Neuropharmacological Profile of an Atypical Antipsychotic, NRA0562

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ABSTRACT

Schizophrenia is a serious and disabling psychiatric disorder affecting approximately 1% of the world’s population. A new generation of atypical antipsychotics has been introduced over the past decade. These atypical antipsychotics have comparable or greater efficacy than traditional antipsychotics in the treatment of the psychotic symptoms of schizophrenia and a much improved neurologic side effect profile. This paper reviews the pharmacological efficacy and safety of a potential atypical antipsychotic, NRA0562.

NRA0562 has a high affinity for dopamine D1, D2L, D4, 5-HT2A receptors as well as α1-adrenoceptors, and has a moderate affinity for H1 receptors. NRA0562 strongly binds to 5-HT2A receptors and α1-adrenoceptors in the frontal cortex, its binding to striatal D2 receptors is weaker, similar to that of clozapine.

NRA562 displayed potent antipsychotic activities in animal models of schizophrenia, such as methamphetamine (MAP)-induced hyperactivity, apomorphine-induced disruption of pre-pulse inhibition and conditioned avoidance test. NRA0562 is more potent in reversing the inhibitory effects of MAP at A10 than at A9 dopamine neurons. It increased Fos-like immunoreactivity in the nucleus accumbens more effectively than in the dorsolateral striatum, indicating that NRA0562 has the profile of an atypical antipsychotic. In vivo assays for extrapyramidal side effect liability showed that NRA0562 has a low rate of neurological side effects. Thus, NRA0562 may have unique antipsychotic activity with a lower propensity for extrapyramidal side effects.