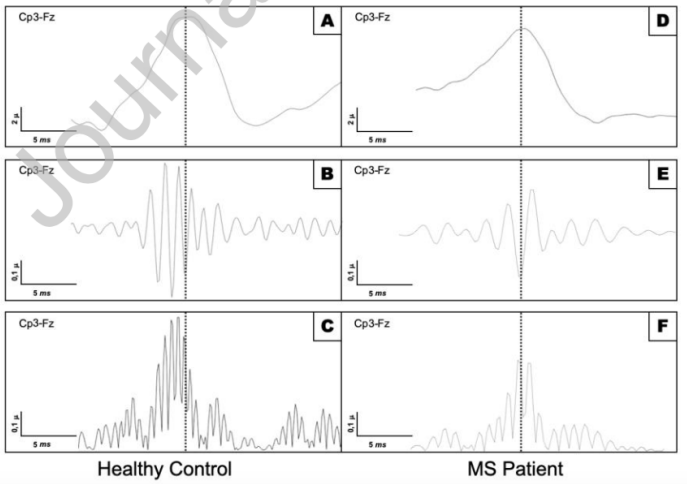


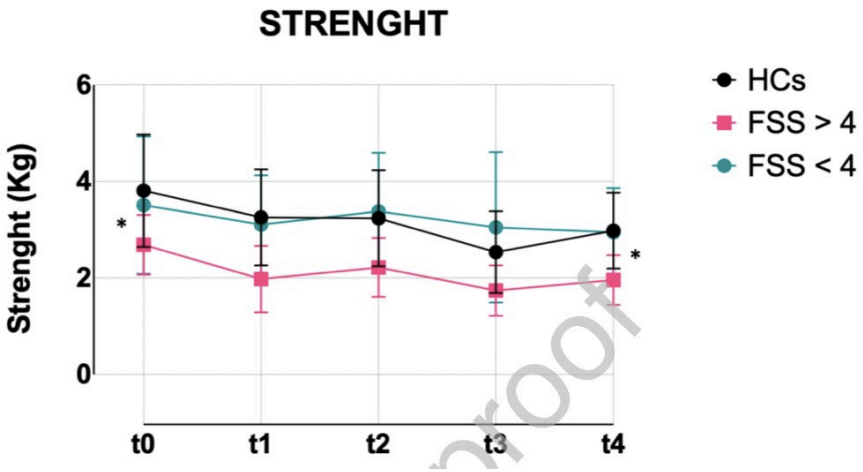


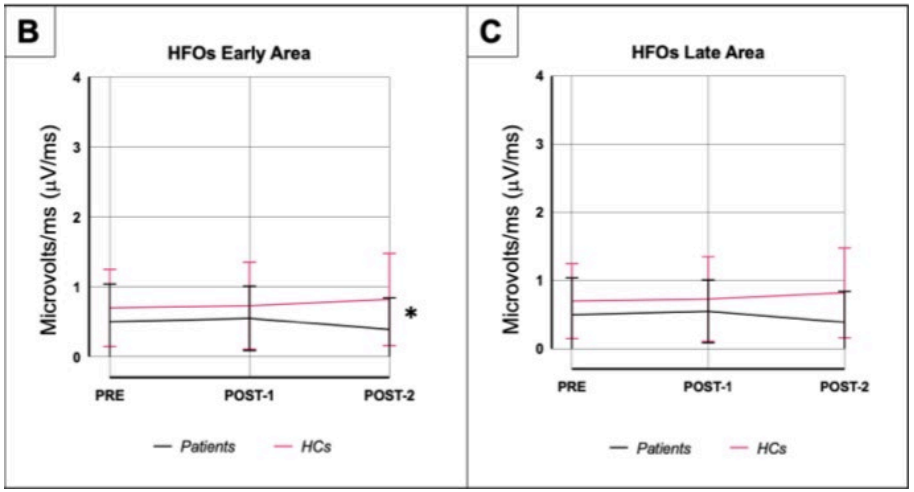
Conte A. et al 2015

Neurophysiological techniques for exploring the pathogenic mechanisms of fatigue





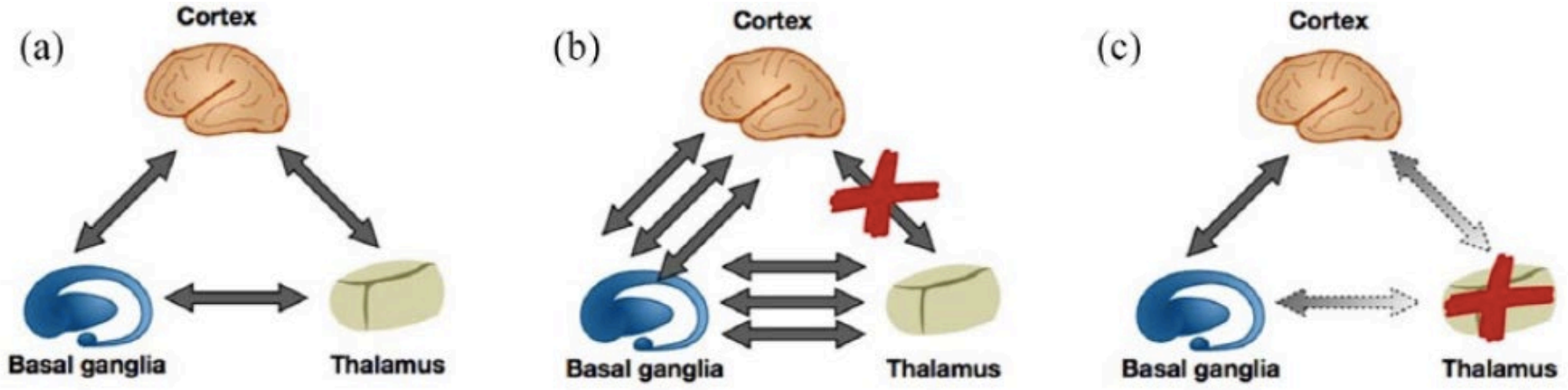




HFOs, a neurophysiological marker of thalamo-cortical pathway, are significantly modified by fatiguing tasks in MS patients, in particular the early component that refers to the functionality of thalamic axons.

Capone F. et al 2019

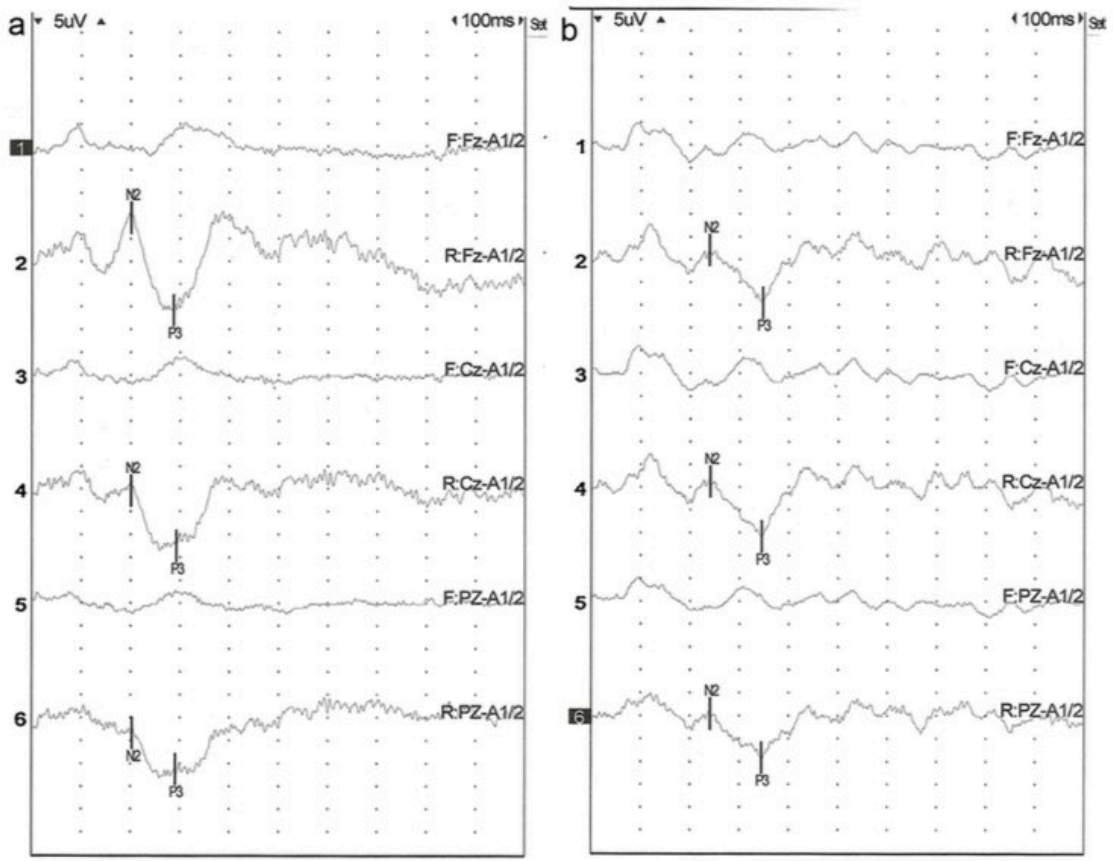
