Extended Essay

Psychology

A Neuropsychological explanation of Fear Conditioning

To what extent does the amygdala explain the role of fear conditioning in humans?

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Contents

Introduction

Pavlovian fear conditioning – or more simply known as fear conditioning – is a form of behavioural associative learning when a neutral stimulus or 'conditioned stimulus' (CS) such as a tone is paired with an aversive stimulus or 'unconditioned stimulus' (US) such as an electrical shock is to elicit a 'unconditional response' (UR), the fear response (Maren, 2001)(Anagnostaras et al., 2014). Over time, through CS-US association formation, the CS on its own is sufficient to elicit the UR. The 'unconditioned response' then transforms into the 'conditioned response' (CR).

A famous example of fear conditioning in humans is during an experiment involving the child known as Little Albert. The child, less than a year old, was shown to display no fear when playing with a white rat (Watson & Rayner, 1920). During the experiment, whenever Little Albert would touch the rat (CS), a hammer was used to produce a large sound (US) close to the child which scared him and made him cry (UR). This CS-US association formation occurred many times and eventually simply close to the rat was enough to trigger Little Albert to cry (CR). The rat triggered the now conditioned response of fear in Little Albert.

This behavioural paradigm has been shown to be an important evolutionary behaviour with significant neurobiological basis, with research having been able to map many of the neural circuits associated with fear conditioning in addition to the adaptive synaptic plasticity within these regions (Maren, 2001). Research has heavily implicated an association of these neural circuits with that of the amygdala (Kim & Jung, 2006). Suggest that fear is fundamentally hard-wired behaviour within human neuropsychology.

To examine the extent to which the amygdala explains fear conditioning, it is important to first understand its structure. The amygdala forms part of the limbic system – considered to be the primitive brain – with the amygdala located in its subcortical areas (Gilbert & Brushfield, 2009)(RajMohan & Mohandas, 2007).

The amygdala – first discovered by Karl Friedrich Burdach – is an almond shaped bilateral structure within the medial temporal lobe (DeLisi et al., 2009)(Pabba, 2013). It consists of multiple sub-regions or nuclei, the four main divisions are known as the basolateral nuclei – often referred to as the basolateral amygdala (BLA), central nucleus, and medial nuclei. Each of which can be further segregated into smaller nuclei such as the lateral amygdala (LA), basal amygdala (BA), and the accessory basal amygdala (Amunts et al., 2005). The LA in particular has be noted to be an area to which fear conditioning is localised (Nader et al., 2001a). The primary functions of the amygdala are to process memory and emotional stimuli, namely fear.

Evidence implicates the amygdala as a neurologically important mechanism of fear conditioning in humans. A variety of evidence was investigated in this essay, such as case studies involving lesioning, brain imaging studies, laboratory experiments and meta-analysis including the use of quantitative and qualitative data analysis. Each evidence will be critically evaluated to determine the degree to which they support their ideas and answer the research question. The thesis put forward states the amygdala plays a key role in fear conditioning.

Thus, this extended essay will aim to examine, *to what extent does the amygdala explain the role of fear conditioning in humans*?

Amygdala's role in fear conditioning

Supporting evidence

One way the link between the amygdala and fear conditioning can be investigated is through lesioning studies. These often occur in animals, the findings of which are then generalised to humans as many studies find that lesioning of amygdalae in animals such as rats inhibits fear conditioning (Moustafa et al., 2013)(Nader et al., 2001b). Rarely is it that lesions in humans can be investigates – due to ethical concerns – which is why patients like SM-046 (abbreviated to SM) presents a rare opportunity for this type of investigation. SM is an American woman who suffered from the bilateral disintegration of her amygdala due to Urbach-Wiethe disease and is involved in many studies regarding this topic (Adolphs et al., 1994).

An investigation was conducted by Feinstein et al in 2011 where they carried out a systematic case study of patient SM to assess the induction and experience of fear in her, an individual with amygdala damage (Feinstein et al., 2011). The researchers attempted to induce fear through exposure to aversive unconditioned stimuli in SM through three methods.

