Conclusion: The lack of standardized protocols and inconsistent methodology limit conclusions on ALS diagnosis using TMS. Furthermore, it becomes difficult to relate the impact of factors such as the onset of symptoms, affected hemisphere, and time of diagnosis with the presence/absence of hyperexcitability. Future research should focus on refining diagnostic criteria based on the standardization of corticospinal activity measurement.
Implications: The study highlights the potential of Single-Pulse TMS for early ALS diagnosis but faces limitations such as methodological heterogeneity, lack of standardized protocols, and inconsistent parameter definitions. These challenges impact result reproducibility and clinical applicability. In clinical approach, improved TMS standardization could enhance early ALS detection, optimizing patient referral for neuroprotective therapies and clinical trials. In physiotherapy, better diagnostic accuracy may guide personalized interventions, delaying functional decline.
Keywords: Motor Neuron Disease, Cortical Hyperexcitability, Neurophysiology

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VOLUNTARY EXERCISE WITH ENRICHED ENVIRONMENT REDUCES ANXIETY- AND DEPRESSION-LIKE BEHAVIOR AFTER NERVE CONSTRICTION IN FEMALE MICE

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Background: Neuropathic pain results from injuries or diseases affecting the somatosensory system, impacting 7—10% of the global population. Additionally, psychological factors such as depression and anxiety are linked to heightened pain perception. Studies using animal models with chronic sciatic nerve constriction injury (CCI) are essential for investigating its pathophysiology. Although pharmacological treatment is widely used, environmental enrichment (EE) and voluntary exercise (VE) have shown efficacy as adjuvant interventions in managing neuropathic pain, including reducing anxiety- and depression-like behaviors associated with pain exacerbation. EE provides motor, sensory, social, and cognitive stimuli, which can be enhanced by VE, consisting of voluntary physical activity performed by the animal on a freely accessible running wheel. However, few studies have compared the effects of EE alone versus EE combined with VE.
Objectives: To compare the effects of EE with or without VE on anxiety- and depression-like behavior in a neuropathic pain model induced by CCI.
Methods: Twenty female BALB-C mice aged 7—8 weeks, weighing 30—35 g, were obtained from the Instituto Evandro Chagas (IEC) animal facility after approval by the animal research ethics committee. The animals were divided into four groups: CCI, CCI + VE, CONTROL, and CONTROL + VE. All groups received EE; the CCI groups underwent nerve constriction surgery, while control groups were not exposed to surgical intervention. Anxiety- and depression-like behaviors were assessed using the Open Field (OF) test, where animals were placed in a $30 \times 30 \times 40$ cm apparatus for 5 minutes and filmed for later analysis. Statistical analyses included the Shapiro-Wilk normality test and one-way ANOVA with Tukey's post-hoc test, using Prism 9 software. p-values < 0.05 were considered significant.
Results: In the OF test, the CCI + VE group maintained total distance traveled like pre-injury measurements, with no significant changes over the 28-day experiment. In contrast, the CCI group showed increased immobility and progressive distance reduction on days 14, 21, and 28 (one-way ANOVA, $F(4,16) = 6.47$; $p = 0.003$). Furthermore, time spent in the corners of the apparatus increased significantly in the CCI group compared to pre-injury (one-way ANOVA, $F(4,16) = 3.34$; $p = 0.03$).
Conclusion: The combination of VE with EE enhanced the reduction of anxiety- and depression-like behaviors in mice subjected to CCI.
Implications: These findings suggest that combined non-pharmacological interventions could be promising strategies for managing neuropathic pain through reducing anxiety- and depression-like behaviors, warranting further studies to explore their mechanisms and clinical applications.
Keywords: Physical Exercise, Hyperalgesia, Nervous System

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ENRICHED ENVIRONMENT WITH VOLUNTARY EXERCISE PROMOTES SENSORY RECOVERY AFTER SCIATIC NERVE CONSTRICTION IN FEMALE MICE

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Background: Neuropathic pain results from injuries or diseases affecting the somatosensory system, impacting 7-10% of the global population. Animal models with chronic constriction injury (CCI) of the sciatic nerve are essential for investigating its pathophysiology. Although pharmacological treatment is widely used for neuropathic pain, non-pharmacological interventions such as environmental enrichment (EE) and voluntary exercise (VE) have shown promising efficacy. EE, which provides motor, sensory, social, and cognitive stimuli, can be enhanced by VE, performed in a freely accessible activity wheel. However, there is a scarcity of studies comparing isolated EE and its combination with VE.
Objectives: To evaluate the effects of EE, alone or combined with VE, on sensitivity modulation in a model of neuropathic pain induced by sciatic nerve constriction in female mice.
Methods: Twenty female BALB-C mice, aged 7-8 weeks and weighing 30-35 g, were used, acquired after approval by the animal research ethics committee. The 29-day experiment divided the animals into four groups: CCI; CCI + VE; SHAM, and SHAM + VE. All groups underwent EE, and the SHAM group consisted of animals without sciatic nerve injury. Sensitivity was assessed using the Von