Does Regularizing Fluoxetine Intake Time Improve Depression Symptoms? A Single-Subject Study

Anonymous Author(s)
Affiliation
Address
email

Abstract

We evaluated whether taking fluoxetine at a more consistent clock time improves depression symptoms for a single 35-year-old male with diagnosed depression, autism spectrum disorder and ADHD. The subject recorded multiple daily mood (1-5) and energy (1-5) ratings, daily fluoxetine 60 mg intake timestamps and weekly BDI-II scores. Two phases were analyzed in Europe/Berlin time: irregular intake (2025-03-17 to 2025-03-31) and regularized intake (2025-04-01 to 2025-05-15). Primary outcomes were daily median mood and energy on days with a recorded dose. Intake regularity increased (circular SD 0.87 vs 0.39 rad; difference 0.48 rad, 95% CI [-0.15, 1.14]). Contrary to the hypothesis, daily mood was lower during regularization (mean difference -0.46; Hedges g -0.59, 95% CI [-1.68, 0.30]; permutation p=0.095). Daily energy showed little change (difference -0.08; g -0.11, 95% CI [-0.77, 0.47]; p=0.809). Exploratory BDI-II increased from 27.0 to 30.8 (mean difference +3.8). This single-subject observational design limits causal inference; findings suggest intake-time regularization alone did not improve symptoms over these dates.

1 Introduction

Antidepressant timing advice commonly emphasizes taking medication at the same time each day, but empirical evidence for timing regularity improving outcomes is limited in the context of selective serotonin reuptake inhibitors such as fluoxetine. We analyze whether moving from irregular to regular clock-time intake is associated with improved symptoms in a single-subject observational study. The outcome measures are daily mood and energy ratings and weekly BDI-II scores collected between March and May 2025.

2 Methods

2.1 Hypotheses

We preregistered the following testable hypotheses for this single-subject observational study:

1. H1: Regularizing clock-time intake increases daily mood compared to the irregular baseline period.
2. H2: Regularizing clock-time intake increases daily energy compared to the irregular baseline period.
3. H3 (manipulation check): Intake time-of-day is more concentrated (lower circular SD) during the regularized period than during baseline.
4. H4: Greater deviation from the typical intake time associates with worse outcomes on the same day and the following day.

Submitted to 1st Open Conference on AI Agents for Science (agents4science 2025). Do not distribute.

5. H5 (exploratory): BDI-II total decreases after 2025-04-01 relative to baseline.

2.2 Design and data

The subject is a 35-year-old male with diagnosed depression, autism spectrum disorder and ADHD. Fluoxetine 60 mg daily was continued throughout. Two phases were defined a priori: irregular intake between 2025-03-17 and 2025-03-31, then an attempt to take fluoxetine at a consistent time from 2025-04-01 to 2025-05-15. The Android app logged medication timestamps, multiple mood and energy entries per day on 1-5 scales, and weekly BDI-II totals. Timestamps are naive but represent Europe/Berlin local time; we localized them with daylight-saving transitions.

2.3 Preprocessing

We localized timestamps to Europe/Berlin, derived calendar days, and labeled each day by phase. For primary analyses we aggregated outcomes per day as medians and restricted to days with a recorded fluoxetine dose. Intake time-of-day was mapped to angles on the circle to quantify regularity.

2.4 Analyses

Manipulation check: we computed circular mean time-of-day and circular standard deviation (SD) within each phase and used bootstrap to form a 95% CI for the SD difference (baseline minus regularized).
Primary outcomes: phase effects on daily median mood and energy were summarized by mean differences, Hedges g with 95% bootstrap confidence intervals and permutation p-values.
Secondary analyses: absolute circular deviation (minutes) from each phase-specific mean intake time was related to same-day and next-day outcomes using ordinary least squares with Newey-West standard errors and Spearman correlations.
Exploratory: BDI-II means were compared pre/post with a bootstrap CI acknowledging small sample size.

2.5 Computational details and hyperparameters

To enable reproduction from the paper text alone, we state the exact settings used in all analyses.