In the first fear-inducing method, SM was taken to a pet store and exposed to snakes and spiders which SM reportedly hated. SM displayed exploratory behaviour around these creatures and even willing to hold a snake and was shown to display no fear with either animal, even attempting to touch the tarantula despite dangers of being bitten. Despite exposure to unconditioned stimulus – the snakes and spider – she failed to produce an unconditioned fear response despite her dislike towards them. The researchers asked SM to rate her levels of fear from 0 (no fear) to 10 (extreme fear). SM's self-reported rating never surpassed 2.

In the second fear-inducing method, SM was taken to the Waverly Hills Sanatorium, a haunted house which is designed specifically to provoke the fear response. SM showed an extreme willingness to explore dark corridors and corners with no hesitation at all. Attempts by the 'monsters' hidden in the walls of the corridors to scare SM only elicited joy and intrigue by SM. In contrast, these tactics elicited screams and fright in those who entered. Throughout the experience, SM was constantly asked about how fearful she was, which remained at a constant zero over the course of the haunted house. Overall, although SM was emotionally stimulated by the Sanatorium though she displayed no conditioned fear.

In the third fear-inducing methods, SM was shown 10 fear-inducing clips from horror films, with some clips spliced between the viewings aimed to elicit emotions such as rage, sadness and joy. As with the other methods, SM showed no conditioned fear but did display the emotions the spliced footage aimed to elicit. Additionally, SM was provided eight clinically supported questionnaires to measure her phobias and fears regarding specific situations over the three years she was studied. Every questionnaire rated her fear as extremely low. Furthermore, SM's past was investigated, having experienced events considered to be traumatic – including near death experiences by domestic abuse, death threats, and held up by gunpoint. When recalling these events, once more no conditioned fear was reported. Considering SM's lack of fear to fearful unconditioned stimuli; the researchers concluded that bilateral lesions of the amygdala impair fear conditioning processes, suggesting the amygdala can explain the role of fear conditioning in humans.

The study had significant construct validity as SM was exposed to a variety of situations specifically aimed at inducing fear to see whether she would elicit it which means the results accurately depict the amygdala's role in fear conditioning. Moreover, the results possess mundane realism as the study was conducted in realistic environments that elicit the fear response in functioning individuals, so the results can be said to have ecological validity. However, there are significant limitations with the study, as with most case studies, it is hard to generalise to the majority of individuals since not only did the sample consist of only SM, she possessed a very rare genetic disease meaning the results of the sample can only represent those with Urbach-Wiethe disease (Parida et al., 2015). Another limitation was the use of

self-report data. SM could have felt pressured by the researchers to show no fear in CS-US association formation, which means social desirability might have altered the results. Thereby making them less accurate.

SM provides a rare opportunity to understand the effect the lack of an amygdala can have on behaviour despite the nature of this investigation being reductionist. A reason for this is because research has shown that plasticity alters brain structure and re-wires neurons to compensate for lost function (Baker & Roth, 2004). It is entirely possible that SM can experience fear, but because of potential neuroplasticity to compensate for her missing amygdala, there was not a sufficient unconditioned stimulus to trigger these new pathways. Nevertheless, Feinstein et al.'s research does show the amygdala to have a clear role in fear conditioning.

Another study supporting the amygdala's role in fear conditioning was conducted by Furmark et al using brain imaging techniques (Furmark et al., 1997). The study's aim was – via positron emission tomography (PET) scans – investigating whether there was direct a involvement of the amygdala in human fear conditioning by determining differences in central nervous system activity through regional cerebral blood flow (rCBF) in the amygdala and electrodermal activity (EDA). Participants consisted of women (mean age of 30) who were psychologically screened for any phobias and cleared for psychological and neurological defects, including medications.