Neurophysiological techniques for exploring the pathogenic mechanisms of fatigue

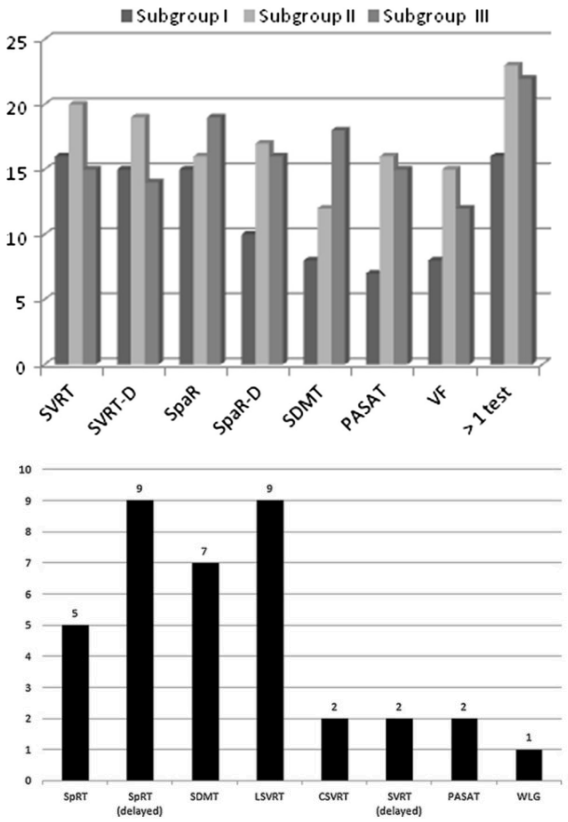


In healthy subjects, thalamus acts as a relay between different cortical and subcortical areas (a). In fatigued MS patients, fatigue can arise from an increase in the activity of the network, as a result of a compensatory mechanism that allows to maintain normal functioning but also produces fatigue (b). Alternatively, fatigue can arise from a global reduction in the activity of the network involving thalamus, basal ganglia, and cortex (c).

