

## The Relationship Between Cortical Excitability and Pain Catastrophizing in Myofascial Pain

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**Abstract:** Pain catastrophizing regularly occurs in chronic pain patients. It has been suggested that pain catastrophizing is a stable, person-based construct. These findings highlight the importance of investigating catastrophizing in conceptualizing specific approaches for pain management. One important area of investigation is the mechanism underlying pain catastrophizing. Therefore, this study explored the relationship between a neurophysiological marker of cortical excitability, as assessed by transcranial magnetic stimulation, and catastrophizing, as assessed by the Brazilian Portuguese Pain Catastrophizing Scale, in patients with chronic myofascial pain syndrome. The Pain Catastrophizing Scale is a robust questionnaire used to examine rumination, magnification and helplessness that are associated with the experience of pain. We include 24 women with myofascial pain syndrome. The Brazilian Portuguese Pain Catastrophizing Scale and cortical excitability were assessed. Functional and behavioral aspects of pain were evaluated with a version of the Profile of Chronic Pain scale and by multiple pain measurements (eg, pain intensity, pressure pain threshold, and other quantitative sensory measurements). Intracortical facilitation was found to be significantly associated with pain catastrophizing ( $\beta = .63, P = .001$ ). Our results did not suggest that these findings were influenced by other factors, such as age or medication use. Furthermore, short intracortical inhibition showed a significant association with pressure pain threshold ( $\beta = .44, P = .04$ ). This study elaborates on previous findings indicating a relationship between cortical excitability and catastrophizing. The present findings suggest that glutamatergic activity may be associated with mechanisms underlying pain catastrophizing; thus, the results highlight the need to further investigate the neurophysiological mechanisms associated with pain and catastrophizing.

**Perspective:** This study highlights the relationship between cortical excitability and catastrophizing. Cortical measures may illuminate how catastrophizing responses may be related to neurophysiological mechanisms associated with chronic pain.

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**Key words:** Catastrophizing, myofascial pain, chronic pain, cortical excitability, Quantitative Sensory Testing, repetitive transcranial magnetic stimulation, glutamatergic system.

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Chronic pain is a major health problem insofar as it reduces quality of life and adversely impacts social and economic outcomes. In most cases, treatment outcomes for chronic pain conditions are unsatisfactory, causing displeasure among physicians and patients.<sup>19,36</sup> For chronic pain disorders, epidemiologic studies have found that myofascial trigger points (MTrPs) might be the source of nociceptive inputs for 30 to 85% of patients seeking pain therapy.<sup>14,46</sup> MTrPs are defined as painful locations in skeletal muscle that can provoke referred pain, motor dysfunction, and autonomic phenomena.<sup>45</sup> Myofascial pain syndrome (MPS) is a common clinical finding that is characterized by the presence of MTrPs.<sup>45</sup> Furthermore, MTrPs have been linked to the activation of pain mechanisms, such as widespread central sensitization.<sup>63</sup> This central sensitization phenomenon involves impaired functioning of brain-orchestrated descending inhibitory mechanisms and is able to alter pain facilitatory pathways.<sup>49,63</sup> Impairment of these pathways and central sensitization cause changes in sensory processing centers of the brain.<sup>49</sup> These neuroplastic changes can lead to behavioral and emotional changes for a person experiencing pain,<sup>15</sup> especially in the context of chronic pain conditions, for which management of symptoms is often ineffective.<sup>36</sup> A lack of treatment response that leads to maintenance of pain can yield negative emotions, such as anger, depression, and anxiety.<sup>22</sup>

Moreover, psychological factors, such as somatization, helplessness, and catastrophizing, might exacerbate chronic pain conditions.<sup>13,16,52</sup> Catastrophizing was first described approximately 40 years ago and describes a phenomenon involving dwelling on the worst possible outcome of a situation and the subsequent results of an unpleasant outcome.<sup>3,4</sup> Sullivan et al showed that measurements of pain catastrophizing are positively associated with measures of physical and psychological disability among subjects with diverse pain conditions. Similar results have confirmed this relationship between catastrophizing and disability over the time during which an individual experiences pain.<sup>54</sup> Thus, it has been suggested that catastrophizing is a stable, person-based construct.<sup>51,54</sup> Overall, these findings highlight the importance of catastrophizing in conceptualizing specific approaches for pain management in clinical practice.

