OMB No. 0925-0001 and 0925-0002 (Rev. 03/2020 Approved Through 02/28/2023)

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.  
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Panayi, Marios Chris

eRA COMMONS USER NAME (credential, e.g., agency login): PANAYIMC

POSITION TITLE: Postdoctoral IRTA Fellow

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)

| INSTITUTION AND LOCATION | DEGREE  (if applicable) | Completion Date  MM/YYYY | FIELD OF STUDY |
| --- | --- | --- | --- |
| University of New South Wales (UNSW), Sydney, Australia | BA(Hons) | 03/2010 | Psychology |
| University of New South Wales (UNSW), Sydney, Australia | PHD | 07/2015 | Psychology |
| University of New South Wales (UNSW), Sydney, Australia | Teaching | 12/2015 | Psychology |
| University of Oxford, Oxford, United Kingdom | PostDoc | 02/2020 | Learning and Decision Making |
| National Institute on Drug Abuse Intramural Research Program | Visiting Fellow | Present | Cellular Neurobiology |

**A. Personal Statement**

**Through many experiences in my academic and personal life, I have developed a keen interest in studying the neural and psychological mechanisms of learning, motivation, and behavior. In particular, how do we come to learn about informative cues in our environment, and how do these representations inform our moment-to-moment behavior? Why am I checking the refrigerator? Why am I refreshing my twitter feed? These processes are fundamental to neurotypical and maladpative learning and behavior characteristic of most neuropsychiatric disorders. I focused on these issues in my first independent undergraduate research thesis in the lab of Dr. Simon Killcross at UNSW, Australia. There I studied how failed feedback from informative cues could be used to model compulsive behaviors in animal models of obsessive-compulsive disorder. This work received the Australian Psychological Society prize and helped me establish a strong background in designing and testing novel behavioral procedures. A desire to understand these processes further led me to study the orbitofrontal cortex (OFC) in the same laboratory, where I learned stereotaxic surgery to perform lesions and micro infusion techniques. My graduate thesis was awarded the The Paxinos Neuroscience Prize and resulted in publications demonstrating greater contribution of the OFC to basic learning phenomena than had previously been thought, and the existence of novel subdivisions within classically defined OFC subregions. During this time, I also collaborated with Dr. Fred Westbrook and Dr. Nathan Holmes to understand how other neural and neurochemical systems contribute to cue-based control of behavior such as the role of benzodiazepines in extinction therapy, oxytocin signaling in the amygdala regulates fear, and nicotine self-administration which resulted in co-authorship on three publications. Throughout my graduate career I also acquired a strong background in statistics and research methods, which started with teaching in undergraduate and postgraduate courses, and led to being hired to develop and teach a new course in statistics and critical thinking.**

**My graduate experience left me with a desire for a finer grained understanding of the relationship between the brain and behavior. This led me to move continent to Europe where I joined the labs of Dr. Mark Walton and Dr. David Bannerman at the University of Oxford to learn how to record real-time dopamine signaling using fast-scan cyclic-voltammetry (FCV) in striatum, to understand how cue learning is disrupted in genetically modified mouse models of aberrant attention in schizophrenia. While some of this work is ongoing, a number of publications from this work have been written up and submitted to journals and I expect they will be published soon. I directly supervised a number of graduate students during my postdoc and continued to teach statistics and research methods. During this time, I also acquired new skills to extend the findings from my graduate work which resulted in three publications. I learned neuroanatomical tracing techniques to provide further evidence of novel subdivisions within OFC and collaborated to develop a novel computational model of OFC function.**

**I am well suited to fill my role in this project for several reasons. First, I have expertise in animal behavioral testing, including extensive experience developing successful novel behavioral assays. I also have experience with behavioral pharmacology and translational models of neuropsychiatric disorders. I have mastered stereotaxic surgery in rats and mice to lesion, infuse viruses and tracers, implant cannula, and FCV microelectrodes for stable chronic in-vivo recordings. Indeed, there are very few labs that have been able to successfully record FCV signals in freely behaving mice. I also have experience and statistical expertise working with large and complex multivariate data sets that are generated when continuously recording signals from a behaving animal. Finally, I have expertise in studying OFC function. A key component of my training in the Schoenbaum lab and this proposal is learning in-vivo electrophysiology. Since accessing the laboratory, I have already begun pilot testing behavior and learning to assemble and implant microelectrode arrays and microdrives. Critically, all the research proposed will enhance my training while building on many areas of in which I already have experience. Being awarded a CCB fellowship will provide me with an opportunity build on my strengths and acquire new skills to advance my career in research, teaching and mentoring.**