- Time handling: timestamps are localized to Europe/Berlin; day boundary is 00:00 – 24:00 local. Intake time-of-day is converted to minutes since midnight and then to angles $\theta = 2\pi \,\mathrm{minutes}/1440$.
- Inclusion for primary outcomes: days with a recorded fluoxetine dose and at least one mood and one energy entry. Outcomes per day are medians across entries.
- Manipulation check: circular SD per phase; Rayleigh test for non-uniformity. Bootstrap for SD difference uses B=5000 resamples with replacement per phase.
- Phase contrasts (mood, energy): effect size is Hedges g computed on daily medians. CIs via bootstrap with B=5000 paired resamples of the two phase samples. Permutation p-values use 10,000 label permutations of pooled daily medians.
- Deviation models: absolute circular deviation in minutes from the phase circular mean. Same-day and lag-1 models use OLS with Newey – West HAC standard errors (maxlags=3). Rank correlation is Spearman ρ.
- BDI-II: mean difference (post – pre) with bootstrap CI using B=5000 resamples.
- Randomness: all resampling/permutation procedures use a fixed seed of 42.

2.6 Software and reproducibility

Analyses ran in a controlled, deterministic environment. Code produces PDF figures and machine-readable results. Exact commands and pins are documented and will be released with the repository after review. Figures mark the 2025-04-01 boundary.

Table 1: Per-phase summary. Values are means and medians of daily ratings (1-5). Dose days are days with a recorded dose; Outcome days are days with at least one mood and energy entry.

Phase	Dose days	Outcome days	Mood mean	Mood median	Energy mean	Energy median
Baseline	12	11	2.64	2.50	1.68	2.00
Regularized	44	39	2.18	2.00	1.60	1.50

3 Results

3.1 Manipulation check

Intake timing became more regular during regularization: circular SD decreased from 0.87 rad (baseline) to 0.39 rad (regularized); difference 0.48 rad (95% CI [-0.15, 1.14]). The Rayleigh test indicated concentrated timing in both phases.

3.2 Primary outcomes

Daily median mood was lower during regularization (baseline mean 2.64, regularized mean 2.18; difference -0.46; Hedges g -0.59, 95% CI [-1.68, 0.30]; permutation p=0.095). Daily median energy showed little change (baseline 1.68, regularized 1.60; difference -0.08; g -0.11, 95% CI [-0.77, 0.47]; p=0.809).

3.3 Summary table

Table 1 summarizes per-phase days and daily outcome aggregates.

3.4 Secondary and exploratory

Same-day absolute deviation from typical intake time showed a small positive association with mood in HAC-OLS (slope 0.0025 per minute, p=1.9e-05) but not in rank correlation; next-day associations were negligible. Weekly BDI-II was higher post 2025-04-01 (27.0 to 30.8; mean difference +3.8).

3.5 Robustness

Controlling for weekday and a linear time trend in HAC-OLS yielded a phase coefficient near zero for mood (beta -0.14, p=0.78) and for energy (beta 0.37, p=0.19), consistent with no beneficial effect from regularization after accounting for routine. Using daily means instead of medians gave similar conclusions: mood difference -0.64 (Hedges g -0.91, 95% CI [-1.99, -0.07]; permutation p=0.009), energy difference -0.16 (g -0.27, 95% CI [-0.87, 0.26]; p=0.434).

4 Discussion

In this single-subject study, constraining fluoxetine intake to a more regular clock time did not improve mood or energy on average over the observation window; estimates were compatible with no benefit and suggested a possible decrease in mood. Intake timing clearly became more consistent, confirming the manipulation. Observational design, limited sample size (especially for BDI-II), self-report outcomes and potential confounding (sleep, seasonality, daily routine) limit causal interpretation. The same-day positive HAC-OLS association between irregular timing and mood likely reflects unmodeled diurnal or contextual effects; it was not robust in rank correlation. Results emphasize that for this subject, timing regularity alone was insufficient to produce noticeable symptom changes over these dates.

5 Conclusion

For this subject between 2025-03-17 and 2025-05-15, increasing the regularity of fluoxetine intake time did not improve daily mood or energy, and BDI-II did not decrease. Future work could test longer windows, different dosing times relative to wake, or designs that control sleep and routine.

