Letter to the Editor: Haloperidol but not dopamine rapidly induces neuronal death: comments on ‘A systematic review of the effects of antipsychotic drugs on brain volume’

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Letter to the Editor

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In a systematic review published in Psychological Medicine, Moncrieff & Leo (2010) come to the conclusion that antipsychotics may be partly responsible for reductions in brain volume. Similar conclusions are reached by other reviewers, such as Navari & Dazzan (2009) and Zipursky et al. (2012), whereby they additionally propose that first-generation antipsychotics (FGAs) make an impact on brain volume more strongly than second-generation antipsychotics (SGAs).

All three papers, however, call for more research into the mechanisms that actually convey these effects. Although Moncrieff & Leo (2010) and Navari & Dazzan (2009) both suggest a potential neurotoxic effect of FGAs, they cite little research that may support the supposition of FGA neurotoxicity on the neuronal (i.e. the effects on the neuron) rather than solely the neural (i.e. the effects on the brain) or phenotypical level.

Noh et al. (2000) reported the dose-dependent induction of apoptosis through haloperidol in primary (not cell lines) mixed (neurons and glia) cortical cell cultures. These findings prove the neurotoxicity of haloperidol, but do not eliminate similar effects of increased dopamine levels (comparing healthy versus sick brains). Taking this into account, we replicated these results (Grant, 2011), but additionally compared effects of dopamine incubation. We found a drastic dose-dependent induction of neuronal death (90% at highest concentrations) after 24 h in haloperidol-treated but not in dopamine-treated primary mixed cortical cultures. Additionally, we examined possible mediators of haloperidol neurotoxicity, finding substantial increases in indicators of oxidative stress. These findings mirror significant increases in oxidative damage markers found in animals induced by haloperidol but not by SGAs (e.g. Parikh et al. 2003) as well as in schizophrenic patients (e.g. Zhang et al. 2006).

I would, therefore, draw two conclusions. First, haloperidol is indeed toxic at the neuronal level. Second, I believe that findings on the cell biology of schizophrenia and related factors may be of great importance and should therefore be incorporated into the field of schizophrenia research more than they currently are.

Declaration of Interest

None.

References


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