

The role of the indirect basal ganglia pathway in a mouse model of repetitive circling behavior

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Introduction

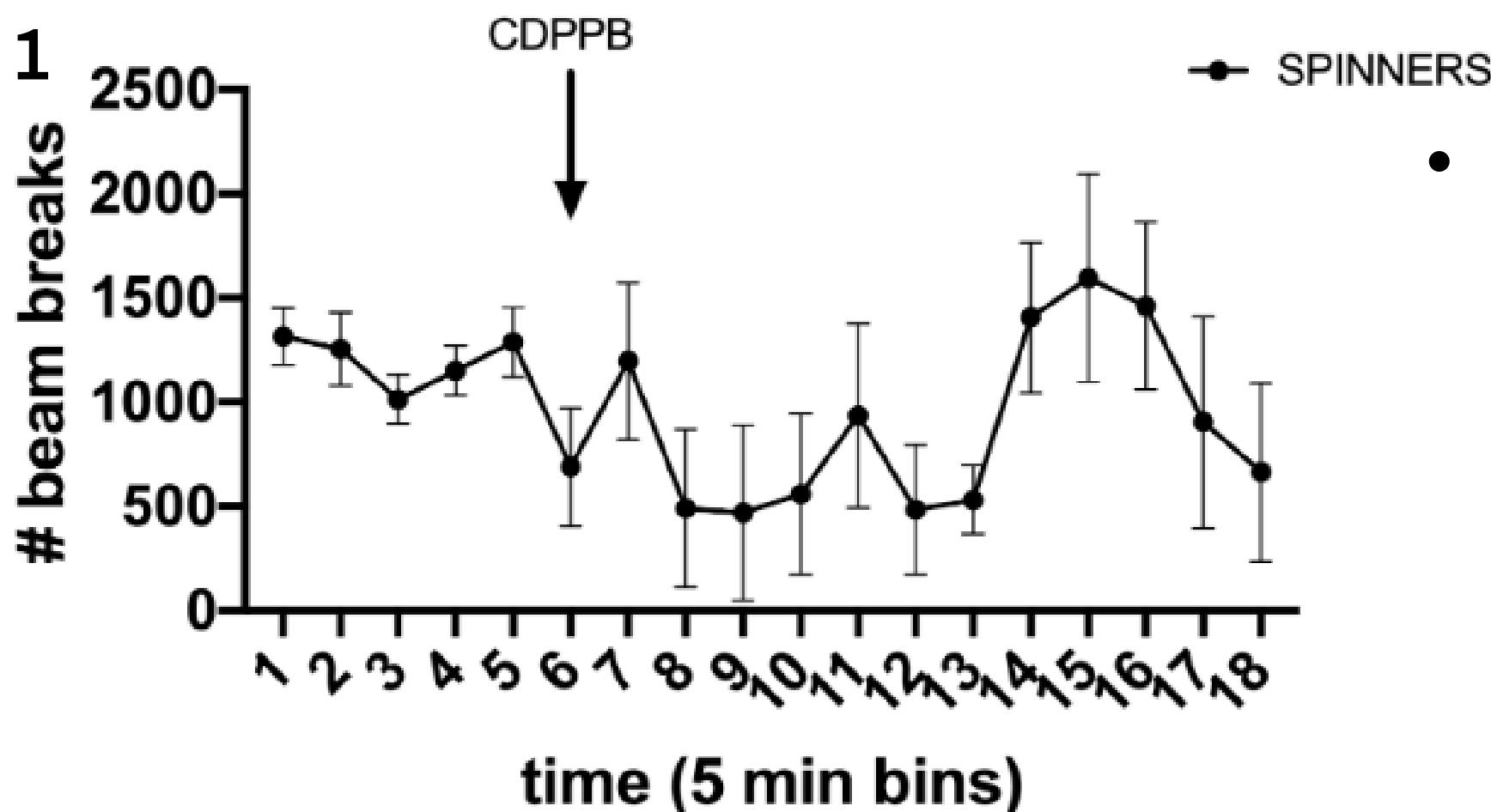
- Repetitive behaviors are associated with a variety of disorders in humans
- Previous investigations have indicated that the ketogenic diet plays a role in neurotransmitter functioning
- We investigated the potential role of neurotransmitters in repetitive behaviors by investigating how three drugs affected circling behavior in mice

