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Influence of osmotic stress on dopaminergic innervation of the mesencephalon and locomotor performance in rats

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The osmotic stress is a powerful stimulus that elicits profound peripheral and central disturbances. In the mammalian brain, osmotic stress has been associated to several glial and neuronal changes. The lack of data regarding the impact on the dopaminergic system and locomotion led us to investigate the effect of prolonged water deprivation in rat on the midbrain dopaminergic system and locomotor performance by dehydrating rats for one two weeks. Locomotor activity and tyrosine hydroxylase (TH) expression were assessed using the open field test and immunohistochemistry respectively. Water deprivation was accompanied with a significant increment of TH expression within substantia nigra compacta (SNc) and ventral tegmental area (VTA) gradually as the duration of dehydration increases. While locomotor activity showed the inverse tendency manifested by a drop of crossed boxes number following one and two weeks of water deprivation. Our data suggest a substantial implication of midbrain dopaminergic system in the central response to the osmotic stimuli accompanied with locomotor deficiencies.

Key words: water deprivation, dopamine, locomotion, substantia nigra compacta, ventral tegmental area

Neuropharmacological evaluation of methanolic extract from mercurialis annua a plant used in moroccan traditional medicine

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Current therapeutic for the treatment of anxiety is associated with a wide variety of prominent side effects. The traditional use of plant extract to health care can indicate an important source of new pharmaceuticals. In Morocco traditional medicine, the use of Mercurialis annua is commonly recommended for relief of anxiety.

Nevertheless, despite its popular use there are no studies related to its possible neuropharmacological effect. Here, we investigated the possible anxiolytic effect of the extract of *M. annua* after acute treatment in mice. The methanolic extract from the aerial parts of *M. annua* (100, 200 or 400 mg/kg) was orally administered, and its anxiolytic effect was evaluated in hole board test, the light-dark box test, and motor coordination with the rota rod test. Diazepam was employed as standard drug 1mg/kg. The methanolic extract of *Ma* 100 mg/kg increased the time spent in the brightly-lit chamber of the light/dark box, as well as in the number of times the animal crossed from one compartment to the other. Performance on the rota rod was unaffected. In the hole board test, the extract significantly increased head-dip counts. These results provide support for anxiolytic activity of *Mercurialis annua*, in line with its medicinal traditional use, and may also suggest a better side-effect profile of *Mercurialis annua* relative to diazepam.

Key words: diazepam, hole board test, rotarod test, plant

General overview of the physiology of nociception

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Nociception is a stimulus whose intensity results in defense reactions aimed at safeguarding the integrity of the organism. The nociceptive message is conveyed from the periphery to the higher centers (periphery, spinal cord, brainstem, thalamus to the cortex). In this transport and at each different stage, there is a modulation, nociceptive information undergoing inhibitory or excitatory influences, including the sensory marrow is an important step of modulation of nociceptive information before they are transmitted to higher centers. The central sensitization mechanisms are almost identical for the different types of pain, whether inflammatory or neuropathic. Central sensitization begins with a cascade of events in the posterior horn of the cord whose dorsal horn neurons can be sensitized in an identical manner to peripheral nociceptors. The excessive release of neurotransmitters by the presynaptic fiber results in a significant increase in the transmission of pain. After the neurotransmitters released in excess by the peripheral fiber will stimulate and sensitize the postsynaptic membrane via phosphorylation of the ion channels, transcriptional changes will affect the molecular machinery of the cell by giving phenotypic changes to the neurons in order to generate the activation of a number of genes that cause long-term cellular activations.

Key words: nociception, neurotransmitters, peripheral nociceptors, central sensitization

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Behavioral and epigenetic effects of paternal exposure to cannabinoids during adolescence on offspring vulnerability to stress

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Chronic cannabinoid exposure during adolescence in male rats induces chronic cognitive and emotional impairments. However, the impact of this form of exposure on offspring vulnerability to stress is unknown. The aim of this study was to evaluate the behavioural and epigenetic effects of stress in the offspring of male rats whose fathers were exposed to cannabinoids during adolescence.

Male adolescent offspring of Win55,212-2 (1.2 mg/kg) treated rats were exposed during one week to variable stressors and subjected to behavioural tests of anxiety and episodic-like memory, followed by an assessment of global DNA methylation and expression of DNA methyltransferases enzymes DNMT1 and DNMT3a mRNA in the prefrontal cortex.

Stress exposure induced a significant anxiogenic-like effect but did not affect the episodic-like memory in the offspring of Win55,212-2 exposed fathers in comparison to the offspring of non-exposed fathers. These behavioural changes were subsequent to a significant increase in global DNA methylation and DNMT1 and DNMT3a transcription in the prefrontal cortex.

These data suggest that the deleterious effect of chronic exposure to cannabinoids during adolescence are not limited to the exposed individuals but may increase the vulnerability to stress-induced anxiety in the offspring and alter their epigenetic programming.