The study was conducted in three phases, the first of what was dubbed the habituation phase. A video of a snake was presented to the participants without additional stimulus. The acquisition phase followed, consisting of CS-US association formation, where the same video was paired with six unconditioned electrical shocks which converted the video into the conditioned stimulus. The third was the extinction phase, now that the participants were conditioned to fear the snake video. The video was played once more without any electrical shocks and their rCBF was measured. PET scans were table twice during the study and during all conditions. The shocks were only strong enough to induce discomfort in participants, not pain. EDA was measured using the second digit finger of participant's left hand. The extent participants were successfully fear conditioned was made through the observation of scans

before and after CS-US association formation, including participant's rCBF and EDA. They found that there was a significantly positive correlation between EDA and rCBF in the right hemi-sphere of the amygdala. The researchers concluded that from their PET scans, for paradigms involving fear conditioning in humans, a higher metabolic demand in the right amygdala was present following fear conditioning. An idea consistent with the idea that the amygdala has a role in fear conditioning.

Their results can be considered reliable since there was evidence of standardised procedure. For example, all participants were exposed to the same videos, the spot the EDA was measured on their bodies was the same and there was no audio for all observations of the conditioned stimuli which should mean the results are replicable. They can be said to easily generalised to neurofunctional humans because participants around the age of 30 were used since human brains reach full maturity at around 25 years of age (*Brain Maturity Extends Well Beyond Teen Years : NPR*, n.d.). This is strength because it reduces potential extraneous variables – in addition to clearing participants of any neurological defects – related to potentially underdeveloped brain regions, namely the amygdala which means the sample represents most humans without neurologic abnormalities and so can be applied to them. However, because of the small sample of eight all-female participants, there is also a lack of representation of male populations as well as a diverse range of humans, there could be some issues with the generalisation of larger populations. Furthermore, the results are – for the most part – correlational in nature given that no causal mechanism was drawn between the skin conductivity and neurological activity in the amygdala data collected during the experiment so the results cannot accurately explain the connection between fear conditioning and the amygdala directly which puts into question how well the study supports it.

Overall, the findings of Furmark et al are consistent with and in agreement with animal research on the topic of the amygdala's involvement of fear conditioning (Goldstein, 1992)(Ressler, 2010). This study is also one of the few that investigate the activation of the amygdala rather than effect on fear after lesioning, such as the case study of SM as discussed earlier (Feinstein et al., 2011). Further, from a holistic perspective it could be said the results do not fully encompass the correlation of fear conditioning since the CS served as only a visual stimuli whereas fear

conditioning is an extremely multi-faceted internal process governed by an extensive conditioning paradigm in real world situations, unlike the single sensory stimuli of the snake video (Veit et al., 2013). As such, for the CS to develop fear conditioning in individuals to its fullest extent, it would be necessary for future research on this topic to ensure the CS involves a multitude of sensory stimuli a kin to real world conditioned stimuli to properly gauge true fear conditioning which in turn would allow for more concrete analysis of the amygdala's role in fear conditioning. In spite of this, it is evident that the amygdala has a clear connection with fear conditioning, even if we do not know exactly why that is.

Opposing evidence

Not all evidence agree that the amygdala has a distinct role in the fear conditioning of humans. For example, a study conducted by Feinstein et al 2013 – the same researchers who conducted the case study on SM earlier in the paper – is one such study as they managed to find fear conditioning when the amygdala was absent (Feinstein et al., 2013). They aimed to investigate the fear responses in patients with complete bilateral amygdala lesions from 35% CO_2 exposure. The experimental group were female patients with Urbach-Wiethe disease, resulting in the complete bilateral destruction of their amygdalae. SM was included in the sample along with a pair of monozygotic twins – known as AM and BG. Their mean ages were 39.33 and mean years of education was 13.33. The control group consisted of women with no reported personal or familial history of neurological disorders (Rassovsky & Kushner, 2003). Prior to the experiment, participants completed the Beck Anxiety Inventory which found them to have low baseline levels of anxiety. Participants were all exposed to inhalation challenges using a plastic mask covering their nose and mouth, whilst laying down on their backs in a reclined chair and secured to the chair to prevent them from falling out. Physiological conditions such as respiratory rate, heart rate and skin conductance were measured throughout the experiment. The volumes which participants inhaled were recorded. This information was used – alongside their heights and weights – to calculate their Forced Inspiratory Vital Capacity (FIVC). Seventy-five percent of

participant's relative FIVCs were inhaled. Single-breath FIVC challenges were undergone, half using atmosphere air, the other using 35% CO_2. Procedure repeated at a later date. Participants were unaware which order these were in. Breaks were spliced between the trials. After each inhalation challenge, multiple self-report questionnaires were given to participants to fill, including an inhalation symptoms checklist by the DSM-IV which collectively rated participant's levels of fear, intensity of the challenge and anxiety levels. They were then asked to rate how they felt during and after their inhalation symptoms were at their maximum in addition to how they currently felt.

