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 α_2-adrenoceptor antagonist yohimbine (1 mg/kg, i.p.), serotonin 5-$HT_{2A/2C}$ 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[4] were evaluated.

The enhancement in the latency of PCA-induced response to thermal stimuli was reversed by yohimbine and naloxone pretreatments in hot-plate test, while it was reversed by yohimbine, naloxone and also 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 Opiodergic, Serotonergic and Noradrenergic Modulation of Ferulic Acid-Induced Central Analgesia

Nurcan BEKTAS[*1], *Rana ARSLAN*[1]
[1]*Anadolu University, Faculty of Pharmacy, Department of Pharmacology, 26470, Eskisehir, TURKEY*
[*]*Corresponding Author*
Name: Nurcan BEKTAS
Address: Anadolu University, Faculty of Pharmacy, Department of Pharmacology, 26470, Eskisehir, TURKEY
Phone: +902223350580-3745
e-mail: nurcanbektas@anadolu.edu.tr

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 α_2-adrenoceptor antagonist, 1 mg/kg ketanserin as a serotonin 5-$HT_{2A/2C}$ 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 mecamylamine 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 mecamylamine, but not ketanserin, reversed the antinociceptive effect of ferulic acid in hot-plate test while yohimbine, naloxone, atropine and mecamylamine, 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.
Acknowledgments
This study was supported by the Anadolu University Scientific Research Projects Unit (Project No: 1505S398), Anadolu University, Eskisehir, Turkey.

PERSONALITY DISORDERS: PT646 – PT647

PT646

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

Kranz GS[1], *Seiger R*[1], *Kaufmann U*[2], *Hummer A*[3], *Hahn A*[1], *Ganger S*[1], *Sladky R*[3], *Windischberger C*[3], *Kasper S*[1], *Lanzenberger R*[1]
[1]*Department of Psychiatry and Psychotherapy* [2]*Department of Obstetrics and Gynecology,* [3]*MR Centre of Excellence, Center for Medical Physics and Biomedical Engineering, Medical University of Vienna, Austria*

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 (FtM, 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. FtM 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 1.64mm^3 acquiring diffusion-weighted images in 30 directions with a b-value of 800s/mm^2. 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 FtM 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.

References

1. Kranz, G.S., W. Wadsak, U. Kaufmann, M. Savli, P. Baldinger, et al., *High-Dose Testosterone Treatment Increases Serotonin Transporter Binding in Transgender People.* Biol Psychiatry, 2015. **78**(8): p. 525–33.

2. Hahn, A., G.S. Kranz, R. Sladky, U. Kaufmann, S. Ganger, et al., *Long-term testosterone administration affects language areas of the human brain.* Hum Brain Mapp, 2016(accepted).
3. Rametti, G., B. Carrillo, E. Gomez-Gil, C. Junque, L. Zubiaurre-Elorza, et al., *Effects of androgenization on the white matter microstructure of female-to-male transsexuals. A diffusion tensor imaging study.* Psychoneuroendocrinology, 2012. **37**(8): p. 1261–9.
4. Kranz, G.S., A. Hahn, U. Kaufmann, M. Kublbock, A. Hummer, et al., *White matter microstructure in transsexuals and controls investigated by diffusion tensor imaging.* J Neurosci, 2014. **34**(46): p. 15466–75.

PT647

Changes in BDNF methylation status before and after receiving Dialectical Behavior Therapy (DBT) in patients with borderline personality disorder

*Shu-I Wu[1,2] MD, PhD;Shen-Ing Liu[1,2] MD, PhD; Hsian-Yu Lin[2,3]MD, PhD; Kai-Liang Kao[*4] MD.*
[1]Mackay Memorial Hospital, Department of Psychiatry, Taipei, Taiwan, [2]Department of Medicine,Mackay Medical College, Taipei, Taiwan, [3]Mackay Memorial Hospital, Department of Pediatrics, Taipei, Taiwan, [4]Far Eastern Memorial Hospital, Department of Pediatrics, Taipei, Taiwan.
**Correspondence*

Abstract

Objective: Borderline personality disorder (BPD) is a chronic and debilitating syndromeassociated with considerable morbidity, mortality, and high rates of medical and psychiatricutilization services. Literature havedemonstrated the therapeutic effects of dialectical behavior therapy (DBT) in patients with BPD. We aimed to explore whether the brain-derived neutrophic factor (*BDNF*) mightbe a natural candidate for a biological correlate of early life stress or an indicator for epigenetic modifications pre- and post- psychotherapeutic treatment.