Capone F. et al 2020

Neurophysiological techniques for exploring the pathogenic mechanisms of fatigue





MS patients with fatigue have worse cognitive performances and delayed latency in the P300 component of the auditory ERP and also in the early stage of the disease.

Pokryszko-Dragan A et al 2016

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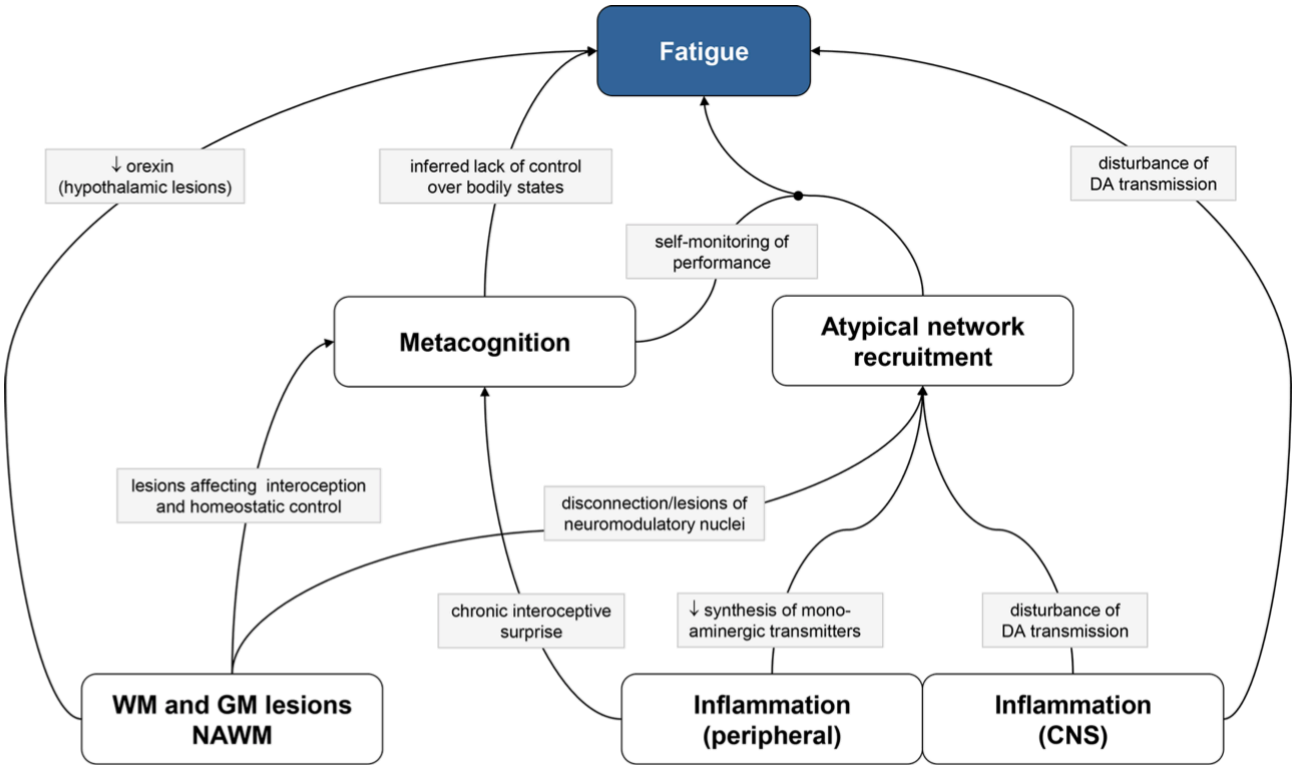
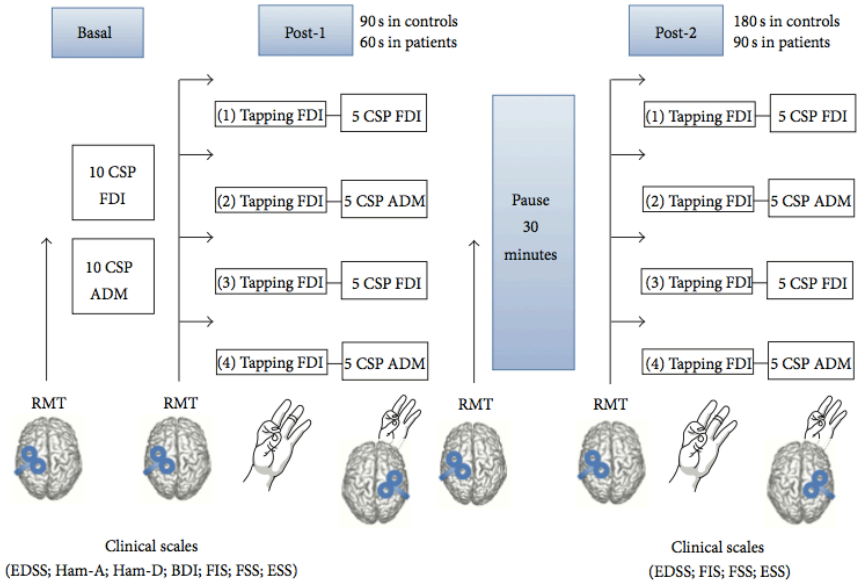


