Review of: "Individual behavioral trajectories shape whole-brain connectivity in mice"

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The Individuality RFID cage system with extensive roaming tracking provides the opportunity for high resolution phenotyping of exploratory behavioural trajectory in mice. The paper demonstrates the potential utility of such trajectory analysis, and suggests the possibility of extending this type of analysis with longitudinal biological read-outs (e.g longitudinal MRI) to develop novel trajectory-based insights in future studies. Comparisons between down-roaming and flat-roaming mice are the primary focus of the results, however, evidence for the validity of these two behavioural trajectory phenotypes should be strengthened.

1. Too many aspects are collapsed into a single data point. Nightly roaming entropy from 21 days is averaged into a single data point, obscuring daily volatility. Given that deeper behavioural phenotyping is available, consider providing the full trajectory. Do the down-roaming and flat-roaming phenotypes persist?
2. Excluding mice with an intermediate phenotype increases the likelihood of false discovery.
3. In Figure 1C, down-roamers are predominantly low-activity mice in the final time block (T4), while flat-roamers are predominantly high-activity mice in T4. It is possible that the sub-group connectome and neurogenesis findings are a consequence of selecting mice with lower activity in the most recent 21-day block preceding biological read-outs. Authors may want to provide evidence this is not the case; for example, by repeating the subgroup analysis pipeline using T4 data as input.
4. It is not clear why relative structure volume is used to construct covariance matrix over absolute structure volume.