Method: We proposed this current randomized control trial to test whether epigeneticchanges happen during and after DBT treatments. Proportions having suicide ornon-suicidal selfinjurious behaviors was followed and tested against changes in *BDNF*methylation levels. Suicidality, depression, hopelessness, quality of life, disability, serviceutilization, and function were assessed. Our inclusion criteria wereadult BPD patients that had at least two episodes of suicidal or non-suicidal self-injurious episodes in the past 5 years, and at least one of which is in the 3 months preceding enrollment. Outcome measures and blood samples were obtained at pre-treatment, 4-month, 8-month and post-treatment (12-month) during 1-year protocol.

Results: In the first year of this study, we recruited19 patients with BPD into case group and 20 healthy controls. Eight BPD patients started receiving DBT and 11 of them were in the TAU group. Two of the BPD were male, with average age being 32.7 years old for case group and 30.2 years old for control group, respectively.After 4 months, 8 people in the case group have received first stage of DBT. Their QLES and PHQ have shown significant improvement. However, their BDNF methylation levels were not significant different from baseline, or to compare with controls.

Conclusion: More participants and longer follow-ups are needed to explore whether there were changes in methylation levels over time after different interventions.

SEXUAL DISORDERS: PT648 – PT649

PT648

The effects of chronic treatment with haloperidol, clozapine and aripiprazole on mice isolated vas deferens

Mehmet Hanifi Tanyeri[a], Mehmet Emin Buyukokuroglu[b], Pelin Tanyeri[b], Oguz Mutlu[c], Güner Ulak[c], Füruzan Yildiz Akar[c], Bekir Faruk Erden[c]
[a]Yenikent Government Hospital, Department of Urology, 54100 Sakarya/Turkey [b]Sakarya University, Faculty of Medicine, Department of Pharmacology, 54100-Sakarya/Turkey [c]Kocaeli University, Faculty of Medicine, Department of Pharmacology, 41380-Kocaeli/Turkey

Abstract

Specific objective of the study: Sexual dysfunctions have commonly been reported as the resulting side effects of psychotropic drugs such as antipsychotics that result in both short and long-term effects on sexual function. This study aimed to determine the influence of haloperidol, clozapine and aripiprazole on noradrenaline and potassium chlorid (KCl)-induced contractions of the vas deferens.

Methods used: 7 weeks aged male inbred BALB/c ByJ mice were randomly divided into experimental groups (n = 7) as follows: saline; haloperidol 0.125 mg/kg; haloperidol 0.25 mg/kg; clozapine 1.25 mg/kg; clozapine 2.5 mg/kg; aripiprazole 3 mg/kg; aripiprazole 6 mg/kg. Mice were treated by ip injection of drugs during 21 days. After 21 days of treatment, epididymal and prostatic portions of vas deferens were surgically removed and immersed in 20 mL organ baths containing Krebs' solution. The effects of chronic treatment with haloperidol, clozapine and aripiprazole were investigated on noradrenaline (10(-8) to 10(-4) M), and 80 mM KCl-induced contractile responses. Statistical comparison between the groups was performed using ANOVA supported by Dunnett's post hoc test.

Summary of results: There were no significant differences in KCl-induced contractile responses in the epididymal and prostatic portions of mice vas deferens strips among the groups. Noradrenaline-induced contractile responses were significantly inhibited in the epididymal portion of the vas deferens obtained from the haloperidol-treatment group and clozapine-treatment group whereas in the prostatic portions there were no change. However, aripiprazole treatment had no effect on noradrenaline responses in both epipdidymal and prostatic portions of mice vas deferens.

Conclusions reached: These results revealed that induced contractions of vas deferens were affected after chronic treatment with haloperidol and clozapine but not aripiprazole. Noradrenergic receptors may, at least in part, contribute to changes in vas deferens contractions in mice with chronic treatment of haloperidol and clozapine but not aripiprazole.

PT649

Problematic sexual behavior in young adults: Associations across clinical, behavioral, and neurocognitive variables.

Eric Leppink[1], Samuel Chamberlain[2], Jon Grant[1], Sarah Redden[1]
[1]University of Chicago, USA, [2]University of Cambridge, UK

Abstract

Objectives: Amongst sexually active young adults, a notable number struggle to control this behavior, resulting in significant impairment and distress. Previous assessments of problematic