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Direct RNAseq reveals postpartum stress isoform and epitranscriptomic changes in BLA

Maternal postpartum stress caused by low resource parenting can produce enduring phenotypes in offspring, including changes in morphine and cocaine self-administration. Yet the effects on the maternal brain are largely unexplored. We aimed to define how postpartum stress reshapes isoform usage and the epitranscriptomic landscape in the female rat basolateral amygdala (BLA). We collected BLA tissue from postpartum female rats parenting in a low resource or control environment (n=10). Poly(A)+ RNA was profiled using ONT direct RNA sequencing (RNA004) on the PromethION platform. Reads were basecalled, aligned to the rat reference genome, and assigned to genes and annotated for isoforms. We performed differential gene expression, differential isoform expression, and isoform-switching analyses, and leveraged raw-signal features to infer stress-associated epitranscriptomic signatures and poly(A) tail-length shifts. Pathway enrichment was used to contextualize regulated programs. Direct RNA sequencing yielded long reads spanning full transcripts, enabling isoform-resolved quantification and simultaneous detection of stress-linked RNA features from the same dataset. Postpartum stress was associated with coordinated changes in BLA transcript usage, including isoform shifts within stress- and synapse-related pathways, alongside distinct RNA modification signatures and poly(A) tail-length alterations consistent with post-transcriptional reprogramming. These results provide an integrated view of how postpartum stress modulates both isoforms and RNA chemistry in the maternal BLA. We plan to expand to additional amygdala subnuclei and time points, add cell-type resolution, and validate priority isoforms/modification sites with targeted long-read and orthogonal biochemical assays.

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