Psychopathology, self-esteem, and self-perceived stigma were also measured using the Positive and Negative Syndrome Scale, the Rosenberg Self-Esteem Scale (SES), the Beck Depression Inventory (BDI), the Beck Hopelessness Scale, and the Korean version of the Internalized Stigma of Mental Illness scale (K-ISMI).

Results
- Of the total of 87 participants, 20 (23%) had attempted suicide. Patients with a history of suicide attempts had significantly higher scores on the BDI (p=0.036) and K-ISMI (p=0.009), and significantly lower scores on the SES (p=0.001). Analysis of covariance revealed that the SES scores were significantly lower in patients with a history of previous suicide attempts than in those with no history, after controlling for K-ISMI and BDI scores (p = 0.039).

Conclusion
- Low self-esteem appears to represent a psychological dimension that is closely related to suicide risk. Therefore, clinical attention should be paid to the evaluation and enhancement of low self-esteem in schizophrenia patients with suicidal-ity. A longitudinal prospective study is required to ascertain whether low self-esteem leads suicide attempts.

PM426
Effect of a glucagon-like peptide 1 (GLP-1) receptor agonist, liraglutide, on cognition and body weight during antipsychotic treatment
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Abstract
Background: Second-generation antipsychotics (SGAs), such as olanzapine, are used to treat schizophrenia; however, they have minimal benefits for cognitive deficits and cause metabolic side-effects such as obesity [1, 2]. Obesity has been linked to increased cognitive impairment [3], complicating the health issues of people with schizophrenia. Liraglutide is a synthetic glucagon-like peptide-1 (GLP-1) receptor agonist with anti-obesity and neuroprotective properties [4, 5]; however, whether liraglutide can improve cognition during olanzapine treatment is unclear. The aim of this study was to examine the effects of liraglutide co-treatment on cognition and metabolic parameters during olanzapine treatment.

Methods: Sprague-Dawley rats were administered olanzapine (2mg/kg), liraglutide (0.4mg/kg), olanzapine+liraglutide co-treatment or vehicle (control) (n=12/group) for six weeks. Body weight, food intake and locomotor activity were recorded. Novel object recognition (NOR) and T-maze tests were conducted to examine recognition and working memory. Post-mortem white adipose tissue weight was recorded.

Results: Olanzapine caused significant body weight gain and increased white adipose tissue mass (p<0.05 vs control), whereas liraglutide co-treatment significantly reduced body weight and adiposity (p<0.001 vs olanzapine). Olanzapine induced hypolocomotion (p<0.001 vs control), whereas liraglutide co-treatment significantly increased locomotor activity (p<0.05 vs olanzapine). In the NOR test, olanzapine-treated rats spent significantly less time exploring the novel object, and this was significantly improved in the liraglutide co-treatment group (p<0.01 vs olanzapine). There was no effect of treatment on correct entries in the T-maze test (p>0.05 vs control).

Conclusion: This study demonstrates that liraglutide co-treatment can improve locomotor activity, decrease adiposity and prevent weight gain side-effects associated with olanzapine administration. Liraglutide co-treatment was able to improve recognition memory impairment caused by olanzapine treatment; however, it had no effect on working memory. Further studies are required to understand the mechanisms underlying these changes, and to elucidate whether a link exists between olanzapine-induced obesity and liraglutide’s effect on cognition.

Reference
1. Keefe, R.E., et al., Neurocognitive effects of antipsychotic medications in patients with chronic schizophrenia in the catie trial. Archives of General Psychiatry, 2007. 64(6): p. 633–647.
2. Weston-Green, K., X.-F. Huang, and C. Deng, Second generation antipsychotic-induced type 2 diabetes: a role for the muscarinic M3 receptor. CNS Drugs, 2013. 27(12): p. 1069–80.
3. Prickett, C., L. Brennan, and R. Stolwyk, Examining the relationship between obesity and cognitive function: a systematic literature review. Obes Res Clin Pract, 2015. 9(2): p. 93–113.
4. McClean, P.L., et al., The diabetes drug liraglutide prevents degenerative processes in a mouse model of Alzheimer’s disease. J Neurosci, 2011. 31(17): p. 6587–94.
5. Porter, W.D., et al., Liraglutide improves hippocampal synaptic plasticity associated with increased expression of Mash1 in ob/ob mice. International Journal of Obesity, 2013. 37(5): p. 678–84.

PM427
Histamine H4 receptor is involved in clozapine-induced hematopoietic toxicity: vulnerability under granulocytic differentiation of HL-60 cells
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Abstract
Background: Second-generation antipsychotics (SGAs), such as clozapine, are the most effective antipsychotic for treatment-resistant schizophrenia, whereas it occurs fatal hematopoietic toxicity as agranulocytosis. To elucidate mechanism of hematopoietic toxicity by clozapine, we tried to develop the in vitro assay systems using HL-60 cells, and investigated the effect on hematopoiesis.

Method: HL-60 cells were differentiated by all-trans retinoic acid (ATRA) to three states according hematopoietic process: undifferentiated HL-60 cells, under granulocytic ATRA-differentiation and ATRA-differentiated granulocytic cells. Hematopoietic toxicity was evaluated by analyzing cell survival, cell proliferation, granulocytic differentiation, apoptosis, and necrosis.

