Efficacy of AUT6, a novel and selective Kv3 channel modulator, to alleviate cognitive and neurobiological dysfunction in the sub-chronic PCP rat model of schizophrenia symptomatology

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Introduction

Schizophrenia is a chronic psychiatric disorder affecting 1% of the population. Although positive symptoms are reasonably well controlled by current medication, cognitive dysfunction and negative symptoms remain poorly treated. Development of improved treatments with efficacy across the spectrum of symptoms and a lower side effect burden is therefore of the utmost importance.

Preliminary data have shown that the voltage-gated ion channel Kv3, mainly expressed on Parvalbumin (PV) GABAergic interneurons, is closely involved in brain circuitry thought to be affected in schizophrenia. Indeed, reduced Kv3.1b channel expression was recently reported in neocortex of untreated patients. Thus, novel Kv3 channel modulators may provide an improved therapeutic strategy for certain symptom domains.

In animals, sub-chronic administration of the NMDA receptor antagonist, Phencyclidine (PCP), has been shown to produce robust cognitive and social behaviour deficits of relevance to schizophrenia. The effects of AUT6 were no longer observed after 1 and 7 days of washout. Our aim here is to explore efficacy of chronic treatment with AUT6 (p.o.; 60 mg/kg) to improve cognitive and neurobiological deficits in the rat PCP model.

Methods

Results

Conclusions