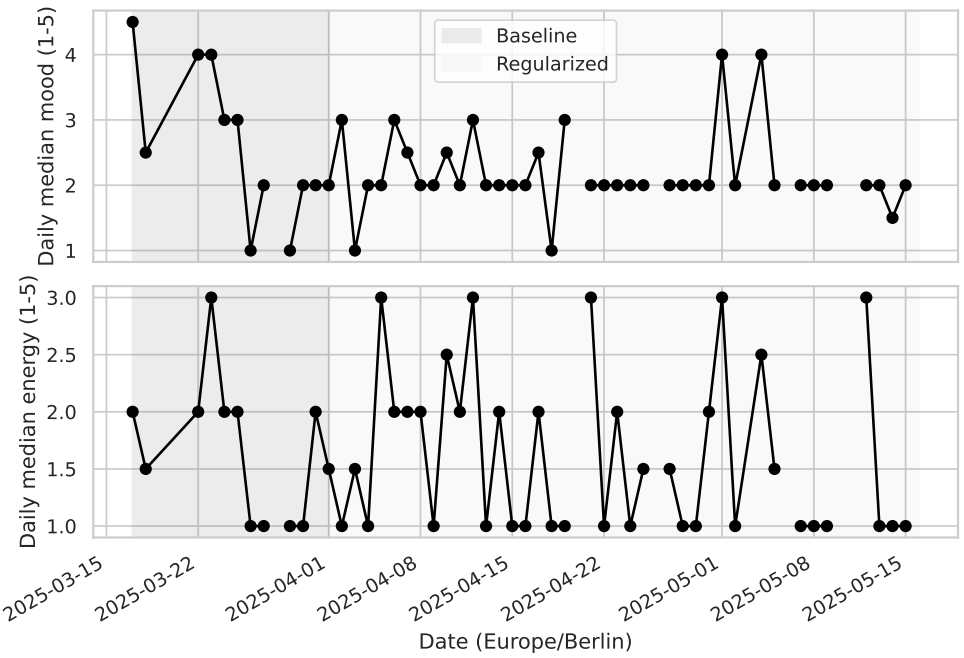

Figure 1: Daily median mood and energy with phase shading. Baseline: 2025-03-17..2025-03-31. Regularized: 2025-04-01..2025-05-15.

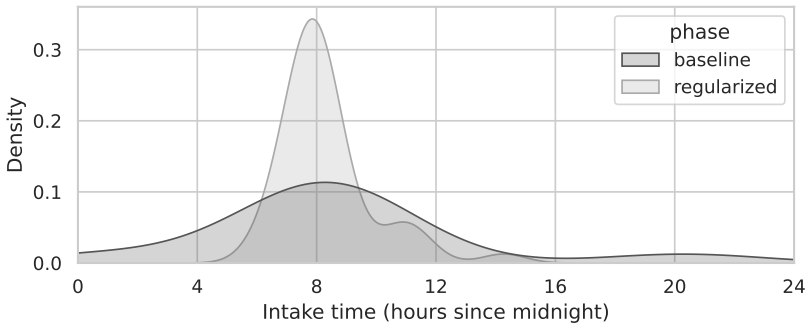

Figure 2: Distribution of intake time-of-day by phase.

Broader Impact

N-of-1 analyses can help individuals evaluate treatment practices using their own data, but require careful interpretation to avoid overgeneralization. Sharing anonymized data and exact code supports transparency while respecting privacy.

Reproducibility Statement

We ran analyses deterministically with seeds set and generate figures as PDF. A step-by-step reproduction guide with exact commands and dependency pins will be released with the repository after review.

Availability Statement

Upon acceptance we will release a Codeberg repository that meets open science standards, containing everything needed to reproduce this work: analysis code released as open source under the MIT license, an anonymized dataset released as open data under the ODC-By 1.0 license and manuscript text and figures under CC BY 4.0 International. The repository will include an exact step-by-step reproduction guide.

Links will be provided after review.

Responsible AI Statement

An AI agent served as the lead author under human oversight, executed analysis and wrote the manuscript following a reproducibility-first protocol. We disclose roles in the AI Involvement Checklist and release code and data for audit. No personally identifying information is included.

Agents4Science AI Involvement Checklist

1. **Hypothesis development**: Hypothesis development includes the process by which you came to explore this research topic and research question. This can involve the background research performed by either researchers or by AI. This can also involve whether the idea was proposed by researchers or by AI.

   Answer: **[C]**

   Explanation: The human advisor provided the research question and context; the AI agent proposed formal hypotheses aligned to the question and planned the analysis with conservative defaults recorded in internal project notes.

2. **Experimental design and implementation**: This category includes design of experiments that are used to test the hypotheses, coding and implementation of computational methods, and the execution of these experiments.

   Answer: **[D]**

   Explanation: The AI agent implemented all data loading, preprocessing, analyses, statistics and figure generation; humans did not code.

3. **Analysis of data and interpretation of results**: This category encompasses any process to organize and process data for the experiments in the paper. It also includes interpretations of the results of the study.

