Australian Learning Group Christmas Workshop
11th December 2015

Chair: Ian Johnston

9:40 The roles of the perirhinal cortex and basolateral amygdala in consolidation of a sensory preconditioned association
*Nathan Holmes*, Mukesh Raipuria, & Fred Westbrook
University of New South Wales

10:00 Dopaminergic mediation of Pavlovian conditioned and unconditioned responding
*Stephanie Roughley* & Simon Killcross
University of New South Wales

10:20 Stimulation of the infralimbic cortex facilitates extinction after reconditioning and renewal
*Nura W. Lingawi*¹, Vincent Laurent¹-², & Fred Westbrook¹
¹University of New South Wales ²University of Sydney

10:40 Rats choose high doses of nicotine in compensation for and anticipation of restricted access to nicotine
*Kelly J. Clemens*, Jiajing Pan, & Nathan M. Holmes
University of New South Wales

11:00 BREAK

Chair: Nathan Holmes

11:20 Are long-term memories stored at synapses? Evidence from recent work in Aplysia
*David Glanzman*, Shanping Chen, Diancai Cai, & Kaycey Pearce
University of California, Los Angeles

11:50 Cannabis cue exposure and renewal: A pilot study
*Ellise Barnier*¹, Gabrielle Weidemann², & Melissa Norberg¹
¹Macquarie University, ²Western Sydney University

12:10 Examining human spatial navigation strategy use with a virtual reality maze
*Blake Segula*, Ian Johnston, & Frans Verstraten
University of Sydney

12:30 Latent inhibition in human nausea learning
*Veronica Quinn*, Ben Colagiuri, & Evan Livesey
University of Sydney

12:50 LUNCH

Chair: Tom Beesley

13:50 Test sensitivity in cue competition effects
*Hilary Don* & Evan Livesey
University of Sydney
14:10 Evidence for the Uncertainty Principle in Human Associative Learning
*Lara Easdale, Tom Beesley & Mike Le Pelley*
University of New South Wales

14:30 There’s nothing automatic about evaluative conditioning—a facial EMG study on the role of relationship on explicit and automatic evaluations
*Tanya Pritchard & Gabrielle Weidemann*
Western Sydney University

14:50 The influence of expectancy and sequence on reaction times and motor excitability in a Go/No Go task
*Gabrielle Weidemann¹, Amy McAndrew², Tobias Stevens², Fredrick Verbruggen², & Ian McLaren²*
¹Western Sydney University, ²University of Exeter

15:10 Learning about nothing: Examining outcome-specific inhibitory associations in humans
*Stephanie L. Quail, Vincent Laurent, & Bernard W. Balleine*
Brain & Mind Centre, University of Sydney

15:30 BREAK

Chair: Evan Livesey

15:50 Eating chow as a contributor to the delay gradient in taste aversion learning
*Bob Boakes & Dorothy Kwok*
University of Sydney

16:10 When does short-term exposure to a high-fat high-sugar diet impair object recognition memory?
*Dominic M. D. Tran & R. Frederick Westbrook*
University of New South Wales

16:30 The effects of partial reinforcement on the extinction of conditioned responding
*Jonas Chan & Justin Harris*
University of Sydney

16:50 Extinction, time and trials
*Justin Harris*
University of Sydney

17:10 DRINKS

18:00 DINNER
Abstracts

The roles of the perirhinal cortex and basolateral amygdala in consolidation of a sensory preconditioned association