**My productivity has been impacted by the SARS-CoV-2 pandemic. I moved continent to start a second position as a NIDA IRP Visiting Fellow and flew into the US on March 16th, 2020 a day before international travel restrictions. I was then required to quarantine for two weeks. During this time, in person government services were suspended, which prevented me from acquiring a social security number and access to NIDA facilities until early November of 2020. During this time my productivity and access to necessary computing resources was significantly limited. I am aware that many have been significantly impacted by this pandemic, I only raise this to highlight the additional barriers that I experienced because of the unfortunate timing of moving to a new country during the pandemic.**

**B. Positions and Honors**

**Positions and Employment**

**2010 - 2014 Undergraduate course tutor and lecturer, UNSW**

**2014 Teaching and Research Fellow, UNSW**

**2015 Curriculum Development and Postdoctoral Fellow**

**2016 - 2020 Postdoctoral Research Associate in Learning and Decision Making, University of Oxford**

**2020 - present Visiting Fellow, Division of Intramural Research, National Institute of Drug Abuse**

**Other Experience and Professional Membership**

**2009 - 2010 Member, Australian Psychological Society**

**2012 Member, Society for Neuroscience**

**2012 Member, Society for Neuroeconomics**

**2012 Member, Pavlovian Society**

**Honors**

**2008 - 2009 The Faculty of Science Dean’s List, UNSW**

**2009 Graduated Hons. Class 1, and awarded the University Medal in Psychology, UNSW**

**2009 The Australian Psychological Society Prize**

**2010 - 2013 Australian Postgraduate Award**

**2010 - 2013 UNSW Research Excellence Award**

**2012 Postgraduate Research Support Scheme Travel Award, UNSW**

**2012 Postgraduate Research Competition, UNSW**

**2016 The Paxinos Neuroscience Prize, PhD thesis UNSW**

**2017 Vice-Chancellor’s Award for Outstanding Contributions to Student Learning, UNSW**

**2018 Monitoring Molecules in Neuroscience Short Oral Communication Award**

**C. Contributions to Science  
URL to a full list of my published work:** [*https://pubmed.ncbi.nlm.nih.gov/?term=Panayi+MC&cauthor\_id=30044220*](https://pubmed.ncbi.nlm.nih.gov/?term=Panayi+MC&cauthor_id=30044220)

**The role of the orbitofrontal cortex in simple and complex environments:** My graduatework tested the dominant idea that the orbitofrontal cortex (OFC) is critical for behavioral flexibility in complex environments, with changing contingencies or multiple cues and/outcomes, but not for simple, single cue-outcome learning. First, I addressed this using both pre- and post-training excitotoxic lesions and muscimol-inactivation of rodent lateral OFC in a simple single Pavlovian cue-reward procedure. I found that pre-training lesions enhanced behavior, whereas post-training lesions and inactivation suppressed behavior. Importantly, given the surprising nature of these results to the field, I demonstrated the reliability and relevance of these effects confirming other standard OFC effects in this preparation and replicated it multiple times with multiple cue modalities. I then confirmed these effects on behavioral expression rather than learning using an associative blocking design. In a separate study, I found that inactivation of OFC disrupted a simple cue-no outcome extinction learning between-sessions, but not within-session extinction, contrary to OFC model predictions. During my postdoc, I sought out a collaboration with Dr. Mehdi Khamassi at the Sorbonne Université to develop a computational model to account for these findings by proposing the OFC as an arbitrator between model-based and model-free reinforcement learning mechanisms. This work has been accepted and will be published in the next edition of the journal. For all these projects I performed all procedures, data analysis, and manuscript preparation.

* + **Panayi MC\*,** Killcross S. Orbitofrontal cortex inactivation impairs between- but not within-session Pavlovian extinction: An associative analysis. Neurobiol Learn Mem. 2014;108:78–87. PMID: 23954805
  + **Panayi MC\*,** Killcross S. The role of the rodent lateral orbitofrontal cortex in simple Pavlovian cue-outcome learning depends on training experience. Cereb Cortex Commun. 2021;(November 2020):1–14.
  + **Panayi MC\*,** Khamassi M**\***, Killcross S. The rodent lateral orbitofrontal cortex as an arbitrator selecting between model-based and model-free learning systems. Behav Neurosci. 2021; *In Press*.

