

Hypothalamic activity in an animal model of paclitaxel-induced neuropathic pain: MEMRI and *ex vivo* spectroscopy studies.

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Abstract

Paclitaxel (PTX) is widely used to cancer treatment but frequently causes chemotherapy-induced neuropathic pain (CINP) [1]. The central nervous system mechanisms underlying CINP are starting to be uncovered [2] [3]. This experimental work aimed to evaluate the effects of PTX at the hypothalamus, using manganese-enhanced magnetic resonance imaging (MEMRI) and *ex vivo* spectroscopy.

CINP was induced in Wistar male rats by intraperitoneal injections in 4 alternate days with PTX dissolved in and DMSO (vehicle) or DMSO. Imaging studies were performed at 0 (T0), 28 (T28) and 56 days (T56) after CINP induction in a 7T MRI system under inhalatory anesthesia (1-1.5%, 1L/min O₂). A solution of MnCl₂ 100mM was intraperitoneally injected (1 mmol/kg) 24h before scanning that consisted in T1 maps were acquired employing a saturation-recovery sequence (7 TRs from 150 to 6000ms).

Rats were sacrificed at T28 and T56 with a focused high-power microwave (5000W). ¹H HR-MAS spectra of hypothalamus were acquired in a 11.7T with CPMG sequence and processed with LCModel.

MEMRI studies showed that PTX treatment decreased the T1 time at T56 in hypothalamus compared to DMSO-injected animals. No differences were observed in T1 time between experimental groups at T28. The analysis of data from *ex vivo* spectroscopy demonstrated that at T28 the paclitaxel-injected rats presented an increase N-acetyl aspartate and a decrease of lactate in the hypothalamus compared to the control group. Together, our results indicate that PTX induces metabolic and functional changes in hypothalamus over time. Due to the role of the analyzed metabolites, the possibility of neuroinflammation at the hypothalamus needs to be evaluated.

Figure 1

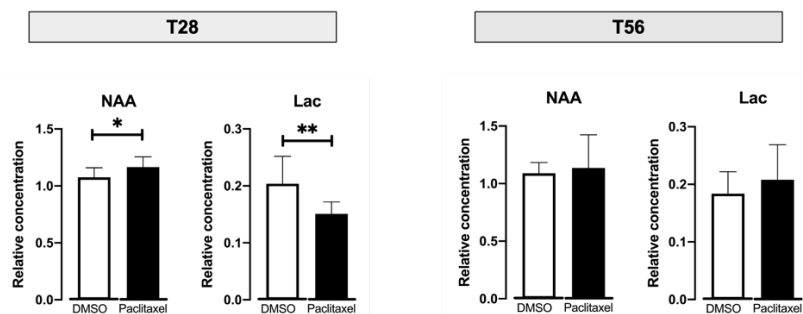


Figure 1 - Metabolic profile determined by ¹H HR-MAS in the hypothalamus of DMSO and paclitaxel-injected rats. Relative concentration of N-acetyl aspartate (NAA) and lactate (Lac) determined by magnetic resonance spectroscopy in the hypothalamus at 28 (T28) and 56 (T56) days after the first injection of DMSO or paclitaxel. Data are presented as mean ± SD. * p < 0.05; ** p < 0.01.

References

[1] Sisignano, M. et al, Nature Reviews Neurology, 10 (2014), 694-707.

[2] Costa-Pereira, J. T. et al, European Journal of Neuroscience, 51 (2020), 1756 – 1769.

[3] Costa-Pereira, J. T. et al, Frontiers in Neuroscience, 13 (2020), 1413.