D-Aspartate drinking solution alleviates pain and cognitive impairment in neuropathic mice.

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D-Aspartate (D-Asp) is a free D-amino acid detected in multiple brain regions and putative precursor of endogenous N-methyl-D-aspartate (NMDA) acting as agonist at NMDA receptors. In this study, we investigated whether D-Asp (20mM) in drinking solution for 1month affects pain responses and pain-related emotional, and cognitive behaviour in a model of neuropathic pain induced by the spared nerve injury (SNI) of the sciatic nerve in mice (Decosterd and Woolf CJ 2000).SNImice developed mechanical allodynia and motor coordination impairment 30days afterSNIsurgery. The cognitive performance was also significantly compromised 30 days after SNI as suggested by the reduction of the recognition index in the object recognition task, alternation in the y-maze test and social recognition memory in the social interaction paradigm. SNI also induced anxiety and depression-like behaviour, since it increased the digging and burying in the marble burying test, time spent in light box in the light/dark box and the time of immobility in the tail suspension test and forced swimming test. The expression of (post synaptic density) NR2B was increased, while, PSD-95 and Shank 1was instead unaffected in the medial prefrontal cortex (mPFC) of theSNImice. Treatment with D-Asp drinking solution, started right after theSNI(day 0), alleviated mechanical allodynia, improved cognition and motor coordination and increased social interaction. D-Asp also restored the levels of extracellular D-Asp, Homer 1a and NR2B subunit of the NMDA receptor to physiological levels and reduced Shank1 and PSD-95 protein levels in the mPFC. Moreover, we used amitriptyline (10mg/Kg, i.p.), a tricyclic antidepressant used also to alleviate neuropathic pain in humans, as a positive control. Amitriptyline reverted mechanical allodynia and cognitive impairment, and unlike D-Asp, was effective in reducing depression and anxiety-like behaviour in theSNImice and increased PSD protein level. Altogether these findings demonstrate that D-Asp improves sensorial, motor and cognitive-like symptoms related to chronic pain possibly through glutamate neurotransmission normalization in neuropathic mice.

References

Decosterd I., Woolf CJ. (2000) Spared nerve injury: an animal model of persistent peripheral neuropathic pain. Pain 87(2):149-158