**Defining novel anterior and posterior subregions within the lateral orbitofrontal cortex.** The rodent lateral orbitofrontal cortex (LO) is the primary experimental target of most orbitofrontal cortex (OFC) research. During my graduate work, I showed that discrete anterior and posterior LO lesions had dissociable effects on the two cardinal OFC sensitive tasks, outcome devaluation and reversal learning. I followed up this work during my postdoc at Oxford using retrograde tracing, by showing that projections to anterior and posterior LO are as distinct as projections to the anatomically adjacent ventral OFC. I conceived of the experiments, performed all procedures, data analysis, and manuscript preparation for these studies. The neuroanatomical work was shared in collaboration with a graduate student I was supervising. These findings are the first demonstration of functionally and neuroanatomically distinct subregions within LO along the anterior-posterior axis and the implications of these findings were proposed in a review. We argued that the field of OFC research often fails to distinguish between classically defined OFC subregions (e.g. ventral, lateral, dorsolateral, and medial), which may account for conflicting results that have been reported. Furthermore, there is now emerging evidence that there are functionally and anatomically distinct OFC subregions along the anterior-posterior axis in rodents, and primates that must also be considered. These ideas will refine how OFC research is conducted and performed. I co-wrote the manuscript as the senior author with the graduate student. This work has been accepted and will be published in the next edition of the journal.

* + **Panayi MC\***, Killcross S. Functional heterogeneity within the rodent lateral orbitofrontal cortex dissociates outcome devaluation and reversal learning deficits. Elife. 2018 Jul 25. PMID: 30044220
  + Barreiros I V**\***, **Panayi MC\*,** Walton ME. Organization of Afferents along the Anterior-posterior and Medial-lateral Axes of the Rat Orbitofrontal Cortex. Neuroscience. 2021 Apr 15; 460:53–68. PMID: 33609638
  + Barreiros I V**\***, Ishii H, Walton ME, **Panayi MC.** Defining an orbitofrontal compass: functional and anatomical heterogeneity across anterior-posterior and medial-lateral axes. Behav Neurosci. 2021; *In Press*.

**Glutamatergic and dopaminergic models of aberrant salience in psychosis and schizophrenia.** The primary focus of my postdoctoral work at Oxford looked explored aberrant salience, a model of inappropriate attention to cues that is thought to underly psychosis in schizophrenia. Aberrant salience models predict that patients fail to reduce attention to irrelevant cues. In my first project, I created a novel task to measure levels of attention paid to specific cues or contexts in models of psychosis. My data show that classic dopaminergic models like amphetamine caused general increases in arousal and attention, whereas glutamatergic models likeGluA1-receptor KO mice (GluA1-KO) and MK-801 (dizocilpine; an NMDA receptor antagonist) caused stimulus specific increases in attention. In my second project, I found novel evidence showing how dopaminergic dysfunction in psychosis can be a secondary consequence of glutamatergic dysfunction. Measuring striatal dopamine using fast-scan cyclic voltammetry in anaesthetized and awake behaving animals, I found that administration of metabotropic glutamate receptor agonist LY354740 in rats and GluA1-KO mice had abnormally high dopamine responses that correlated with abnormally high attention to specific cues. These findings show for the first time how glutamatergic dysfunction can lead to a behaviorally relevant hyperdopaminergic phenotype thought to underlie increased attention in aberrant salience. In a third project, I showed that the aberrant salience phenotype found in GluA1-KO mice can lead to the formation of inappropriate associations between cues using a sensory preconditioning paradigm. I found that GluA1-KO mice were more likely to form inappropriate associations between cues when there were multiple cues within the session, but enhanced association formation when no competing cues were present. Together, these projects show how glutamatergic dysfunction thought to underlie psychosis can create increased attention to specific cues that is tied to hyperdopaminergic midbrain signaling and inappropriate cue i.e. direct tests of the mechanisms thought to underlie aberrant salience in schizophrenia. During these projects I supervised 4 masters students and a graduate student. I performed all procedures, data analysis, and manuscript preparation in these studies independently as well as in collaboration with the graduate student. These projects have recently been completed and manuscripts have been completed or submitted. Corresponding presentation of these projects at conference proceedings cited below.

* + **Panayi, M. C.\*, Jahans-Price, T., Boerner, T., Huber, A., Harrison, P. J., Walton, M. E., Bannerman, D. M., (2017). Glutamatergic dysfunction leads to a hyper-dopaminergic phenotype: Aberrant salience and aberrant actions. Associative Learning Symposium (XXI), Gregynog Hall, Cardiff, UK.**
  + **Panayi, M. C.\*, Jahans-Price, T.\*, Boerner, T., Huber, A., Walton, M. E., Bannerman, D. M., (2018). Glutamatergic dysfunction leads to a hyper-dopaminergic phenotype: Linking dopamine to aberrant salience. Monitoring Molecules in Neuroscience, Oxford, UK.**
  + Blackmore, T., Stahr, L. B., Samborksa, V., Gilmour, G., Walton, M. E., Bannerman, D. M., **Panayi, M. C.** (2019). Fractionating aberrant salience in rodent models of psychosis. Society for Neuroscience, Chicago, IL, USA.

**D. Additional Information: Research Support and/or Scholastic Performance**