

Summary for Authors

This Summary for Authors was adapted from an actual review carried out by an AJE content reviewer. The study describes protein changes in rat frontal cortex exposed to chronic mild stress (CMS) and an antidepressant using different dosing schedules. Factual information was altered to maintain confidentiality.

Title, Authorship	<p>The title is clear and accurately describes the study.</p> <p>Not all the affiliations of all authors are listed; please include them.</p> <p>The corresponding author and contact information should appear on page 1.</p>
Abstract, Keywords, Running Title	<p>The abstract provides appropriately succinct statements on the Background, Methods, and Results. Please also include a concluding statement; e.g., refer to the potential relevance of this research to the clinical application of paroxetine.</p> <p>Most target journals will include up to five key words. Please consider medical subject headings (MeSH terms) that indicate, e.g., the dosing strategy tested such as “dose” or “dosing regimen”; the drug name should also be included.</p> <p>The Running Title is nicely descriptive.</p>
Introduction	<p>Overall, the Introduction is well written and provides appropriate justification for their animal model and the rationale for the study of paroxetine.</p> <p>The authors have included a good justification for the research, indicated at the end of the Introduction, and they cite an older review from 2001 to describe the changes in the frontal cortex after CMS exposure. Please consider including more recent references that examine proteomic changes in the presence of antidepressants, such as that of Mu, et. al., Proteomic analysis of a rat model of depression; Expert Review of Proteomics, Vol. 5, 315-320, 2008.</p>
Methods	<p>In the Methods section, please consider including information on whether any of the experimentation was conducted in a “blinded” manner in which the researcher was unaware of the treatment group.</p> <p>In the Methods section, the CMS rats are divided into four groups, which include vehicle-treated, treated daily + paroxetine, and treated weekly + paroxetine. Please consider using a key control group comprised of animals that are treated as controls (i.e., no CMS) but receive paroxetine (both daily and weekly). This control group would help to interpret the data for the identified proteins on 2-D gels that remained abundant after CMS in animals that received paroxetine.</p> <p>The authors discuss teraxin-1 changes with chronic administration of other same-class drugs (page 19), which supports their view that the change in the level of this protein in their study is an expected response.</p>
Results, Discussion	<p>The Results and Discussion should be in separate sections.</p> <p>In the discussion, the authors claim their results are in agreement with their working hypothesis that daily drug administration is more important for triggering changes in protein expression compared to weekly dosing schedules. However, the authors have only tested one dose of paroxetine (i.e., 5 mg/kg). Furthermore, they have only tested 2 time schemes (i.e., daily vs. weekly). Expanding their dosing/timing strategy would strengthen their conclusions. At the very least, the authors should justify why this dose and these times were chosen and how they were optimized.</p>

	<p>As mentioned in the text comments, the authors need not discuss every protein that showed alterations in expression. However, they might consider discussing the examples where there is a change in the weekly dose but not in the daily dose (i.e., annexin A3, synapsin IIb, galactokinase 1). The authors claim the dosage-dependent responses represent different underlying molecular mechanisms for the effects of treatments. However, this point is barely discussed, and no explanation is put forth. Please consider including a discussion paragraph that will provide some explanation of these findings.</p>
Figures	<p>The figures are clear and well presented, but please see comments for the legend of Figure 1 concerning dosing.</p>
Comment	<p>This study demonstrates that paroxetine treatment can reverse distinct protein expression changes that occur during CMS in a rat model. Furthermore, the authors suggest that drug treatment does this in a time-dependent manner (i.e., daily vs. weekly). The latter of these points is extremely novel and may have direct implications for the clinical administration of paroxetine.</p> <p>Overall, the manuscript is well written and well presented. However, the clinical implications of these results should be discussed, and the possibility of using a non-biased proteomic approach for identifying new therapeutic targets for paroxetine treatment should be included as a major aim of this work.</p>