

Date of submission: 29/10/2007  
Project title: Investigation into  
Predictive Error Signal Abnormality  
in Psychiatric Disorders.

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## SINAPSE PhD Project Proposal Template for PhDs starting in 2008

**SINAPSE Centre (i.e. primary university to which this studentship will be attached\*):**

University of Aberdeen

**First supervisor: contact details**

**Name:** Dr Douglas Steele  
**Department:** Department of Mental Health, University of Aberdeen  
**Address:** Clinical Research Centre, Royal Cornhill Hospital, Aberdeen  
**Email:** d.steele@abdn.ac.uk **phone:** 01224-557-602

**Second supervisor: contact details**

**Name:** Dr Jeremy Hall  
**Department:** Department of Psychiatry, University of Edinburgh  
**Address:** Kennedy Tower, Royal Edinburgh Hospital, Edinburgh  
**Email:** Jeremy.hall@ed.ac.uk **phone:** 0131-537-6313

**Speciality of first supervisor:**

Psychiatry (mood disorder) , fMRI  
quantitative models of dopamine

**Speciality of second supervisor:**

Psychiatry (schizophrenia), fMRI  
neuroscience of associative learning

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### PROJECT

**Title:**

Investigation into Predictive Error Signal Abnormality in Major Depression and Schizophrenia.

**Planned start date (year of intake):**

2008

**Likely background of suitable student (eg. Neuroscience, MR Physics, Chemistry, Psychology) and essential skills required prior to starting this PhD:**

The successful candidate will require a background in mathematical/computational studies/modelling and have a strong interest in applying these techniques to psychiatric disorder neuroscience research. The successful candidate will not have to recruit patients, nor be involved with their treatment or undertake clinical assessment, as this will be done by medically qualified collaborators. However, they will be expected to assist with the image acquisition. Statistical analysis of fMRI data and computational modelling of dopamine will be a central feature of their project. Previous experience of fMRI analysis is not required as training will be provided.

\*usually this would be the university in which the first supervisor is based.

**Summary of proposed project (approximately 200 words):**

There is robust empirical clinical evidence that antidepressants are effective treatments for patients with a moderate to severe depressive illness. There is similarly robust clinical evidence for the efficacy of antipsychotics in patients with schizophrenia. Nevertheless, whilst antidepressants have a common action of increasing monoamine levels, and antipsychotics have a common action of dopamine blockade, there are no consistent studies demonstrating that depressed patients have low monoamine levels or that schizophrenic patients have high dopamine levels. One possible explanation is that previous studies have investigated “tonic” (or long timescale) background levels of monoamines. Over the past decade, there has been considerable interest in investigating “phasic” (fast timescale) monoamine activity in humans. Building on recent clinical fMRI work (computational modelling of dopamine, *under review*) in major depression at Aberdeen University, and work on the aberrant attribution of salience to neutral stimuli in schizophrenia (*under revision, Biological Psychiatry*) at Edinburgh University, the proposed study will investigate hypothesised abnormal phasic dopamine signals in depressive illness and schizophrenia using fMRI.

**Key references (up to five):**

1. Kapur, S., 2003. Psychosis as a state of aberrant salience: a framework linking biology, phenomenology, and pharmacology in schizophrenia. *Am J Psychiatry* 160, 13-23.
2. O'Doherty, J., Dayan, P., Schultz, J., Deichmann, R., Friston, K., Dolan, R.J., 2004. Dissociable roles of ventral and dorsal striatum in instrumental conditioning. *Science* 304, 452-454.
3. Steele JD, Kumar P, Ebmeier KP (2007): Blunted response to feedback information in depressive illness. *Brain* 130:2367-2374.
4. Kumar P, Waiter G, Ahearn T, Milders M, Reid I, Steele JD (2007) “Temporal difference signals and human social group inclusion” (*under review*)
5. Kumar P, Waiter G, Ahearn T, Milders M, Reid I, Steele JD (2007) “Blunted temporal difference reward-learning signals in major depression unresponsive to antidepressant medication” (*under review*)

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**In what way does this PhD proposal meet the SINAPSE criteria as described in the call for proposals? (50 words)**

The study has been approved by Aberdeen University for a PhD but funding has not yet been obtained. The proposed project builds on existing work, is fundamentally interdisciplinary in nature, involves translating replicated neuroscience findings into clinical research, and expanding collaboration with Edinburgh University Department of Psychiatry.

**Please state the name of the local SINAPSE Centre Lead with whom you have discussed this project (Leads are listed on the Call for Proposals):**

Dr Alison Murray