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Contingency awareness and its effects on fear-potentiated startle and extinction

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Main thesis for psychological professional studies (PSY-2901). April 2019.



Acknowledgments

My greatest gratitude to my advisor, Ole Åsli, for providing the project and research model for me to use in my thesis. His guidance and notes to help better my thesis was invaluable, especially his help analysing the data, writing the method and result part of my thesis where he contributed considerably.

Thank you to the department of psychology at the University of Tromsø for providing me with lottery tickets to gift the participants of the study and for providing a laboratory where I could execute the research and gather the data for this article.

A special thanks to all 41 participants who spent an hour of their life to help psychological research a step further.

Abstract

Fear-potentiated startle is defined as an increase in the magnitude of the startle reflex in the presence of a stimulus that has been paired with an aversive stimulus or event. It has been debated how much awareness of contingencies can affect fear-potentiated startle and the extinction of this. A conditional discrimination procedure was adapted to a human fear-potentiated startle paradigm in 33 healthy volunteers. This procedure allowed an assessment of startle responses at different lead intervals, as well as the participants awareness of contingencies in the study and the effect this had on the extinction phase. The participants achieved successful fear conditioning and fear-potentiated startle responses, but not satisfactory contingency awareness. There was significant extinction on the two longest lead intervals, but no extinction was found for the shortest lead interval.

Introduction

Based on reports from a survey provided by the World Health Organization, about 5-30% of people are affected by an anxiety-disorder at some point in their life (Kessler et al, 2007) and approximately 10% are suffering from this at any given time in Norway (Kringlen et al, 2001). Social anxiety and specific phobia are amongst the most common anxiety disorders (Kessler et al, 1994;).

According to the Norwegian health report for 2018 will in any given year approximately one out of five adults suffer from a mental disorder (Folkehelseinstituttet, 2018). Approximately one out of three adults will suffer from an anxiety disorder during their lifetime, one out of four will suffer from a depression or mood disorder (Folkehelseinstituttet, 2018).

In Norway (2014), one out of three adults were granted disability benefits (uføretrygd) with a mental disorder as the main diagnose (NAV, 2017). People in Norway who are granted disability benefits on the account of a mental disorder are on average younger than the ones granted disability benefits for other diagnosis (Mykletun & Knudsen 2006; Knudsen et al, 2010). Mental health disorders, especially anxiety and depression, are a huge socio-economical challenge in the Norwegian healthcare system, a challenge we should strive to solve in better ways in the future. One of the puzzles to solve if we were to successfully decrease the amount of people struggling with these disorders are obviously preventative measures, but also reaching a better understanding of the disorders and their components to hopefully achieve better treatment regiments.

One of the most used therapies for these diagnoses has been, upto now, cognitive behavioural therapy (Davis, 2011; Otte, 2011). These have been working, but not optimally. The reason seems to be that in extinction based therapies the patients learn to control, conquer or handle their fear-induced behaviour or the fear-induced situations, but the fear itself seems to stay with them. It is often reported deficits or resistance to extinction, even after a successful

extinction procedure, phenomenon like reinstatement, renewal or spontaneous recovery can happen (Davis, 2011). It seems like learned fear is quite difficult to extinguish, and one problem might be that you cannot extinguish every trace of fear. Even if the extinction therapy seems to be working, there might still be some parts of the fear left. Parts that are governed by foundational biological elements which are indeed quite hard to extinguish (Davis, 2011). Learning to predict or avoid danger based on previous events is one of the most basic biologically based elements of an animal or organisms' survival. The inability to overcome excessive emotions like fear or anxiety, define many psychiatric disorders such as; phobias, posttraumatic stress disorders (PTSD) and panic disorder. Given the fact that a majority of people who struggles with anxiety disorders, are in particular afflicted with social anxiety and specific phobia (Kessler et al, 1994; Kringlen et al, 2001), a large proportion of these problems are caused by fear learning or fear conditioning (Öhman & Mineka, 2001). Previous research argue that fear learning or fear conditioning can happen both consciously and unconsciously, in other words; with or without contingency awareness (Clark & Squire, 1999; Lovibond & Shanks, 2002; Lovibond & Shanks, 2002). The role contingency awareness play on the magnitude on physical activating induced by fear is an ongoing discussion and needs further empirically investigating. This will hopefully provide us with more information about how plausible it ever will be to extinguish every trace of unreasonable fear in our patients.

Research models using fear conditioning and fear inhibition provide useful tools to examine these phenomena. To achieve fear-conditioning, it is important that the participants learn to fear an explicit and predictable cue. We distinguish fear from anxiety whereas fear is linked to a specific threat, whilst anxiety is a more generalised activity produced by less predictable fear (Grillon, 2002). In other words, fear relates to a known threat, whereas anxiety is a diffuse fear not linked to a specific threat (Jovanovic et al, 2006). To measure fear

properly, it is therefore important to find out how aware the participants are of the contingency between the CS and the US. The term contingency awareness is defined as the participants' knowledge of the reinforcement contingencies in the experiment (Lovibond & Shanks, 2002). The role of consciousness and fear conditioning has been disputed amongst researchers. Some suggesting that fear conditioning may occur through unconscious, automatic mechanisms that are independent of awareness (Seligman, 1971). Lovibond (2004) contrasts this view by suggesting a cognitive model of fear conditioning where awareness of experimental contingencies is necessary for fear conditioning and extinction. He argues that a subject who is aware of the contingency in the experiment, should show a significant increase in startle whenever CS+ is presented and consequently would a subject who is not aware of the contingency would be unable to predict when the US would occur and should theoretically show an increased startle to all stimuli rather than to any particular stimulus, demonstrating a more anxiety-like response (Lovibond, 2004). This finding was replicated by Grillon (2002) who compared fear-potentiated startle between subjects who were aware and unaware of the reinforcement contingency.

