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Abstract

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Does Olanzapine change Orexin A expression?

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Schizophrenia is a serious mental illness that today is treated with second generation atypical antipsychotic drugs such as Olanzapine. Second generation atypical antipsychotic drugs have a lower incidence of extrapyramidal side effects than the first generation of antipsychotic drugs. Unfortunately, they also have distinct metabolic side effects in up to 80% of treated patients. Numerous studies have investigated the central and peripheral side effects of atypical antipsychotics in rodents as well as humans. The mechanisms underlying the dysmetabolic effects of the atypical antipsychotics are, however, still not fully understood. This study aims to investigate the effects of Olanzapine in the lateral hypothalamus of female rats that have been treated with Olanzapine or vehicle for 2 days (acute). This study is a part of a bigger project investigating Olanzapine's effect on the entire appetite regulating center in the hypothalamic region of the brain.

Immunohistochemistry was used to visualize Orexin A neuropeptides in rat brain sections, cut in 50 µm thick sections and sampled across the entire lateral hypothalamic region. The region of interest, lateral hypothalamus, was delineated in all sections, and a *z*-axis analysis was performed to test for staining penetration, shrinkage and loss of cells. The number of Orexin A neuropeptide expressing neurons were quantified using the optical fractionator. In addition, Orexin A concentrations in rat plasma has been quantified using competitive enzyme immune assay (EIA). The EIA results revealed that there was no significant difference between Olanzapine and vehicle treated rats. This indicates that peripheral levels of Orexin A are not associated with the dysmetabolic side effects of Olanzapine.

This study will hopefully result in better understanding of the side effects of atypical antipsychotic drugs which can help develop a more specific medical model for Schizophrenic patients using atypical antipsychotic drugs.