The Pain Catastrophizing Scale (PCS) has been used to assess 3 dimensions of catastrophizing in response to pain: 1) rumination (repeated thoughts of pain), 2) magnification (increased severity and importance of pain), and 3) helplessness (a general feeling that it is not possible to escape from pain-related suffering).<sup>51,55</sup> The PCS has been widely used in research and clinical practice. In fact, catastrophizing has been extensively investigated in chronic pain patients with various pain disorders and in healthy subjects via experimentally induced pain.<sup>21,51-53</sup> These studies have shown that catastrophizing is significantly correlated with a patient's subjective experiences of the severity of pain and his or her disability due to the pain. Moreover, a study conducted in chronic neuropathic pain subjects has shown that catastrophizing is positively correlated with affective

aspects of experiencing pain.<sup>51</sup> The impact of emotional regulation is highlighted by the fact that inappropriate emotional responses worsen clinical pain outcomes. Although it is important to underscore that catastrophizing and depression have different mechanisms,<sup>52</sup> some of the neural pathways associated with affective regulation involve the same subcortical nuclei, such as the amygdala, nucleus accumbens, ventral striatum, dorsal raphe nucleus, and several areas of the prefrontal cortex.<sup>10,48,59</sup> The dorsolateral prefrontal cortex is an important brain region for emotional processing and the downregulation of negative affective conditions.<sup>1,11,12,35</sup>

Collectively, these findings suggest that catastrophizing refers to various negative pain-related thoughts, including exaggerating the severity of a pain sensation, focusing on pain, and worrying about the possible consequences of pain. Past research has primarily focused on the psychological, social, and emotional aspects of pain catastrophizing, with little attention given to neurophysiological correlates. Consequently, the exact neural mechanisms underlying pain catastrophizing and its close relationship with many other factors involved in pain remain unclear. It is not known whether catastrophizing is associated with changes in cortical plasticity.

Transcranial magnetic stimulation (TMS) may offer an opportunity to investigate whether pain catastrophizing is linked to cortical excitability in chronic pain. The assessment of cortical plasticity using the noninvasive technique of TMS is a well-established method applied in routine clinical diagnostics. TMS consists of the application of a nonpainful magnetic pulse to a person's head, which secondarily elicits a motor-evoked potential that can be recorded via electromyogram in a peripheral muscle. TMS parameters can be used to assess the activity of different neurotransmitter systems, including glutamatergic, gamma-aminobutyric acid (GABA)<sub>A</sub>ergic, and GABA<sub>B</sub>ergic functions. Using TMS, it has been found that different pain disorders are linked to specifically impaired neurotransmitter systems, such as GABA<sub>A</sub> in chronic neuropathic pain<sup>29</sup> and a hyperexcitable state in migraines.<sup>2,9</sup> Given recent findings that chronic pain syndromes are associated with a specific neural signature characterized by a defective inhibitory state in the primary motor cortex,<sup>29</sup> we aimed to further explore the mechanistic relationships between catastrophizing, motor cortex excitability, and pain measures. Thus, in this exploratory study, we tested the hypothesis that measurements of cortical excitability are significantly associated with pain catastrophizing scores. To address this hypothesis, we assessed the PCS, several subjective and objective pain measures (the behavioral outcome), and motor cortex excitability via transcranial magnetic stimulation (the neurophysiological outcome) in chronic pain subjects with long-term musculoskeletal MPS.

## Methods

### Study Design

This study was carried out at the Hospital de Clínicas de Porto Alegre in Porto Alegre, Brazil. The study protocol

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