Acute Effects of Social Defeat on Neuroinflammatory Signaling in Mice

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INTRODUCTION

Psychosocial stress negatively affects both physical and mental health; and stress-related psychiatric disorders are more common in women. Interestingly, preclinical studies have predominately studied the effects of psychosocial stress on male mice. These studies suggest that adverse effects of psychosocial stress are due in part to the disruption of inflammatory signaling; however, the extent to which these findings translate to females remains unclear. In the few instances where the effects of social defeat have been studied in female mice, a male mouse was used as the aggressor. There is still much to learn about the effects of psychosocial stress on inflammatory signaling in female mice, particularly in the context of female-mediated aggression. Our working hypothesis is that social defeat impacts stress and inflammation in a sex-dependent manner.

METHODS

To test our working hypothesis, we investigated the effects of a single, 2 h bout of social defeat on biomarkers of stress and inflammation in male and female C57BL/6J mice: importantly, the CD-1 aggressor mice were the same sex as the subject mice. Plasma corticosterone (CORT) levels were measured using an enzyme-linked immunosorbent assay (ELISA) and used a biomarker of stress. Levels of the proinflammatory chemokine, monocyte chemotactic protein-1 (CCL2), were measured in plasma and brain by ELISA. The inflammatory signaling protein, transforming growth factor beta activated kinase 1 (TAK-1), and glial fibrillary acidic protein (GFAP), a marker of astrocyte activation, were assessed in the brain by western blot analysis.

RESULTS

Single Bout Social Defeat "bully protocol"

C57BL/6J

CD-1 "bully"

Three C57Bl/6J mice where placed in a cage with one CD-1 mouse where a social defeat baseline was established with a Single 2h bout. CD-1 aggressor mice were the same sex as the subject mice.

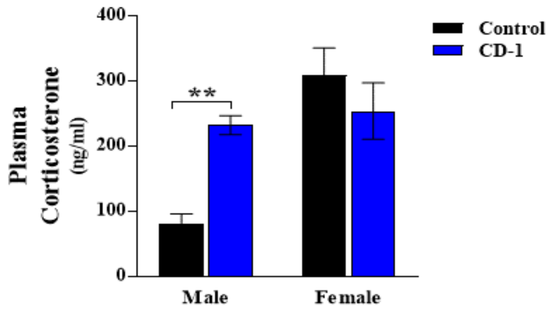

Fig 1: Effects of social defeat on plasma CORT. Mice were subjected to a single 2 h bout of social defeat followed immediately by collection of brain sample; plasma CORT was measure by ELISA. Data were analyzed by two- way ANOVA and Fisher's LSD, **p<0.01; ****p<0.0001

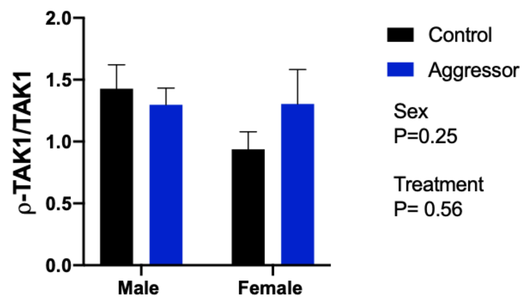

Fig 2: Effects of social defeat on TAK1 activation. Mice were subjected to a single 2 h bout of social defeat. Brains were collected immediately after social defeat. p-TAK1 and TAK1 were measure in brain homogenates by Western Blot Analysis. Data were analyzed by a two-way ANOVA, n= 8-9.

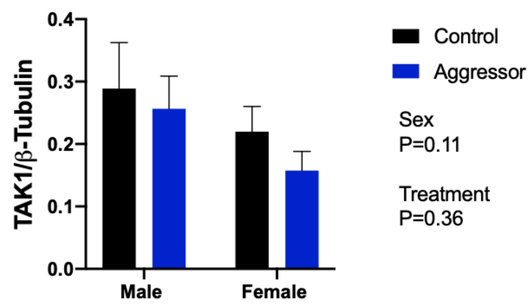

Fig 3: Effects of social defeat on TAK1 expression. Mice were subjected to a single 2 h bout of social defeat. Brains were collected immediately after social defeat. TAK1 and β-Tubulin were measure in brain homogenates by Western Blot Analysis. Data were analyzed by a two-way ANOVA, n= 8-9.

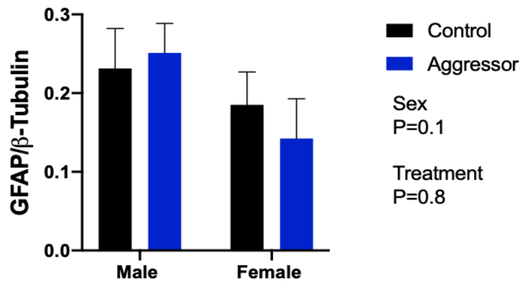

Fig 4: Effects of social defeat on GFAP. Mice were subjected to a single 2 h bout of social defeat. Brains were collected immediately after social defeat. GFAP and β-Tubulin were measure in brain homogenates by Western Blot Analysis. Data were analyzed by a two-way ANOVA, n= 8-9.

CONCLUSION

A single bout of social defeat induces stress as indicated by an increase in plasma CORT. The biomarkers of inflammation in the brain and astrocyte activation were not significantly impacted in males or females by a single bout of social defeat. These insights into the effects of acute psychosocial stress on inflammatory signaling warrant further investigation.

FUTURE DIRECTIONS

Future investigations will assess additional inflammatory mediators and the effects of repeated bouts of social defeat. Together, these findings are expected to be instrumental in efforts to advance the development of novel therapeutic strategies to combat the detrimental effects of psychosocial stress.

REFERENCES

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