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# A meta-analysis and critical review of the effects of conventional neuroleptic treatment on cognition in schizophrenia: opening a closed book

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## Abstract

### Background

In recent years, numerous studies have examined whether new-generation antipsychotic agents impact cognitive impairment in patients with schizophrenia when compared with conventional antipsychotic treatment. The working assumption of such studies, supported by narrative reviews, is that the conventional antipsychotic medications have little or no effect on cognition. The studies concerning the effects of conventional neuroleptics on cognition, however, have never been analyzed quantitatively. In this

meta-analysis, we revisit the question of whether typical agents might have enhancing effects on cognition.

## Methods

The meta-analysis included studies that 1) compared the effects of typical neuroleptic agents with those of placebo or no medication on cognition; 2) examined adult patients identified as having schizophrenia; and 3) produced adequate data to estimate an effect size. Studies were identified by searches of computerized literature databases and by cross-referencing included studies. The effect size calculated was $d$, the difference between the means in cognitive measures of patients with schizophrenia taking and not taking conventional neuroleptic medication, divided by the pooled SD. Critically, when multiple measures were reported in a single article, effect sizes were combined so as to minimize the possibility that one study had undue weight simply because of the number of cognitive outcome variables that it contained. These results were corrected for bias due to sample size, with each of the effect sizes weighted by the reciprocal of its variance. The final sample after exclusion of outliers comprised 208 effect sizes from 34 studies.

## Results

With a random-effects model, effect sizes from the primary studies were weighted according to sample size and averaged. The resulting mean effect size was .22 (95% confidence interval = .10, .34). The result is positive, in that the range did not include zero and was of low moderate size. No moderating effects of study design or patient qualities were found to be significant. With the same procedures, effect sizes for individual neurocognitive domains were computed. Effect sizes were generally in the .13â€“.29 range for the majority of cognitive functions, whereas motor function was impacted negatively (â^'.11). Unexpectedly, medication dose did not correlate with effect size.

## Conclusions

Typical antipsychotic medication provides modest-to-moderate gains in multiple cognitive domains. Given unavoidable methodologic limitations of the primary studies, current findings suggest that the impact of conventional medication on cognitive function should be re-evaluated.

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Keywords

Antipsychotic; neuroleptic; neuropsychology; schizophrenia; meta-analysis



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