Neuropsychological change to second generation antipsychotic treatment in schizophrenia: a meta-analysis.

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Abstract

Objective: Cognitive impairment represents a core feature of schizophrenia and a major impediment to social and vocational rehabilitation. First generation antipsychotic (FGA) medications do not elicit robust cognitive changes, but over the past 15 years a number of studies have claimed benefits from various second generation antipsychotics (SGAs).

Method: Two meta-analyses of the cognitive changes elicited by clozapine, olanzapine, risperidone, and quetiapine were carried out. The first analysis included studies that randomized subjects in a double blind fashion to one or more SGA arms and an FGA comparator. The second analysis included all prospective investigations of SGAs that were published or ‘in press’ studies that examined neuropsychological change to clozapine, olanzapine, risperidone, or quetiapine.

Results: Both analyses identified significant benefits from the SGAs on seven cognitive domains: motor, attention, verbal, visuospatial, executive, immediate, recall, and delayed recall. Within-class comparisons identified differences between SGAs on several measures including attention, verbal fluency, visuospatial processing, and delayed recall.

Conclusions: SGAs improve a wide array of cognitive functions in schizophrenia and preliminary findings suggest that there may be differences between treatments.

Introduction

Cognitive impairment is fundamental to schizophrenia and readily demonstrated on a variety of neuropsychological instruments (Heinrichs & Zakzanis, 1998).

People with schizophrenia typically perform one to two standard deviations below controls on tests of executive function, memory, attention, and verbal fluency.

Several meta-analyses have identified direct links between specific cognitive skills and discrete areas of functional outcome (Green, 1996; Green et al., 2000). For example, secondary verbal memory is strongly linked to psychosocial skill acquisition, daily living skills, and social problem solving skill.

The strong associations between cognition and functional outcome suggest that improvements in cognition, possibly through pharmacotherapy, might translate directly to improvement in functional outcome.

FGA treatments are largely ineffective at improving cognition, however, cognitive improvements to the newer SGA treatments have been reported. Two meta-analyses were carried out to examine the postulated gains with SGAs and compare medications within the SGA class.

Methods

Published or ‘in press’ studies that examined neuropsychological change to clozapine, olanzapine, risperidone, or quetiapine in schizophrenia were included.

Two analyses were done. The first analysis included double blind random assignment studies that included an FGA control arm and the second analysis included all prospective SGA studies.

Analysis One

Nudge g was used to estimate effect sizes. A weighted average effect size estimate was calculated for each neuropsychological test by combining data from all double blind, randomized, FGA comparator studies that examined cognitive change to clozapine, olanzapine, risperidone, or quetiapine.

Effect sizes were combined according to the fixed effects model described by Shadish & Haddock and a Q statistic, a measure of effect size variation, was calculated for each neuropsychological test. When the Q statistic exceed the p=.05 threshold, effect sizes were combined according to the random effects model.

Results

11 studies were included in Analysis One. Significant effect sizes were observed on at least one test from each of the seven domains examined. (See Table 1).

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Table 1: Neuropsychological Change with Second Generation Treatment: Analysis 1.

<table>
<thead>
<tr>
<th>Domain</th>
<th>Clozapine</th>
<th>Olanzapine</th>
<th>Risperidone</th>
<th>Quetiapine</th>
<th>Mean Effect Size</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attention</td>
<td>0.15</td>
<td>0.16</td>
<td>0.14</td>
<td>0.18</td>
<td>0.15</td>
<td>-0.01 to 0.31</td>
</tr>
<tr>
<td>Immediate Recall</td>
<td>0.16</td>
<td>0.15</td>
<td>0.14</td>
<td>0.18</td>
<td>0.16</td>
<td>-0.01 to 0.32</td>
</tr>
<tr>
<td>Verbal Fluency</td>
<td>0.16</td>
<td>0.15</td>
<td>0.14</td>
<td>0.18</td>
<td>0.16</td>
<td>-0.01 to 0.32</td>
</tr>
<tr>
<td>Visuospatial</td>
<td>0.16</td>
<td>0.15</td>
<td>0.14</td>
<td>0.18</td>
<td>0.16</td>
<td>-0.01 to 0.32</td>
</tr>
<tr>
<td>Motor Skills</td>
<td>0.16</td>
<td>0.15</td>
<td>0.14</td>
<td>0.18</td>
<td>0.16</td>
<td>-0.01 to 0.32</td>
</tr>
<tr>
<td>Delayed Recall</td>
<td>0.16</td>
<td>0.15</td>
<td>0.14</td>
<td>0.18</td>
<td>0.16</td>
<td>-0.01 to 0.32</td>
</tr>
</tbody>
</table>

Figure 1. Mean within domain effect size and 95% CI: Analysis One.

Discussion

SGAs are superior to FGAs at improving cognition in schizophrenia. The cognitive gains observed with SGAs are typically within the range of 0.2 to 0.4 standard deviations and can be seen on a variety of neuropsychological instruments from several domains.

Preliminary evidence suggest there are differences between SGAs on several measures including tests of attention (i.e. Stroop), delayed recall (i.e. visual reproduction), and verbal fluency.

The improvements in cognition observed with SGAs are likely to benefit functional outcome and the differences between SGAs suggest that the newer treatments might have unique effects on outcome.

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