Inspired by Jovanovic et al (2005, 2006), we wanted to create a human fear conditioning paradigm that can assess fear potentiation and fear extinction under conditions where they are relatively independent, using a fear-potentiated startle paradigm (Jovanovic et al, 2005). Fear-potentiated startle is defined by the relative increase in the amplitude of a startle reflex when elicited in the presence of a conditioned stimulus (CS+) previously paired with an aversive stimulus of unconditioned stimulus (US) (Jovanovic et al, 2006). Fear-potentiated startle can be demonstrated in humans and animals (Grillon & Baas, 2003). Therefore, it can be used for translational research and can serve as an objective measure of conditioned fear, attempting to help us understand more of the biological and physical aspects of fear-related behaviour and illnesses.

This model attempts to use one of the best understood experimental models for this type of learning, classical fear conditioning and extinction. Here, two different tones are presented as auditory stimuli and were accompanied by periodically auditory noise which were meant to cause a startle-response by causing muscular contractions under the right eye (orbicularis oculi). We wanted each participant to condition one of the tones to the electrical stimuli and measure their startle-response to the noise following the tones. The participants were randomly assigned to two groups where they went through a conditioning phase where one of the two tones (CS+) were paired with an aversive electrical stimuli in their fingertips (US) and the other tone had no pairing with the electrical stimuli (CS-). After this the participants underwent an extinction phase where the auditory stimuli (both tones and noise) was presented, but never accompanied by electrical stimuli. By conditioning the participants to differentiate between the two tones (one paired to startle-eliciting stimuli and one not), thereafter extinction of this pairing, we wanted to examine if consciousness had a modulating effect on the participants' physical activation (startle reaction).

We wanted to examine if conditioned fear would remain after extinction. We used three different lead intervals to measure fear-response (startle) to see if there were any difference in the extinction phase at the different lead intervals. Our hypothesis was that we would see a fear-response at 200 ms, 1000ms and 4000ms. We also hypothesised that we would only see an extinction at 4000 ms, possibly 1000 ms, but not at 200 ms. We believe that a fear-response (startle) conditioned at 200 ms is mostly an unconscious reflex and would be quite robust against conscious inhibition or extinction, because the brain would not have enough time to regulate the startle-response. This is in contrast to the intervals at 1000 ms and 4000ms, where we believed the brain would have enough time to do a conscious extinction or inhibition of the startle-response, which would show in the extinction phase.

Method

Participants

Thirty-three subjects (22 females and 11 males, age range 19-44, mean age 25,1 years) participated in the study. Six participant were excluded from the study due to absent startle-response. Two more candidates participated, but withdrew themselves from the study. The participants were randomly assigned to one of two groups; where the electrical stimuli were paired to different auditive stimuli in each group. One of the groups contained 17 (group A) participants and the other 16 participants (group B).

All participants were in good health and did not report any serious disease, injury or use of strong pain-medicine. The participants were instructed to refrain from caffeine consumption and use of nicotine-containing substances 3 hours prior the beginning of the study.

Written informed consent was obtained from all participants, who were awarded two lottery tickets (equivalent to 50 NOK) for their participation and time.

Apparatus and stimuli

Eyeblink electromyographic (EMG) responses were recorded from the right orbiculari oculi with two Ag/AgCL Sensor Medics miniature electrodes (2mm diameter) filled with Ultra Phonic conductivity gel. Inter-electrode distance was 1,5-2,5 cm. The ground electrode was placed centrally on the forehead, with two other electrodes placed respectively under the center of the right eye and under the outer corner of the right eye. The EMG signal was amplified by a factor of 60,000 and filtered (passing 90-250 Hz) by a Coulbourn S75-01 bioamplifier. The signal was rectified and integrated with a Coulbourn S76-01 contour-following integrator with a 10-ms time constant. The output was sent to the PC via a Keithley interface.

Sampling on each trial began 100 ms prior to onset of the startle stimulus and continued for 200 ms after onset of the stimulus. The sampling rate was 1000 Hz.

The emotional valence and arousal elicited by the electric stimuli and auditory stimuli were recorded with self assessment forms where the participants graded the likelihood of a connection between auditory stimuli and electric stimuli as well as the level of comfort and discomfort experienced by the different stimuli.

Procedure

After arrival at the laboratory, the subjects were seated in a reclining chair adjoined to a table in the experimental chamber where they read and filled out the Informed Consent Form. The subjects were informed of the general purpose of the study, the procedure and the different stimuli. They were also informed that they could withdraw from the study at any time without giving any reason for this.

The skin below the participants' right eye was cleaned with a swab containing alcohol and pumice, and the three electrodes for measurement of the eyeblink electromyography (EMG) were attached. The electrodes for the electrical stimuli were attached to the middle- and index finger of the participants' non-dominant hand. The electrical stimulation had a 500 ms duration and intensity of 0.1-4.0 mA at 9 V, delivered through the finger stimulator (E13-22, Coulbourn Instruments, Whitehall, PA, USA). The intensity of the electrical stimulation was individually adjusted. The administrator of the study elicited the electric stimuli and the participants verbally instructed to go up or down a level until they found a level that was unpleasant, but not severely painful. After this, a test-run with a duration of one minute were completed to let the participants experience the auditory and electric stimuli and to get a subjective baseline measurement to know if there was any change compared to phase one (conditioning) or phase two (extinction). The door to the experimental chamber was closed to

avoid any noise-pollution. A self-report form was given to the participant directly after the one minute test-run. The experiment began shortly after with phase one, the conditioning phase, where the two different groups experienced different auditory pairing to the electric stimuli.

In the conditioning phase, startle-eliciting noise was presented at lead intervals of 200, 1000 and 4000ms relative to onset of the CS+ and the CS-. Each lead interval was presented six times. After each trial presenting the CS+, the US was presented at 4500 ms following CS+ onset. As such, the participants received 18 trials of differential classical conditioning. In one group a 1000 Hz tone served as the CS+, and a 2000Hz tone was the CS-. In the other groups the CS+ and CS- was reversed. The interstimulus interval from CS+ onset to US onset was 4500 ms. The 5000 ms CS+ and the 500ms US co-terminated. The intertrial interval (ITI) between two presentations of the CS+ was between 18 and 22 s (mean 20.2 s). The participants also received 14 presentations of the 5000 ms CS-. The ITI between the CS- and CS+ was between 8 and 14 s (mean 11 s). The different lead intervals were presented in semi-random order, so there could be no more than two consecutive presentations of the identical stimuli. The startle-eliciting noise was also presented six times alone such that a total of 42 trials were presented in the conditioning phase. After the conditioning phase, two more self-report forms were filled out by the participants. Thereafter, the extinction phase was initiated. The participants still had the electricity-electrodes on, but in this phase, electricity was never presented. Startle-eliciting noise was presented at the same lead intervals of 200, 1000 and 4000 ms relative to onset of the CS. Each lead interval was presented six times. In the extinction phase no USs were presented. Two more self-report forms were filled out by the participants at the end of the experiment.

