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PO.159

Enhancement of the respiratory response to metabolic acidosis in newborn rat by a progestin: possible involvement of orexin neurons

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Introduction: Ondine's curse is a neuro-respiratory disease characterized by sleep-related life-threatening hypoventilation due to dysfunction of the CO₂/H⁺ chemosensitive neurons of the retrotrapezoid nucleus/parafacial respiratory group. A clinical observation have shown on two women patients a recovery of CO₂/H⁺ chemosensitivity concomitantly with oral contraception using desogestrel (Straus et al 2010). Recently, we have shown on *ex vivo* preparations of central nervous system that etonogestrel (active metabolite of desogestrel) induced a potentiation of the respiratory response to metabolic acidosis (MA: a model of hypercapnia) (Loiseau et al 2014). Our aim was to determine the encephalic subdivisions and structures involved in order to surround the action mechanisms of the progestin.

Methods: Under MA, etonogestrel's effect on respiratory frequency, was appreciated on *ex vivo* preparations from newborn rats containing either the medulla oblongata with or without pontine, mesencephalic and diencephalic regions. On preparations with diencephalon, etonogestrel's effect was examined under exposure with a specific antagonist of orexin receptors and appreciated in comparison to control preparations. In addition, immunohistological detection of *c-FOS* was performed concomitantly with detection of orexinergic neurons.

Results: Etonogestrel enhanced the acidosis-induced hyperventilation only when diencephalic structures were present. Under antagonization of the orexinergic signalization, this effect was abolished. Immunohistological quantification suggest that etonogestrel significantly increased *c-FOS* expression in orexin-containing neurons of the lateral hypothalamic area.

Conclusion: These data suggest that etonogestrel acts by activating the orexinergic signalization. Further experiments are required to highlight all the downstream structures involved and contribute to develop pharmacological treatment for CCHS.

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Direct-current stimulation of posterior tibial nerve modulates the Soleus H-reflex amplitude

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Introduction: Several studies demonstrated that transcranial direct current stimulation (tDCs) is a promising non-invasive tool able to modulate the excitability of several CNS structures. Its effect is usually facilitatory when using anodal polarity and inhibitory for the cathodal one. In most studies, DC stimulation was applied on cortical or spinal structures, while little is known about its effect on peripheral nerves fibres. This research aims at highlighting such effect.

Methods: In twenty subjects, electrical stimulation of the posterior tibial nerve (1 ms current pulses, 1 shock every 9 s) was used to elicit the H-reflex in the Soleus muscle. Once the H-reflex amplitude was stable for at least 15 min, DCs (either cathodal or anodal) was applied proximally to the same nerve for 10 min, looking for changes in reflex amplitude. Then, the H-reflex was measured for 30 further minutes, looking for after-effects.

Results: Cathodal DCs induced a significant increase of the H-reflex amplitude (about +35%) with respect to the control value. In this configuration the after-effect lasted about 25 min. Anodal DCs induced instead a significant decrease (about -25%) of the reflex amplitude. A significant after-effect was observed for just about 5 min.

Discussion: This study shows that DCs applied to a peripheral nerve is able to elicit neuromodulation. Its polarity dependence suggests a local change in the excitability of nerve fibres rather than a central modulation of the spinal reflex circuit. Moreover it is worth to note that the polarity dependence was opposite to what found for tDCS.

PO.161

The mouse isolated detrusor strip preparation as a useful model for exploring the paralyzing potency of botulinum neurotoxins at the urological level

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Introduction: Botulinum Neurotoxin type A (BoNT/A) has been clinically used for 15 years to treat several lower urinary tract (LUT) conditions as a second