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Augmenting atypical antipsychotics with a cognitive enhancer (Don 

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Augmenting atypical antipsychotics with a cognitive enhancer (donepezil) improves regional brain activity in schizophrenia patients: a pilot double-blind placebo controlled BOLD fMRI study.

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Abstract

Cognitive impairments are cardinal features of **schizophrenia** and predictors of poor vocational and social outcome. Imaging studies with verbal fluency tasks (VFT) lead some to suggest that in **schizophrenia**, the combination of a failure to deactivate the left temporal lobe and a hypoactive frontal lobe reflects a functional disconnectivity between the left prefrontal cortex and temporal lobe. Others have theorized that an abnormal cingulate gyrus modulates such fronto-temporal connectivity. Thus addition of a **cognitive** enhancing medication to current antipsychotic therapy might improve functionality of networks necessary in working memory and internal concept generation. To test this hypothesis, we serially measured **brain activity** in 6 subjects on stable **atypical antipsychotics** performing a VFT, using **BOLD fMRI**. Measurements were made at baseline and again after groups were randomized to receive 12 weeks of **donepezil** (an acetylcholinesterase inhibitor) and **placebo** in a blind cross-over design. **Donepezil** addition provided a functional normalization with an increase in left frontal lobe and cingulate **activity** when compared to **placebo** and from baseline scans. This **pilot study** supports the cingulate's role in modulating cognition and neuronal connectivity in **schizophrenia**.

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