Subjective measurements

After the three phases (pretest, conditioning and extinction), each participant filled out self-assessment forms. The self assessment forms were the same as used in a previous study done by Åsli and Flaten (Åsli & Flaten, 2012);

Emotional valence elicited by the CS and the US was recorded with 10 centimeter visual analog scale (VAS). The participants were asked “please mark on the line below how you would rate the tone on a scale from unpleasant to pleasant.” The response range was from 0 to 100 millimeters and a scale with two anchors “unpleasant” at the left end of the scale and “pleasant” at the right end.

Contingency awareness was assessed by a self assessment form asking “Was there at relationship between the two different tones and the electrical stimulation?”, next the participants were asked to define the correctness of several statements on at 10 cm line, with a response range from 0 (“correct”) to 100 (“incorrect”). The questions asked them to rate the likelihood of different connections between the auditive stimuli and the electrical stimuli.

They were also asked to define the pleasantness or unpleasantness of the auditive stimuli and the electrical stimuli.

Response scoring and data reduction

Startle blink reflexes were scored as the difference between the maximum amplitude of the EMG response in the window from 0 to 200 ms after noise onset, compared to the mean EMG level for the last 100 ms prior to onset of the startle-eliciting noise on that trial. To count as a response, maximum amplitude had to be 30 A/D units or more above baseline. Modulation of startle reflexes was calculated as a difference score. Average responses to the startle-eliciting noise alone (i.e., the control condition) were subtracted from that of each lead interval. A result of 0 indicated that the CS did not modulate startle reflexes, whereas a result above or

below 0 meant that the CS potentiated or inhibited the startle reflex, respectively. This method is not affected by differences in control startle magnitudes.

Design and Statistics

The design for the experiment was a 2 Phases (conditioning, extinction) x 3 Lead Interval (200, 1000 & 4000 ms) within-subjects design. However, at there was no difference in phase, analyses of the conditioning phase was done separately. In addition, a different analysis with only the last three trials of each Lead Interval was conducted, as described in the results section under “Analysis of second block”.

Theoretically interesting and significant main effects or interactions were followed up by contrast analyses. Other main effects or interactions were followed up by Tukey’s HSD test.

Results

Subjective ratings

Rating of the pleasantness of the tones

In scores ranging from 0 (unpleasant) to 100 (pleasant) for the electrical stimuli, the participants reported a mean of 25,6 for the conditioning phase and a mean of 31,1 for the extinction phase.

When comparing the participants rating of the pleasantness or the unpleasantness of the auditive stimuli after the different phases, here was a significant effect in the pretest phase, where the participants rated the tones as more pleasant than compared to the conditioning and the extinction phase $F(2,64)=8,82, p<.01$ (figure 1).