Nathan Holmes, Mukesh Raipuria and Fred Westbrook
University of New South Wales

The present study examined whether fear changes how the brain stores an association between a neutral sound and a neutral light (sensory preconditioning). We focused on the roles of medial temporal lobe structures which we have previously shown to be involved in sensory preconditioning, the perirhinal cortex (PRh) and basolateral amygdala (BLA). Rats with cannulas targeting the PRh or BLA were exposed to pairings of a sound and light. These pairings occurred in a safe environment or a dangerous environment – one in which rats had been exposed to foot-shock and were fearful. Immediately after sound-light pairings, rats were infused with a drug that blocked neuronal activity (bupivacaine) or inhibited ERK/MAPK activation (U0126). Thereafter, they were then exposed to pairings of the light and foot-shock, and finally, tested for freezing responses to the sound. When the sound and light were paired in a safe environment, consolidation of the sound-light association required neuronal activity, including ERK/MAPK activation, in the PRh but not the BLA. Conversely, when the sound and light were paired in a dangerous environment, consolidation of the sound-light association required neuronal activity, including ERK/MAPK activation, in the BLA but not the PRh. The final experiments extended these findings: when danger was encountered either before or after sound-light pairings, consolidation of the sound-light association required activation of AMPA receptors in the BLA. These findings are discussed in relation to the cellular processes involved in consolidation of conditioned fear, and the role of the amygdala in processing of environmental stimuli with respect to motivational states like fear.

Dopaminergic mediation of Pavlovian conditioned and unconditioned responding

Stephanie Roughley and Simon Killcross
University of New South Wales

Dopamine is known to be necessary for acquisition and performance of Pavlovian conditioned approach behaviour. However, some research suggests that the importance of dopamine in performance of Pavlovian CRs decreases with extended training, such that these responses can occur in the absence of dopamine signaling (Choi, Balsam, & Horvitz, 2005). We investigate this further using a design that manipulates CS duration in order to tease apart dopaminergic involvement in CS-generated and US-generated responding. Rats were trained for 7 sessions on a conditioning procedure where presentations of a click CS were paired with food rewards. This click CS was either 400ms (in replication of previous studies) or 3s in duration. A dopamine D1 receptor antagonist was administered on sessions 3 (early) and/or 7 (late) in various groups to assess dopaminergic mediation of responding at different stages of training. Results indicate that dependence on dopamine activity decreases across training for US-generated responding, but not CS-generated responding.
Stimulation of the infralimbic cortex facilitates extinction after reconditioning and renewal

Nura W. Lingawi¹, Vincent Laurent¹-², Fred Westbrook¹
¹University of New South Wales
²University of Sydney

It is now well-established that the infralimbic region of the medial prefrontal cortex (IL) is critical for the consolidation and retrieval of fear extinction. Not only does IL inactivation impair long-term retention of fear extinction (Sierra-Mercado, et al 2011), but electrophysiological and pharmacological stimulation of the IL have been shown to facilitate extinction learning (Vidal-Gonzalez, et al 2006; Thompson, et al 2010). Similarly, previous research in our lab has shown that neuronal activity in the IL is required to relearn extinction after reconditioning (i.e., re-extinction). For instance, inactivation of the IL impairs long-term inhibition of fear to a context that has previously been extinguished and then reconditioned (Laurent & Westbrook, 2009). However, it remains unclear whether the IL plays this same role in re-extinction when fear to a cue has returned due to restoration phenomena, such as renewal. We tested this by blocking NMDA receptors and stimulating the IL during extinction of renewed fear. Blocking NMDA receptors in the IL impaired initial extinction and re-extinction, whereas stimulation of the IL only facilitated re-extinction. We also examined the specificity of this facilitation by conditioning two cues, and extinguishing either one or both of the cues. Facilitation of extinction was specific to the cue to undergo re-extinction. These results suggest that the IL plays a similar role in extinction of restored fear as it does to standard extinction: activity in the IL is required to learn and consolidate information about an extinguished CS and transmit this information to the amygdala causing a reduction in fear responses.

Rats choose high doses of nicotine in compensation for and anticipation of restricted access to nicotine