Several structural and functional abnormalities in various cortico-subcortical neural networks (e.g., fronto- striatal network, cortico-striato-thalamo-cortical loop) occur during MS as a result of inflammation, neurodegeneration, and compensatory neuroplasticity processes.

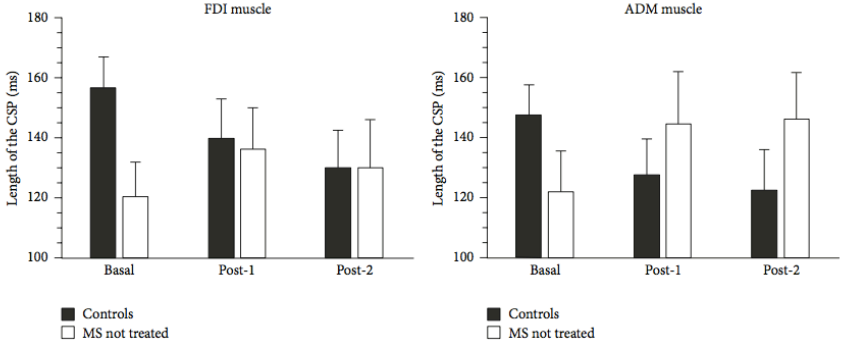
The development of fatigue could depend on the dynamic balance between damage and restorative processes during the disease's course. Indeed the latter can be predominant in the initial phase of the disease, thus masking the clinical occurrence of fatigue, while, later on, the damage could prevail so that patients experience clinically relevant fatigue.

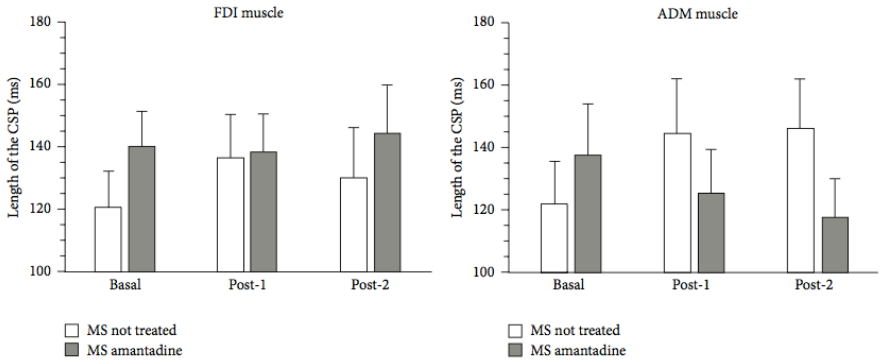
Neurophysiology for measuring fatigue and monitoring the response to symptomatic therapies



Chronic therapy with amantadine annulled differences in CSP duration between controls and patients, possibly through restoration of more physiological levels of intracortical inhibition in the motor cortex.

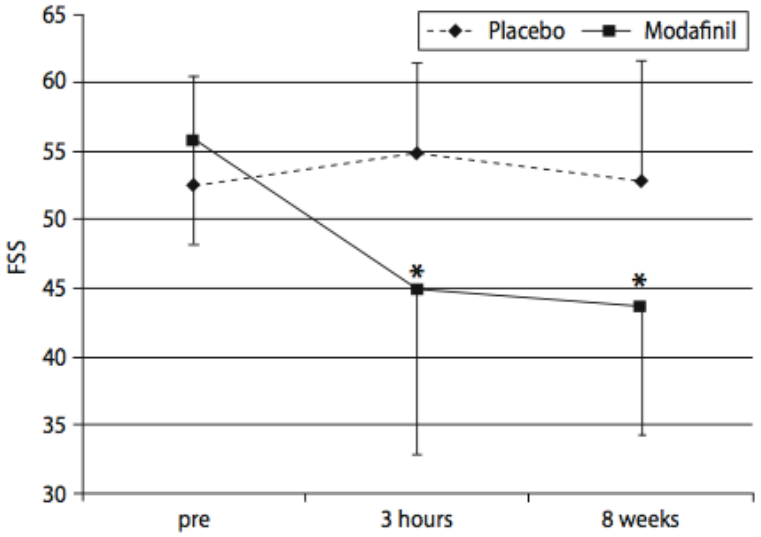
These inhibitory changes correlated with the improvement of fatigue scales.



