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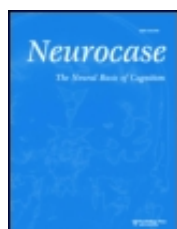
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Abstract

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 BOLDfMRI. 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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