Kelly J. Clemens, Jiajing Pan and Nathan M. Holmes
University of New South Wales

People adapt to restrictions on when and where they can smoke by adjust their smoking patterns: they increase their rate of nicotine intake both before and after a period when they cannot smoke. The present study used an animal model, nicotine intravenous self-administration in rats, to investigate the factors that underpin the shift towards greater nicotine intake under restricted access conditions. In Experiment 1, rats were trained to choose between three doses of nicotine (15, 30 or 60 µg/kg/infusion). Restricted access was modelled by progressively increasing the post-infusion time-out interval from 20 s (free access) to 300 s (restricted access). Experiment 2 used a procedure in which a signalled time-out interval varied within each self-administration session. Rats equally sampled all doses of nicotine under free access conditions, but exhibited a preference for the highest dose (60 µg) as access was restricted across sessions. This preference was immune to treatment with a partial nicotine receptor agonist, Varenicline, but decreased when the response requirement for the highest dose increased and when rats were returned to conditions of free access. Experiment 2 showed that rats can use a signal of future access conditions to regulate their current dose selection. Together these results indicate that rats, like people, seek higher doses of nicotine under restricted access conditions. Critically, the preference for a higher dose is not simply a consequence of extended nicotine exposure, but instead, reflects both compensation for and anticipation of a restricted access period.
Are long-term memories stored at synapses? Evidence from recent work in *aplysia*

*David Glanzman, Shanping Chen, Diancai Cai, Kaycey Pearce*
University of California, Los Angeles

It is generally believed that long-term memories are stored in the brain as changes in synaptic connections. However, we have recently found that long-term memory (LTM) and synaptic change can be dissociated in *aplysia*. We trained cocultures of sensory and motor neurons with serotonin, a transmitter that mediates behavioral sensitization and long-term facilitation (LTF) in *aplysia*. Serotonin (5-ht) triggered the growth of new presynaptic varicosities, a synaptic mechanism of long-term sensitization (LTS). Blockade of reconsolidation of the memory for LTF eliminated this increase in varicosity number. But inspection of the reconsolidation-induced alterations in synaptic structure indicated that the removal of the varicosities appeared random, and involved elimination of both original varicosities—varicosities present prior to 5-ht treatment—and varicosities whose growth was triggered by 5-ht. Thus, the LTM did not appear to reside in the new synapses produced by 5-ht. In behavioral experiments we observed that the LTM for LTS could be reinstated after reconsolidation blockade, which suggests that this antimnemonic treatment does not actually erase LTM. However, the LTM could not be reinstated if sensitized animals were treated with rg-108, a DNA methyltransferase inhibitor. This, together with other evidence, suggests that LTM is stored in *aplysia* as epigenetic changes.

**Cannabis Cue Exposure and Renewal: A Pilot Study**

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**AIM:** The decision to abandon cue exposure therapy nearly 20 years ago due to its inability to reduce drug use was perhaps premature. Associative learning theory and basic laboratory studies highlight that conditioning generalises across contexts, but that extinction learning is context dependent. Thus, drug cues can trigger cravings in any context, but individuals will only retrieve the extinction memory in the extinction context. Perhaps cue exposure failed since researchers provided it within therapeutic settings, a context where drug use rarely, if ever, occurs.

**METHOD:** Seventeen regular cannabis users (53% male) completed pre- and post- cannabis cue-reactivity sessions in a living room. Individuals were randomised to receive two, 90-minute cue exposure sessions in either the living room (AAA) or a therapist's office (ABA). Exposure sessions focused on violating CS-US (conditioned stimulus-unconditioned stimulus; bong-drug taking) expectancies and having participants tolerate their reactions to their cannabis paraphernalia. Sessions occurred daily or intensively (all in one day) to accommodate participants' schedules and enhance recruitment.

**RESULTS:** Cannabis cravings decreased throughout the study for three of the four groups, with the Daily groups experiencing the largest reductions (AAA=59%; ABA=41%) However, the ABA Intensive group experienced a 19% increase in their cravings from the pre- to post-cue reactivity sessions. Additionally, the ABA Daily group evidenced renewal of craving from their final cue exposure session to the post-cannabis cue reactivity session, while the AAA Daily group evidenced a 53% reduction in their cravings during this period. Lastly, EDA increased from the pre- to post-cue reactivity sessions for the ABA Daily group, but decreased for the AAA Daily group.

