IV. ABSTRACT

Predicting the occurrence of future events based on previous experience is an important, adaptive ability. For instance, learning to predict that a snake signals danger and subsequently responding to this signal with an appropriate (fear) response may indeed be life-saving. However, when contingencies change, it might be equally important to learn that previous signals of danger are safe and no longer need to be avoided, especially in cases of excessive or phobic fear. This kind of learning is termed extinction learning and, simply put, refers to the unlearning of a previously acquired response or behavior as a consequence of changing contingencies. However, extinction is not always successful and permanent, as indicated by recovery effects showing a return of extinguished responding. Contextual cues seem to play an important role, as a recovery of extinguished responses is more pronounced when retrieval is tested outside the extinction context (renewal effect). Investigating factors which modulate extinction memory is highly relevant both for basic science as well as for potential clinical applications (e.g., for optimizing the treatment of anxiety disorders). Acute stress and the associated mediators of the bodily stress response are known to influence learning and memory processes. Based on the observation that brain areas which are involved in extinction memory processes are those which are also critically affected by stress, it seems likely that stress may also be a potent modulator of extinction memory. In order to systematically examine the influence of stress on extinction memory along the time course of extinction learning, its consolidation and retrieval, five studies were carried out. By manipulating contextual cues and focusing on the renewal effect, the modulatory role of the context was taken into account, which might be especially relevant for the understanding of extinction memory.

The first three studies applied the same three-day predictive learning paradigm in which participants acquired an association between critical stimuli and an outcome in one context (A) on the first day, underwent extinction of these associations in another context (B) on the second day and were tested for retrieval in both contexts on the third day. By inducing stress prior to testing retrieval of extinction memory, the first study found a stronger recovery of responding in stressed compared to non-stressed participants, which may reflect an impairing effect of stress on the retrieval of extinction memory. The second study showed that stress after extinction led to reduced spontaneous recovery of extinguished associations when memory was tested one day later in the extinction context. This finding was most likely due to an enhancing effect of stress on the consolidation of extinction memory. Study 3 showed that pre-extinction stress again enhanced the consolidation of extinction memory while not affecting extinction learning. In contrast to study 2, this effect was not context-
specific, indicating that pre-extinction stress made extinction memory less dependent on the context. Taken together, the three predictive learning studies demonstrated that stress exerts a marked influence on extinction memory, which can be modulated by contextual cues and critically depends on which memory phase is affected.

In order to allow for a comparison between aversive and non-aversive learning and to enable drawing more direct conclusions regarding the clinical applicability of the results, the next two studies investigated stress effects on the extinction of aversive memories by applying a fear conditioning paradigm. Pre-retrieval stress (study 4) reduced the return of fear in the retrieval test, as indicated by diminished renewal in the acquisition context and generally attenuated fear responses in the extinction context. This can be interpreted as an impairing effect of stress on the retrieval of fear memories. In contrast, post-extinction stress (study 5) increased the differentiation between the extinguished stimulus and the safe stimulus in the retrieval test. This was probably caused by an enhancing effect of stress on the consolidation of contextual cues, which made extinction memory more context-dependent and thus led to a stronger return of fear in the acquisition context.

In conclusion, the results of this thesis add to the understanding of the complex interactions between stress and context in modulating extinction memory. Based on the comparison of the predictive learning and fear conditioning studies, a likely explanation of the observed effects is that stress context-dependently enhances the consolidation of extinction memory, while impairing retrieval of the more arousing memory (i.e., it reduced retrieval of fear memory in the fear conditioning paradigm and retrieval of extinction memory in the predictive learning paradigm). The findings are largely consistent with the known, timing-dependent effects of stress on declarative memory and may ultimately contribute to the optimization of extinction-based psychotherapeutic treatments.