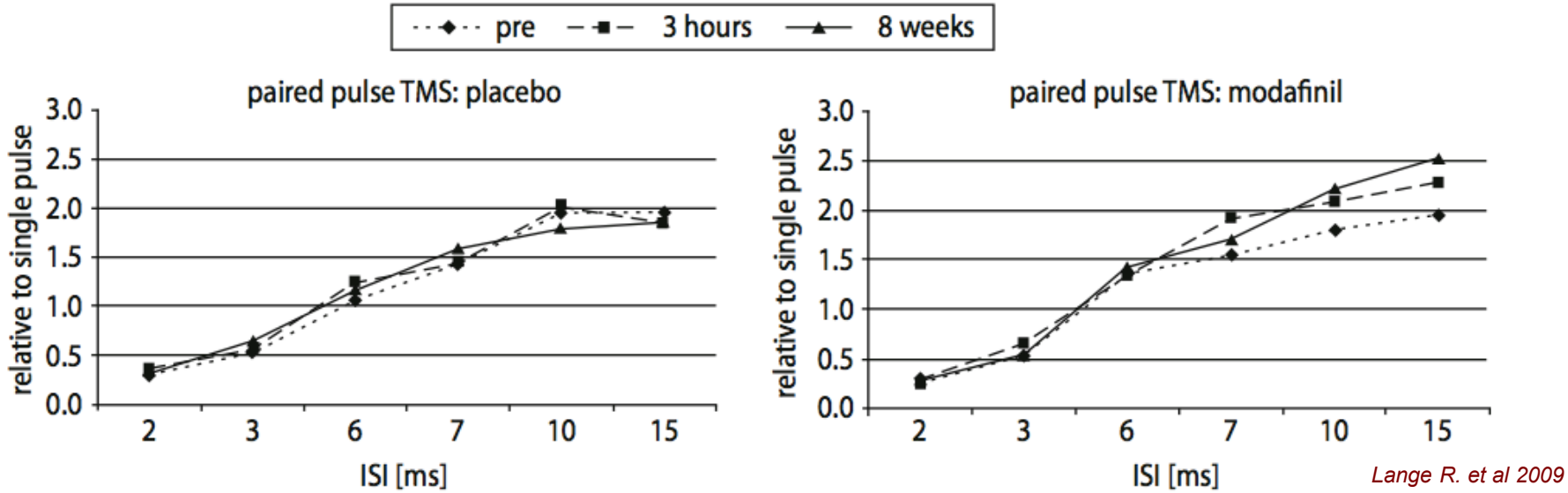


Santarnecchi E. et al 2015

Neurophysiology for measuring fatigue and monitoring the response to symptomatic therapies

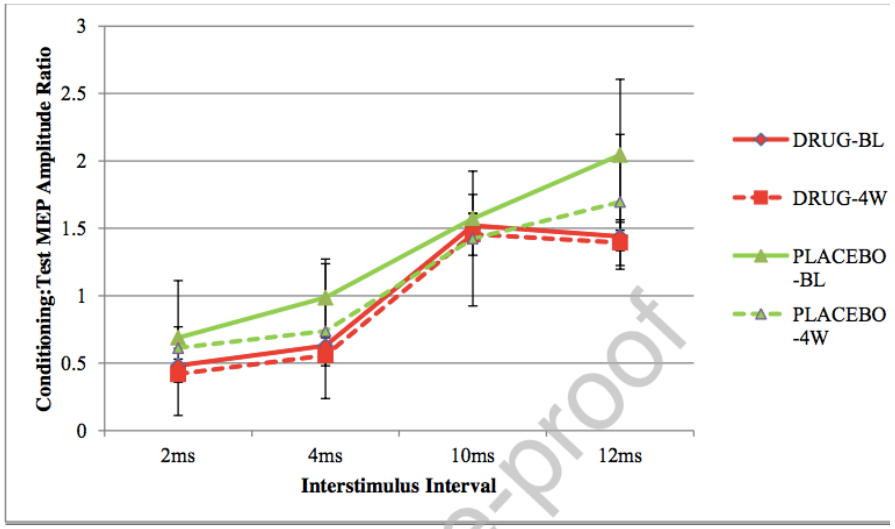


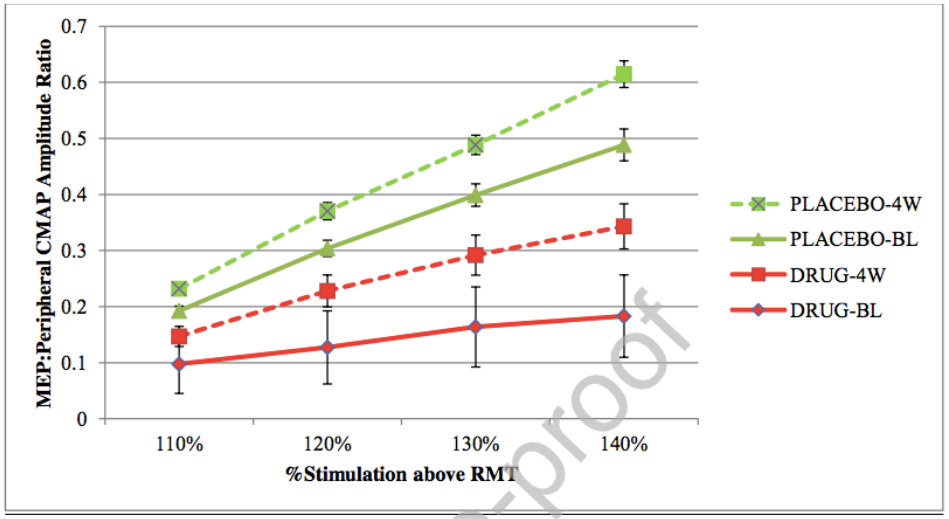
Modafinil improved fatigue, focused attention and dexterity and enhanced motor cortex excitability in MS patients with fatigue. Modafinil may be helpful in MS patients with fatigue to improve cognitive and motor abilities.