**CONCLUSIONS:** Providing cue exposure sessions in naturalistic settings may improve their effectiveness. When sessions occurred daily, individuals who received cue exposure in the living room and the therapist's office both improved. However, those who received cue exposure sessions in the therapist's office relapsed when they returned to the living room, a context where participants regularly smoked cannabis. Additionally, providing cue exposure therapy intensively provided little benefit, with individuals receiving treatment in the therapist's office experiencing a worsening of craving.
Examining human spatial navigation strategy use with a virtual reality maze

Blake Segula, Ian Johnston, and Frans Verstraten
University of Sydney

There is a great deal of evidence supporting the central role played by two learning systems, place learning and response learning, in human spatial navigation. Research suggests that there is typically a shift from place learning dependent, which involves finding one's way around with reference to the self-independent relationships between environmental cues, to response learning dependent, which involves movement via learned, self-dependent stimulus-response behaviours, navigation as a person becomes more familiar with an environment. However this transition, or at least the empirical observation of it, in humans requires an environment complex enough to allow place navigation to be a viable strategy, at least early on. Teasing apart when place and response-based systems of navigation become available to use also requires environments that are dynamically flexible enough to switch between necessitating the use of one or the other, or to put both in conflict. Therefore my research so far has involved the design and testing of a complex virtual maze to observe this strategy transition and to tease out what cognitive processes may potentially underpin them.

Latent inhibition in human nausea learning

Veronica Quinn, Ben Colagiuri, Evan Livesey
University of Sydney

The role of conditioning in the experience of nausea has been well documented both in the laboratory and clinic, but less is known about how this maladaptive conditioning can be prevented. One successful method of preventing conditioned associations from forming in animals is the latent inhibition procedure. Latent inhibition refers to the phenomenon whereby pre-exposing a subject to a stimulus retards subsequent learning about that stimulus. Replicating this effect in human learning has been difficult due to the inability to reproduce certain parameters present in the animal latent inhibition paradigm. The human nausea learning paradigm using Galvanic Vestibular Stimulation (GVS) solves many of these problems, and an experiment was conducted to determine if pre-exposure to placebo-GVS could reduce conditioned nausea to GVS on test. Self-report and physiological correlates of nausea were assessed, as well as expectancies and contingency awareness. Experiment 1 found that pre-exposure to GVS on day one reduced conditioned nausea on day two and three. Experiment 2 sought to determine whether this effect was contingent upon the deception involved in the first design, which would reduce its clinical applications, through the addition of a group given “informed” pre-exposure. It was found that latent inhibition occurred in both the uninformed and informed groups to an equivalent extent.
Test Sensitivity in Cue Competition Effects

Hilary Don & Evan Livesey
University of Sydney

Cue competition effects in human contingency learning appear to be influenced by the causal nature of cue-outcome relationships. For instance, while blocking effects are reliably demonstrated in scenarios where cues are presented as causes, several studies have failed to find blocking in non-causal scenarios, which is typically taken as evidence for the contribution of sophisticated reasoning processes that consider the causal structure of events. Other cue competition effects, such as highlighting and the inverse base-rate effect seem to be far less sensitive to the causal properties of the scenario. However, blocking is typically measured with continuous causal ratings of single cues, while highlighting and the IBRE are measured with discrete choices about combinations of cues. Although these measures may be differentially sensitive to learning and reasoning effects, surprisingly little effort has been made to compare their properties, for instance their sensitivity to causal information. This study therefore aimed to assess the sensitivity of blocking and other cue competition effects to causal scenarios across different test measures. The results suggest that contributions of associative memory and causal reasoning to cue competition effects may depend substantially on the test measure used.

Evidence for the Uncertainty Principle in Human Associative Learning

Lara Easdale, Tom Beesley & Mike Le Pelley
University of New South Wales

Prior research has shown that human attention is allocated according to both a predictiveness principle and an uncertainty principle. The predictiveness principle ensures that we attend to meaningful cues: stimuli which reliably predict an outcome are allocated more attention. The uncertainty principle ensures that we attend to the cues we are unsure about: stimuli which are associated with the greatest degree of uncertainty are allocated more attention. The two principles together suggest an interaction between exploitation of known predictive cues and exploration of unknown cues. Recently, a study that systematically manipulated both predictiveness and uncertainty showed evidence for the role that each of these principles play in attentional processing (Beesley, Nguyen, Pearson & Le Pelley, 2015). The present study sought to examine whether preferential allocation of attention to uncertain cues leads to more rapid learning about these cues in the future. It was found that those participants who experienced an increase in uncertainty showed a higher initial rate of learning compared to those participants for whom uncertainty was constant. We will argue that this represents evidence for an effect of exploratory attention on rate of learning in humans.
There’s nothing automatic about evaluative conditioning — A facial EMG study on the role of relationship on explicit and automatic evaluations

