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Modafinil enhances cognitive, but not emotional conflict processing via enhanced inferior frontal gyrus activation and its communication with the dorsomedial prefrontal cortex

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One of the essential executive functions is inhibitory control task-irrelevant conflicts. Previous neuroimaging studies demonstrated separate conflict processing, with cognitive conflict particularly engaging the inferior frontal cortex (IFG) and emotional conflict recruiting the rostral anterior cingulate cortex (rACC) (Egner, Etkin, Gale, & Hirsch, 2007). Whereas initial findings suggest the putative neuroenhancer modafinil (MOD) may improve inhibition (Turner et al., 2003), it is unknown whether MOD shows distinct effects in cognitive versus emotional conflict processing.

72 healthy males were randomly assigned to either 200mg MOD (n = 35) or placebo (PLC; n = 37). Affective Stroop paradigm incorporating emotional and cognitive conflict was employed. Behavioral performance and fMRI data served as primary outcomes. Functional connectivity analyses (gPPI) were performed for distinct conflict processes. Imaging data analysis focused on conflict network including the bilateral dorsomedial prefrontal cortex (dmPFC), IFG and rACC ($p_{svc\text{-}FWE} < 0.05$) (Egner et al., 2007; Feng et al., 2018).

The congruence × treatment interaction effect on behavioral accuracy was significant during cognitive, but not emotional conflict, with MOD specifically enhancing accuracy on cognitive distracters (**Fig. 1a**). Similarly, brain activation analyses indicated a treatment × congruence × task interaction effect located in the left IFG (**Fig. 1b**), with parameter estimates showing MOD enhancing effects on cognitive, but not emotional conflict relative to PLC (**Fig. 1c**). During cognitive conflict MOD increased right IFG coupling strength with bilateral dmPFC relative to PLC (**Fig. 2**).

Overall, MOD selectively enhanced cognitive but not emotional conflict processing, with stronger engagement of the left IFG and communication between the right IFG and dmPFC, which suggest specific neuroenhancing effects of MOD on cognitive deficits