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Letter to the Editor

Anti-viral properties of antipsychotic medications in the time of COVID-19



Dear Editor,

The study by Gordon et al. in *Nature* (Gordon et al., 2020) identified human proteins with which SARS-CoV-2 interacts, then examined the affinities of FDA-approved compounds for these proteins and their potential antiviral effects. Among the drugs that had significant affinity was haloperidol, a first-generation antipsychotic drug which interacts with sigma receptors and was proposed as an agent with potential antiviral properties. This finding follows prior studies that found antiviral and antimicrobial effects of specific antipsychotic medications. For example, chlorpromazine, a phenothiazine drug, may inhibit endocytosis (Dutta and Donaldson, 2012) of coronaviruses. In fact, several studies have demonstrated that chlorpromazine substantially inhibits MERS-CoV and/or SARS-CoV-2 related viruses in vitro (Cong et al., 2018; Dyal et al., 2014; Inoue et al., 2007). One group made the observation that patients in their psychiatric hospital seem to have a lower rate of symptomatic COVID-19 infection than staff (Plaze et al., 2020) and propose to conduct a clinical trial of chlorpromazine for symptomatic COVID-19 infection.

These antiviral effects are mediated by off-target (non-D2 receptor effects) extra-CNS effects on Sigma and Histamine receptors, among other potential targets. One question is whether the potential antiviral effects of antipsychotic medications are achievable at concentrations which produce their behavioral effects. For example, many antipsychotic drugs are active at nanomolar concentrations, whereas their antiviral effects appear to require at least micromolar concentrations.

Despite this limitation, a potential clinical application of such drugs with putative antiviral activity (like haloperidol and chlorpromazine) could be their prioritization among the various drugs in their class for behavioral control of patients in treatment settings such as nursing homes with vulnerable populations to SARS-CoV-2 infection.

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