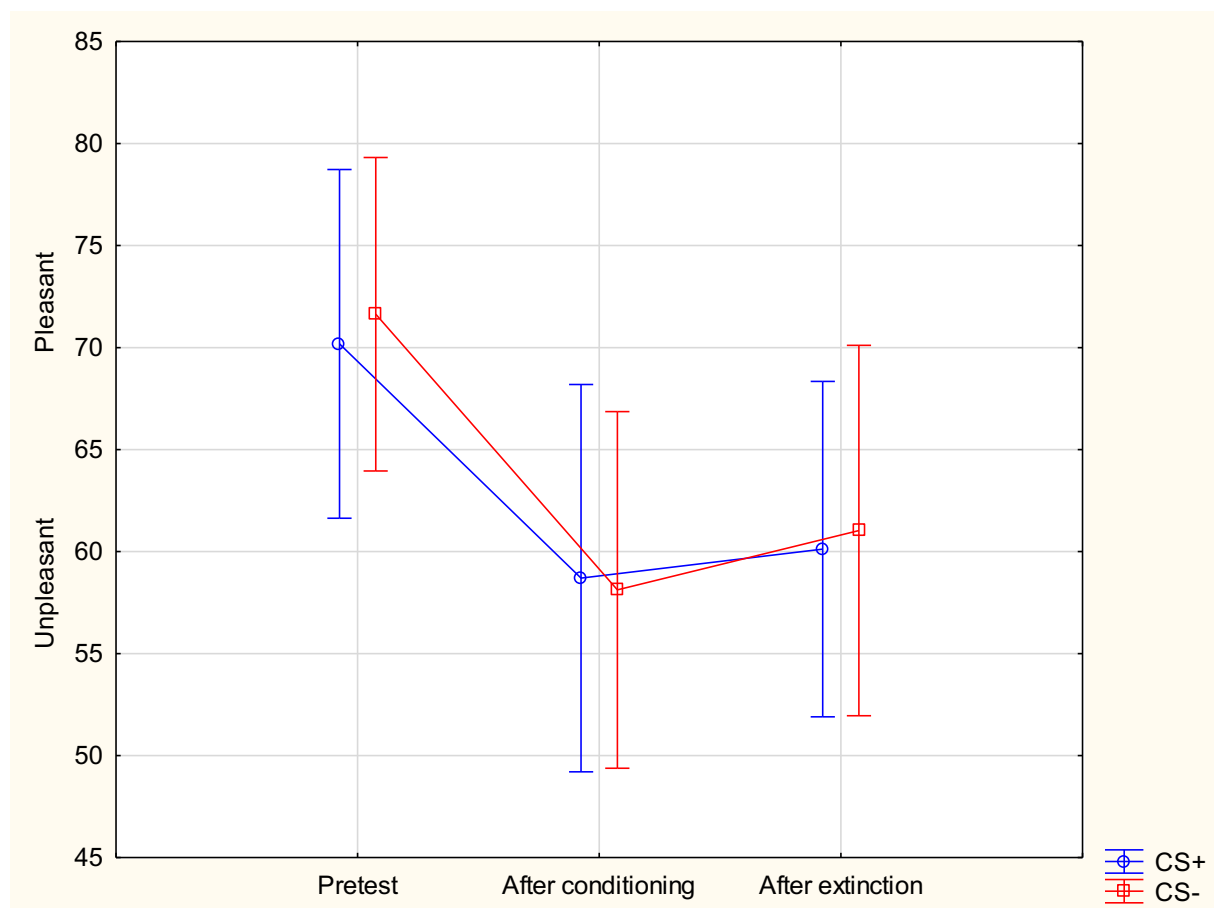


Figure 1. Rating of pleasantness/unpleasantness of the auditive stimuli in the different phases.

Contingency awareness

With scores ranging from 0 (full contingency awareness) to 100 (no contingency awareness), the participants reported a mean of 34,5 after the conditioning phase, and a mean of 12,6 after the extinction phase. Results show that after the conditioning phase, the participants were unsure about the connection between CS+/- and US. After the extinction phase the participants report a more certain and correct connection between the CS+/- and the US ($F(1,32) = 9,03, p < .05$).

Startle

The interaction of Phase x Lead Interval x CS was not significant $F(2, 64) = 1,70, p > .19$ (Figure 2). This analysis included all trials. However, for the first trials there were no effect of conditioning (and extinction in the second phase). A second analysis included only the second block (the last three trials) of each phase.

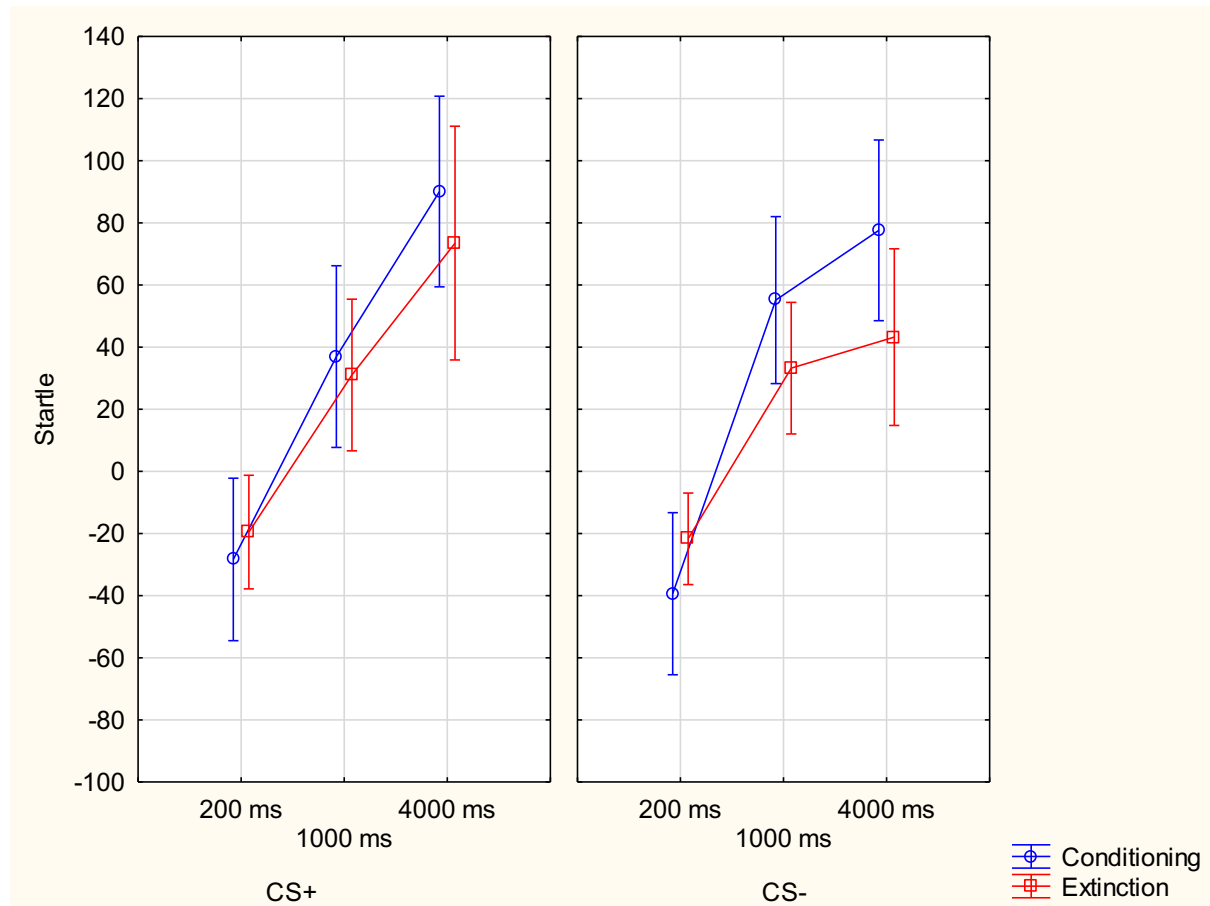


Figure 2. Startle responses at different lead intervals during the conditioning phase and the extinction phase. Error bars represent +/-1 standard error of the mean.

Analysis of second block

There was a significant main effect of Phase $F(1, 32) = 8,78, p < .01$, as the startle responses was smaller in the extinction phase compared to conditioning phase. The main effect of Lead interval was also significant $F(2, 64) = 29,10, p < .01$. The interaction of Phase x Lead interval was significant $F(2, 64) = 5,40, p < .01$. The interaction of Phase x Lead interval x CS was not significant $F(2, 64) = ,23, p > .79$.

Analysis of CS+ second block

There was a significant main effect of Phase $F(1, 32) = 5,40$, $p < .05$, as the startle responses was smaller in the extinction phase compared to conditioning phase. The main effect of Lead interval was also significant $F(2, 64) = 26,27$, $p < .01$. The interaction of Phase x Lead interval revealed a tendency toward significance $F(2, 64) = 2,85$, $p < .07$ (Figure 3).