Method

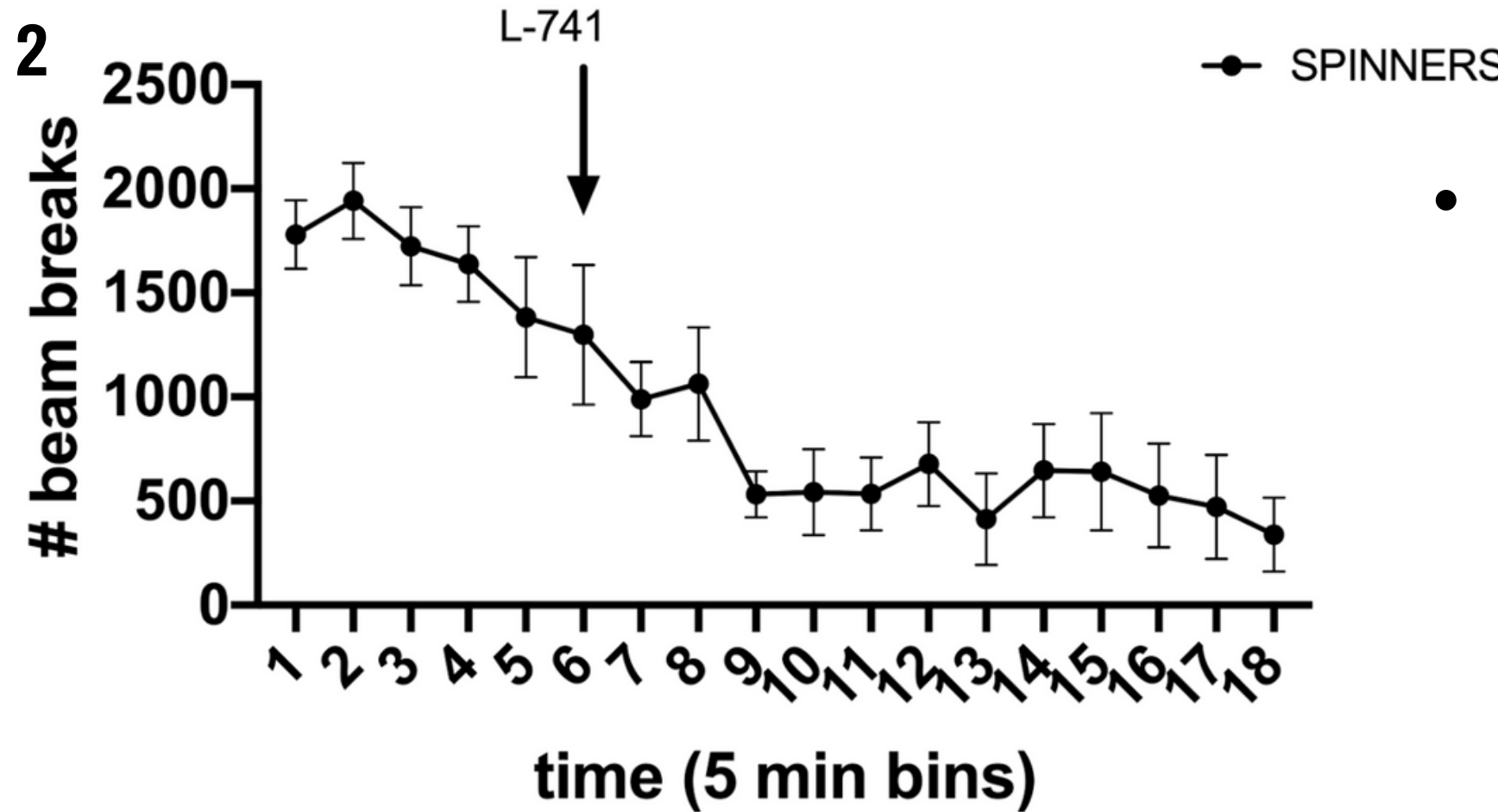
- Circling behavior was measured using photobeam activated locomotor chambers
- Drugs utilized:
 - L-741,626: Dopamine receptor antagonist
 - CGS21680: Adenosine agonist
 - CDPBPB: Gutamate positive allosteric modulator
- Drugs were administered in either a triple cocktail or as single drugs

