Review of Literature

Fear and pleasure- those two words seem like polar opposites in terms of how humans and other animals generally experience the two feelings. But when examined more closely in terms of the brain and the mind, fear and pleasure are more complicated than associations with negative and positive stimuli or the responses they elicit. If it were as simple as fear being a response to threatening stimuli and pleasure being a response to rewarding stimuli, then why would there be people who experience pleasure and fear in response to the same stimuli, such as when skydiving? Or why are there people who experience pleasure from dangerous and life threatening drugs such as heroin, and vice versa (those who experience fear from stimuli that typically are associated with pleasure, or even the fear of pleasure itself). There has been much research done on both fear and pleasure, and it turns out that although very different in definition, similar areas of the brain seem to be implicated in processing both fear and pleasure; these areas include the amygdala, hippocampus, anterior cingulate cortex (ACC), the prefrontal cortex (PFC), and components of the striatum ( Burke, Tobler, Baddeley & Schultz, 2010; Golkar, Haaker, Selbing & Olson, 2016; Olsson, Nearing & Phelps, 2007; Shane, Stevens, Harenski & Kiehl, 2008). In relation to fear and pleasure are both fear conditioning and reward learning, as well as the extinction of these acquired fear and reward associations. Although there is still a lot to learn about many aspects of conditioning and extinction, this topic has been explored for quite a while.

In the late 1800s, Dr. Ivan Pavlov became interested in a type of learning where a previously neutral stimulus would become associated with a reward (classical conditioning). Pavlov became interested in this subject after realizing that after a period of time, dogs that would be fed began to salivate not only every time a lab assistant brought them food, but every time the assistant entered the room. The food was an unconditioned stimulus (a stimulus that evokes a response instinctively), which would cause the dogs to salivate (which is an unconditioned, instinctive response). In order to observe the phenomenon he witnessed when the dogs associated the lab assistant with food, he needed a neutral stimulus that did not cause the dogs to salivate. He used a bell as the neutral stimulus and had it rung every time the dogs were to be fed. After a while, Pavlov would have the bell rung even when it was not feeding time. And just like the dogs salivated whenever the lab assistant who would feed them came into the room, they now salivated whenever the bell was rung; the bell was no longer a neutral stimulus, but a conditioned stimulus (since it was now associated with the unconditioned stimulus: food). Pavlov also observed that this association could be broken through a process now known as extinction; if the bell is consistently rung without the reward of food, the dogs would no longer salivate in response to the bell (the bell was once again a neutral stimulus).

In the mid 1900’s, Dr. B.F. Skinner studied what is known as operant conditioning, a more complex form of conditioning than classical conditioning. Operant conditioning focuses on how positive or negative reinforcements can influence behavioral learning. Skinner studied this form of conditioning in rats using a mechanism known as the Skinner Box; one aspect of this experiment involved an electrical grid built into the box where the rats were kept, that could be controlled by a lever also inside the box. Shocks would be administered to the rats acting as a negative reinforcer, and the rats learnt that if they pressed the lever, they would be rewarded with no more shocks. The other aspect of the study involved positive reinforcement; the rats were placed inside a box with a lever, and when they pushed the lever, food would be released. Knowing that food (a positive reinforcer) would be released as a result of pressing the lever, the rats began to press the lever whenever they were hungry.

Since the work of Pavlov and Skinner, much has been discovered about affective and emotional learning, and now a major focus of research on conditioning is extinction learning, and the parts of the brain involved in this type of learning. There has been a great deal of research done on the neural circuits involved in fear extinction, which is important in treating many disorders such as phobias and certain anxiety disorders, but there has not been as much research done on the extinction of reward learning in relation to the brain. This is a critical area of study as psychiatric conditions such as addiction related disorders have to do with dysfunctions within the reward pathway.

