

# Pharmacological and Exercise-Induced Changes in Beta EEG Oscillations as a Possible Indication of Analgesic-Related GABAergic Neurotransmission Improvement: a Single Case Study

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Background and research question: Chronic pain (CP) is a major public health problem often unsuccessfully treated. The mechanistic approach of pain management, targeting one neurotransmission system, namely the gamma-aminobutyric acid (GABA) system, is one potential strategy, owing to the important role played by GABA in pain regulation and considering modifications noticed in the GABAergic signaling in CP situation. Electroencephalographic (EEG) fast oscillations (including beta ( $\beta$ ) waves) constitute an easy way to measure the GABAergic neurotransmission in the brain. Furthermore, studies suggest that balance training (BT), while being analgesic, increases the activity of the GABAergic system. Thus, like other pain therapies, the analgesic effect could also be studied in relation with changes in brain GABAergic activity. We hypothesized that analgesia induced by therapeutic measures (including drugs and BT) would parallel increase  $\beta$  EEG oscillations (considered as a GABAergic marker). Aim: This study aimed at measuring changes in EEG  $\beta$  oscillations (considered as a possible marker of brain GABAergic signaling) after analgesic therapeutic interventions, in parallel with clinical pain reduction. Methods: In this single case study, a 62-year-old patient with CP of unknown origin, resistant to usual analgesic drugs, was submitted to clinical pain evaluation and to high density (68 electrodes) resting-state EEG recording in standing and seated positions, in order to evaluate low  $\beta$  (L $\beta$ ; 13-20 Hertz, Hz) and high  $\beta$  (H $\beta$ ; 20-30Hz) Global Power Spectrum (GPS). These measures were performed before and after therapeutic interventions consisting in analgesic dose increase (gabapentin from 800mg per day to 2g per day) respectively a four-week BT. Results: After gabapentin increase, pain intensity did not change, contrary to the affective and sensory components of pain, which both decreased. In parallel, the L $\beta$  GPS and the H $\beta$  GPS increased in standing position (L $\beta$ : 44%; H $\beta$ : 30%), but not in seated position (L $\beta$ : -0.2%; H $\beta$ : -32%). After BT, all 3 pain scores decreased and both EEG markers improved in all recording positions (L $\beta$ : 26% in seated; 30% in standing position; H $\beta$ : 27% in seated and 29% in standing position). Concluding discussion: Upon dose increase of gabapentin, sensory-affective-discriminated subscores depicted better the subjective reduced pain than pain intensity, while  $\beta$  EEG GPS increase was observed only in standing position. In contrast, after BT, all evaluated pain indicators decreased in parallel with all EEG markers increase in standing as in seated position. Thus, although all therapeutic interventions induced the expected clinical and electrophysiological changes, BT appeared to have a more global effect than pharmacological treatment modification, which more likely to be effective in a CP situation.

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