All participants of the experimental group reported experiencing fear during the challenge which were consistent amongst the repeats, with only 3/12 of participants in the control group matching this. All participants who panicked found the aversive stimuli of CO_2 inhalation to be a more stimulating and fearful experience than those in the control group who did not panic. Interestingly, the experimental group denied feelings of anger, which meant that it was only their fear responses that were induced by the CO_2 inhalation. There was also a significant increase in physiological processes between the experimental group and non-panicking members of the control group. This was not the case between the control's panicking members and the experimental group. The experimental group were surprised by their reactions as it was their first experience with conditioned fear. They concluded that bilateral amygdala lesions did not inhibit the experience of fear in humans which contradicts the Feinstein's earlier research.

A strength of this study was that they were able to replicate their results since they found participants reacted similarly between the repetitions of the inhalation challenge which means the results can be said to be reliable. Moreover, the studies use of a control group establishes a baseline in neurologically-intact individuals to be used as a point of reference for effective comparison with the experimental group, which is important in determining the extent to which the experimental group bilaterally lesioned amygdala group differed from the control group, showing accuracy in their results. The study however, appear to be largely correlational for the most part, no causal mechanism for why exactly the experimental group showed fear conditioning when exposed to CO_2 inhalation compared to typical visual or auditory aversive stimuli such as scary movies or haunted houses in the case of SM was established, meaning the

result's ability to explain the phenomenon is lacking, which decreases construct validity. Additionally, ecological validity is absent from the results as inhalation of 35% CO_2 is an unrealistic real-life situation, so the results lack mundane realism and thereby, difficult to apply to real-world scenarios.

The atypically aversive US that is CO_2 smoke inhalation suggests that to consider the amygdala as the only processor of fear is reductionist in nature. This evidence clearly shows that some sort of dormant pathway was activated by the inhalation challenge. A discrepancy which could have a few explanations to it. The unconditioned stimulus provided by this challenge compared to other stimuli tested by Feinstein et al may have induced fear as CO_2 works internally on the acid-activated chemoreceptors in the body which detects when the blood becomes acidic, something excessive CO_2 inhalation can cause (Preter & Klein, 2008)(Ziemann et al., 2009). Thereby triggering the fear response interoceptively compared to the visual and auditory stimuli used in Feinstein's past research which acts in an exteroceptive way to induce fear. Which could also suggest that different brain regions may correspond to different types of fear (Killcross et al., 1997). This could explain SM's lack of fear conditioning in Feinstein's previous study with her, the CO_2 inhalation happened to activate the appropriate fear pathways. There are important generalisability issues to consider as – similar to the first two studies – only women were used, which means men are not being represented in these experiments.

In summary, given that it was established earlier than individuals like SM understand the concept of fear and had experienced for first time – in addition to the study's findings – there is more to the fear conditioning than the amygdala.

A study that sheds light on this complex interaction between fear conditioning and human neurophysiology was conducted by Sehlmeyer et al. They conducted a meta-analysis aimed to review research pertaining to aversive fear conditioning in humans via PET and functional magnetic resonance imaging scans to allow for the consolidation of their results to arrive at a generalised conclusion (Sehlmeyer et al., 2009). Forty-six neuroimaging studies were collated using the PubMed research database between 1994 and 2008 using keywords such as "fear",

“humans”, “conditioning” “neuroimaging”, etc… There was a criterion the researchers used to prune irrelevant studies by analysing their abstracts, determining if they used PET or fMRI, participants were neurologically sound, and if there was an explicit focus on fear conditioning. Additionally, the experimental designs for fear conditioning being measured by fMRI and PET were compared, with a focus on the significance of experimental variables. The data for the studies were extracted by multiple individuals, the first initial author followed by an independent double-checking of inclusionary criteria by a second author. Any inconsistent or conflicting findings were then reviewed by a senior author who reviewed the conflict and determined the correct viewpoint. Variables from the data were extracted and then organised based on six attributes such as variables used to measure the fear conditioning process. During analysis of the extracted data, the frequency of brain area activation during fear conditioning were assessed, including the identification of common and different areas of activation across the studies. Those that reported activation of brain areas that could form a core fear network were further examined for validity, in terms of experimental method, or explanations provided by the studies themselves. The researchers avoided the statistical combination of results in the studies individually given that each one differed in their experimental procedure.