**Fear Conditioning and Extinction**

One famous and very early example of fear conditioning was the “Little Albert” experiment by Dr. John B. Watson. In this study, a nine month old baby named Albert was exposed to stimuli such as white rats. Upon entering the study, Albert was unafraid of the rat (neutral stimulus). One time as Albert was playing with the rat though, loud noises were made and Albert would cry (an unconditioned stimulus causing an unconditioned response). After continuously pairing the white rat with the loud noise, Albert began to show signs of fear, such as crying, upon exposure to the rat (and other white, furry items). His crying was a conditioned response to a conditioned stimulus. Research on the neural circuits involved in this type of conditioned learning suggest that the amygdala plays a large role in the acquisition of conditioned fears such as those of Little Albert, though it is simplistic to assume that learning is due to fear conditioning only by the amygdala. For example, humans are social by nature and their learning is aided by social cues, social norms, etc. (Olsson et al., 2007).

**Vicarious learning.** One method of fear and reward learning that is a focus of current research is vicarious learning, which is learning from observing others. Vicarious extinction learning in particular, involves a person with a conditioned fear watching others who lack that fear, react to the fear-causing stimulus in a typical way. A 2016 study by Golkar et al. examined the efficacy of vicarious extinction learning as compared to direct extinction, and the different parts of the brain involved in vicarious extinction learning. In the study, the procedure included three phases: Acquisition, Extinction, and reinstatement testing. Reinstatement testing is when a previous, but currently extinguished fear (that had been acquired due to fear conditioning) is made to return. The results of Golkar et al., 2016 suggest that vicarious safety learning (learning that a previously threatening CS is still safe by watching others demonstrate the safety of the CS) is an effective way of preventing fear reinstatement. Specific areas of the brain that are correlated with the decreased fear reinstatement during vicarious safety learning were the Ventromedial PFC (vmPFC), which showed enhanced activity and increased connectivity with the amygdala and anterior hippocampus. Interestingly, during the vicarious extinction learning itself there was less connectivity between the vmPFC and amygdala, than during non-vicarious extinction; this suggests that the vmPFC which typically works to integrate sensory information to determine appropriate responses, does not exhibit as much of an influence when aided by factors such as social cues, and observational learning (Golkar et al., 2016).

This association of the vmPFC with sensory integration (specifically in relation to extinction recall) is supported by another study that saw decreased activity in the vmPFC in individuals who showed higher levels of social anxiety (Pejic, Hermann, Vaitl & Stark, 2013). What this study suggests is that a failure to activate the vmPFC during extinction learning and recall can be a cause of increased social anxiety. This ties in with Golkar et al., 2016 which shows increased activity in the vmPFC to be associated with less successful fear reinstatement. And interestingly, although the findings of Pejic et al., 2013 were based upon fear conditioning in healthy participants, unlike Golkar et al., 2016, this study dealt with the acquisition and attempted extinction of social anxiety disorder. The model for generating social anxiety disorder was flawed though, with one of these flaws being that social anxiety disorder involves the fear of negative evaluation, rather than the direct negative evaluation participants experienced. People who are made fun of or disrespected get mad and upset, but those with social anxiety may dwell on these happenings and fear similar occurrences, while those without social anxiety can rationalize that not everyone will be mean to them, despite specific occurrences. Yes, there have been instances in which the disorder has manifested following negative experiences regarding social interaction, but for many individuals there is no known environmental trigger for the disorder (Carleton, Peluso, Collimore & Asmundson, 2011). Despite this, the study still gave important insight regarding the possible biological etiology of social anxiety disorder in terms of the involvement of the vmPFC (Pejic et al.,2013). These findings are especially important as this was one of the few studies to use unconditioned stimuli that were socially relevant to social anxiety disorder (such as direct insults to the participant); other studies aimed to be able to make conclusions about the neural networks of social anxiety disorder through general fear conditioning and extinction testing, but findings were inconclusive (Veit et al., 2002, Hermann et al., 2002).