Results

- Results indicated systemic injection of the triple drug cocktail was not able to reduce circling behavior



- Fig 1: Number of locomotor beam breaks by minute in circling mice (n=5) before vs. after injection of CDPBPB ($F(17, 68) = 1.9, p = 0.058$)



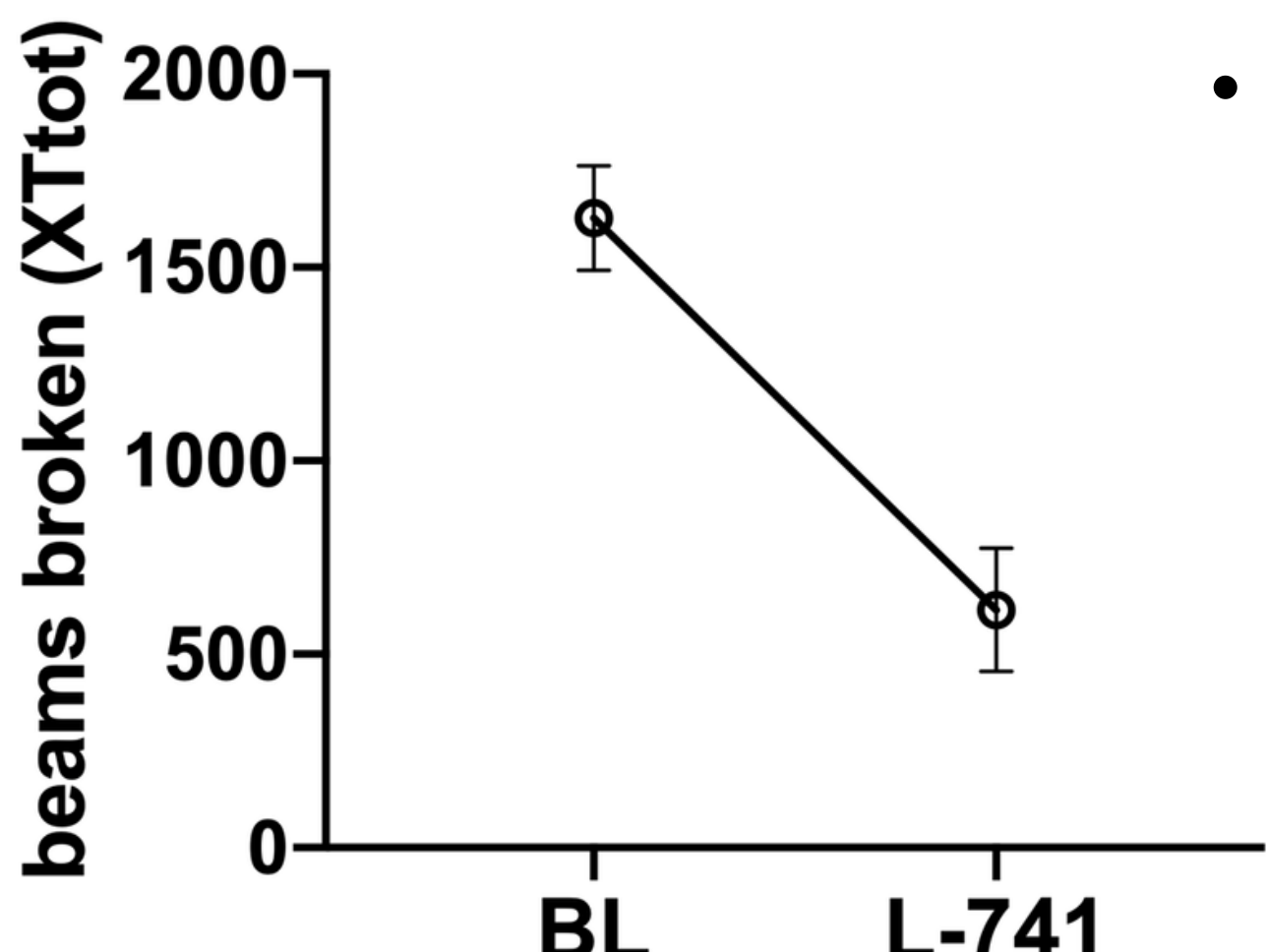
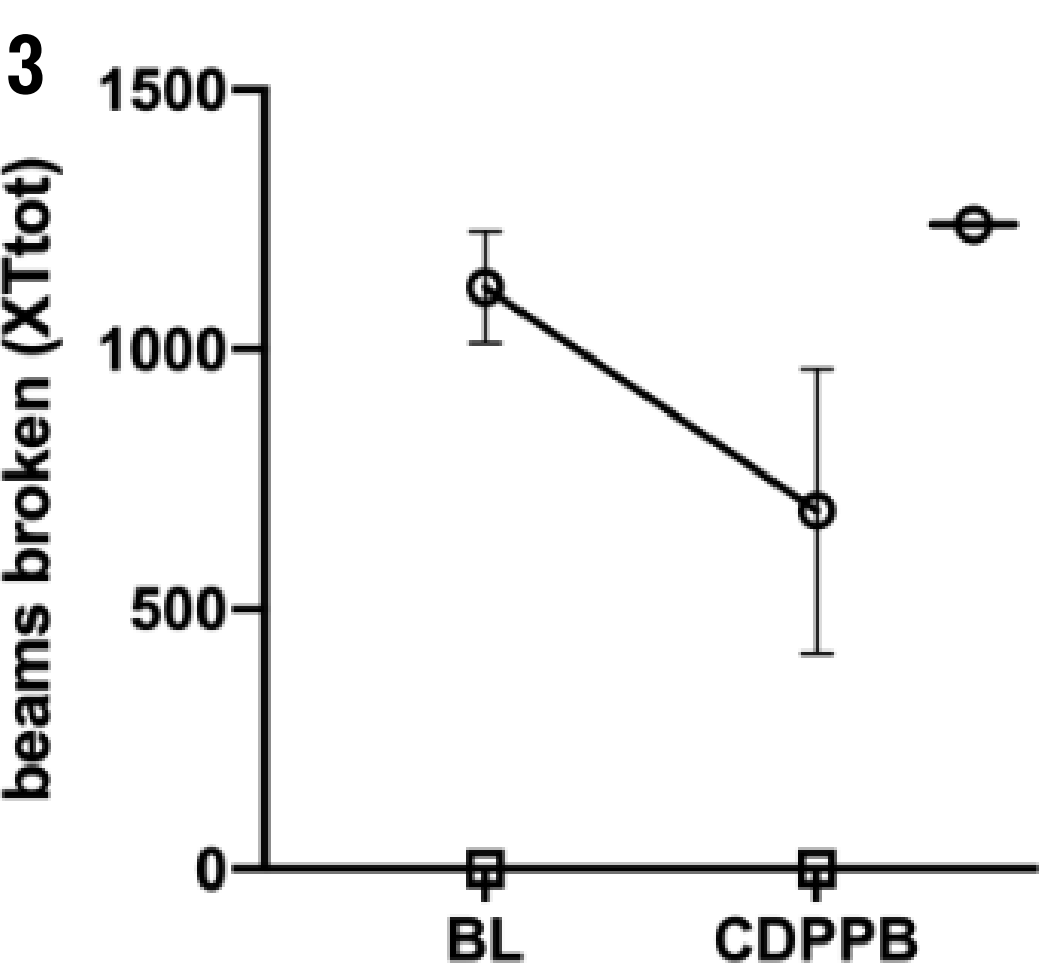
- Fig 2: Number of locomotor beam breaks by minute in circling mice (n=5) before vs. after injection of dopamine ($F(17, 85) = 7.06, p < 0.0001$)

