

BAP *in vivo* training initiative pilot scheme

BAP launched the *in vivo* training initiative earlier this year. The pilot funding scheme was successfully run in the summer of 2009 with 4 highly-deserving recipients submitting excellent *in vivo* vacation studentship project proposals.

Full reports on the projects from the recipients appear below. The successful applicants were:

- Ros Brett, University of Strathclyde. *Cannabinoids and depression: effect of chronic delta-9-tetrahydrocannabinol on conditioned place preference to sucrose.*
- Helen Cassaday, Nottingham University. *Amended title; Testing for behavioural dissociations of the effects of catecholaminergic depletion within the medial prefrontal cortex. (original title; Does intra-accumbens amphetamine reproduce the effect of 6-OHDA depletion in a trace conditioning procedure?)*
- Michael Harte, University of Bradford. *Investigation into cognitive and pathological deficits in an animal model of schizophrenia: effects of antipsychotics.*
- Emma Robinson, Bristol University. *Effects of ADHD medications on performance in the stop signal reaction time task for rats.*

Each of those named above received £500 from BAP towards running the project and also paid reduced costs for animals from Harlan (www.harlan.com).

The scheme will be expanded in 2010. Details will be available on the website soon and the deadline for applications will be 1st April.

Jo Neill and Mohammed Shoab

Reports from 2009 Projects:

Cannabinoids and depression: effect of chronic Δ^9 -tetrahydrocannabinol (Δ^9 -THC) on conditioned place preference to sucrose

Student; Deborah Clark

Deborah Clark has just entered final year of a Biomedical Sciences and Psychology degree at Strathclyde, specialising on the biomedical sciences side in pharmacology. This summer we obtained funding under the BAP's *In vivo* Training Initiative for a project studying the effect of cannabinoid treatment on measures of anhedonia in mice. Deborah wished to have experience of an *in vivo* pharmacology project to complement her psychology dissertation in which she plans to do empirical human research. For my part, I wanted to investigate if we could condition a place preference to sucrose to use as a measure of anhedonia. We already use the sucrose preference test in mice, but a second methodology would be invaluable. From elsewhere we obtained funding for Deborah's living costs from elsewhere, but not for animal costs and consumables – the most expensive aspect of doing *in vivo* research. So we were delighted to get the BAP funds!

Deborah gained her Home Office licence, and administered drugs and carried out behavioural testing. More importantly, she learnt a great deal about validation and optimisation of behavioural methodology, as the method proved less than easy. In the end we failed to 'get it working' in the six weeks available (what behavioural scientist will be surprised about that?), but produced lots of ideas for improvement. From my point of view it was an opportunity to try something out, and I plan to continue working on it this autumn. We went on to test mice chronically treated with Δ^9 -THC in the sucrose preference test, and found that chronic treatment with the cannabinoid tended to increase sucrose preference. This requires repetition and further investigation, but suggests that mice are more sensitive to reward after chronic cannabinoid – which could argue for a 'gateway' effect of cannabis. Certainly it would not be consistent with a depression-inducing effect of cannabis use.

Deborah will leave the University with an accredited degree in psychology but has also gained valuable experience in *in vivo* pharmacology, an excellent combination towards a future career. We are most grateful to the Association for facilitating this.

Dr Ros Brett
Strathclyde Institute of Pharmacy and Biomedical Sciences
University of Strathclyde

Testing for behavioural dissociations of the effects of catecholaminergic depletion within the medial prefrontal cortex.

Student; Molly Cooper. Supervised by Andrew Nelson and Helen Cassaday; School of Psychology, University of Nottingham.

Nottingham School of Psychology was delighted to be in receipt of funding under the new BAP *in vivo* training initiative. This was used in partial support of one of our second year undergraduates, Molly Cooper. The School regularly supports up to 8 summer interns. In this case, Molly was also in receipt of a Wellcome Trust Biomedical Vacation Scholarship that provided her stipend, topped up by the School to our standard rate of payment.

The laboratory work on the neuropharmacological substrates of associative learning and memory in the rat was part of an ongoing project supported by the Wellcome Trust (ref. 082940). The BAP funding contributed to the maintenance of 60 rats over 9 weeks

Over the course of her 8 week internship, Molly observed surgery and provided invaluable assistance with our post-operative care regime. Then, under delegated Home Office Licence authority, she assisted with a series behavioural tests, including conditioned emotional response procedures and object recognition variants. Karen Thur will complete the assay on the lesions (by HPLC) in due course. The behavioural results are very promising and we look forward to feeding back full details to BAP when the work is submitted for publication. The results will also be presented to the membership at the summer meeting 2010.

Molly is now entering her final year of Psychology at Nottingham. As a matter of course, we offer final year projects in a different area of training so it is too soon to say whether Molly will apply for a PhD in the area of training provided by her internship. Prospective PhD supervisors who may have a suitable project are invited to contact Molly via Nottingham Psychology (lpybmtc1@nottingham.ac.uk). She is due to graduate summer 2010.

Dr Helen Cassaday October 2009

My experience as a psychopharmacologist

Molly Cooper

One of the most interesting aspects of the research was the surgery performed on the animals in the first weeks of the internship. Although text books describe pharmacological manipulations in general terms, observing surgery made me appreciate the selectivity that is now possible. I observed the precision required for each surgery, this was especially evident during location of co-ordinates (from the atlas of Paxinos and Watson) in relation to bregma and the dura mater.

A second aspect of the research that I found particularly interesting was the range of behavioural measures that can be taken in order to assess the effect of a particular pharmacological manipulation. Within the single project all animals were tested in a LI conditioning procedure, a trace interval conditioning procedure, three tests of object memory (measuring novel object recognition, spatial memory, and temporal order memory), and in tests of activity in the Elevated Plus Maze (EPM).