**Reward Learning and Extinction**

**Decisions based on reward to self and others.** Although the majority of research on reward conditioning does not focus on its extinction, many studies have been done regarding the acquisition of reward associations. This research can be done in organisms other than humans such as the Rhesus macaque monkey, as like humans, they learn from social observation, understand and infer others intentions, and care for their children amongst other similar attributes (Chang, Winecoff & Platt, 2011). Using both operant and classical conditioning, a 2011 study by Chang et al. examined how monkeys respond to rewards (juice) directed to either themselves (M1), the other monkey in a pair (M2), both monkeys (M1+M2), or neither monkey. M1 monkeys made less errors when a reward was predicted to M2 than when a reward was predicted to neither M1 or M2, but when an M1 was faced with a decision to solely get a reward or both M1 and M2 getting a reward, the M1 chose for themselves only to get the reward. Chang et al., 2011 theorizes that the preference of M1 to give juice to M2 rather than nobody can be due to it being the only option that allows the monkey feel that they are being rewarded (by seeing the other monkey satisfied). But then it would be assumed that M1 monkeys, if able to decide if they alone, or them and M2 should receive juice, would choose for both of them to receive juice (since there would be pleasure of receiving the juice themselves and pleasure of seeing that they helped another monkey get juice) but this was not the case. Factors at play here seem to be ones of pleasure of self reward, pleasure through charity, but also jealousy and competition. Studies such as Chang et al., 2011 can be expanded or built upon, if a jealousy evoking aspect can be introduced such as to see if M1s will still choose for M2s to get juice when they have the option of M2 or nobody getting the juice, if M2 is being treated better in general than M1 (such as better home, more care, etc.) or if M1 monkeys will be more likely to choose for M1 and M2 to get rewards if M2 if getting slightly less of a reward than M1.

Although the participants were not monkeys, a 2010 study by Tricomi, Rangel, Camerer & O’Doherty studied inequality aversion, a factor that may have played a role in Chang et al., 2011, in human participants. The study was not specifically related to reward learning nor the extinction of reward based learning, but it looked at factors that influence decisions one makes for themselves as well as examining the brain during self-related decision making. This can help determine areas for future studies related to reward learning and extinction. fMRI was used to see whether activity in the human brain (specifically the ventral striatum and the ventromedial prefrontal cortex) supports the theory of inequality- averse social preferences in humans, meaning that humans do not only make decisions based on personal benefit, but decisions that are based on equality and fairness to others. Examining brain changes during these decisions would further support evidence towards the theories on inequality- averse social preferences. Participants in Tricomi et al., 2010 were divided into a high pay (given a $50 bonus in the beginning of the study, “rich”) and low pay group (given $0 bonus in the beginning of the study, “poor”) in order to test the hypotheses that (1) The low pay group would make decisions that caused them to stop falling more behind from the high pay group, even if this meant not taking an offer that would benefit them, because it would also benefit the already “winning” high pay group (disadvantageous inequality aversion) and (2) The high pay group would make decisions that decreased the inequality between them and the low pay group, since they were still getting money themselves but also were helping the people with lesser gains (advantageous inequality aversion). These hypotheses are supported by the results of the study and also suggested by this study is that by focusing on inequality aversion, humans may make irrational decisions (such as missing out on opportunities for personal gain). In terms of fMRI results, the ventral striatum and vmPFC showed higher levels of activities when participants were making decisions that decreased the inequality gap between self and other (Tricomi et al., 2010). Although decision making and reward learning are two different areas of study, they relate in many ways including their potential evolutionary backgrounds (i.e the satisfaction of drinking when thirsty ensures people will aim to stay hydrated; rationalizing that studying for a standardized exam is better than catching up on a tv show makes one more likely to succeed academically). It is important to note that the findings of Tricomi et al., 2010 suggest that the reward pathway can be influenced by inequality aversion; utilizing the theory of inequality- aversion may help in understanding factors that can influence the extinction of reward associations. In terms of clinical applications, it seems as if other theories regarding the extinction of reward associations are being studied, including appetitive conditioning and extinction.

