

School/ Department: School of Biosciences

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This brief report aims to present the corrections that have been made as requested by the examiners following the viva examination of the PhD thesis with title: "Cannabidiol regulation of extinction and relapse of learned fear". For convenience purposes, the requested corrections will appear at the left-side column of the list, while the amendments made by the student will be provided at the right-side column, along with the new page number that these correspond:

<p>P40; please clarify when the effective infusion in the Rossignoli study was delivered. This is not currently clear in the text.</p>	<p>The effective infusion of CBD into PFC was delivered 5hrs post-conditioning. (now found at p. 41)</p>
<p>In the methods of each chapter, the full housing conditions of the rats should be reported (including details of any environmental enrichment in the home cages).</p> <p>It should also be made clear whether and how the assumptions of ANOVA were tested (e.g. homogeneity of variance and sphericity assumptions).</p>	<p>Housing conditions are described in detail in 2.2.1 Subjects section (p. 47). Temperature, humidity, illumination, access to food, numbers of rats housed per cage.</p> <p>For environmental enrichment, wooden chew sticks and cardboard tunnels were used. These conditions were identical across all experiments, therefore for avoiding repetition, the reader is referred to Chapter 2, for more details.</p> <p>Two-way Anova with Geisser-Greenhouse correction was applied to adjust for lack of sphericity, when the within-subject factor had more than two levels. Bartlett's test and F test were used to test for homogeneity of variance in ANOVA and t-test, respectively. This will be found in the data analysis section of each chapter.</p>
<p>In relation to the statistical approach, it should be clearer whether post-hoc analyses were fully pairwise, or limited. One example is that for the dose-response studies, doses were seemingly</p>	<p>Information regarding the type of post-hoc multiple comparisons has been added in data analysis section of each chapter.</p>

compared against vehicle, but not against each other. This should be clear from the statistical methods section.	
Within the figures, the legends should be revised so that the figures can be viewed and interpreted in isolation and without reference to the text (or other figures). The "(n/a)" within the data labels should also be removed.	Figures have been amended according to the recommendation of the examiners. Emphasis was given in the figures explaining protocol design, and experimental results, containing also information regarding sample size, routes of drug administration, statistical analysis information etc.
In all of the results reporting, when there is no statistically significant effect, please word as, for example "there were no reliable differences between...", rather than "there were no differences".	Amended accordingly where indicated across the result sections of each chapter, and in legends of results figures.
An explanation of the selection of group sizes would be appropriate in the methods sections.	Information about the power analysis and sample size calculation is now added in 2.2.1 Subjects section (p. 48) and applied in all the studies (8-12 rats/group were sufficient).
P53; you say that ANOVA revealed increased freezing during trial 1 vs trials 2 & 3, but no statistical evidence is actually quoted.	Statistical evidence was added for all the comparisons of the study (pp. 57-62).
P141; it would help to present the one-way ANOVA of the test results more clearly as the <i>a priori</i> confirmatory analysis, with the trial-by-trial analysis as an exploratory follow-up.	Confirmatory one-way Anova and exploratory two-way Anova with trial-by-trial analysis are mentioned in p. 154.
In chapters 4 and 5, some cited information on the selectivity of the drugs used to potentially block the effects of CBD would be useful.	A dedicated paragraph describing the selectivity of CB1R antagonist AM251, and 5-HT1AR antagonist WAY100,635 was added in the introduction section of chapter 4 (p. 94-95) and 5 (p. 123), respectively.
Throughout, there are multiple instances of citations being formatted incorrectly (e.g., in parentheses even when the author name is part of the sentence text. The candidate may wish to take the opportunity to "clean up"	Typographical, syntactical, reference errors were corrected accordingly.

<p>the presentation (and any typographical errors) as part of the correction process. An annotated copy of the thesis has been given to the candidate to help with this.</p>	
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