Discussion

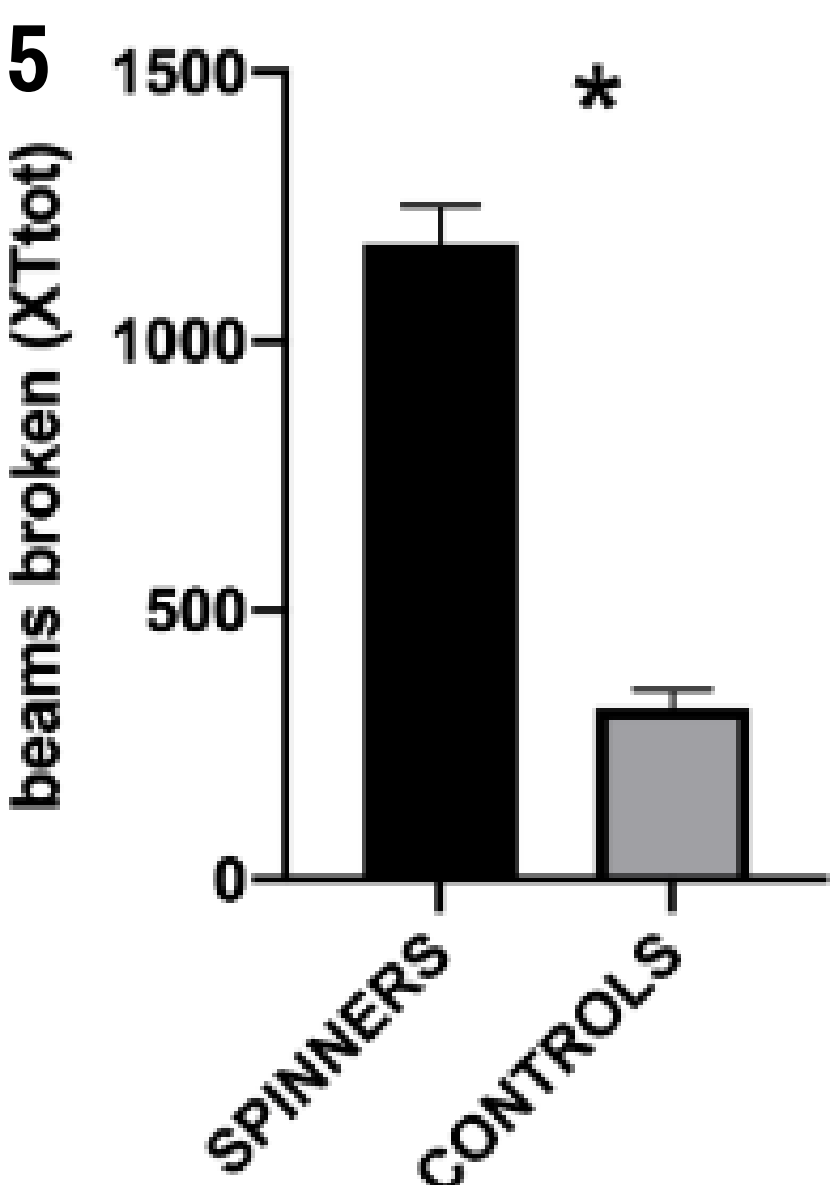
- These drugs have been shown to reduce striatal indirect basal ganglia pathway cell function
- Results implied the role of the indirect basal ganglia pathway in repetitive behavior, as well as the potential to reduce this behavior through pharmacological means
- The results of this study recapitulate the importance of dopamine in repetitive behaviors, and suggest that dopamine may be a key neurotransmitter implicated in the ketogenic diet's ability to reduce stereotypy

Future Directions

- This experiment suggests the potential of a single drug injection in reducing repetitive behavior, future studies may further investigate the the single drug effects of CGS21680
- It is unclear why the triple drug injection did not have the same attenuating effects as the single drug trials. A future study may attempt to reinvestigate the use of the triple drug cocktail



- Fig 3 and 4: Difference in XTtot breaks in circling mice before and after a single injection of CDPBPB ($F(1,4) = 2.32, p = 0.202$) and dopamine ($F(1, 5) = 18.54, p = 0.008$)



- Fig 5: Differences in XTtot locomotor activity between circling and non-circling mice
- Fig 6: Correlation matrix of relationship between scan focal sampling of circling behavior and XTtot beam breaks ($r = 0.641$ and $p = 0.024$)

