Fear conditioning and context learning in relation to treatment outcome: a study in patients with partially remitted anxiety disorders

Duits, P.[1], Baas, J.M.P.[3], Engelhard, I.M.[1,2], van den Hout, M.A.[1], Heitland, I[3] & Cath, D.C.[1,2]

1. Dept. of Clinical and Health psychology, Utrecht University, Utrecht, the Netherlands
2. Altrecht Academic Anxiety centre, Altrecht, Utrecht, the Netherlands
3. Dept. of Experimental Psychology, Utrecht University, Utrecht, the Netherlands

ECNP Workshop, 7 – 10 March 2013, Nice, France

Background

Patients with anxiety disorders often experience a chronic state of anxiety and aversion of specific situations/contexts. During fear acquisition of a conditioned stimulus (CS) - unconditioned stimulus (US) contingency, an initial fear towards the context becomes cue specific[1]. Being unable to identify specific danger cues in a dangerous context can result in contextual fear and chronic anxiety. When the CS is no longer followed by the US, extinction of the contingency takes place. Extinction is at the core of exposure treatment, the most commonly used treatment in anxiety disorders.

Aims

1. Studying the ability to learn fear associations in a dangerous versus safe context in patients with anxiety disorders and healthy control subjects.
2. Exploring the predictive value of fear acquisition and extinction mechanisms in patients with anxiety disorders on treatment outcome.

Methods

- 30 patients with an anxiety disorder partially remitted* and a control group participated in a fear conditioning task in a virtual reality (VR task). Groups were matched on sex, age and education.
- In the VR task, participants visited two virtual environments: a threat context (in which the CS could be followed by the US) and a safe context (in which presentation of the CS was never followed by the US). See also figure 1.
- An increase in background illumination was used as CS (see figure 2).
- The US was a mild electrical shock. Reinforcements rates varied between 37,5% and 75%.
- The VR task included 4 phases, each consisting of multiple blocks:

I. Habituation: presentation of startle probes in the virtual environment to get used to the setting (2 blocks).
II. Acquisition: learning the CS-US association within the dangerous context (6 blocks).
III. Post-instruction: participants were informed on the contingencies to ensure contingency learning before extinction (5 blocks).
IV. Extinction: CS was never followed by the US (4 blocks).

- Outcome measures: physiological fear potentiated startle for objective anxiety and visual analogue scales (VAS) for subjective fearfulness.
- Analyses: repeated measures ANOVA's for group differences in conditioning and exploratory linear regression analyses for fear conditioning as predictor of treatment outcome.

*15 patients treated for panic disorder and 15 patients treated for social phobia in the past three years. The patient and control group differed significantly ($p<0.05$) on clinical characteristics (table 1).

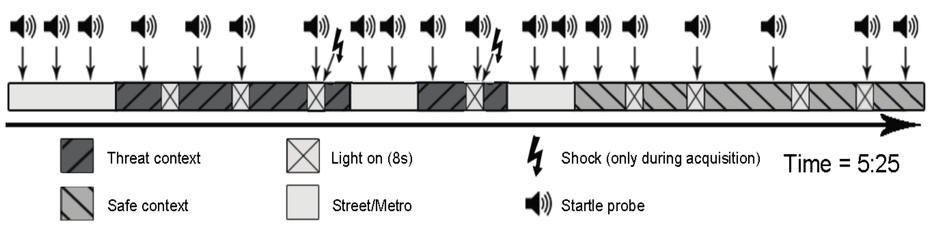

Figure 1. Design VR task

Context without and with CS presentation

No CS (light off) Presentation of CS (light on)

Figure 2. Example of one of the contexts from the VR world without and with CS presentation

Questionnaire	*Patient group M (SD)*	*Control group M (SD)*
State-Trait Anxiety Inventory	48,8 (7,0)	41,2 (5,6)
Anxiety Sensitivity Index	18,0 (10,1)	5,8 (4,5)
Beck Anxiety Inventory	15,1 (11,7)	4,8 (4,7)
Beck Depression Inventory	13,6 (10,3)	6,2 (7,4)

Table 1. Means (M) and standard deviations (SD) of clinical characteristics by group

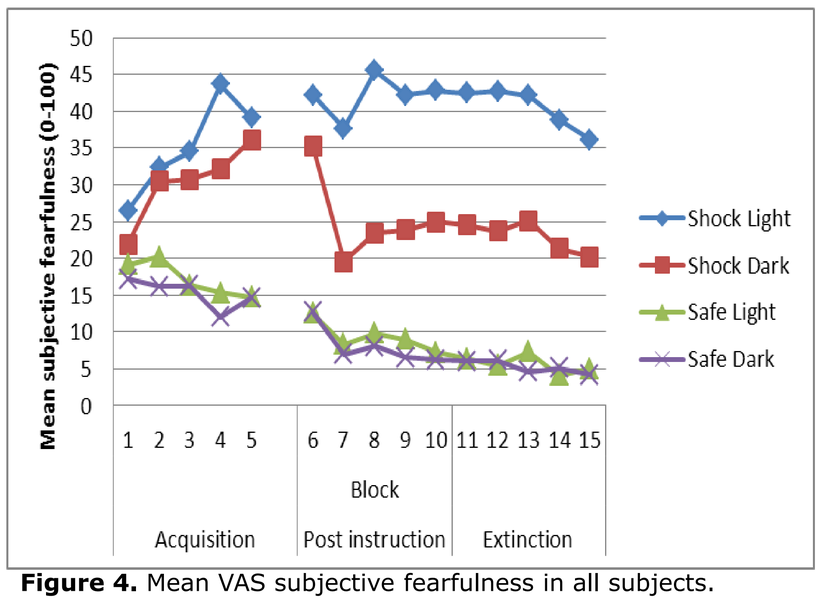

Figure 4. Mean VAS subjective fearfulness in all subjects.

