Different Associations Between Cognitive Impairment and Severity of Symptoms Among ADHD, Schizophrenia & MDD

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Keith A. Wesnes1,2,3; Seth C. Hopkins4; Kenneth S. Koblan4

BACKGROUND
- CNS diseases impact cognitive functioning and different psychiatric conditions are believed to exhibit characteristic deficits in cognitive performance across major cognitive domains.
- The purpose of the present study was:
  1. To compare the profile of cognitive impairment between three conditions: Major Depressive Disorder (MDD), Adult ADHD and schizophrenia.
  2. To evaluate the relationship between symptom severity and the degree of cognitive impairment in the three conditions.

METHODS
- Pre-dosing performance data were collected from various clinical trials.
- All patients were evaluated on the CDR system - a set of 9 automated tests of attention, information processing, working memory, executive control and episodic memory which take 20 minutes to perform in total.
- Performance on the CDR measures was compared to that of a large database of age-matched normal volunteers.

RESULTS
- The interest-activity symptom dimension (reflecting low interest, reduced activity, indecisiveness and lack of enjoyment) at baseline strongly predicted poor treatment outcome in GENEDP, irrespective of overall depression severity, antidepressant type and outcome measured.
- Conclusions: Loss of interest, diminished activity and inability to make decisions predict poor outcome of antidepressant treatment even after adjustment for overall depression severity and other clinical covariates.

VALIDATED CDR SYSTEM™

- Power of Attention
  - focussed attention & information processing
- Continuity of Attention
  - sustained attention/vigilance
- Reaction Time Variability
  - the ability to sustain concentration at constant levels
- Quality of Working Memory
  - the ability to store and retain episodic information in long-term memory and subsequently recall it
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  - the ability to store and retain episodic information in long-term memory and subsequently recall it

<table>
<thead>
<tr>
<th>Cognitive Domain</th>
<th>ADHD</th>
<th>MDD</th>
<th>Schizophrenia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Power of Attention</td>
<td>-0.02</td>
<td>0.09</td>
<td>0.06</td>
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<tr>
<td>Continuity of Attention</td>
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<td>-0.03</td>
<td>-0.06</td>
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<tr>
<td>Fluctuations in Attention</td>
<td>-0.02</td>
<td>0.01</td>
<td>0.06</td>
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<tr>
<td>Quality of Working Memory</td>
<td>-0.02</td>
<td>0.03</td>
<td>0.01</td>
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<tr>
<td>Speed of Memory</td>
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<td>0.05</td>
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</table>

<table>
<thead>
<tr>
<th>Interest-Activity Dimension</th>
<th>Activity Interest Quotient</th>
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<tr>
<td>ADHD</td>
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<tr>
<td>MDD</td>
<td>4</td>
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<tr>
<td>Schizophrenia</td>
<td>5</td>
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</tbody>
</table>

**REFERENCES**

Neurosci 2000;250:186–193


Uher et al's Interest-Activity dimension is a novel finding, and consistent with the proposal that 'fatigue' could be a prodrome for MDD (Fava, 2003).

The finding of a relationship between attention in this study and Uher et al's Interest-Activity dimension is a novel finding, and consistent with the proposal that 'fatigue' could be a prodrome for MDD (Fava, 2003).

Antidepressants can reduce the cognitive impairment in MDD, but these effects appear to be independent of their ability to treat the symptoms of depression, and more likely due to direct actions on mechanisms which govern cognitive function.

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In conclusion, these findings suggest that cognitive impairment or a susceptibility to it may precede the onset of MDD, and/or that an early trigger for depression also triggers cognitive impairment; but thereafter these two impairments appear to take independent courses.

DISCUSSION & CONCLUSIONS

- The cognitive deficits in the 3 conditions are most marked on all domains for schizophrenia, the impairments in MDD and ADHD being progressively smaller, yet still notable with large effect sizes.
- MDD & ADHD patients do not show impaired accuracy scores on working & episodic memory tasks, but they do show marked deficits in the time taken to retrieve information from these memory stores, which will impair everyday behaviour.
- The most notable finding was that unlike ADHD & schizophrenia, MDD showed no evidence of any relationship of these notable cognitive deficits to the various core clinical symptoms which characterise the condition. The MDD sample was large and typical for such clinical trials, and the absence of any such relationship is surprising.
- I could suggest that cognitive impairment is not a symptom of depression, but a co-existing disorder. Reschies & Neu (2000) found no normalisation of cognitive performance despite complete recovery of affective symptoms in MDD, and many other studies have detected cognitive impairment in recovered patients. In an MDD study reboxetine improved speed of retrieval and speed of memory on the CDR system but there was no relationship between these changes and improvement in either the Hamilton or MADRS (Ferguson et al, 2002).

Thus antidepressants can reduce the cognitive impairment in MDD, but these effects appear to be independent of their ability to treat the symptoms of depression, and more likely due to direct actions on mechanisms which govern cognitive function.

The finding of a relationship between attention in this study and Uher et al's Interest-Activity dimension is a novel finding, and consistent with the proposal that 'fatigue' could be a prodrome for MDD (Fava, 2003).

It does indicate that lowered motivation and interest can be related to the extent of cognitive impairment in MDD, but does not account for the marked impairments even in patients with low scores on the Interest-Activity dimension.

In conclusion, these findings suggest that cognitive impairment or a susceptibility to it may precede the onset of MDD, and/or that an early trigger for depression also triggers cognitive impairment; but thereafter these two impairments appear to take independent courses.