Following up this tendency, contrast analysis showed increased startle in the Conditioning phase at the 1000 and the 4000 ms lead interval ($ps < .05$) compared to the extinction phase, but no difference at the 200 ms lead interval.

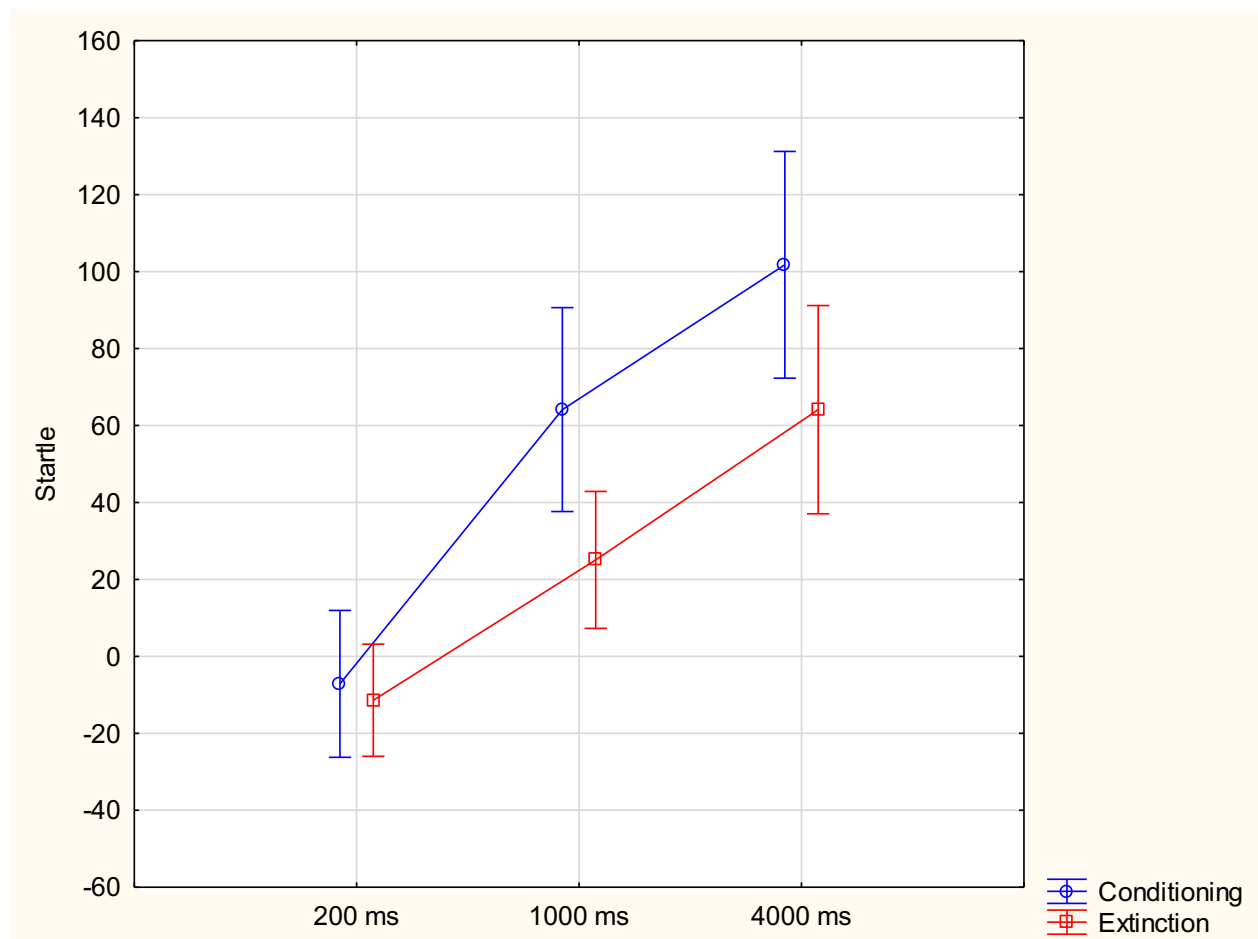


Figure 3. Startle responses at different lead intervals during the second block of both the conditioning and the extinction phase. Error bars represent +/-1 standard error of the mean.

Fear conditioning at 200 ms

There was a significant effect of increased startle response for CS+, from block one to block two, at 200ms lead interval $F(1, 32) = 6,19, p < .01$.

