**Supplementary Results**

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**Supplementary Figure 1. Time courses of skin conductance responses (SCR) for each session and group are consistent with the model-bases analysis and show that stimulus discrimination was similar in both groups during acquisition but increased in the prazosin group during extinction and re-extinction.** The level of SCR response was determined by taking the base-to-peak difference for the first waveform (in microSiemens, mS) with the base within the 0.5–4.5 s window after stimulus onset. The minimal response criterion was 0.02 mS. The raw SCR scores were square-root transformed and scaled according to each subject’s unconditioned response by dividing each response by the mean response to the shock. Responses for acquisition, extinction, and re-extinction after administration of placebo (top) and prazosin (bottom) are shown. Extinction and re-extinction started with a CS- presentation and thus involved one additional CS- (trial 0); subsequent presentations of CS+ and CS- were counterbalanced. Error bars denote standard errors.

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**Supplementary Figure 2. Time courses of aSNA responses for each session and group confirm that stimulus discrimination was similar in both groups during acquisition but increased in the prazosin group during extinction and re-extinction.** Mean logarithmized anticipatory sudomotor nerve activity estimates (aSNA) for acquisition, extinction, and re-extinction after administration of placebo (top) and prazosin (bottom) are shown. Estimates of aSNA indicate the anticipation of an aversive event within the time window of stimulus presentation. These were calculated by inverting a forward model that describes how (hidden) SNA translates into an (observable) SCR using a variational Bayes approximation. A unit increase in aSNA corresponds to an increase in SCR of 1 μ S. Extinction and re-extinction started with a CS- presentation and thus involved one additional CS- (trial 0); subsequent presentations of CS+ and CS- were counterbalanced. Error bars denote standard errors.

**Supplementary Table 1: Stimulus discrimination (CS+ minus CS-) for each group, session, and phase using model-based SNA and base-to-peak scored SCR data.**

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| **Base-to-peak scored SCR** | | | | | | | |
| **Group** | **Session** | **Phase** | ***t*** | **df** | ***P*** |  | **Cohen's *d*** |
| Placebo | Acq | all | 4.57 | 18 | 0.0002 | \*\*\* | 1.05 |
| Placebo | Acq | early | 4.01 | 18 | 0.0008 | \*\*\* | 0.92 |
| Placebo | Acq | late | 3.67 | 18 | 0.0017 | \*\* | 0.84 |
| Placebo | Ext | all | 2.51 | 18 | 0.0217 | \* | 0.58 |
| Placebo | Ext | early | 1.17 | 18 | 0.2569 |  | 0.27 |
| Placebo | Ext | late | 4.6 | 18 | 0.0002 | \*\*\* | 1.05 |
| Placebo | Reext | all | 1.54 | 17 | 0.1414 |  | 0.36 |
| Placebo | Reext | early | 2.3 | 17 | 0.0343 | \* | 0.54 |
| Placebo | Reext | late | 0.37 | 17 | 0.7166 |  | 0.09 |
| Prazosin | Acq | all | 2.55 | 18 | 0.0202 | \* | 0.58 |
| Prazosin | Acq | early | 0.6 | 18 | 0.5581 |  | 0.14 |
| Prazosin | Acq | late | 3.51 | 18 | 0.0025 | \*\* | 0.81 |
| Prazosin | Ext | all | 4.3 | 18 | 0.0004 | \*\*\* | 0.99 |
| Prazosin | Ext | early | 4.49 | 18 | 0.0003 | \*\*\* | 1.03 |
| Prazosin | Ext | late | 2.28 | 18 | 0.0353 | \* | 0.52 |
| Prazosin | Reext | all | 3.83 | 18 | 0.0012 | \*\* | 0.88 |
| Prazosin | Reext | early | 3.61 | 18 | 0.002 | \*\* | 0.83 |
| Prazosin | Reext | late | 2.34 | 18 | 0.031 | \* | 0.54 |
| **Model-based SNA** | | | | | | | |
| Placebo | Acq | all | 2.9 | 18 | 0.0097 | \*\* | 0.66 |
| Placebo | Acq | early | 2.83 | 18 | 0.011 | \* | 0.65 |
| Placebo | Acq | late | 1.76 | 18 | 0.095 | + | 0.4 |
| Placebo | Ext | all | 1.55 | 18 | 0.1394 |  | 0.35 |
| Placebo | Ext | early | 0.83 | 18 | 0.4198 |  | 0.19 |
| Placebo | Ext | late | 3.71 | 18 | 0.0016 | \*\* | 0.85 |
| Placebo | Reext | all | 1.3 | 17 | 0.21 |  | 0.31 |
| Placebo | Reext | early | 1.72 | 17 | 0.1032 |  | 0.41 |
| Placebo | Reext | late | -0.01 | 17 | 0.9916 |  | 0 |
| Prazosin | Acq | all | 4.1 | 18 | 0.0007 | \*\*\* | 0.94 |
| Prazosin | Acq | early | 2.44 | 18 | 0.026 | \* | 0.56 |
| Prazosin | Acq | late | 2.93 | 18 | 0.009 | \*\* | 0.67 |
| Prazosin | Ext | all | 5.04 | 18 | 0.0001 | \*\*\* | 1.16 |
| Prazosin | Ext | early | 2.44 | 18 | 0.026 | \* | 0.56 |
| Prazosin | Ext | late | 3.9 | 18 | 0.001 | \*\* | 0.9 |
| Prazosin | Reext | all | 4.76 | 18 | 0.0002 | \*\*\* | 1.09 |
| Prazosin | Reext | early | 2.44 | 18 | 0.026 | \* | 0.56 |
| Prazosin | Reext | late | 3.67 | 18 | 0.0017 | \*\* | 0.84 |

*Abbreviations*: Acq, acquisition; Ext, extinction; Reext, re-extinction; df, degrees of freedom; SNA, sudomotor nerve activity; SCR, skin conductance response. +, P < 0.1; \*, P < 0.05; \*\*, P < 0.01; \*\*\*; P < 0.001.

