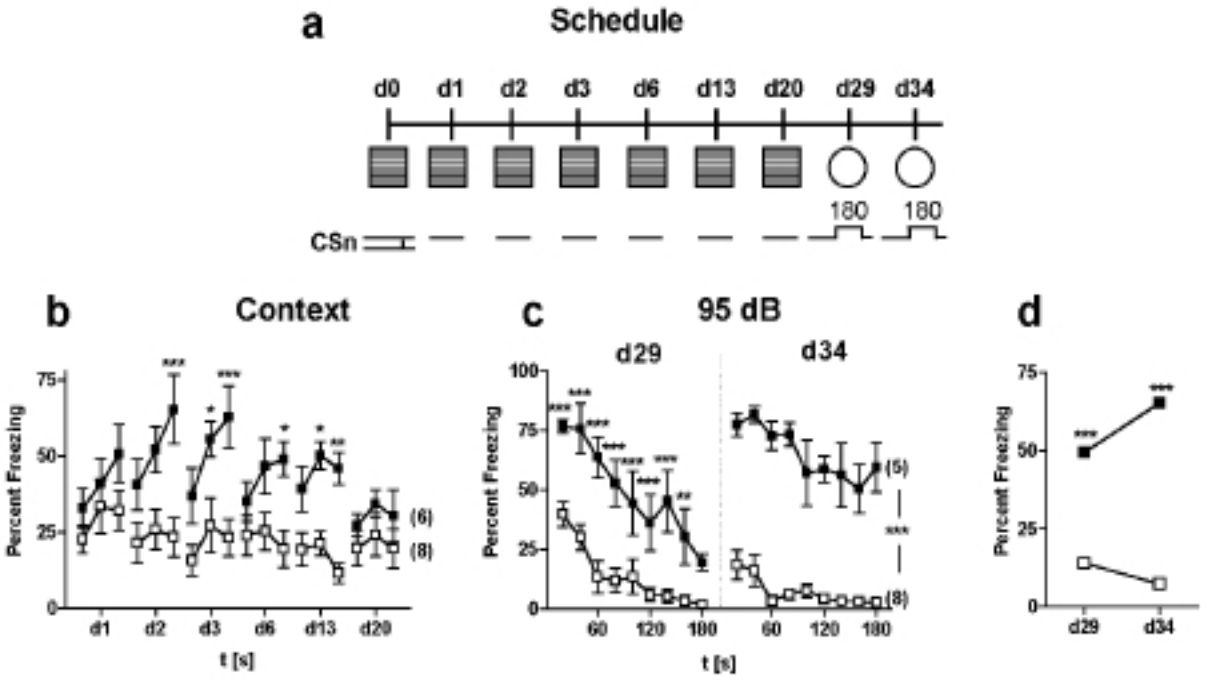


***Supplementary Figure 2: Impairments in adaptation of sensitized fear in CB1$^{-/-}$ mice are independent from extinction of contextual fear.***

**(a)** Experimental procedure: CB1$^{-/-}$ (■, n = 6) and CB1$^{+/+}$ (□, n = 8) were sensitized with a single footshock in the conditioning chamber, and repeatedly re-exposed to the conditioning chamber for 3 min without tone or footshock presentation at days 1, 2, 3, 6, 13 and 20 after the sensitization procedure. At days 29 (d29) and 34 (d34), mice were exposed to 3-min tones of 95 dB in the test context. **(b)** Freezing in the conditioning chamber in absence of tone presentation. With repeated context exposure, CB1$^{-/-}$ mice initially showed significantly more contextual freezing than wild-type controls. However, these differences disappeared towards day 20 (statistics not shown). **(c)** Freezing to a tone of 95 dB at d29 and d34. Although the differences in contextual freezing between the two genotypes disappeared towards the end of context exposures, CB1$^{-/-}$ froze significantly more to the tone both at d29 (*Genotype:* $F_{1,11} = 22.0$, $P < 0.001$; *Genotype x Interval:* $F_{8,88} = 2.2$, $P = 0.036$) and at d34 (*Genotype:* $F_{1,11} = 179.0$, $P < 0.0001$). It is of note that one CB1$^{-/-}$ mouse died during tone presentation because of an audiogenic seizure. Together with the data of the freezing response to the context, these data indicate that freezing to the tone does not simply reflect generalized contextual fear. **(d)** Development of the freezing response to the tone from d29 to d34. The highly significant differences in tone freezing between CB1$^{-/-}$ and CB1$^{+/+}$ became evident also if the development of the total freezing response from day 29 to day 34 was considered (*Genotype*: $F_{1,11} = 137$, $P < 0.0001$; *Genotype x Day* interaction: $F_{1,11} = 5.7$, $P = 0.036$). The significant interaction of the two main factors relates to the fact that CB1$^{+/+}$, but not CB1$^{-/-}$, showed a decrease in freezing from day 29 to day 34 (statistics not shown). Data were normalized either to 20-s (c), or to 60-s (b) or to 3-min (d) observation intervals. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$ vs. CB1$^{+/+}$ (2-way ANOVA for repeated measurements, followed by Newman-Keuls post-hoc test).