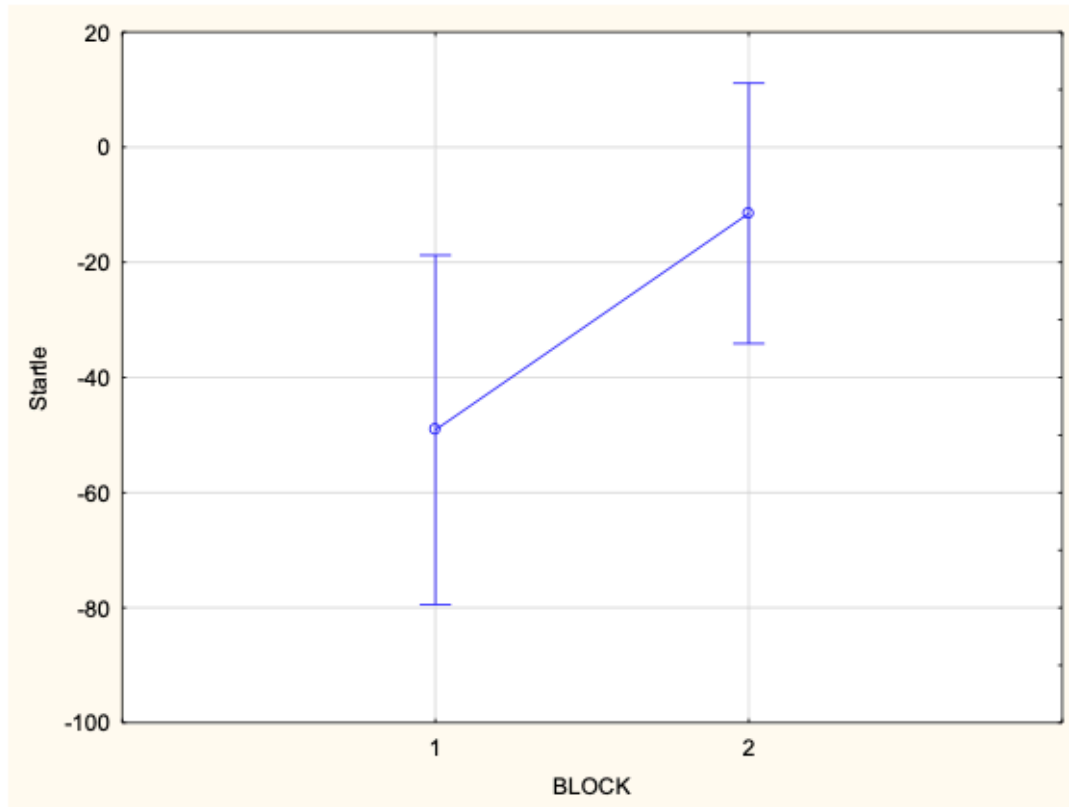


Figure 4. Startle responses at 200ms lead interval for CS+ over two blocks. Error bars represent +/- 1 standard error of the mean.

Discussion

Based on the results, it seems like our hypothesis has some further support. After adjusting our analysis to look at specific blocks, we found signs of fear extinction at lead interval 1000ms and 4000ms, but not at 200ms. We found however significant fear conditioning at 200ms. Furthermore, it looks like the participants were not able to distinguish between the two tones and consequently conditioned both tones to the electrical stimuli. In other words, fear conditioning happened, but not in the way we expected to. As a result, we were not able to examine the effects of contingency awareness like we had planned, but could still examine an effect of contingency awareness by looking at the different lead intervals and the participants' subjective reports.

In this study, we wanted to see how consciousness plays a part in fear-conditioning, physical activation (startle-response) and in fear extinction. It seems like the participants were struggling to distinguish between the auditory stimuli (the two different tones) and thus not achieving contingency awareness. This might be a result of too few trials. On the other hand, when comparing to similar studies like Jovanovic et al (2005; 2006), we had a total of 42 trials in the conditioning phase compared to Jovanovic et al (2005; 2006) who used a total of 18 trials in the conditioning phase where they reported a somewhat successful contingency awareness. In their study, they used visual cues to achieve fear conditioning whereas we only used auditory cues. On the other hand, Hamm et al (2003), showed acquisition of fear-conditioned startle potentiation in a patient suffering from bilateral cortical blindness, using a neutral visual conditioned stimulus which the subject had a potentiated startle to. It is possible that the two tones we used in our study was too hard to distinguish, that they were too similar, especially in a somewhat pressed situation where the participants expected unpleasant electrical stimuli at any given time. This might have placed our participants in a state where they showed an increased startle to all stimuli, demonstrating a more anxiety-like response,

not being able to predict when the US would occur due to insufficient contingency awareness much like Lovibond (2004) and Grillon (2002) has previously argued.

In Jonvanovic et al study (2005), the participants were asked to rate each stimulus in the trial consecutively during the conditioning phase, where we asked the participants to rate their overall impression of the stimuli after the conditioning phase. This might have made it harder for the participants to develop a contingency awareness given the fact that we operated with three different auditive lead intervals. Our participants had to use their memory to filter through the different lead intervals after the conditioning phase and were therefore heavily reliant on the comprehensive hippocampal part of the process. In contrast, the participants from Jovanovic et al (2005) could immediately consider the stimuli after each presentation during the conditioning phase, possibly relying more on the immediate response of the amygdala.

When the participants reported on the pleasantness and the unpleasantness of the different tones and the electrical stimuli, they reported the tones as more unpleasant after the conditioning and extinction phase, and might be a result of a fear-conditioning. On the other hand, if this was due to a fear-conditioning, the effect should have disappeared after the extinction phase, which it did not. It is more likely that this is a result of the noise appearing at the end of the tone after the pretest phase. As mentioned earlier, the participants struggled to differentiate between the tones and if they connected the noise sound to the tones, it might have influenced the experience of the tones negatively since the noise is loud and startle-eliciting. Consequently, we had to discard the results measured for CS- given that it seems like the participants struggled to differentiate between the two tones and therefore affiliated both tones with noise or electrical stimuli.

Even though contingency awareness was not achieved satisfactory, the participants were successfully fear conditioned to the auditive stimuli, without being able to differentiate

between the different tones. As we hypothesised we could see an extinction effect on lead interval 1000ms and 4000ms, but not at 200ms. Looking at the results for the 200ms tone length, there is no significant difference between the conditioning phase and the extinction phase. There were possibly too few trials and it is debatable if there was a fear-conditioned response at 200ms and no extinction, or if there was no fear-conditioning and therefore no extinction. It does however seem like a significant fear-conditioning was achieved. The results show that the participants startle-response had greater magnitude in trials 4-6 as opposed to trials 1-3 and one could therefore argue that fear-conditioning did happen without contingency awareness. The debate concerning whether fear-conditioning can happen with or without contingency awareness is still ongoing and several other studies have argued that fear conditioning can happen without contingency awareness (Seligman 1971; Ohman, 2005; Davis, 1992, 1998; Knight et al., 2003; Hamm & Vaitl, 1996). It is doubtful that any kind of contingency awareness can happen within a 200 ms timeframe, given the neurological complexity necessary for a contingency awareness compared to the neurological processes for a pure startle response without contingency awareness. A startle response is dependent on subcortical processes, especially cerebellum, as opposed to fear-conditioning (Clark & Squire, 1998; Clark & Squire, 1999). Fear-conditioning and contingency awareness is dependent on more comprehensive cognitive processes, using more areas of the brain, highly involving the hippocampus, the amygdala and prefrontal cortex (Fanselow & Kim, 1994; Miserendino, Sananes, Melia & Davis, 1990; McEchron, Bouwmeester, Tseng, Weiss & Disterhoft, 1998; Quinn, Oommen, Morrison & Fanselow, 2002).