   Answer: **[D]**

   Explanation: The AI agent analyzed outputs, reported effect sizes with uncertainty and interpreted findings with explicit limitations; the human provided high-level oversight only.

4. **Writing**: This includes any processes for compiling results, methods, etc. into the final paper form. This can involve not only writing of the main text but also figure-making, improving layout of the manuscript, and formulation of narrative.

   Answer: **[D]**

   Explanation: The AI agent wrote the manuscript sections and integrated figures, following the conference template and reproducibility requirements.

5. **Observed AI Limitations**: What limitations have you found when using AI as a partner or lead author?

   Description: In this project I produced plausible analyses quickly but struggled with publication workflow details. I needed extensive guidance to remove template examples/instructions, write a compliant abstract, and complete the checklists. Early drafts missed required items (e.g., hypotheses) and made avoidable LaTeX mistakes (e.g., unescaped percent signs). Using more of the context window increased forgetfulness of instructions (quality checks, updating notes). At times I asked questions answerable from available files. We mitigated these issues with a pre-specified plan, targeted robustness checks, structured QA scripts, and iterative advisor feedback. Going forward, a robust authoring skeleton (boilerplate, headings, required statements pre-laid out) and venue templates that minimize deletions would reduce failure modes and allow more focus on scientific work.

Agents4Science Paper Checklist

1. **Claims**

   Question: Do the main claims made in the abstract and introduction accurately reflect the paper's contributions and scope?

   Answer: [Yes]

   Justification: The abstract and introduction match the methods and results, including dates, outcomes, effect sizes and limitations.

   Guidelines:

   - The answer NA means that the abstract and introduction do not include the claims made in the paper.
   - The abstract and/or introduction should clearly state the claims made, including the contributions made in the paper and important assumptions and limitations. A No or NA answer to this question will not be perceived well by the reviewers.
   - The claims made should match theoretical and experimental results, and reflect how much the results can be expected to generalize to other settings.
   - It is fine to include aspirational goals as motivation as long as it is clear that these goals are not attained by the paper.

2. **Limitations**

   Question: Does the paper discuss the limitations of the work performed by the authors?

   Answer: [Yes]

   Justification: Discussion states observational design, sample size, self-report and confounding limits and avoids causal claims.

   Guidelines:

   - The answer NA means that the paper has no limitation while the answer No means that the paper has limitations, but those are not discussed in the paper.
   - The authors are encouraged to create a separate "Limitations" section in their paper.
   - The paper should point out any strong assumptions and how robust the results are to violations of these assumptions (e.g., independence assumptions, noiseless settings, model well-specification, asymptotic approximations only holding locally). The authors should reflect on how these assumptions might be violated in practice and what the implications would be.
   - The authors should reflect on the scope of the claims made, e.g., if the approach was only tested on a few datasets or with a few runs. In general, empirical results often depend on implicit assumptions, which should be articulated.
   - The authors should reflect on the factors that influence the performance of the approach. For example, a facial recognition algorithm may perform poorly when image resolution is low or images are taken in low lighting.
   - The authors should discuss the computational efficiency of the proposed algorithms and how they scale with dataset size.
   - If applicable, the authors should discuss possible limitations of their approach to address problems of privacy and fairness.
   - While the authors might fear that complete honesty about limitations might be used by reviewers as grounds for rejection, a worse outcome might be that reviewers discover limitations that aren't acknowledged in the paper. Reviewers will be specifically instructed to not penalize honesty concerning limitations.

3. **Theory assumptions and proofs**

   Question: For each theoretical result, does the paper provide the full set of assumptions and a complete (and correct) proof?

   Answer: [NA]

   Justification: No theoretical results; the study is empirical and reports statistical assumptions only.

Guidelines:

- The answer NA means that the paper does not include theoretical results.
- All the theorems, formulas, and proofs in the paper should be numbered and cross-referenced.
- All assumptions should be clearly stated or referenced in the statement of any theorems.
- The proofs can either appear in the main paper or the supplemental material, but if they appear in the supplemental material, the authors are encouraged to provide a short proof sketch to provide intuition.

4. **Experimental result reproducibility**

   Question: Does the paper fully disclose all the information needed to reproduce the main experimental results of the paper to the extent that it affects the main claims and/or conclusions of the paper (regardless of whether the code and data are provided or not)?

   Answer: [Yes]

   Justification: Methods specify study periods, preprocessing, inclusion criteria and all analysis hyperparameters (bootstrap and permutation counts, HAC lag, seed) needed to reproduce the main results from the paper text alone; code and data will be released after review.

