Introduction
The importance of serotonin for the regulation of anxiety is illustrated by the efficacy of long-term administration of selective serotonin reuptake inhibitors in most anxiety disorders [1]. However, much is yet to explore on the complex influence of serotonin on anxiety.

Objective
The aim of this study was to assess to what extent an anxiety-related behaviour in rat, context-conditioned fear, is dependent on brain serotonergic activity [2]. To this end, rats were studied with respect to context-conditioned freezing in the presence or absence of brain serotonin, respectively, the latter situation being obtained by administration of a serotonin synthesis inhibitor, para-chlorophenylalanine (PCPA). The effects of PCPA on both the acquisition and the expression of context-conditioned fear were evaluated.

Results
In the first experiment (Experiment 1), the effect of PCPA administration prior to expression of context-conditioned fear was evaluated. The time spent freezing was significantly reduced by PCPA versus control (p<0.001) (Figure 1). In the second experiment (Experiment 2), the effect of PCPA administration prior to acquisition of context-conditioned fear was evaluated. Also under these conditions there was a significant anxiety-reducing effect of PCPA versus control with respect to reduction of freezing in PCPA-treated animals (p < .05) (Figure 2). There was however no significant difference in the amount of freezing between treatment groups (PCPA and control) for animals that was not fear conditioned to the context.

Conclusions
The results indicate that an intact serotonergic neurotransmission is important for both expression and acquisition of contextual fear. We suggest that serotonin should be regarded as an anxiety-enhancing or anxiety-modulating rather than as an anxiety-reducing transmitter.

References

Method
Male Sprague Dawley rats were housed with three individuals per cage. Food and water were supplied ad libitum. Rats were ten weeks of age at arrival and were habituated to human handling at a regular basis during two weeks before testing. All rats were subjected twice to a fear-conditioning system with two identical cubicles. Each rat was assigned to the same cubicule at both tests. Rats received injections of either PCPA (300 mg/kg) or 1 ml of 0.9% saline. Injections were given on three consecutive days, i.e. at a dose regimen that causes an almost complete depletion of serotonin while leaving catecholamine levels intact [3]. In Experiment 1, rats received injections prior to testing. In Experiment 2, rats received injections prior to fear-conditioning to the context. Hence, while Experiment 1 evaluated the effect of PCPA on expression of context-conditioned, fear, Experiment 2 evaluated the effect of PCPA on acquisition of contextual fear. The unconditioned stimulus was electric foot-shock (5 x 1s, 0.6 mA). The time between fear-conditioning and testing was 21 days in Experiment 1 and 14 days in Experiment 2. The time spent freezing was assessed by automated scoring of video recordings and was computed as lack of motion for more than 1 s. Effects of treatments were analysed with Student’s t-tests.

Figure 1. Top) Comparison of time freezing for context-conditioned animals (Mean + SEM). Time freezing was significantly reduced by PCPA administration prior to fear expression versus control. Bottom) Time freezing for all groups divided into two minute intervals (Mean + SEM). (** p<0.001)

Figure 2. Top) For context-conditioned animals time freezing was significantly reduced by PCPA administration prior to fear acquisition versus control (Mean + SEM). There was no significant difference between treatment groups for animals that was not fear conditioned to the context. Bottom) Time freezing for all groups divided into two minute intervals (Mean + SEM). (*) p<0.05