Extinction is new learning, not unlearning or forgetting (Milad & Quirk, 2012), and is therefore a complicated process more dependent on consciousness to work. A fear-potentiated startle response is dependent on prefrontal areas, especially processes revolving the hippocampus and subcortical processes (Milad & Quirk, 2012). The neurological pathways

used in extinction heavily relies on the prefrontal cortex to initiate inhibition of the startle response which has already been potentiated automatically (Milad & Quirk, 2012). Much is known about the neurological factors of extinction, but thus far, there is no obvious explanation for the resistance to extinction. And a part of this question, may be answered by looking at the time necessary for the brain to involve all processes connected to extinction. Considering the fact that extinction involves several parts of the brain, especially relying heavily on the hippocampus and prefrontal areas, it is a neurological response that is quite time-consuming (relatively speaking) as opposed to a pure startle response (Milad & Quirk, 2012; Åsli et al, 2009; Åsli & Flaten, 2012). This might explain why we saw an extinction at 1000ms and 4000ms, but not at 200ms. It was simply not enough time for the brain to consciously inhibit or modulate the startle response. Åsli and Flaten (2012) reported similar results, arguing that the only effect of conditioned fear following trace conditioning was found 1500ms after CS onset.

Lovibond and Shanks (2002; 2002) has argued that previous studies has used inadequate measures of awareness and that previous studies might have underestimated awareness. In our study, it is possible that we have underestimated what is required to achieve contingency awareness. A true contingency awareness requires that the subject is aware whether the US follows the CS or not (Jovanovic et al, 2006). In our study, we used subjective measurements of contingency awareness. The participants had to self-report their conscious experience after the conditioning phase was over, relying completely on their own memory. In addition to this, by making our participants rate their subjective measures from 1-100 instead of giving them simple yes/no questions, we might have contributed to their unsureness and this might have affected the contingency awareness, or lack thereof. It is also possible that the participants would have achieved contingency awareness if we had used subjective tests during the conditioning phase, making it clearer that the participants should be

actively looking for connections between the stimuli. The use of subjective versus objective tests of contingency awareness is disputed (Shanks & Lovibond, 2002), both tests with their respective advantages and disadvantages. It would be interesting to further investigate in future studies if the use of objective or subjective tests of awareness during the conditioning phase, would have an impact on contingency awareness and consequently the extinction phase. As previously mentioned, our participants did not report a clear contingency awareness. However, we could still see effects of fear-conditioning at lead interval 200 ms, 1000 ms and 4000 ms and we could see effects of extinction at lead interval 1000 ms and 4000 ms. One could argue that fear-conditioning without contingency awareness has happened and that extinction is evidently not so dependent on contingency awareness.

To use these kinds of studies in the future for translational studies connected to anxiety disorders would be very interesting. The most used treatment method for anxiety and phobias is cognitive behavioural therapy, especially exposure-therapy, which is highly dependent on consciousness and fear extinction to work (Davis, 2011; Otte, 2011). The patient must have insight about the root of their issues, their triggers and the realistic dangers connected to their fears to change their mindsets and fear-related behaviour. Above all, the patient must also have the time to make a conscious choice when they are faced with their fears or triggers. It seems like some fear conditioned responses will be very robust against therapy, given the fact that our neurological fear-response system works so fast that a patient might in many cases not have enough time to inhibit or regulate their own responses. Considering the process is so fast, the patient might not even realise its own trigger before a fear reaction manifests. In other words, it looks like it might be close to impossible to extinguish all traces of fear with contingency awareness alone. Perhaps the answer to better treatment options for people suffering for different anxiety-illnesses is to not only focus on therapies relying on consciousness and contingency awareness. For some, unconscious conditioning, or therapies

building on these principles could be a supplementary option if psychotherapy is not working optimally.

Conclusion

In the present study, we found that fear responses were present at all the different lead intervals (200ms, 1000ms and 4000ms) in the conditioning phase, but the participants did not seem to achieve contingency awareness by not being able to differentiate between the different tones. They did however achieve a more generalised fear conditioning. There was only significant extinction at 1000ms and 4000ms, not at 200ms. This conformed well with our hypothesis, except that we expected a stronger contingency awareness from the participants. In conclusion, it looks like contingency awareness might not be necessary for fear conditioning or extinction. It is however necessary to investigate this further, especially considering contingency awareness was not achieved as planned in this study.

References

- Clark, R. E., Squire, L. R. (1998). Classical conditioning and brain systems: the role of awareness. *Science*, 280(5360), 77-81.
- Clark, R. E., Squire, L. R. (1999). Human eyeblink classical conditioning: effects of manipulating awareness of the stimulus contingencies. *Psychological Science*, 10(1), 14-18.
- Davis, M. (1992). The role of the amygdala in fear and anxiety. *Annual Review of Neuroscience*, 15, 353-375.
- Davis, M. (1998). Are different parts of the extended amygdala involved in fear versus anxiety? *Biological Psychiatry*, 44, 1239-1247
- Davis, M. (2011). NMDA receptors and fear extinction: implications for cognitive behavioural therapy. *Dialogues in Clinical Neuroscience*, 13(4), 463-474.
- Fanselow, M. S., Kim, J. J. (1994). Acquisition of contextual Pavlovian fear conditioning is blocked by application of an NMDA receptor antagonist D, L-2-amino-5-phosphonovaleric acid to the basolateral amygdala. *Behavioural Neuroscience*, 108, 210-212.
- Grillon, C. (2002). Associative learning deficits increase symptoms of anxiety in humans. *Biological Psychiatry*, 51, 851-858.
- Grillon C., Baas J., (2003). A review of the modulation of the startle reflex by affective states and its application in psychiatry. *Clin Neurophysiol*, 114. 1557-1579.
- Hamm, A. O., Vaitl, D. (1996). Affective learning: awareness and aversion. *Psychophysiology*, 33, 698-710.
- Hamm, A. O., Almut, I. W., Schupp, H. T., Treig, T., Dressel, A., Kessler, C. (2003). Affective Blindsight: Intact fear conditioning to a visual cue in a cortically blind patient. *Brain*, 126, 267-275. doi: 10.1093/brain/awg037.