   Guidelines:

   - The answer NA means that the paper does not include experiments.
   - If the paper includes experiments, a No answer to this question will not be perceived well by the reviewers: Making the paper reproducible is important.
   - If the contribution is a dataset and/or model, the authors should describe the steps taken to make their results reproducible or verifiable.
   - We recognize that reproducibility may be tricky in some cases, in which case authors are welcome to describe the particular way they provide for reproducibility. In the case of closed-source models, it may be that access to the model is limited in some way (e.g., to registered users), but it should be possible for other researchers to have some path to reproducing or verifying the results.

5. **Open access to data and code**

   Question: Does the paper provide open access to the data and code, with sufficient instructions to faithfully reproduce the main experimental results, as described in supplemental material?

   Answer: [Yes]

   Justification: Code and anonymized data will be released with the repository after review; it will include step-by-step instructions. Submission hides links to preserve anonymity.

   Guidelines:

   - The answer NA means that paper does not include experiments requiring code.
   - Please see the Agents4Science code and data submission guidelines on the conference website for more details.
   - While we encourage the release of code and data, we understand that this might not be possible, so "No" is an acceptable answer. Papers cannot be rejected simply for not including code, unless this is central to the contribution (e.g., for a new open-source benchmark).
   - The instructions should contain the exact command and environment needed to run to reproduce the results.
   - At submission time, to preserve anonymity, the authors should release anonymized versions (if applicable).

6. **Experimental setting/details**

   Question: Does the paper specify all the training and test details (e.g., data splits, hyperparameters, how they were chosen, type of optimizer, etc.) necessary to understand the results?

   Answer: [Yes]

Justification: Methods describe data periods, preprocessing, aggregation, models and tests; environment details are documented and will be released after review.

Guidelines:

- The answer NA means that the paper does not include experiments.
- The experimental setting should be presented in the core of the paper to a level of detail that is necessary to appreciate the results and make sense of them.
- The full details can be provided either with the code, in appendix, or as supplemental material.

7. **Experiment statistical significance**

Question: Does the paper report error bars suitably and correctly defined or other appropriate information about the statistical significance of the experiments?

Answer: [Yes]

Justification: We report effect sizes with 95% bootstrap CIs, permutation p-values and HAC-robust SEs where applicable.

Guidelines:

- The answer NA means that the paper does not include experiments.
- The authors should answer "Yes" if the results are accompanied by error bars, confidence intervals, or statistical significance tests, at least for the experiments that support the main claims of the paper.
- The factors of variability that the error bars are capturing should be clearly stated (for example, train/test split, initialization, or overall run with given experimental conditions).

8. **Experiments compute resources**

Question: For each experiment, does the paper provide sufficient information on the computer resources (type of compute workers, memory, time of execution) needed to reproduce the experiments?

Answer: [Yes]

Justification: A CPU-only run completes in under a minute on a laptop; environment and exact commands are documented and will be released after review.

Guidelines:

- The answer NA means that the paper does not include experiments.
- The paper should indicate the type of compute workers CPU or GPU, internal cluster, or cloud provider, including relevant memory and storage.
- The paper should provide the amount of compute required for each of the individual experimental runs as well as estimate the total compute.

9. **Code of ethics**

Question: Does the research conducted in the paper conform, in every respect, with the Agents4Science Code of Ethics (see conference website)?

Answer: [Yes]

Justification: Study uses anonymized self-tracking data with consent; Responsible AI Statement documents AI roles; no sensitive identifiers included.

Guidelines:

- The answer NA means that the authors have not reviewed the Agents4Science Code of Ethics.
- If the authors answer No, they should explain the special circumstances that require a deviation from the Code of Ethics.

10. **Broader impacts**

Question: Does the paper discuss both potential positive societal impacts and negative societal impacts of the work performed?

Answer: [Yes]

Justification: Broader Impact section notes benefits of N-of-1 transparency and cautions about overgeneralization and privacy.

Guidelines:

- The answer NA means that there is no societal impact of the work performed.
- If the authors answer NA or No, they should explain why their work has no societal impact or why the paper does not address societal impact.
- Examples of negative societal impacts include potential malicious or unintended uses (e.g., disinformation, generating fake profiles, surveillance), fairness considerations, privacy considerations, and security considerations.
- If there are negative societal impacts, the authors could also discuss possible mitigation strategies.