Conclusions: Our findings provide valuable information for personalized pain treatment after LAC, in which the C allele of the rs2076222 SNP is associated with lower opioid sensitivity and/or higher pain sensitivity and requires more opioid analgesic after LAC.

PT642

The effects of caffeine on acupuncture analgesia
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Abstract

Objective: In the animal study, analgesic effect of acupuncture is reported that there is another route by an adenosine receptor except for opioid system[1]. This study was investigating the effects of acupuncture analgesia by an adenosine receptor. We stimulated to electro-acupuncture (EA) stimulation administered caffeine as an adenosine receptor blocker[2].

Methods: 20 volunteers (male:15, female:5, mean age:24.2 ± 4.4 years) who had chronic lumbar pain. Randomly divided into two groups: shame group (n=10), administration of caffeine group (n=10, 100mg/kg).

Conditions: EA stimulation-100Hz optimum intensity stimulation-15min once a week for weeks. Acupoints - Shenshu (BL-23)-Dachangshu (BL-25), evaluation-by using the Visual Analog Scale (VAS), highest blood pressure, muscle hardness, numerical value of adrenalin and recurrence time of pain.

Results: In VAS, highest blood pressure and muscle hardness showed significant differences (p<0.05). The shame group showed a long lasting effects in recurrence of pain. No significant changes were observed in numerical value of adrenalin.

Conclusion: It is suggested that administration of caffeine may be effective for preventing from acupuncture analgesia.

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PT643

Potassium and TRP Channels Are Involved in Analgesic Effects of NSAIDs in Tail Immersion Test
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Nonsteroidal anti-inflammatory drugs (NSAIDs), which main mechanism is the inhibition of cyclooxygenases (COXs), are commonly used in management of pain, fever and inflammation. In recent years, it has been asserted that NSAIDs induce central antinociception via various central analgesic mechanisms (1–2). Transient receptor potential (TRP) channels and potassium (K’) channels are widely distributed in the central and peripheral regions related with pain (3–5).

It is aimed to investigate the possible involvement of Kv7 potassium channels and TRP channels in antinociceptive mechanism of central action of selected NSAIDs, dipyrone (500mg/kg, i.p.), etodolac (70mg/kg, i.p.), ketoprofen (50mg/kg, i.p.) and diclofenac (50mg/kg, i.p.) by using tail-immersion test in mice. Mice were pre-treated with 3mg/kg (i.p.) ruthenium red (RR), non-competitive TRPV1 antagonist, and XE-911 (1mg/kg, i.p.), the potent and selective blocker of Kv7 channel, 30 and 15 minutes before NSAIDs administration, respectively. The tail withdrawal responses to thermal stimuli (52.5 ± 0.2 °C hot water) (6) were measured 45 minutes after NSAIDs administration.

The results of experiments showed that dipyrone, etodolac, diclofenac and ketoprofen exhibit statistically significant analgesia. Dipyrone and etodolac induced antinociception was significantly reversed (P<0.001, P<0.01) by pre-treatment with XE-911 while dipyrone, etodolac and also ketoprofen induced antinociception was significantly reversed (P<0.001, P<0.01) by pre-treatment with RR.

In conclusion, Kv7 channels are involved in the central analgesic activity of dipyrone and etodolac. TRP channels play a role in central antinociceptive effects of dipyrone, etodolac and ketoprofen. It may be suitable approach to use these agents as adjunctive therapeutics with other central analgesics to provide more effective therapy with less side-effects.

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PT644

The Possible Action Mechanisms of Central Analgesic Effect of Protocatechuic Acid
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Abstract

Protocatechuic acid (PCA) is a common bioactive polyphenolic in medicinal plants and human diet. The various pharmacological activities such as antioxidant, anticancer, anti diabetic and anti-inflammatory, have been identified1. However, the studies focused on the analgesic effect of this polyphenolic are limited1 and the action mechanisms of PCA still remain unclear.

Previously, we found that PCA has a central analgesic effect in hot-plate and tail-immersion test at the doses of 75, 150 and 300mg/kg3. This study aimed to investigate the involvement
of noradrenergic, serotonergic, cholinergic and opioidergic mechanisms in PCA-induced central analgesia in mice. The mice administered 300 mg/kg PCA (p.o.) were pre-treated with α2-adrenoceptor antagonist yohimbine (1 mg/kg, i.p.), serotonin 5-HT2 receptor antagonist ketanserin (1 mg/kg, i.p.), non-specific muscarinic antagonist atropine (5 mg/kg, i.p.) and non-specific opioid antagonist naloxone (5 mg/kg, i.p.), respectively. The analgesia test procedures were performed 45 minutes after PCA administration. The hot-plate (integrated supraspinal response) and tail-immersion (spinal reflex) tests were used and pain thresholds which are indicated by the withdrawal response latency to the thermal stimuli were evaluated.

