The Effects of Early Life Stress on Altered Gene Expression

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Background

Childhood trauma increases the lifetime risk of depression, drug addiction, and other mood disorders[1]. Previous studies have suggested that the brain is sensitive to environmental factors such as stress during early development, linking early life stress to increased sensitivity to future stress[2,3]. The molecular mechanisms driving this effect are still unknown. The purpose of this experiment is to revalidate directionality and significance of altered gene expression[4] in separate cohorts of mice.

Research Questions

How does early life stress (ELS) increase sensitivity to stress? Does ELS alter gene expression in the brain's reward circuitry?

Methods and Materials

Bilateral punches of VTA, NAc, and PFC tissue were collected from female and male C57BL/6J mice in both ELS and standard-reared groups. RNA was extracted with RNeasy Micro Kits (Qiagen) and converted into cDNA (Thermocycler). The cDNA was used in qPCR with primers designed for the target genes. Hprt1 acted as the housekeeping gene. qPCR allows for the quantification of gene expression, but is limited by the efficiency and accuracy of the primers.

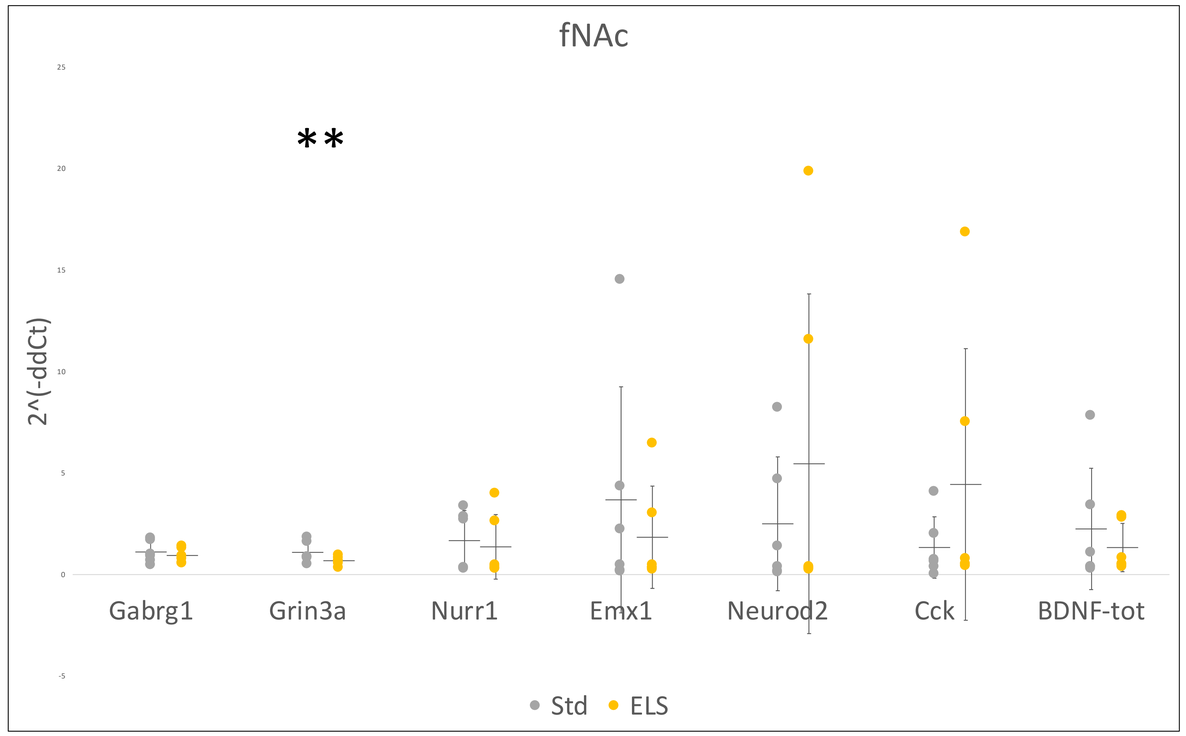

Fig 1. Relative gene expression in female NAc, Std vs. ELS; *Grin3a* has a trend of downregulation in ELS. **p<0.1

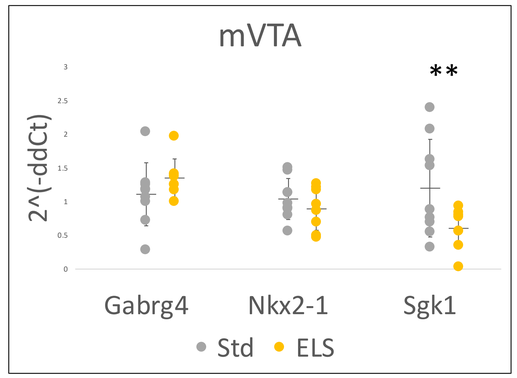

Fig 4. Relative gene expression in male VTA, Std vs. ELS; *Sgk1* has a trend of downregulation in ELS.**p<0.1

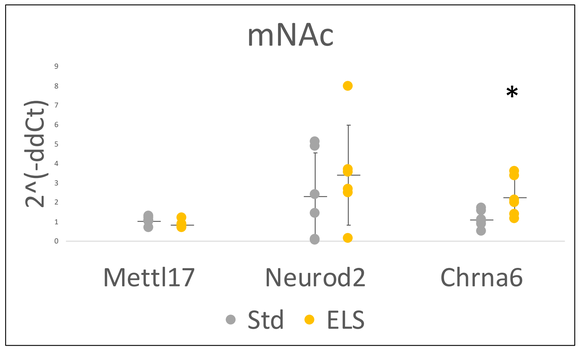

Fig 2. Relative gene expression in male NAc, Std vs. ELS; *Chrna6* is upregulated in ELS.*p<0.05

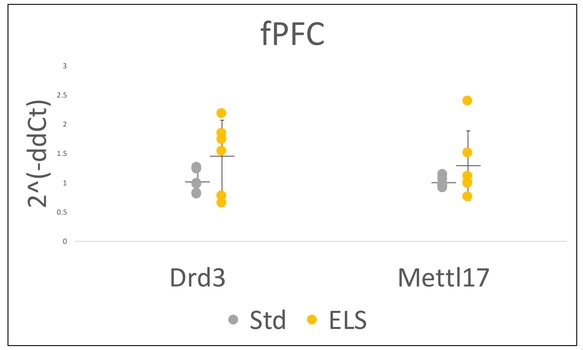

Fig 3. Relative gene expression in female PFC, Std vs. ELS. No significant altered gene expression in the target genes.

Results

I used a fold change to represent gene expression and compared the results between the Std and ELS groups. In female NAc, *Grin3a* was downregulated for ELS (**Figure 1**, Std mean=1.094, ELS mean=0.683, p=0.099). In male NAc, *Chrna6* was upregulated for ELS (**Figure 2**, Std mean=1.09, ELS mean=2.24, p=0.029). There was no significant altered gene expression for the target genes in female PFC (**Figure 3**). In male VTA, *Sgk1* was downregulated for ELS (**Figure 4**, Std mean=1.202, ELS mean=0.605, p=0.093).

Conclusion

The data suggests that ELS alters gene expression in the brain reward circuitry of male and female mice, revalidating previous data of altered gene expression found with RNA-seq. These findings confirm our understanding of the transcriptional effects of ELS. Some gene expression changes were different in directionality and significance from the original RNA-seq, so further study in this area may be necessary.

Acknowledgments

I would like to thank Dr. Peña for her mentorship throughout this project. I would also like to thank Shannon, Julie-Anne, Cero, Rebekah, and Anne-Elizabeth from the Peña lab for their help.

References

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