Lange R. et al 2009

Neurophysiology for measuring fatigue and monitoring the response to symptomatic therapies

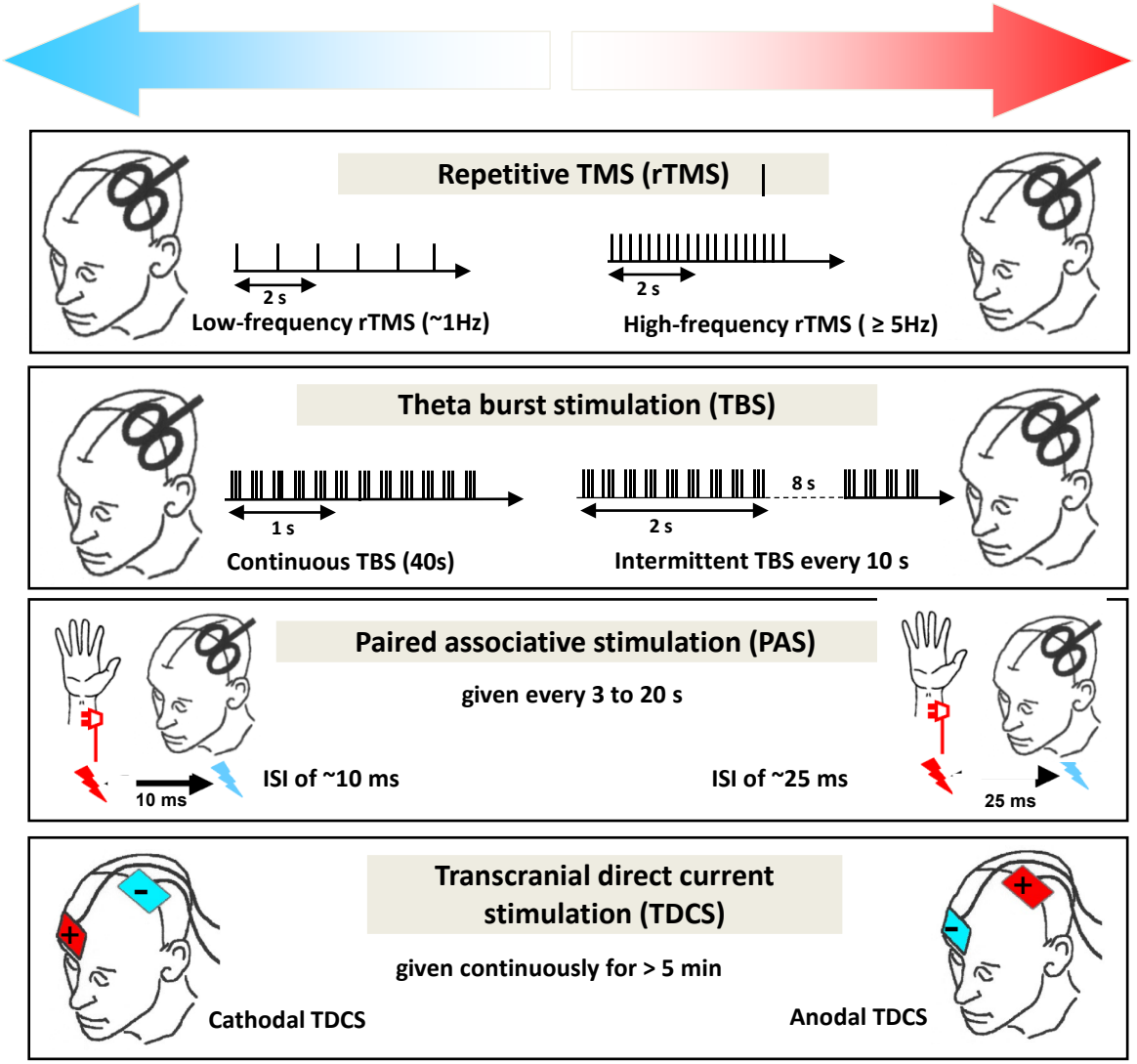




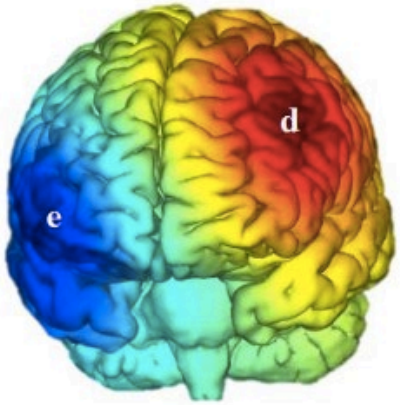
Fampridine (10 mg bd, for eight consecutive weeks) did not produce significant changes in upper limb function, fatigue, and neurophysiological parameters

