

## REVIEWER A

The authors report that early (preweaning) exposure to the serotonin reuptake inhibitor clomipramine (CLI) reduced motionless time in the forced swimming test (Exp 1) and facilitated recovery from incentive downshift in the cSNC situation (Exp 2). The former is a replication of previously reported results and was used to validate the early-infancy intervention. The latter is an original result worth considering for publication in *Psicologica*. I have a number of suggestions that might help clarify some issues that appeared to me confusing as I was reading the MS. I will list them in the order in which they appear in the MS.

(1) Abstract: a brief discussion of the results is missing at the end of the paragraph.

(2) P. 3 and other parts in the MS: the authors should try to be specific when describing results. For example, they say that CLI treatment “produces permanent alteration of plasma corticosterone levels.” Do they mean “increase” or “decrease”? In the following paragraph, where they say “lower increase of plasma hormone levels,” could they specify the hormone? In p. 4, could they specify the drug used by Grigson and Flaherty (1991) and by Becker (1986)?

(3) P. 4: Nikiforuk & Popik’s (2009) results are not accurately described. First, they found no evidence of contrast in their operant situation (progressive ratio schedule) involving sucrose solutions, which is consistent with a large body of literature since the 1960s on failures to find SNC when sucrose solutions are downshifted. Second, despite the absence of SNC, antidepressants (fluoxetine and citalopram) did have an effect on the breaking point measure.

(4) P. 6: briefly describe goal-tracking time so readers have a more accurate notion of what this measure actually involves.

(5) P. 6: the 3-way ANOVA reads, “...Trial (4-10 trials)...” I think they meant, “...Trial (1-10 trials)...” Also, are the follow-up ANOVAs one-way analyses? If so, then the word “simple” should be deleted. Why did they compute these analyses for Trials 4-10, excluding Trials 1-3?

(6) P. 7: since the authors report on one-way ANOVAs with LSD ad hoc tests, it would be interesting to note whether CLI 32 and VEH 32 were different on Trials 11 and 12 (and the same for CLI 4 and VEH 4). There is substantial evidence that performance on these two key trials is based on different mechanisms (i.e., trial-selective effects of various drugs, including CDP; see Flaherty, 1996). They could perhaps make a similar argument from the present results.

(7) Figures: if they number the figures as 1a and 1b, only one legend would be required and both figures should be presented in the same page, perhaps one on top of the other. This would seem the correct way to present the data.

(8) Finally, the lack of cSNC on CLI groups (Fig 1a) seems to be the result of a drop in performance in the CLI 4 condition. It is possible that a repeated-measure analysis of Trials 11 vs. 12 for CLI 4 animals would show the decrease in goal-tracking times to be significant. The authors should discuss this issue as a possible limitation of their study.

## **REVIEWER B**

Previous research has shown that neonatal administration of clomipramine (CLI), a serotonin and norepinephrine reuptake inhibitor produces effects resembling endogenous depression in adult rats and modifies the reactions to aversive situations. The authors analyse whether neonatal application of this tricyclic antidepressant (clomipramine) affects the behaviour of adult rats when faced with an incentive downshift or frustration using a consummatory successive negative contrast paradigm (Experiment 2). In Experiment 1, as a preliminary step and in order to determine the effectiveness of this manipulation in the induction of "endogenous depression", the researchers analyzed the behaviour of animals in a forced swim test, an experimental paradigm of unconditioned response widely used as an animal model of depression. Animals treated with clomipramine remained motionless longer than rats from control group showing the efficacy of neonatal treatment. In Experiment 2, the results showed that in the consummatory successive negative contrast, CLI group showed faster recovery of consummatory behavior than control group.

This manuscript reports well-conducted experiments directed to a topic of interest generating potentially important results and I consider that these data should be published. The rationale for this research is clear, the methodology is sound, and the application and interpretation of the statistical analyses is appropriate. Therefore, pending a suitable revision, I recommend publication of this work in *Psicológica*

As noted above, I found the experimental components of this report (Methods; Results) to be acceptable, but I found some of the sections of the Introduction and General Discussion to be less effective. I recommend the authors consider revising the following points:

1. Although the main objective of the research is clear, I think that it is necessary a clarification of the specific objectives of each of the experiments.

Experiment 1. Although, it is true that the specific use of the forced swim test is presented in the Introduction section, I consider that, given the relevance that this test has for the present research, the proposal of this experiment should appear fully justified and clarified.

Experiment 2. Consummatory successive negative contrast (cSNC) has widely been used as an animal model of depression, mainly in relation to the anhedonia. The usual result after application of a procedure inducing analogous behavior to the depression is a decrease in both negative and positive contrast, so I think that based on these studies, researchers could establish a hypothesis in this direction. I suppose it would bolster their argument.

2. Experiment 1. The means and standard errors of the groups should appear. Also I miss a theoretical interpretation of the results related to the effectiveness of neonatal treatment with clomipramine in inducing symptoms resembling endogenous depression in adult animals.

Experiment 2. The transformation of the data based on animal body weight despite being right should be justified. Also I consider necessary a justification for the removal of the first four trials from data analysis in the pre-shift analysis.

It is noteworthy that the Contrast x Trial interaction is significant and analyses of simple effects are not significant.

3. The General Discussion must be extended. I think the discussion would improve if theoretical models developed to explain the differential processes involved in the first post-shift trial and subsequent trials were applied (Amsel, 1992; Flaherty, 1996)

In general, these theories postulate that during cSNC there is a reaction to change in solution which involves a search for the 'missing' substance (first post-shift trial, first stage), this leads to the activation of a stress response (second post-shift trial, second stage). The first stage is described as cognitive while the second stage involved an emotional reaction of frustration. The results of Experiment 2 are consistent with previous research that showed that neonatal administration of clomipramine may play an important role on the regulation of the stress responsiveness in adulthood and represent the evidence that the neonatal clomipramine administration has effects that are similar to those of anxiolytic drugs, in alleviating contrast similar in the timing of those effects time period corresponding to a second post-shift day once this stress response has been activated.