

Convergence of clinically relevant manipulations on dopamine-regulated prefrontal activity underlying stress-coping responses

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Manuscript Source: <https://www.biorxiv.org/content/10.1101/2021.03.20.436282v1>

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- Depending on the source of the input text, the Sentence Audit may contain occasional html artefacts that are parsed as sentences (E.g. "Download figure. Open in new tab").
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Contact Information:

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All queries, feedback or suggestions are also very welcome.

Research Paper Sections:

The sections of the research paper input text parsed in this audit.

[illegible]

Title

Convergence of clinically relevant manipulations on dopamine-regulated prefrontal activity underlying stress-coping responses

S1 [001] ABSTRACT

S1 [002] Background

Background

S1 [003] Depression is a pleiotropic condition that can be produced or ameliorated by diverse genetic, environmental, and pharmacological manipulations.

Depression is a pleiotropic condition ...
... that can be produced ...
... or ameliorated ...
... by diverse genetic, ...
... environmental, ...
... and pharmacological manipulations.

S1 [004] In this context, identifying patterns of circuit activity on which many of these manipulations converge would be important, because studying these patterns could reveal underlying biological processes related to depression and/or new therapies.

In this context, ...
... identifying patterns ...
... of circuit activity ...
... on ...
... which many ...
... of these manipulations converge would be important, ...
... because studying these patterns could reveal underlying biological processes related ...
... to depression ...
... and/or new therapies.

S1 [005] In particular, the prefrontal cortex and dopaminergic signaling have both been implicated in depression.

In particular, ...
... the prefrontal cortex ...
... and dopaminergic signaling have both been implicated ...
... in depression.

S1 [006] Nevertheless, how dopamine influences disease-relevant patterns of prefrontal circuit activity remains unknown.

Nevertheless, ...
... how dopamine influences disease-relevant patterns ...
... of prefrontal circuit activity remains unknown.

S1 [007] Methods

Methods

S1 [008] We used calcium imaging in brain slices to identify depression-relevant patterns of activity in prefrontal microcircuits, and measure how these are modulated by dopamine D2 receptors (D2Rs).

We used calcium imaging ...
... in brain slices ...
... to identify depression-relevant patterns ...
... of activity ...
... in prefrontal microcircuits, ...
... and measure how these are modulated ...
... by dopamine D2 receptors ...
... (D2Rs).

S1 [009] Then, we used optogenetic and genetic manipulations to test how dopamine and D2Rs contribute to stress-coping behavior in a paradigm commonly used to assay how manipulations promote or ameliorate depression-like states.

Then, ...
... we used optogenetic ...
... and genetic manipulations ...
... to test how dopamine ...
... and D2Rs contribute ...
... to stress-coping behavior ...
... in a paradigm commonly used ...
... to assay how manipulations promote ...
... or ameliorate depression-like states.

S1 [010] Results

Results

S1 [011] Patterns of correlated activity in prefrontal microcircuits are enhanced by D2R stimulation as well as by two mechanistically distinct antidepressants: ketamine and fluoxetine.

Patterns ...
... of correlated activity ...
... in prefrontal microcircuits are enhanced ...
... by D2R stimulation ...
... as well ...
... as by two mechanistically distinct antidepressants: ...
... ketamine ...
... and fluoxetine.

S1 [012] Conversely, this D2R-driven effect was disrupted in two etiologically distinct models of depression: a genetic susceptibility model and chronic social defeat.

Conversely, ...
... this D2R-driven effect was disrupted ...
... in two etiologically distinct models ...

... of depression: ...
... a genetic susceptibility model ...
... and chronic social defeat.

S1 [013] Phasic stimulation of dopamine afferents to prefrontal cortex increased effortful responses to tail suspension stress.

Phasic stimulation ...
... of dopamine afferents ...
... to prefrontal cortex increased effortful responses ...
... to tail suspension stress.

S1 [014] Conversely, deleting prefrontal D2R receptors reduced the duration of individual struggling episodes.

Conversely, ...
... deleting prefrontal D2R receptors reduced the duration ...
... of individual struggling episodes.

S1 [015] Conclusions

Conclusions

S1 [016] Correlated prefrontal microcircuit activity represents a point of convergence for multiple depression-related manipulations.

Correlated prefrontal microcircuit activity represents a point ...
... of convergence ...
... for multiple depression-related manipulations.

S1 [017] Prefrontal D2Rs enhance this activity.

Prefrontal D2Rs enhance this activity.

S1 [018] Through this mechanism, prefrontal dopamine signaling may promote network states associated with antidepressant actions that manifest as effortful responses to stress.

Through this mechanism, ...
... prefrontal dopamine signaling ...
... may promote network states associated ...
... with antidepressant actions ...
... that manifest ...
... as effortful responses ...
... to stress.

S2 [019] INTRODUCTION

S2 [020] Numerous mechanistic studies have implicated prefrontal circuits in human depression or depression-like states in animal models (1–6).

Numerous mechanistic studies have implicated prefrontal circuits ...
... in human depression ...
... or depression-like states ...
... in animal models ...
... (1–6).

S2 [021] Indeed, directly modulating activity in prefrontal circuits can relieve many symptoms associated with clinical depression (7–9).

Indeed, ...
... directly modulating activity ...
... in prefrontal circuits can relieve many symptoms associated ...
... with clinical depression ...
... (7–9).

S2 [022] A wide range of genetic and environmental factors influence depression susceptibility (10), and a similarly broad range of interventions, including medications, electrical stimulation, and exercise, can alleviate depressive symptoms.

A wide range ...
... of genetic ...
... and environmental factors influence depression susceptibility ...
... (10), ...
... and a similarly broad range ...
... of interventions, ...
... including medications, ...
... electrical stimulation, ...
... and exercise, ...
... can alleviate depressive symptoms.

S2 [023] Here, we take advantage of this heterogeneity by searching for convergent microcircuit processes engaged by these disparate factors.

Here, ...
... we take advantage ...
... of this heterogeneity ...
... by searching ...
... for convergent microcircuit processes engaged ...
... by these disparate factors.

S2 [024] Seeking convergence is a tactical approach for filtering pleiotropic changes in neural circuits in order to identify those mechanisms which are most likely to have broad clinical relevance.

Seeking convergence is a tactical approach ...
... for filtering pleiotropic changes ...
... in neural circuits ...
... in order ...
... to identify those mechanisms ...
... which are most likely ...
... to have broad clinical relevance.

S2 [025] We adopted a multi-step process.

We adopted a multi-step process.

End of Sample Audit

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