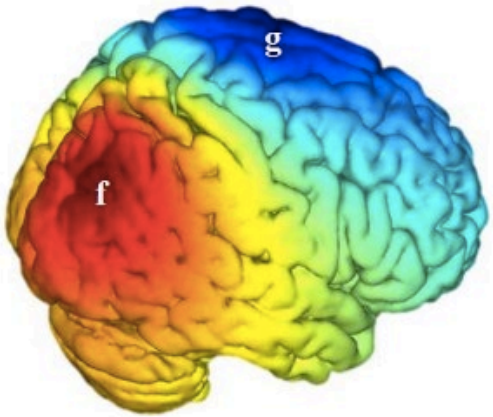
Marion S.. et al 2020

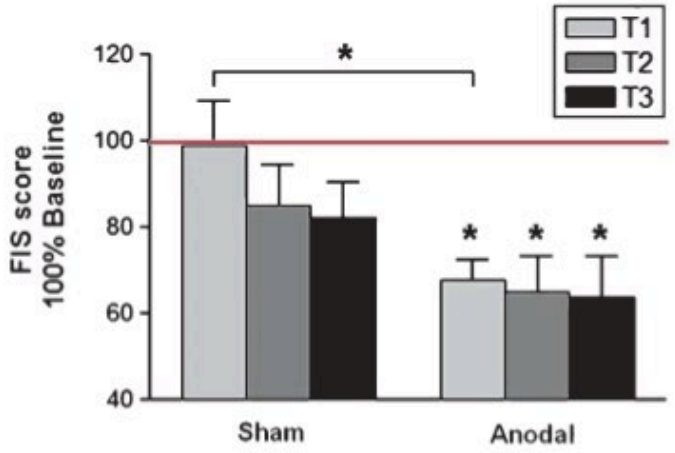
Application of neuromodulation as an innovative treatment for fatigue