*Tanya Pritchard* and Gabrielle Weidemann
Western Sydney University

Recent research suggests that evaluative conditioning (EC) of deliberate responses is moderated by relational information between the CS and US; however, there is conflicting evidence for the role of relational information on the formation of automatic affective responses. In the current study, neutral faces (CSs) were shown to ‘love’ or ‘hate’ affective and neutral images (USs). Participants then rated the faces for likeability and took part in an affective priming task to assess both deliberate and automatic affective responses towards the CSs. Facial electromyography across the corrugator region was also measured to assess emotional responding towards the images. It was found that EC occurred only for faces that loved (but not hated) positive and negative things, however, there was no evidence for an affective priming effect despite participants showing emotional responses towards the affective images. These results indicate that relational information do not change the automatic evaluative response toward the USs during conditioning, and EC of deliberate and automatic affective responses is not the automatic result of pairing neutral and affective stimuli.

The influence of expectancy and sequence on reaction times and motor excitability in a Go/No Go task

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Under most circumstances our goal directed actions are driven by executive function and we behave according to our expectations about the world. However, under some circumstances particularly when there is uncertainty about what we expect to happen it is possible to dissociate expectancy and voluntary behaviour. After repeated pairings between a cue and a stimulus which signals that participants must perform an action, participants show faster reaction times (RTs) even though their expectancy for the signal is low and they are uncertain about whether the signal will occur. In order to examine the influence of the previous response and the presence of the cue on the neural processes driving behaviour we conducted two experiments in which we stimulated participants motor cortex with TMS pulses at various points in the trial. The TMS pulse was designed to elicit a motor evoked potential (MEP) which could be used to infer the pre-activation of the motor network. These experiments revealed that top-down expectancies are not the main driving force for action control both when participants are uncertain and when they have just repeated the same action several times. Residual activation of the motor system following an action appears to be much longer lasting than previously thought and is probably contributing to subsequent responses when there is repeated activation of the same action.
Learning about nothing: Examining outcome-specific inhibitory associations in humans

Stephanie L. Quail, Vincent Laurent & Bernard W. Balleine

Brain & Mind Centre, University of Sydney

Our ability to extract predictive information from our environment, allowing cues to become associated with the delivery or absence of outcomes, is important for adaptive and effective guiding of behaviour and choice. The development of both general and outcome-specific excitatory associations has been extensively examined in both rats and humans, with the ability to assess the distinct features of the outcome associated with the cue clearly established. However, the evidence regarding the development of inhibitory Pavlovian associations in humans is less clear. Inhibitory conditioning procedures have been found to generate both general and outcome-specific inhibitory associations in rats, however the ability for cues to become associated with the specific identity of an omitted outcome is less clearly demonstrated in humans. Additionally, as the majority of research examining conditioned inhibition in humans has employed causal learning tasks, which have been found to be particularly sensitive to instruction and framing, we intended to examine the development of outcome-specific inhibitory cues in humans using a feature-negative conditioned inhibition procedure that more closely mimics the procedure established in the rat literature. Whilst indirect assessments of the associations developed using a Pavlovian-Instrumental transfer test provided initial evidence of the development of outcome-specific inhibitory associations in humans, further experiments directly examining the development and nature of these inhibitory associations after the feature-negative conditioned inhibition procedure alone did not reveal evidence of this specificity. Implications for our understanding of the potential conditions that may promote the development of outcome-specific inhibitory associations in humans will be discussed.

