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Genetic basis for substance use exacerbation of COVID-19

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Background COVID-19 pandemic is a global infectious disease crisis causing more than 102 million infected and more than 2 million deaths during the last year. Patients with COVID-19 develop various clinical manifestations, from asymptomatic to mortality forms. Substance use disorders (SUDs) are recently implicated in the COVID-19 development especially among African Americans but the molecular underpinnings remain unclear.

Rationale/significance Genetics play an important role in the substance use exacerbation of COVID-19 based on the facts that both SUDs and severe COVID-19 carry significant genetic etiologies.

Hypothesis SUDs and severe COVID-19 share genetic risks.

Results In a SUDs-related 60-gene network, eight genes were associated with severe COVID-19, including *LZTFL1*, *PDYN*, *BDNF*, *ENTPD6*, *ADH1C*, *HEY1*, *PLAGL1*, and *HIVEP2*. A half of them encoded neuronal transcription factors (TFs), which was a 4-fold enrichment comparing to non-TF associations. This network displayed an overall 17-fold enrichment for nominal association significance while *LZTFL1* might help explain the greater vulnerability in African Americans than in European Americans.

Discussion Substance use as a risk for severe COVID-19 is manifest by shared genetic etiology, and likely by additional classified roles, such as damaging the immune system, facilitating the coronavirus entry, injuring various organs and causing behavioral exposure to infection.