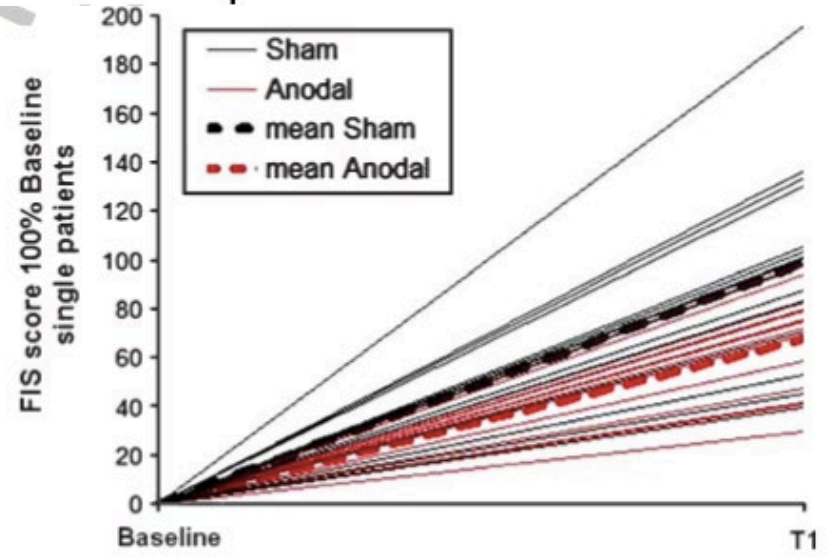


Application of neuromodulation as an innovative treatment for fatigue





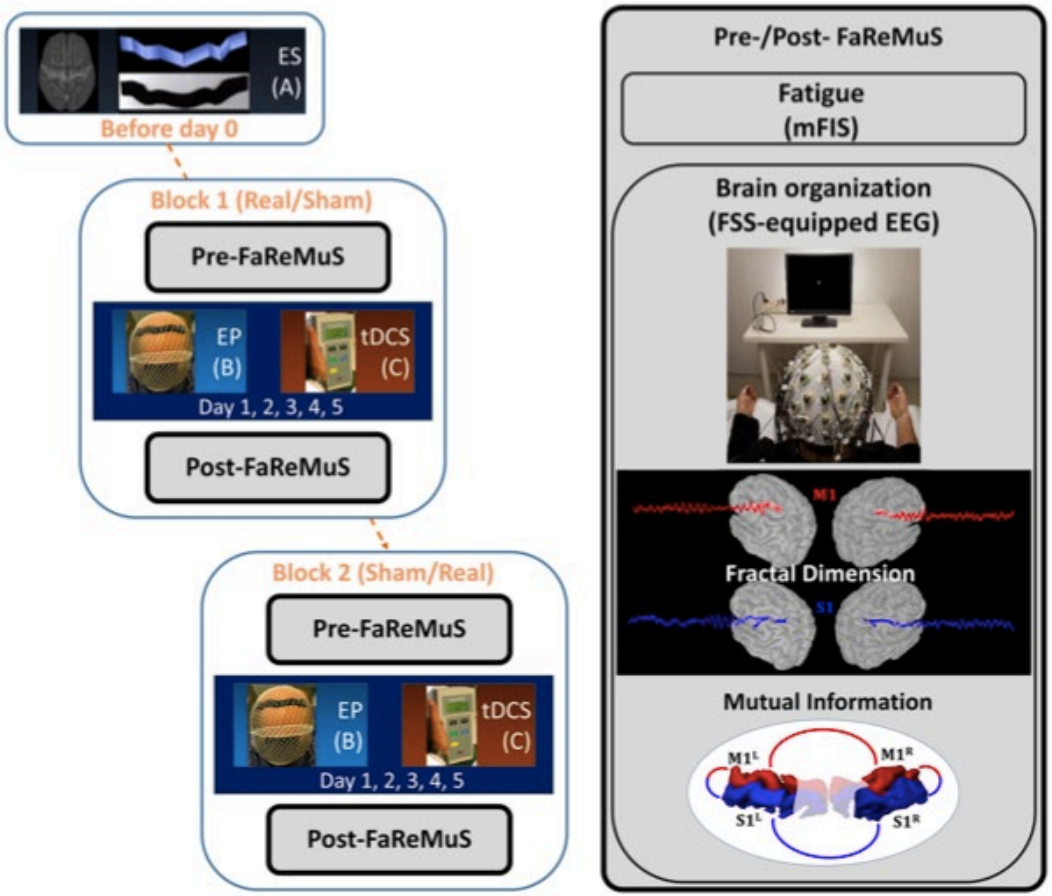




anodal tDCS applied over the motor cortex or DLPFC improve fatigue in patients with MS.

Ferrucci R et al 2014; *Chalah MA et al 2017*

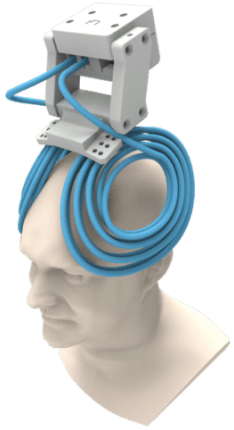
Application of neuromodulation as an innovative treatment for fatigue

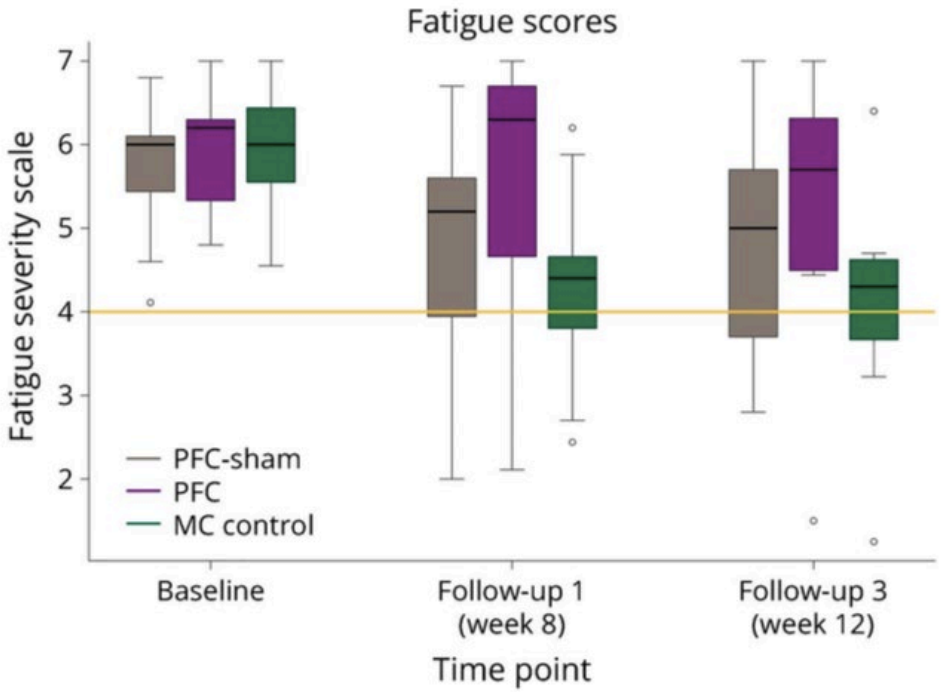


The sensorimotor networks activity at rest in fatigued MS people was modulated after the personalized FaReMuS 5-day non-pharmacological treatment in a way that partly explained the fatigue symptoms amelioration. The neuronal activity of the primary sensorimotor counterpart was altered more than the motor one before the treatment. The neuromodulation can effectively revert the unbalanced functional connectivity among interconnected target networks involved in the fatigue symptom.

Porcaro C.. et al 2019

Application of neuromodulation as an innovative treatment for fatigue





H-coil rTMS is safe and well tolerated in patients with MS.

Subthreshold MC stimulation reduced fatigue in MS patients

Gaede G. et al 2018

Application of neuromodulation as an innovative treatment for fatigue

The mechanisms by which NIBS could improve fatigue are still unclear.

Different hypothesis have been proposed such as:

- presynaptic increase of spinal drive from motor cortex
- modulation of premotor areas
- increase in motivation
- promotion of changes in cortical resting state activity and cortico-cortical connectivity
- induction of long-term potentiation-like and long-term depression-like neuroplastic changes at a local and/or network level.

Capone F. et al 2020

LA FATICA NELLA SCLEROSI MULTIPLA

Valutazione neurofisiologica

The neurophysiology could play a role in the management and evaluation of MS-related fatigue.

Despite of heterogeneity in results and methodological limitations, current evidence supports further studies on the role of neurophysiology in the management of fatigue.

In particular, for therapeutic purpose, tailored approaches based on individual network dysfunctions, individual plasticity impairment, and other neurophysiological variables should be explored.

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REVIEW
published: 22 April 2020
doi: 10.3389/fneur.2020.00251

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The Potential Role of Neurophysiology in the Management of Multiple Sclerosis-Related Fatigue

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