**Appetitive conditioning and extinction**. Research into psychiatric disorders such as addiction, is exploring processes such as appetitive conditioning and extinction . A typical procedure for appetitive extinction involves a neutral stimulus (CSb) being paired with a chance of a reward (UCS) and there is another case in which another neutral stimulus (CS) is never paired with the chance of a reward. In the extinction part of the study (following the appetitive conditioning phase) the CSb, like the CS is not to be paired with a chance of reward. This procedure can be done based on both classical and operant conditioning. Parts of the brain implicated in appetitive conditioning and extinction are the dorsal anterior cingulate cortex (dACC) which is shown to be involved in a continued expectation of rewards, the ventral anterior cingulate cortex (vACC) which is associated with extinction of rewards, as inferred based on subjective ratings compared with fMRI data. Parts of the brain such as the dACC and vACC appear to be involved in early phases of extinction, while areas such as the nucleus accumbens (NAcc) and amygdala appear to be involved in late phases of extinction (Delgado, Jou, & Phelps, 2011; Kruse, Leon, Stark, & Klucken, 2016). Appetitive conditioning is very important to study in people due to its implication in certain mental health conditions such as addictive disorders. Many studies looking into methods for treating addiction in humans have focused on aversive conditioning, rather than appetitive conditioning. It is possible that the reason most studies choose to focus on aversive conditioning is because an aversive stimuli such as a shock will always be aversive, while in appetitive conditioning, a typically rewarding stimuli such as food may be rewarding to different extents based on contextual factors such as the participant’s current hunger level, time of day, etc. ( Andreatta and Pauli, 2015). There are ways around this issue such as by using secondary rewards such as monetary rewards rather than food, water, etc., which are primary rewards; there have been issues in using secondary rewards in appetitive conditioning studies though, as studies including Delgado, Jou, & Phelps, 2011 and Levy & Glimcher, 2011 suggest that primary reinforcers and secondary reinforcers activate different areas of the brain; for example, it appears that although the striatum is involved in similar degrees in extinction trials with both primary and secondary reinforcers, the amygdala and hypothalamus are more active during extinction trials that use primary reinforcers and the posterior cingulate cortex is more active during extinction trials that use secondary reinforcers.

Andreatta and Pauli, (2015) also compared both aversive and appetitive extinction, and the results of their study suggests that appetitive extinction occurs more rapidly than aversive extinction; being that appetitive conditioning has rarely been tested in humans, it is important that this form of extinction (as well as aversive extinction) was evaluated on different levels including the explicit verbal level, the implicit behavioral level, and the physiological level. And the results of the study show that both aversive and appetitive conditioning are effective in all three of those levels. (Pauli and Andreatta, 2015).

Although both classical and operant conditioning have been used in studies for decades, there is a large focus on fear conditioning and extinction as compared to reward conditioning and the extinction of behaviors associated with certain rewards. Although it is important to study fear conditioning due to its implications in the acquisition and treatment of certain anxiety and panic related disorders, there is a great benefit of studying reward conditioning; for example, people with addiction related disorders most likely have a dysfunction in their brain’s reward circuit. Extinction techniques may help them directly, or studies that use reward conditioning as part of their method, combined with brain imaging techniques such as fMRI could allow for the studying of neural circuits of those with addiction related disorders. That way, the disorders can be better understood and new preventative and treatment methods may eventually be developed. Parts of the brain currently implicated in reward based learning are the ventral tegmental area (VTA), nucleus accumbens, and prefrontal cortex as well as the amygdala and hippocampus) Future studies should continue to examine the extinction of behaviors associated with reward through both aversive and appetitive conditioning, using both primary and secondary reinforcers.

**Method**

**Participants**

Adelphi University undergraduate students were recruited to participate in this study through the use of Sona Systems, which allowed them to receive class credit (2 credits) for their participation in this study. Upon entering the room in which the experiment would take place, participants provided informed consent.

**Subjective Ratings**

Following informed consent, participants filled out the following questionnaires: The Adult Autism Spectrum Quotient, The Interpersonal Support Evaluation List (ISEL-12), The Facebook Intensity Scale, The Rosenberg Self-Esteem Scale (RSES), The Behavioral inhibition system/ behavioral activation system scale (BIS/BAS) and the Multidimensional Scale of Perceived Social Support.