The summarised results of the meta-analysis go as follows. The anterior cingulate cortex and insular cortex were key imperative to the development of delay fear conditioning – findings which were independent of overall experimental procedure of the studies and with sixteen studies supporting either brain region each. Sixteen of the studies also found left and right hemi-sphere activation of the amygdala but both were not present at the same time. Nineteen of the studies reported no amygdala activation. Many of the results of these studies overlapped. The researchers concluded that the amygdala, insula, and ACC played a significant role in fear conditioning and appear to interact with each other given the simultaneous activation of these areas during fear conditioning, suggesting these areas form a fear network.

The results of the study can be said to have high internal validity since multiple individuals reviewed which studies to reject for their final collection. Having a first, second and senor authors assist in preventing bias within the inclusionary and exclusionary criteria and as so it can be said the meta-analysis was completed with a large degree of accuracy. Another strength

of this meta-analysis was that the results can be considered reliable, this is because findings were mostly consistent amongst the studies included in the meta-analysis as to which brain areas were activated during the onset of fear conditioning, thereby making the results highly replicable. The construct validity of the study can be put to question, though the meta-analysis sought to acquire a full picture of the neurology of fear conditioning, the studies used may not have had an experimental procedure explicitly measuring the activity of multiple brain regions during fear conditioning, rather the focus could have been on single brain regions, meaning the meta-analysis might not accurately represent data on the neuroimaging of fear conditioning as a hole.

As is the nature of meta-analysis, the research of Sehlmeyer et al provides a holistic and more complete view as to the neurological basis of fear conditioning. Their analysis found there was both amygdala activation and non-activation in the studies. Additionally, the heavy that the insula and ACC not only activate during fear conditioning is consistent with the identification of core neural networks about these areas that contribute to fear (Maren, 2001). In short, these findings could possibly implicate the amygdala, insula, and ACC to form a core fear network within humans. As such, rather than the amygdala being the direct contributor to fear conditioning fear conditioning is instead facilitated by a core fear network. Although, it is important to acknowledge the meta-analysis did not explicitly aim to investigate the amygdala's role in fear conditioning directly and as such could have excluded studies that would support its involvement.

Conclusion

Taking into account the analysis of the evidence discussed in this essay, research into the amygdala's role in fear conditioning is robust enough to reasonably suggest that it does play a significant part in the explanation of fear conditioning within humans. However, according to said evidence, there is very clearly more to fear conditioning than just the amygdala and as such would be reductionist to claim solely explains it. Though these studies suffer from methodological weaknesses, namely the correlational nature between the amygdala and fear conditioning, they are useful in discerning the full extent of the amygdala's involvement with fear. This makes sense – as discussed earlier – fear is a multi-faceted, complex process. Whilst it is fundamentally a repeated process of CS-US association formation, simplifications of it on a neuropsychological basis can result in contradictory perspectives as seen in both of Feinstein's studies. Furthermore, three out of the four evidences covered consisted only of women, which makes generalisation of the amygdala's role in fear conditioning difficult to apply to men.

Additionally, the meta-analysis did show there to be a large possibility that other brain areas do contribute to fear conditioning despite evidence of amygdala activation and because of this, more focused research is required to determine if the amygdala simply contributes to fear conditioning or plays a central role in the core fear networks underlying it. The amygdala's involvement in fear conditioning is certain but more research is required to elucidate an understanding of how neurological networks underlie this process and its interaction with other brain areas. In conclusion, based on the evidence and critical analysis put forth, the amygdala cannot fully explain the role of fear conditioning in humans.

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