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Effect of a glucagon-like peptide 1 (GLP-1) receptor agonist, liraglutide, on cognition and body weight during antipsychotic treatment

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Effect of a glucagon-like peptide 1 (GLP-1) receptor agonist, liraglutide, on cognition and body weight during antipsychotic treatment

Abstract
abstract of poster that was presented at the 30th CINP World Congress of Neuropsychopharmacology, 3-5 July, Seoul, Republic of Korea.

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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 suicidality. 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.

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PM427

Histamine H4 receptor is involved in clozapine-induced hematopoietic toxicity: vulnerability under granulocytic differentiation of HL-60 cells

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Abstract

Objective: Clozapine is 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

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