Key words: *adolescence, anxiety, cannabinoids, DNA methylation, offspring, stress*

Polysomnographic recording of sleep in dromedary camel

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Sleep is known to show significantly different patterns across species and taxa. In human and laboratory animals, sleep is widely investigated, but less information is available for mammals living in harsh environments such as the dromedary camel in the desert. In a previous study we observed that this camel exhibits a specific nocturnal behavior that might be related to sleep and we aimed at investigating the camel's sleep pattern in more detail. However, since this was a first attempt to record camel sleep, we faced several difficulties. First, we used non-invasive techniques which is a transcutaneous polysomnography: electroencephalography (EEG), electromyography (EMG) and electrooculography (EOG). We were concerned that these electrophysiological signals would be of low quality because of high impedance linked to the thickness of the camel skull bone and skin. Between different recording devices, we chose one often used in human, the Actiwave® (CamNtech-UK). Handmade systems were developed to adapt to the camel and to protect the device from possible

damages. Eight gold-plated electrodes were fixed on the head skin of six female camels. EEG was recorded at occipital and frontal positions, EOG from the upper and lower eyelids and EMG from electrodes on the masseter and nuchal muscles were recorded. First results showed that the recording device was well-tolerated by the camels. The EEG, EOG and EMG recording showed a good signal to noise ratio. Preliminary analyses revealed differences between awake, sleep and rumination states. Thus, we have been successful in using this non-invasive technique for polysomnograph recording in the camel for the first time. This technic can now be used for further investigations of the sleep architecture in the camel.

Key words: *sleep, non-invasive, EEG, EMG, EOG, camel*

Intestinal microbiote and neurological diseases: Targeting for the development of a new generation of probiotics

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Commensal bacteria that we harbor within our digestive tract play a key role in many physiological processes including the regulation of immune and metabolic responses, leaving the microbiota considered as a true organ in itself that is essential to preserve.

The alteration of this bacterial ecosystem is indeed associated with many chronic diseases whose incidence is increasing, such as inflammatory bowel diseases, obesity, diabetes, allergies and neurological disorders. In this context, the targeting of the microbiota has become an important research focus in human health.

The use of bacteria beneficial to health, called probiotics, is experiencing a considerable increase. My study aims to:

- To highlight the possible interactions between dysbiosis and neurobehavioral change,
- To better understand their role in immune and metabolic homeostasis and
- Selected future probiotic candidates of therapeutic interest.

This work is carried out within two teams providing complementary skills in the field of microbiota, probiotics, neuroscience, immune and metabolic responses and should eventually lead to a partnership with an industrialist.

Key words: *autism spectrum disorders-gut microbiota-probiotic*

Evaluation of the analgesic, anti-inflammatory and antioxidant activity of ficus carica L. in Morocco

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People have always given themselves the means to fight pain by first using the means offered by his environment and in particular plants. Ficus carica L is a medicinal plant used in the treatment of many diseases including inflammatory diseases. The aim of the work was to study the analgesic, anti-inflammatory and antioxidant activity of Ficus carica hydro-ethanol extract (FCEE) in order to promote its use in traditional medicine.

The first part is to study the analgesic activity. It is evaluated by the Writhing test, the hot plate test and the formalin test. The obtained results show that the FCE extract has an inhibitory effect on abdominal. The hot plate test shows also that FCEE has a strong analgesic effect against heat compared to Paracetamol taken as a reference. The last test showed an inhibitory effect of FCEE on acute pain in both its early phase and its late phase characterized by formalin-induced nociceptive inflammation.

The second part allows quantifying the anti-inflammatory power of FCEE during the carrageenan test and the xylene test. The obtained results during the injection of carrageenin show that the FCEE has a high anti-inflammatory activity.

The third part consists in evaluating the antioxidant activity using the following tests: DPPH scavenging activity and the test of the antioxidant power. The antioxidant activity of FCEE studied by the DPPH method shows a high activity. A remarkable reducing activity was also recorded with the reducing power test.

The results of this work allowed us to affirm that the hydro-ethanol extract of *Ficus carica* has very good antioxidant, analgesic and anti-inflammatory properties. Indeed, the fig tree will represent an excellent natural alternative to non-steroidal anti-inflammatory drugs and analgesics. Its pharmacological power lies in its phytochemical composition.

Key words: *ficus carica*, analgesic, anti-inflammatory, antioxidant

Effect of pomegranate (*Punica granatum* L.) fruit peel extract on locomotor activity and spontaneous alternation in rats

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Pomegranate is extensively used in numerous folkloric medicines for various ailments like rheumatism, inflammation, jaundice, pain. Many scientific investigations, in vivo and in vitro as well, showed its potency as an antioxidant, an anti-inflammatory, and an antibacterial agent, but very few investigated its effect on animal behavior.

This work aims to investigate in rats, the effect of *P. granatum* on two behaviors: locomotion in the open field and spontaneous alternation the T-maze. Treated groups (fruit peel extract (50 and 150 mg/kg doses, ip)) were compared to a control group (saline, ip).

Results show that animals treated with the extract exhibit a reduction of the locomotor and exploratory activity in the open field, and a decrease in the spontaneous alternation behavior in the T-maze apparatus. In both behaviors, these effects were dose dependent.

On the basis of these findings, we may say that the treatment with the *P. granatum* extract produced a myorelaxant-like effect in rats.

Key words: *punica granatum* L, spontaneous alternation, locomotion, open field, t-maze