**Stimuli**

**Money (1M).** The CS+ was a magenta rhombus for female participants/ a yellow circle for male participants and the CS- was a magenta pentagon for female participants/a yellow pentagon for male participants. For trials in which the CS+ was reinforced,

+$2 would appear over the shape. For the trials in which the CS- was reinforced, $0 would appear over the shape. For the trials in which the CSs were not reinforced, nothing would appear over the shapes.

**Social (2S).**The CS+ was a yellow circle for female participants/ a blue octagon for male participants and the CS- was a yellow square for female participants/ a blue triangle for male participants. For trials in which the CS+ was reinforced, a happy face the same gender as the participant would appear over the shape. For the trials in which the CS- was reinforced, a neutral face of the same gender as the participant would appear over the shape. For the trials in which the CSs were not reinforced, nothing would appear.

over the shapes (The faces shown for the CS+/CS- were of the same person).

**Experimental Procedure**

Developed and run on E-Studio Professional, the experimenter went through the slides that included the introduction to the computerized part of the study, for which the spacebar key on the keyboard was used to proceed from slide to slide. The instructions included an example of how the trials will look, with one slide showing the “+” fixation, the next slide showing a shape that was not to appear in the actual trials, and the next slide showing the shape with a question mark (representing the reinforcer) superimposed onto the center of the shape. There were two main phases of the study, the monetary phase (1M) and social phase (2S). There were instructions more specific to both phases of the study presented directly prior to the commencement of the habituation stage of both phases. Each of these phases had the following stages (participants were not aware of the presence of three stages as there was no direct indication of the move from one stage to another).

**Habituation.** There were six trials during the habituation stage, with both unreinforced CSs were presented 3 times each, with a duration of 4000 milliseconds (random order); there was a 4-6 second interval before each trial in which a “+” appeared on the screen.

**Acquisition.** During the acquisition stage there were 30 trials for which the CS+ and CS- were both presented 15 times (for which 60% of both the CS+ and CS- trials were reinforced) (random order). For the trials in which the CSs were not reinforced, the CS remained on the screen for 4000 milliseconds uninterrupted, but for the trials in which the CSs were reinforced, the blank shape would be on the screen for 3250 milliseconds followed by the superimposing of the reinforcer onto the shape for the remaining 750 milliseconds; the shape and the superimposed item co-terminate. there was a 4-6 second interval before each trial in which a “+” appeared on the screen. Participants were to press the “1” key on the keyboard whenever the reinforcer appeared on the screen, which helps to infer whether the participants were attentive or not.

**Extinction.** During the extinction stage, there were 20 trials for which the unreinforced CSs were presented 10 times each, with a duration of 4000 milliseconds (random order); there was a 4-6 second interval before each trial in which a “+” appeared on the screen.

**Ratings**. Following both phase 1M and 2S, there were a set of rating the participants would complete on the computer. The stimuli (both the CSs and reinforcers) were rated on a scale of -3(negative)-3(positive) in terms of valence and intensity. For these questions, the “select” option was automatically on “0” and participants could use the 1 key to move left and the 3 key to move right, and the 2 key to select their answer. There were also questions in which the participant had to rate their preference of the unreinforced and reinforced trials of both the CS+ and CS- (The unreinforced option appears on the left (1 key to select), and the reinforced option appears on the right (3 key to select)).

**Physiological Data Collection**

**Galvanic Skin Response (GSR).** Biopac Systems, Inc. technology (MP150) was used to acquire the participants’ Electrodermal Activity. Following the use of an abrasive cleaning pad necessary fingers, electrodes were attached to gel pads on the pointer and middle finger of each participant’s non-dominant hand. Participants were told to place that hand in a comfortable position prior to the commencement of the computerized task, and to keep that hand still. The system was calibrated to acquire data during phase 1M and 2S of the study.

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