Result: In undifferentiated HL-60 cells and ATRA-differentiated granulocytic cells, clozapine (50 and 100 µM) and doxorubicin, but not olanzapine decreased survival rate. Under granulocytic differentiation for 5 days, clozapine, even at 25 µM, decreased survival rate without affecting granulocytic differentiation, increased caspase activity, and resulted in induction of apoptosis rather than necrosis. Lower concentrations of clozapine (1
and 10 μM) decreased live cell counts, but not survival rate in undifferentiated HL-60 cells and under granulocytic differentiation. Histamine H4 receptor mRNA was expressed in HL-60 cells, whereas the expression gradually decreased under granulocytic ATRA-differentiation. Thioperamide, a histamine H4 receptor antagonist or DEVD-FMK, a caspase-3 inhibitor protected clozapine-induced decrease of survival rate, but not of live cell counts. 4-Methylhistamine, a histamine H4 receptor agonist as well as clozapine decreased survival rate and live cell counts.

Conclusion: HL-60 cells under granulocytic differentiation were vulnerable for cytotoxicity of clozapine and would be in vitro assay systems for hematopoietic toxicity. Histamine H4 receptor is involved in development of clozapine-induced hematopoietic toxicity with apoptosis, and may be one of the target for preventing it in process of granulocytic differentiation.

PM428
Combination of Clozapine with Long Acting Injectable Antipsychotics in Treatment Resistant Schizophrenia: Preliminary Evidence from Health Care Utilization Indices
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Abstract
Objectives: Clozapine is indicated for Treatment Resistant Schizophrenia (TRS) yet only 30-60% of patients will respond to optimum treatment. There have been studies of clozapine augmentation with oral second generation antipsychotics (SGA) with mixed results but no studies considering the combination with long acting injectable (LAI) antipsychotics. This study attempts to establish the efficacy of the combination of clozapine and LAI antipsychotics in TRS.
Methods: A mirror-image study design was employed to review health care utilization measures 2 years pre and post combination of clozapine with a LAI (either first generation antipsychotic (FGA) or SGA) in a small sample of patients (N=20) with chronic psychotic disorders followed by the Assertive Community Treatment service in Calgary, Alberta.
Results: Paired sample t tests showed a statistically significant reduction in average ED visits in the two years post combination with an average 1.8 fewer ED visits (95%CI = [0.58 to 3.02], p=0.024). There was also a statistically significant reduction in number of hospital admissions in the 2 year post combination with a mean reduction of 0.85 admissions (95%CI = [0.36 to 1.34], p=0.008). There was no statistically significant reduction in hospital bed days between pre- and post-combination.
Conclusions: The combination of clozapine and a long acting injectable antipsychotic appears to reduce health care utilization in terms of ED visits and number of hospital admissions. Future research will investigate the effects of this combination on psychopathology and health related quality of life outcomes in this patient population.

PM429
Comparison of haloperidol and blonanserin on development of dopamine supersensitivity after chronic treatment
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Abstract
Objectives: Blonanserin (Blon) is an atypical antipsychotic drug, which has high affinity for D2R, dopamine D3 receptor (D3R), and 5-HT2A receptor and weak or very low affinity for other receptors. The present study investigated whether chronic treatment with BNS causes DSP.
Methods: Male Wistar rats (6-week-old) were orally administered haloperidol (HPD) and BNS, at doses of 1.1 mg/kg and 0.78 mg/kg, respectively, or vehicle twice daily for 28 days. These doses were equivalent to two times the 50% effective doses of HPD and BNS in a methamphetamine-induced hyperlocomotion test in rats, respectively. Seven days after drug discontinuation, a quinpirole (0.5 mg/kg, sc)-induced hyperlocomotion test or a radioligand binding assay using [3H]-raclopride for striatal D2R was conducted. We also investigated the effects of chronic treatments with HPD and BNS on D2R and D3R mRNA levels in five brain regions.
Results: Chronic treatment with HPD significantly increased locomotor activity and D2R density (i.e. Bmax) compared with vehicle treatment. In contrast, chronic BNS treatment did not affect both locomotor activity and D2R density. There were no changes in D3R and D3R mRNA levels in chronic HPD- and BNS-treated groups, respectively.
Conclusion: The present results suggest that long-term treatment with BNS is less likely to cause DSP compared to treatment with the typical antipsychotic drug, HPD.

PM430
Blonanserin reversed phencyclidine-induced novel object recognition deficit and induced cortical dopamine and acetylcholine efflux through dopamine D3 receptor antagonism
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Abstract
Objectives: Blonanserin (Blon) is an atypical antipsychotic drug (AAPD) with comparable affinity to D2 and D3 receptors. The purpose of this study was to determine the ability of Blon to enhance cortical neurotransmitters efflux, determine the role of D3 receptor antagonism in that process, and determine the role of D3 receptor blockade to improve the deficit in novel object recognition (NOR) in sub-chronic phencyclidine (PCP)-treated rats, a model of schizophrenia.
Methods: Guide cannula with dummy probes were placed to the medial prefrontal cortex (mPFC) and dorsal striatum (dSTR) for microdialysis in mice. Rats received vehicle or PCP for 7 days, followed by a 7-day washout for the NOR study. The D3 receptor antagonist, NGB2904 (NGB) or Blon was administered to rats 30min prior to acquisition. Another group of rats received a combination of sub-effective doses (SED) of NGB and Blon.
Results: Blon increased DA, norepinephrine (NE) and Ach efflux in mPFC and dSTR. NGB increased DA and Ach, but not NE efflux,