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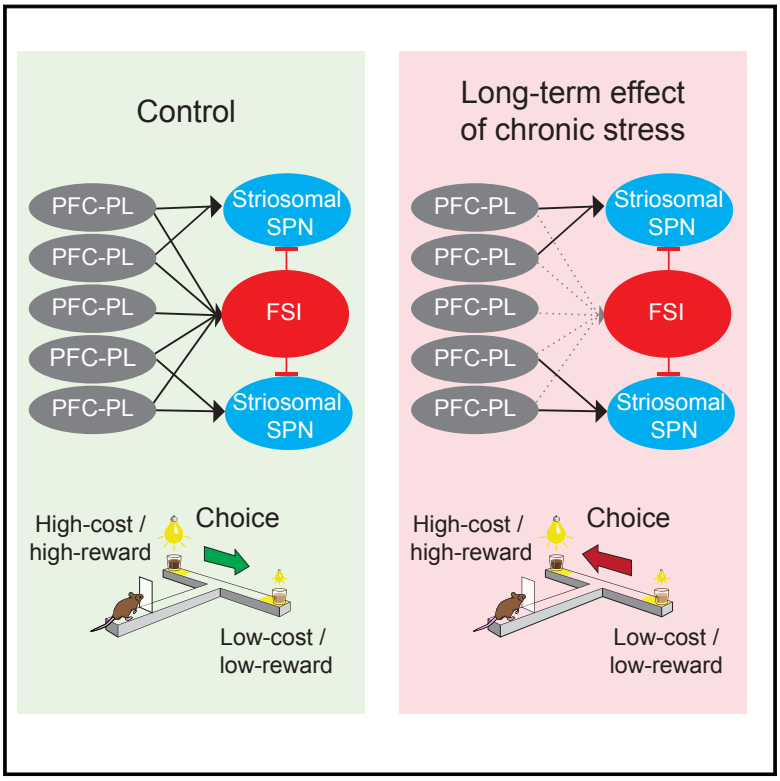
Chronic Stress Alters Striosome-Circuit Dynamics, Leading to Aberrant Decision-Making

Graphical Abstract



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In Brief

A brain circuit that connects the prefrontal cortex with striosomes in the striatum is activated in cost-benefit decision-making and becomes severely impaired after chronic stress, producing abnormal weighing of cost and benefit.

HIGHLIGHTS

- Chronic stress produces abnormal cost-benefit integration in decision-making
- This reflects abnormal in-task firing dynamics of prefrontal and striatal cells
- This circuit disorder leads to highly elevated firing of striosomal output neurons
- Optogenetic manipulations can mimic or reverse these behavioral effects of stress

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Chronic Stress Alters Striosome-Circuit Dynamics, Leading to Aberrant Decision-Making

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SUMMARY

Effective evaluation of costs and benefits is a core survival capacity that in humans is considered as optimal, "rational" decision-making. This capacity is vulnerable in neuropsychiatric disorders and in the aftermath of chronic stress, in which aberrant choices and high-risk behaviors occur. We report that chronic stress exposure in rodents produces abnormal evaluation of costs and benefits resembling non-optimal decision-making in which choices of high-cost/high-reward options are sharply increased. Concomitantly, alterations in the task-related spike activity of medial prefrontal neurons correspond with increased activity of their striosome-predominant striatal projection neuron targets and with decreased and delayed striatal fast-firing interneuron activity. These effects of chronic stress on prefronto-striatal circuit dynamics could be blocked or be mimicked by selective optogenetic manipulation of these circuits. We suggest that altered excitation-inhibition dynamics of striosome-based circuit function could be an underlying mechanism by which chronic stress contributes to disorders characterized by aberrant decision-making under conflict.

INTRODUCTION

The ability to perform integration of costs and benefits is essential for resolution of motivational conflict during value-based decision-making (Glimcher and Fehr, 2013). Abnormal decision-making, including risky or irrational choices leading to negative outcomes, can emerge as a symptom in neurologic and neuropsychiatric disorders, including anxiety and depression, bipolar disorder, Huntington's disease, schizophrenia, and suicidal ideation (Amemori and Graybiel, 2012; Aupperle and Paulus, 2010; Gleichgerrcht et al., 2010; Szanto et al., 2015). The development of such disorders can be facilitated by exposure to chronic stress (Pittenger and Duman, 2008; Selye, 1936), and prolonged stress can itself induce aberrant decision-making (Schwabe and Wolf, 2009; Soares et al., 2012; Sousa and Almeida, 2012). These findings and other pioneering work demonstrates that the induction of dysfunctional neuronal circuitry due to prolonged environmental stress can deleteriously affect mental health (Lucassen et al., 2014; Pittenger and Duman, 2008; Selye, 1936; Sousa and Almeida, 2012). Within the brain, widespread effects of chronic stress have been reported (Dias-Ferreira et al., 2009; Lucassen et al., 2014; Sousa and Almeida, 2012), but the cell- and circuit-level mechanisms underlying these effects still are not fully understood (Dias-Ferreira et al., 2009; Lucassen et al., 2014; Sousa and Almeida, 2012).

Here, we examined the effects of chronic stress on a prefrontal corticostriatal circuit that has been implicated in evaluation of cost, effort, and reward (Amemori and Graybiel, 2012; Friedman et al., 2015; Rushworth et al., 2011) and is related to cortical regions that in humans are affected in individuals suffering from anxiety, depression, and related problems (Aupperle and Paulus, 2010). This circuit preferentially targets the neurochemically specialized striosomes in the rodent dorsomedial "associative" striatum, a striatal region affected by chronic stress along with the prefrontal cortex itself (Arnsten, 2015; Dias-Ferreira et al., 2009). We earlier found that this prefronto-striosomal circuit selectively modulates decision-making under conditions of motivational conflict in which cost-benefit decisions must be made (Amemori and Graybiel, 2012; Friedman et al., 2015). Optogenetic disconnection of the prelimbic region of the prefrontal cortex (PFC-PL) from its putative striosomal targets in the dorsomedial striatum provoked rats to make abnormal choices in which they increased their choices of high-cost/high-reward options, mimicking abnormal decision-making and reflecting abnormal utility functions (Friedman et al., 2015). Within the striatum, both projection neurons (SPNs) and fast-spiking interneurons (FSIs) (Gage et al., 2010; Tepper et al., 2004) were affected by this circuit disconnection.

We trained rats and mice on the same cost-benefit conflict (CBC), benefit-benefit (BB), and cost-cost (CC) tasks and then exposed them to chronic stress and retested their performance. To our surprise, the behavioral effects of the chronic stress were nearly indistinguishable from those that we had found by optogenetically disconnecting the medial prefrontal cortex from its striosomal targets in the dorsomedial striatum (Friedman et al., 2015). Behavioral performance was abnormal in the CBC task, but not in the other decision-making tasks. This striking similarity