Eating chow as a contributor to the delay gradient in taste aversion learning

Bob Boakes and Dorothy Kwok

University of Sydney

Experiments on long-delay conditioned taste aversions (CTA) have varied in whether all procedures, other than lithium chloride (LiCl) injections, are carried out in the animals’ home cages or in drinking chambers where they are given the target solution. Whichever of these procedures is used, it appears that the majority of such CTA experiments have allowed access to chow during the delay interval between receiving the target solution and being injected. One reason why access to chow might be important is that it could contribute to the CTA delay gradient, in that the greater the delay, the greater the opportunity for consuming chow to partially overshadow conditioning of the target taste. Experiment 1 used a 2 x 2 factorial design, in which one factor was whether or not chow was available during the delay interval (Chow vs. No Chow) and the second factor was whether the target solution, sucrose, was given in the home cages or in drinking chambers (Chamber vs. Home). In the single conditioning session rats in the Chamber condition were given access to sucrose in the drinking chambers, while those in the Home condition were given 10-min sucrose in the home cages. During the subsequent 90 min all rats remained in their home cages where a weighed amount of chow was available for half the rats in each condition. At the end of the 90-min delay all rats were injected with lithium chloride. At sucrose test, stronger aversions in the Home than in the Chamber groups were found, and an effect of chow availability in that sucrose aversions were stronger in the Chamber-No Chow than in the Chamber-Chow condition. Experiment 2 confirmed the latter result. In conclusion, overshadowing by chow consumption does appear to contribute to the CTA delay gradient.
When does short-term exposure to a high-fat high-sugar diet impair object recognition memory?

Dominic M. D. Tran & R. Frederick Westbrook
University of New South Wales

Exposure to an energy-rich diet causes impairments on various cognitive tasks in rodents. We and others have shown that within a week of exposure to a high-fat high-sugar (HFHS) diet rats become impaired on spatial memory tasks. Novel object recognition memory however, has been relatively impervious to short-term HFHS diet exposure. In a series of experiments we manipulated the standard novel object task to test the limits of object recognition memory in chow fed and HFHS fed rats. Experiment 1 tested the strength of the object-memory trace by varying the interval of time between initial familiarisation to two objects and subsequent test where one of the old objects was replaced with a new object. Novel object recognition was just as good in the HFHS rats as in chow fed controls across all retention intervals. Experiment 2 tested the effect of increasing working object-memory load by varying the number of objects previously presented before the test phase. The number of object interference items ranged between 0 and 3 objects, and no between-group differences were found. Finally, Experiment 3 again tested the strength of the object-memory trace but controlled for relative familiarity of object identity by separately familiarising both objects presented at test and varying the interval of time between these two familiarisation sessions. For the first time, we found a between-group difference in the object recognition memory; HFHS rats showed a faster rate of object memory decay compared to chow rats.

The effects of partial reinforcement on the extinction of conditioned responding

Jonas Chan and Justin Harris
University of Sydney

Information-based theories of learning (e.g., Gallistel & Gibbon, 2000) assert that, in the face of extinction, animals make the decision to cease responding by comparing the current overall rate of reinforcement with the expected rate of reinforcement learned during training. Specifically, the rate of extinction is dependent on the number of expected reinforcers that have been omitted. According to this account, the partial reinforcement extinction effect (PRE) is observed due to the fact that a partially reinforced schedule is leaner than the corresponding continuously reinforced schedule, and therefore the animal takes longer to detect the change in reinforcement during extinction. We compared the rate of extinction between two stimuli trained with matched reinforcer rates, presented as either a long continuously-reinforced CS, or a short partially-reinforced CS. A PRE effect was found despite identical rates of reinforcement during training, supporting the alternative account that PRE occurs due to relatively greater detectable change in a continuously reinforced schedule.
Extinction, time and trials

Justin Harris
University of Sydney

Extinction of conditioned responding is presumed to depend on an unfulfilled expectation of the US. This has been formalized in two distinct ways. One theory uses a simple error correction rule: expectation of the US, represented by a one-dimensional variable such as associative strength, is reduced on each trial when the US is predicted but does not occur. An alternative theory holds that extinction depends on cumulative non-reinforced exposure to the CS. As the animal accumulates non-reinforced experience with the CS during extinction, it eventually recognizes that the previous rate of reinforcement has changed, and quits responding. The time taken to recognize the change in reinforcement depends on the number of expected USs that have been omitted (the expected number being based on the previously learned rate of reinforcement). I will present experiments that specifically examine how extinction of Pavlovian conditioning is related to the cumulative duration of non-reinforced exposure to the CS or the number of non-reinforced trials.