The enhancement in the latency of PCA-induced response to thermal stimuli was reversed by yohimbine and naloxone non-specific opioid antagonist naloxone and atropine in tail-immersion test.

These results indicated that PCA induces central antinociception via spinally/supraspinally mediated noradrenergic, opioidergic and spinally mediated cholinergic modulation. However, further studies are required to understand how PCA organizes the interactions of these modulatory systems.

**PT645**

The Opioidergic, Serotonergic and Noradrenergic Modulation of Ferulic Acid-Induced Central Analgesia

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**Abstract**

Ferulic acid is a caffeic acid derivative and a common phenolic compound quite abundant in various medicinal plants that used for pain relief. The antinociceptive effect of ferulic acid has been shown; however, the action mechanisms of ferulic acid still remain unclear. The purpose of the present study was to investigate the possible mechanism of action of ferulic acid-induced antinociception in vivo by using hot-plate and tail-immersion tests. The involvement of noradrenergic, serotonergic, opioidergic and cholinergic mechanisms on the antinociception induced by 80 mg/kg ferulic acid were investigated by examining the effects of 1 mg/kg yohimbine as an α2-adrenoceptor antagonist, 1 mg/kg ketanserin as a serotonin 5-HT2 receptor antagonist, 5 mg/kg naloxone as a non-specific opioid antagonist, 5 mg/kg atropine as a non-specific muscarinic antagonist and 1 mg/kg mecaminylamine as a non-specific nicotinic antagonist pretreatments in mice. Ferulic acid at the doses of 80 mg/kg (p.o.) produced an antinociception in hot-plate tests and at the doses of 40 and 80 mg/kg in tail-immersion test. Yohimbine, naloxone, atropine and mecaminylamine, but not ketanserin, reversed the antinociceptive effect of ferulic acid in hot-plate test while yohimbine, naloxone, atropine and mecaminylamine, but not ketanserin, reversed the antinociception in tail-immersion test. These results indicated that ferulic acid possesses central antinociception through mechanisms that involve an interaction with supraspinal/spinal noradrenergic, opioidergic and spinal cholinergic systems, except serotonergic system. In particular, ferulic acid acts as µ-opioidergic agonists.

**Keywords:** Ferulic acid; antinociception; cholinergic pathway; noradrenergic pathway; opioidergic pathway.

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**PERSONALITY DISORDERS:**

**PT646 – PT647**

**PT646**

Effects of sex hormone treatment on white matter microstructure in patients with gender dysphoria

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**Abstract**

**Objective:** Sex hormones influence our behavior and shape associated brain structures and functions [1, 2]. Here, our aim was to investigate the effects of sex hormones on brain white matter microstructure using the cross-sex hormone treatment of patients with gender dysphoria as a model.

**Methods:** 24 Female-to-Male (PtM, 27.24 ± 2.4y) and 12 Male-to-Female (MtF, 26.17 ± 5.6y) transsexuals wanting sex reassignment were included. They were measured before, 4 weeks after, and 4 months after treatment start using diffusion tensor imaging on a 3T scanner. PtM received 1000mg testosterone undecanoate every 12 weeks. MtF received 50mg cyproterone acetate daily and additionally estradiol 0.75–1.5mg transdermally. DTI acquisition was performed with an isotropic resolution of 1.64mm3 acquiring diffusion-weighted images in 30 directions with a b-value of 800s/mm2. Calculation of fractional anisotropy (FA), mean diffusivity (MD), axial and radial diffusivity (AD, RD) maps was done in FSL. Tract-based spatial statistics were used for spatial normalization. Statistics included repeated measures ANOVA and post-hoc pairwise comparisons at p<0.05 FWE corrected using threshold-free cluster enhancement.

**Results:** 4 months but not 4 weeks of testosterone treatment in PtM led to significant increases in FA in a variety of tracts including fornix, corticospinal tract and superior longitudinal fasciculus, among others. Conversely, MD decreased in these tracts. These changes were based on reductions in RD and to a lesser extent AD for the investigated fibers. No significant changes were found for MtF at the two time points.

**Conclusions:** Our results concur with a previous study [3] and match well with our recent finding of a sex difference in MD, showing higher MD values in females than in males in most white matter tracts [4]. The absence of changes in MtF may be attributed to the small sample size. These data highlight the strong impact of testosterone on white matter morphology even after puberty.

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