For this, we measured functional connectivity by using resting MRI and presynaptic dopamine capacity by using [18F]DOPA PET in healthy volunteers (n=12) and patients with schizophrenia who were treated with first-line antipsychotic drugs (n=12) and clozapine (n=12), respectively.

Clozapine group showed lower ki values from [18F]DOPA than other groups and functional connectivity from resting MRI was negatively correlated with ki values. This might suggest that clozapine might make the functional connectivity stronger, leading to reduced presynaptic dopaminergic synthesis.

**PM439**

Chronic effects of aripiprazole on the GSK3β-dependent pathways, NMDA receptor and CREB1 in the rat brain

Bo Pan*a, Xu-Feng Huangb, Chao Deng*a

*a Antipsychotic Research Laboratory, Illawarra Health and Medical Research Institute, Wollongong, 2522, NSW, Australia  b Centre for Translational Neuroscience, School of Medicine, University of Wollongong, Wollongong, 2522, NSW, Australia

**Abstract**

**Background:** Aripiprazole is a D2 receptor (D2R) partial agonist with a favourable clinical profile, compared with other antipsychotics. Previous in vivo studies indicated that acute and short-term administration with aripiprazole affected the GSK3β (glycogen synthase kinase 3β)-dependent pathways, NMDA receptor and CREB (cAMP-dependent element-binding protein 1), which may contribute to its therapeutic efficacy. Aripiprazole is widely used for chronic treatment of various mental disorders, however the chronic effects of aripiprazole on cellular signalling are not clear.

**Aim:** The present study investigated the chronic effects of aripiprazole on the relevant signalling pathways, in comparison with haloperidol (a D2R antagonist) and bifeprunox (a potent D2R partial agonist).

**Method:** Rats were orally treated with aripiprazole (0.250 mg/kg), bifeprunox (0.267 mg/kg), haloperidol (0.033 mg/kg) or vehicle three times per day for 10 weeks. The levels of Akt (protein kinase B)-GSK3β, Dvl (dishevelled)-β-catenin, NMDA-CREB1 signalling pathways were measured in the prefrontal cortex (PFC), caudate putamen (CPU) and nucleus accumbens (NAc) by Western Blots.

**Results:** Akt-GSK3β pathway was activated by both aripiprazole and haloperidol in the PFC, and by all three drugs in the NAc. Both aripiprazole and haloperidol increased the expression of Dvl-3 and β-catenin in the NAC. Both aripiprazole and haloperidol increased NMDA NR1 expression and CREB activity in the NAC; aripiprazole also promoted NMDA NR2A expression and CREB activity in the NAc. Both aripiprazole and bifeprunox increased the expression of Dvl-β-catenin and NMDA-CREB1 in the PFC, and by all three drugs in the NAc.

**Conclusion:** All drugs tested had chronic effects on Akt-GSK3β signalling. Aripiprazole and haloperidol had similar effects on Dvl-β-catenin and NMDA-CREB1 signalling in the NAC, which indicates that a D2R partial agonist with relatively low intrinsic activity may affect Dvl-β-catenin and NMDA-CREB1 signalling. The chronic effects of aripiprazole on these signalling pathways may contribute to its long-term clinical efficacy.

**PM441**

Long term atypical antipsychotic treatment improves cognitive performance in schizophrenia but not surpassing conventional antipsychotic drugs effects.

Gabriel Selva Vera (1), Aroa Borrás Barrachina (2).

(1) Teaching Unit of Psychiatry and Psychological Medicine. University of Valencia (Spain). (2) University Jaime I, Castellón (Spain).

**Abstract**

**Background and Objectives:** Atypical antipsychotics provide better control of the negative and affective symptoms of schizophrenia when compared with conventional neuroleptics. Nevertheless, their heightened ability to improve cognitive dysfunction remains a matter of debate. This study aimed to examine the changes in cognition associated with long-term antipsychotic treatment and to evaluate the effect of the type of antipsychotic (conventional versus novel antipsychotic drugs) on cognitive performance over time.

**Methods:** In this naturalistic study, we used a comprehensive neuropsychological battery of tests to assess a sample of schizophrenia patients taking either conventional (n = 21) or novel antipsychotics (n = 32) at baseline and at two years after.

These tests were used to measure seven neurocognitive domains, (Executive Functions, Working Memory, Verbal Memory, Visual Memory, Visual-Motor Processing, Semantic Verbal Fluency and Motor Speed).

The clinical evaluation of each patient was rated according to the Positive and Negative Symptom Scale and to the Hamilton Rating Scale for Depression. Premorbid adjustment was assessed using the Phillips Adjustment Scale.