***Assessment of early and late phases within and between sessions using aSNA data***

To assess aSNA responses by phase and stimulus within session, we calculated a 2 (placebo, prazosin) x 2 (early, late) x 2 (CS-, CS+) mixed ANOVA for each of the three sessions. For acquisition, there was a main effect of phase (*F*(1, 35) = 30.4, *P* < 0.001) and a main effect of stimulus (*F*(1, 35) = 18.8, *P* < 0.001) but no drug x phase x stimulus interaction. For extinction, there was a main effect of phase (*F*(1, 35) = 42.3, *P* < 0.001) and a main effect of stimulus (*F*(1, 35) = 27.3, *P* < 0.001) but no drug x phase x stimulus interaction. There was, however, a drug x stimulus interaction that did not quite reach significance (*F*(1, 35) = 3.0, *P* = 0.09). For re-extinction, there was a main effect of phase (*F*(1, 35) = 68.2, *P* < 0.001) and a main effect of stimulus (*F*(1, 35) = 23.3, *P* < 0.001) but no drug x phase x stimulus interaction. There was a drug x stimulus interaction (*F*(1, 35) = 8.8, *P* = 0.005).

The fact that there was no three-way interaction of drug x phase x stimulus in any of the sessions indicates that stimulus discrimination did not vary significantly over time between the groups in any of the experimental stages. The phase effect in each session reflects the overall decrease in aSNA response with time, possibly due to habituation, while the stimulus effect corresponds to the higher response to CS+ compared to CS-. The interactions of drug x stimulus in extinction and re-extinction reflect the lower response to the CS- in the prazosin compared to the placebo group.

To assess the change in aSNA from acquisition to extinction, we compared the stimulus discrimination between the late phase of acquisition (second half) and the early phase of extinction (first half) between groups. Stimulus discrimination was similar in late acquisition in both groups (*P* = 0.9) and increased from late acquisition to early extinction in prazosin but not placebo, although this interaction of group x stage did not quite reach significance (*F*(1, 35) = 3.01, *P* = 0.09).

Regarding spontaneous recovery, threat discrimination in late extinction and early re-extinction were not significantly different in placebo (*F*(1, 17) = 0.11, *P* = 0.74) or prazosin (*F*(1, 18) = 3.34, *P* = 0.08) and similar in both groups, i.e., no group x session interaction (*F*(1, 35) = 2.25, *P* = 0.14) was evident. Thus, although there was some evidence for spontaneous recovery in the prazosin group, the effect did not quite reach statistical significance, and it did not significantly differ from the placebo group.

***Analysis of manually scored base-to-peak SCR data***

The results of the manually scored base-to-peak SCR data were consistent with the model-based SNA data; the three-way interaction was significant (χ2 (2) = 6.14, *P* = 0.046; this interaction was also evident when we used ANOVA instead of linear mixed models (*F*(2, 70) = 3.81, *P* = 0.0268). Post hoc *t*-tests comparing CS+ to CS- in each stage and phase in each group are reported above (Supplementary Table 1) and are consistent with the aSNA data. Regarding group differences in base-to-peak SCR to each stimulus separately, again we found that the response was lower to the CS- in the prazosin compared to placebo group during extinction (*t*(36.05) = -1.27, *P* = 0.21) and re-extinction (*t*(36.05) = -1.36, *P* = 0.18) while the CS- response was slightly higher during acquisition (*t*(36.69) = 0.23, *P* = 0.82). Responses to the CS+ did not significantly differ between groups in any session (all *P* > 0.4). Although the post-hoc comparisons of CS- were not statistically significant, note that it is perfectly possible to obtain a statistically significant interaction without the simple effects (the responses to the CS-) being statistically significant. Importantly, the direction of the group differences in the post hoc comparisons of the CS- obtained with the aSNA data is replicated with the conventional base-to-peak method. In addition, the fact that we find differences in statistical significance between the model-based and the conventional peak-to-peak method is, although not meaningful by itself, not unexpected, as that it has been shown that the model-based approach may be more sensitive to detect experimental manipulations (e.g. Bach *et al.*, 2010). A potential reason for this increased sensitivity is that the model-based approach might be less susceptible to over fitting noise in the SCR data.

Within session assessment of phase and stimulus yielded comparable results to the aSNA data: For acquisition, there was a main effect of phase (*F*(1, 35) = 33.2, *P* < 0.001) and a main effect of stimulus (*F*(1, 35) = 24.0, *P* < 0.001) but no drug x phase x stimulus interaction. For extinction, there was a main effect of phase (*F*(1, 35) = 56.7, *P* < 0.001) and a main effect of stimulus (*F*(1, 35) = 25.2, *P* < 0.001), and the drug x phase x stimulus interaction did not quite reach significance (*F*(1, 35) = 3.5, *P* = 0.07). For re-extinction, there was a main effect of phase (*F*(1, 35) = 31.9, *P* < 0.001) and a main effect of stimulus (*F*(1, 35) = 16.0, *P* < 0.001) but no drug x phase x stimulus interaction. The drug x stimulus interaction was not significant (*F*(1, 35) = 2.7, *P* = 0.1).

Overall, these results are in line with the findings obtained with the aSNA data. A formal comparison of the model-based and the base-to-peak methods has been done in previous studies (e.g., Bach *et al.*, 2010) and is beyond the scope of the current study.