

# Abstract

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## Changes in the concentrations of amino acids in the cerebrospinal fluid that correlate with pain in patients with fibromyalgia: implications for nitric oxide pathways.

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**BACKGROUND:** Substance P (SP), a putative nociceptive transmitter, is increased in the CSF of patients with fibromyalgia syndrome (FMS). Because excitatory amino acids (EAAs) also appear to transmit pain, we hypothesized that CSF EAAs may be similarly involved in this syndrome.

**RESULTS:** We found that the mean concentrations of most amino acids in the CSF did not differ amongst groups of subjects with primary FMS (PFMS), fibromyalgia associated with other conditions (SFMS), other painful conditions not exhibiting fibromyalgia (OTHER) or age-matched, healthy normal controls (HNC). However, in SFMS patients, individual measures of pain intensity, determined using an examination-based measure of pain intensity, the tender point index (TPI), covaried with their respective concentrations of glutamine and asparagine, metabolites of glutamate and aspartate, respectively.

**CONCLUSIONS:** This suggests that re-uptake and biotransformation mask pain-related increases in EAAs. Individual concentrations of glycine and taurine also correlated with their respective TPI values in patients with PFMS. While taurine is affected by a variety of excitatory manipulations, glycine is an inhibitory transmitter as well as a positive modulator of the N-methyl-D-aspartate (NMDA) receptor. In both PFMS and SFMS patients, TPI covaried with arginine, the precursor to nitric oxide (NO), whose concentrations, in turn, correlated with those of citrulline, a byproduct of NO synthesis. These events predict involvement of NO, a potent signaling molecule thought to be involved in pain processing. Together these metabolic changes that covary with the intensity of pain in patients with FMS may reflect increased EAA release and a positive modulation of NMDA receptors by glycine, perhaps resulting in enhanced synthesis of NO.

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