During my internship I gained a range of skills. At the beginning of the internship I was trained in animal handling and weighing. Though weighing may seem a relatively simple skill, accurate recording of daily weights is important since weight-loss may indicate ill health in the animal, especially post-surgery. During the surgery I was responsible for the set-up of the post-operative care room (including a specific food mix and recovery cage set up) and behavioural checks while the animals were recovering.

I was trained in the use of conditioning chambers. This included testing of the equipment, placing the animals into the boxes and removing them, initiating the specific computer program, and recording the data. During the course of the project I was able to assist with the running of two different conditioning procedures using the conditioning chambers. As such, I gained a practical understanding of how different conditioning procedures are conducted in a controlled environment through use of operant chambers.

I was also trained in several methods of behavioural testing. I assisted with running tests of novel object recognition, spatial memory for object place, and temporal order memory for relative recency of objects. The behavioural testing in particular made me aware of the need for attention to all potential confounding variables when conducting experiments; for example, in order to avoid odour cues the test arena and all objects were cleaned with an alcohol solution between all trials. After having been trained on behavioural tests based on object memory, I was able to independently conduct behavioural tests of activity in the Elevated Plus Maze (EPM). Throughout the scholarship, it was working and testing independently that gave me an understanding of the sense of responsibility that a researcher feels; it is the researcher who is responsible for the safety of their participants, for ensuring that variables are controlled, and ultimately for the validity of the data collected.

Molly Cooper October 2009

Investigating behavioural and pathological changes in the sub-chronic phencyclidine animal model.

Student; Samuel Marsh (Samuel has just started the final year of his Biomedical Science degree) joined my laboratory in June 2009. Samuel was funded by a Wellcome Trust Summer Studentship.

Samuel has always indicated to me his interest in the area of in vivo research. With this in mind we initiated a project that would provide him with the opportunity to engage in a programme of work that involved both in vivo behavioural studies and ex vivo work involving post-mortem tissue analysis, using standard immunohistochemical techniques followed by microscopic analysis. Throughout the summer Samuel has worked hard on the immunohistochemical aspects of the project. Alongside these studies Samuel was been trained in a number of in vivo behavioural techniques (e.g. novel object recognition, hole board, attentional set shifting, reversal learning). As part of his degree programme the student will return to my laboratory to do his final year project in January 2010.

Throughout the summer Samuel has observed all of the behavioural techniques used in the laboratory. As Samuel has demonstrated a commitment to this area of research we utilised the project funds from the BAP to get Samuel a personal licence (including the appropriate training courses) from the home office. With this in place he will be responsible for conducting his own behavioural project, commencing in January 2010. This will be mainly focused on in vivo behavioural studies.

The funds from the BAP have provided Samuel the opportunity to get the appropriate training and licences to undertake his own in vivo project in January 2010. It is Samuel's intention to pursue a PhD in this area in the future.

Brief summary of results/conclusions

Samuel has been fully trained in conducting both behavioural and pathological studies. In terms of the pathological studies he has found deficits in parvalbumin neurons in the phencyclidine model, two weeks post dosing. He is currently investigating the density of these neurons, eight weeks post phencyclidine.

Dr Mike Harte October 2009

Effects of atomoxetine and reboxetine on the stop-signal reaction time task and the stop-change task.

Student: Christian Wood is on an MSci programme and has now started his third year industrial placement at GSK where he will be continuing *in vivo* work

Funding: The funds provided by the BAP were used to contribute to the maintenance costs for the animals used in the study. We also purchased a new cohort of animals to start operant training using the scheme set-up with Harlan UK. This provided us with a 50% reduction in the price of the animals.

Project overview and outcomes: This project aimed to investigate the actions of noradrenaline re-uptake inhibitors on performance variables in an operant task to test the ability of rats to stop an already initiated motor response. The first series of experiments undertaken compared results for atomoxetine and reboxetine in the stop task. The second series of experiments also compared results for atomoxetine and reboxetine but using a stop-change task where rats were required to stop the go response and switch to making a response in an alternative location. A final experiment looked at the training procedure for a new cohort of rats. Analysis of the results is still ongoing but the outcomes for the basic task variables revealed that both drugs acted in a similar manner suggesting that their effects in the stopping process involve actions at the noradrenaline re-uptake transporter.

In the standard stop task, atomoxetine and reboxetine induced dose-dependent improvements in stop accuracy but also slowed the animals' reaction time and tended to reduce go accuracy. Although these data support the hypothesis that actions at the noradrenaline re-uptake transporter improve stopping of an already initiated motor response, there were non-specific effects on other variables at the doses used. As part of this project, we also examined the actions of atomoxetine and reboxetine on performance in a stop change task. The basic task is the same as the SSRT task but in this case, presentation of the stop cue is paired with the animals stopping their response in one location and switching to respond in another location. This provides the same outcome measures as the SSRT task but also allows for a stop-change time and anticipatory stops to be recorded. In this pilot study atomoxetine and reboxetine were used at lower doses than the SSRT task and improved stop accuracy was observed but a slowing of reaction time and reduced go accuracy occurred at the higher dose tested. No significant effects on stop change or anticipatory stop were observed but this cohort showed a high level of variability and the study lacked overall power. Overall, this study was a useful comparison of noradrenaline re-uptake inhibitors and two methods to assess stopping in rats. Further work is needed to determine if lower doses can induce a selective effect on stopping without slowing the go reaction time and reducing go accuracy.

Dr Emma Robinson October 2009