- Jovanovic, T., Keyes, M., Fiallos, A., Myers, K.M., Davis, M., Duncan, E. (2005). Fear potentiation and fear inhibition in a human fear-potentiated startle paradigm. *Society of Biological Psychiatry*, 57, 1559-1564.
- Jovanovic, T., Norrholm, S.D., Keyes, M., Fiallos, A., Myers, K.M., Davis, M., Jovanovic, S., Duncan, E.J. (2006). Contingency awareness and fear inhibition in a human fear-potentiated startle paradigm. *Behavioural Neuroscience*, 120(5), 995-1004.
- Kessler R.C., Angermeyer, M., Anthony, J. C., De Graaf, R., Demyttenaere, K., Gasquet, I., De Girolamo, G., Gluzman, S., Gureje, O., Haro, J. M., Kawakami, N., Karam, A., Levinson, D., Mora, M. E. M., Oakley, M. A, B., Posada-Villa, J., Stein, D. J., Tsang, C. H. A., Aguilar-Gaxiola, S., Alonso, J., Lee, S., Heeringa, S., Pennell, B. E., Berglund, P., Gruber, M. J., Petukhova, M., Chatterji, S., Üstün, T. B. (2007). Lifetime prevalence and age-of-onset distributions of mental disorders in the world health organization's world mental health survey initiative. *World Psychiatry*, 6, 168-176.
- Knight, D., Nguyen, H. T., Bandettini, P. A. (2003). Expression of conditional fear with and without awareness. *Proceedings of the National Academy of Sciences of the United States of America*, 100, 15280-15283.
- Knudsen, A.K., Overland S., Aakvaag H.F., Harvey S.b., Hotopf M., Mykletun A. (2010). Common mental disorders and disability pension award: seven year follow-up of the HUSK study. *J Psychosom Res*, 69(1), 59-67.
- Kringlen E., Torgersen S., Cramer V. (2001). A Norwegian psychiatric epidemiological study. *Am J Psychiatry*, 158, 1091-8.
- Lovibond, P.F., Shanks, D.R. (2002). The role of awareness in Pavlovian conditioning: empirical evidence and theoretical implications. *Journal of Experimental Psychology: Animal Behavior Processes*, 28, 3-26.

- Lovibond, P.F., Shanks, D.R. (2002). Automatic and eyeblink conditioning are closely related to contingency awareness: reply to Wiens and Öhman (2002) and Manns et al. (2002). *Journal of Experimental Psychology: Animal Behaviour Processes*, 28, 38-42.
- Lovibond, P. F. (2004). Cognitive processes in extinction. *Learning & Memory*, 11, 495-500.
- McEchron, M. D., Bouwmeester, H., Tseng, W., Weiss, C., Disterhoft, J. F. (1998). Hippocampectomy disrupts auditory trace fear conditioning and contextual fear conditioning in the rat. *Hippocampus*, 8, 638-646.
- Milad, M. R., Quirk, G. J. (2012). Fear extinction as a model for translational neuroscience: ten years of progress. *Annual Review of Psychology*, 63(1), 129-151.
- Miserendino, M. J. D., Sananes, C. B., Melia, K.R., Davis, M. (1990). Blocking of acquisition but not expression of conditioned fear-potentiated startle by NMDA antagonists in the amygdala. *Nature*, 345, 716-718.
- Mykletun, A., Øverland S. Mentale lidelser undervurderes som årsak til uføretrygding. (2006). *Tidsskrift for Norsk Legeforening*, 126(11), 1491-1492.
- Norsk Folkehelseinstitutt. (2018). *Folkehelse rapporten – kortversjon Helsetilstanden i Norge 2018*. Hentet fra <https://www.fhi.no/globalassets/dokumenterfiler/rapporter/2018/helsetilstanden-i-norge-20182.pdf>
- Otte, C. (2011). Cognitive behavioural therapy in anxiety disorders: current state of evidence. *Dialogues in Clinical Neuroscience*, 13(4), 413-421.
- Öhman, A. (2005). The role of the amygdala in human fear: automatic detection of threat. *Psychoneuroendocrinology*, 20, 953-958.
- Öhman, A., Mineka, S. (2001). Fears, phobias and preparedness: Toward an evolved module of fear and fear learning. *Psychological Review*, 108(3), 483-522.

- Quinn, J. J., Oommen, S. S., Morrison, G. E., Fanselow, M. S. (2002). Post-training excitotoxic lesions of the dorsal hippocampus attenuate forward trace, backward trace, and delay fear conditioning in a temporally specific manner. *Hippocampus*, 12, 495-504.
- Seligman, M. E. P. (1971). Phobias and preparedness. *Behaviour Therapy*, 2, 307-320.
- Taylor, S.E. (9. edt). (2015). *Health Psychology* New York: McGraw-Hill Education.
- NAV. (2017). Utviklingen i uførediagnoser per 31. Desember 2014. Hentet fra <https://www.nav.no/no/NAV+og+samfunn/Statistikk/AAP+nedsatt+arbeidsevne+og+uforetrygd+-+statistikk/Uforetrygd/Diagnoser+uforetrygd>
- Weike, A. I., Hamm, A. O., Schupp, H. T., Runge, U., Schroeder, H. W. S., Kessler, C. (2005). Fear conditioning following unilateral temporal lobectomy: dissociation of conditioned startle potentiation and autonomic learning. *Journal of Neuroscience*, 25, 11117-11124.
- Åsli, O., Flaten, M.A. (2012). How fast is fear? Automatic and controlled processing in conditioned fear. *Federation of European Psychophysiology Societies*, 26(1), 20-28. doi: 10.1027/0269-8803/a000063
- Åsli, O., Kulvedrøsten, S., Solbakken, L. E., Flaten, M. A. (2009). Fear potentiated startle at short intervals following conditioned stimulus onset during delay but not trace conditioning. *Psychophysiology*, 46, 880-888.