Background and Rationale

- Imagine living trapped in a body that acts on its own, often against your will. This is ‘Knowledge-Action-Dissociation’ and accompanies all abnormal repetitive behaviors (e.g. compulsive behaviors and stereotypies).
- Stereotypy (repetitive, unvarying, and seemingly goal-less behavior) is documented in many animal species and in humans with neuropsychiatric conditions.
- In humans, stereotypy is correlated with knowledge-action dissociation and distressing affective states.
- There is strong evidence of shared pathophysiology between spontaneous stereotypy in animals and stereotypy in humans (e.g. dysregulation of the indirect pathway of the premotor corticostriatal loop and basal ganglia dysfunction in general).

Do Measures of Redox Balance Predict Severity of Stereotypy?

- In the log-log multiple regression, both reduced (F(1,10)=7.805; P=0.0234) and oxidized (F(1,10)=8.189; P=0.0311) plasma-based glutathione positively predicted stereotypy, but each relationship weakened with age (reduced glutathione: F(1,10)=7.4487; P=0.0259; oxidized glutathione: F(1,10)=6.6538; P=0.0447).
- Given the similar effects of reduced and oxidized plasma-based glutathione, we repeated this analysis using total plasma-based glutathione as the only predictor. Total glutathione positively predicted stereotypy (F(1,10)=13.50; P=0.0043), but again, this relationship weakened with age (F(1,10)=11.54; P=0.0068).
- Standardized (to creatinine) excreted antioxidant capacity did not predict stereotypies (F(1,10)=7.453; P=0.0082), nor was there a significant effect of age on this relationship (F(1,10)=0.6223; P=0.4485).

What Does This Mean?

- Plasma-based total glutathione is predictive of stereotypies in mice.
- The relationship between total glutathione and stereotypies diminishes with age.
- The relationship between glutathione and stereotypies in mice parallels the relationship between glutathione and compulsive behaviors in mice and humans.
- These results further support the interpretation of stereotypies as an indicator of neural injury and poor animal welfare.

Why Do We Care?

- Given the established relationships between knowledge-action dissociation and stereotypies in mice and humans, and that these behaviors are ego-dystonic in humans, we hypothesize that stereotypies are also distressing for mice.
- The results from this study suggest REDOX imbalance as a potential neurodevelopmental etiology of stereotypy and highlight potential intervention strategies.

What’s Next?

- Investigate therapeutic potential of antioxidants in preventing or mitigating severity of stereotypy in mice.
- Examine the relationship between stereotypies and plasma-based measures of glutathione in clinical populations.