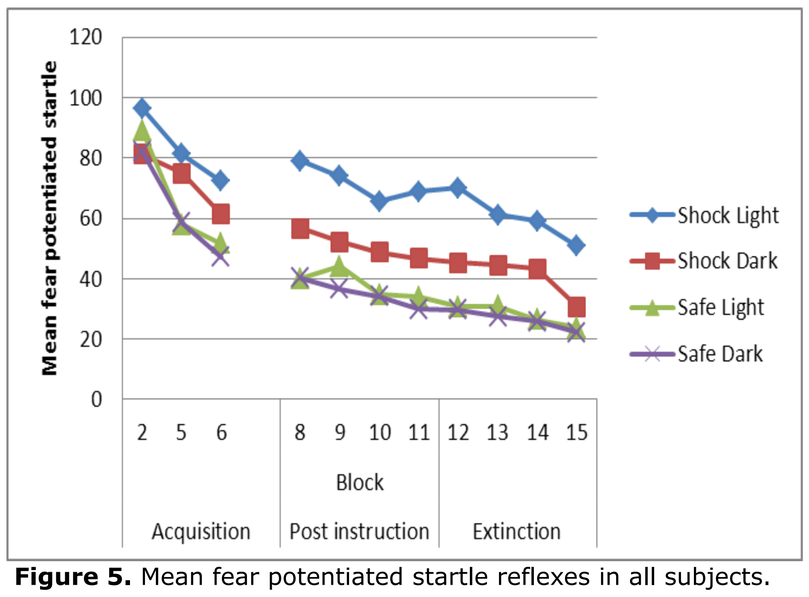

Figure 5. Mean fear potentiated startle reflexes in all subjects.

Results

No significant cue*context*block*group interactions during acquisition, post-instruction and extinction on the physiological and subjective outcome measurements. This indicates no group differences between patients and controls in the ability to learn fear associations during acquisition and extinction. Despite the absence of between group effects, results for all fear conditioning parameters were significant.

Subjective fearfulness (figure 4):
Significant main effects for cue and context, and significant interaction effects on cue*context were demonstrated in all phases (acquisition, post-instruction and extinction). During acquisition, a significant interaction effect on context*block was demonstrated and a significant main effect for block during extinction. Results indicate that both groups significantly differentiated the conditions in which the shock was expected (during presentation of the light cue in the shock context) compared to the other conditions during all phases. The significant context*block interaction indicated stronger habituation of the startle reflex in the safe context compared to the shock context during acquisition.

Fear potentiated startle (figure 5):
During habituation, a significant main effect for block was demonstrated and groups differed significantly on the average startle response. The mean startle response was higher in the patient group compared to the control group. Significant main effects for cue, context and block, and significant interaction effects for cue*context were demonstrated in all phases. The interaction effect context*block was significant during acquisition.

Explorative regression analyses with treatment outcome:
No significant correlations between fear conditioning and treatment outcome.

Conclusion

The patient and control group differentiated equally between shock context and safe context, and between presence and absence of the cue. Both physiological and subjective outcome measurements showed that patients and controls were able to discriminate context and cue during acquisition, post-instruction and at extinction. This implicates successful acquisition of fear, but lack of extinction in patient and control groups. Results from earlier studies, in which pathological fear conditioning was demonstrated, could not be replicated[2]. The exploratory analyses indicated no predictive value of fear conditioning on treatment outcome.

An explanation for the failure of demonstrating effects is that fear conditioning is not a stable trait characteristic, but represents a state function. Normalization of fear conditioning would then occur after treatment and in the case of (partial) remission of anxiety symptoms. Given that this was the case for the patients participating in the current study, this could explain the unexpected results.

To study the relationship between fear conditioning and trait versus state, additional exploratory analyses are planned in which the patient group will be subdivided based on the current clinical characteristics.

References

1. Baas, J. M. P., van Ooijen, L., Goudriaan, A., & Kenemans, L. (2008). Failure to condition to a cue is associated with sustained contextual fear. *Acta Psychologica, 127,* 581 - 592.
2. Lissek, S., Powers, A. S., McClure, E. B., Phelps, E. A., Woldehawariat, G., Grillon, C., & Pine, D. S. (2005). Classical fear conditioning in the anxiety disorders: A meta-analysis. *Behaviour Research and Therapy, 43*(11), 1391-1424.

Dept. of Clinical and Health Psychology, Dept. of Experimental Psychology, Utrecht University, The Netherlands

No potential conflict of interest