

**NUS Graduate School for Integrative Sciences and Engineering  
Research Project Write-up**

**Title of Project :** Mechanisms of action and adverse effects of atypical antipsychotic drugs

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**Short Description**

1 in 100 people have schizophrenia and require treatment with antipsychotic drugs for much of their adult life. Major problems with current antipsychotics medications include limited efficacy against the cognitive symptoms of schizophrenia and adverse side effects including weight gain and diabetes.

**Cognitive effects of atypical antipsychotics:** We are investigating the pharmacology of the effects of antipsychotics on hippocampo-prefrontal cortical-dependent functions. Experiments involve both behavioural studies of cognitive function (e.g. Morris water maze tasks) and measures of synaptic plasticity (e.g. long-term potentiation) in hippocampo-prefrontal cortical pathways. Interested students would also have the opportunity to interact with the Department of Electrical & Computer Engineering in the development of novel techniques to analyze data on brain activity and neuronal firing on this project.

**Weight gain and metabolic syndrome:** More than 1 in 100 people need to take antipsychotic medications for much of their lives, yet the newest and most effective of these medications, the atypical antipsychotic drugs, cause weight gain and related problems such as diabetes, high blood pressure and heart disease. One of the effects of these drugs appears to be to make people eat more, particularly in binges. We have recently discovered that these drugs activate a cluster of cells in the brain that release relaxin-3, a newly discovered small protein related to insulin which is involved in the control of appetite and eating. We will use rodent models to further understanding of the role of these cells in the weight gain caused by atypical antipsychotic drugs. Understanding the mechanisms by which these drugs cause weight gain will help the future development of better antipsychotic drugs. Knowledge of how these drugs cause the relaxin-3 releasing cells to fire may also lead to the development of new drugs that can treat severe obesity.