Psychotropic drugs and mild cognitive impairment: findings from the Sydney Memory and Ageing Study

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Psychotropics and Cognition in Late Life

- Acute side effects of psychotropic drugs in older people include impaired cognition mainly due to sedative effects upon attention, concentration and hence memory.
- In general, the extent of these acute effects relates to the degree of sedation involved & usually resolves with cessation of the agent in question.
- There are mixed findings about whether the long term administration of psychotropic medication can affect cognition in older people & increase the risk of MCI and/or dementia.
Antidepressants and Cognition in Late Life

- Some studies suggest that the continued long term use of all classes of antidepressants is associated with lower rates of dementia (see review Kessing 2012)
- However Women’s Health Initiative Memory Study found that antidepressant use (SSRI & TCA) was associated with 70% increased risk of developing MCI over 7.5 years, with effects noted also for depression severity (Goveas et al, 2012)
Antipsychotics and Cognition in Late Life

• The long term effects of antipsychotics upon cognition has not been well studied in older people.
• Most studies are of younger people with schizophrenia or bipolar disorder where results are mixed.
• One study of 119 euthymic bipolar patients found that those being treated with atypical antipsychotics had worse cognitive performance (Torrent et al, 2011).
• CATIE-AD – patients on atypical antipsychotics had increased cognitive decline consistent with 1-year deterioration compared with placebo (Vigen et al, 2011).
Benzodiazepines and Cognition in Late Life

• The long term effects of benzodiazepines upon cognition are also mixed but mainly suggestive of increasing risk of cognitive impairment (Stewart 2005)

• Some longitudinal studies indicate chronic Bz consumption can increase risk of cognitive decline (e.g. Paterniti et al, 2002) and dementia (e.g. de Gage et al, 2012) in older people

• The extent to which Bz and other sedative/hypnotics are associated with MCI are unclear
Aims of Current Study

- To determine the relationships between categories of psychotropic drug use and mild cognitive impairment (MCI) in older community dwelling people without dementia
Sydney Memory and Ageing Study (MAS)

- initiated in 2005 to examine clinical characteristics and prevalence of MCI and predictors of cognitive decline
- non-demented community-dwelling participants aged 70-90 years

Exclusion criteria:
- dementia
- major psychiatric disorders
- neurological disorders
- developmental disability
- active malignancy
- insufficient English to test

Sydney Memory and Ageing Study (MAS)

- neuropsychological and medical examination, medical history interview, self-report questionnaires, informant interview

Wave 1
2005-2007
n = 1037

MRI n = 542
Blood n = 943
GWAS n = 925

Wave 2
2007-2009
n = 889

MRI n = 425
Blood n = 722

Wave 3
2009-2011
n = 791

Wave 4
2011-2013

MRI
Blood

MCI criteria

• Petersen criteria revised\(^1,2\)
• Not normal, not dementia
• Self and/or informant complaint
• Generally intact global cognition
  – MMSE > 24
• Preserved basic ADLs and minimal impairment of complex function

\(^1\) Petersen et al, Arch Neurol 1999;56:303–308
Pharmaceutical Benefits Schedule (PBS) Data

- PBS data includes information about PBS listed drugs dispensed including the drug, dosage, & number dispensed.
- We obtained PBS data for the 2 years pre and 2 years post-baseline assessment of the participants
- Antidepressants (SSRIs, SNRIs, tricyclics & others)
- Antipsychotics (Atypical and traditional)
- Sedative hypnotics (Benzodiazepines & others)
- All Psychotropic (antidepressant + antipsychotic + sedative hypnotics)
- Anticonvulsants & Antiparkinsonian
Sample and Measures

- Data available on psychotropics for 791 participants, 511 with normal cognition & 280 with MCI, for the 2 years pre and post baseline assessment.
Psychotropic Usage 2 years pre- and post baseline assessments (Wave 1) (n = 791)

- Sedative/hypnotics (benzodiazepines +) 298 (37.7%)
- Antidepressants 169 (21.4%)
- Antipsychotics 8 (1.0%)
- Any psychotropic 360 (45.5%)
- Anticonvulsants 25 (3.2%)
- Antiparkinsonian 19 (2.4%)
<table>
<thead>
<tr>
<th></th>
<th>Normal (%)</th>
<th>MCI (%)</th>
<th>Normal (mean scripts)</th>
<th>MCI (mean scripts)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Psychotropic (Sed Hyp/Antidep/Antipsych)</td>
<td>43%</td>
<td>48%</td>
<td>17*</td>
<td>23*</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>20%</td>
<td>23%</td>
<td>19</td>
<td>20</td>
</tr>
<tr>
<td>Sedative/hypnotics</td>
<td>34%*</td>
<td>41%*</td>
<td>10*</td>
<td>15*</td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>1%</td>
<td>2%</td>
<td>1*</td>
<td>10*</td>
</tr>
<tr>
<td>Anticonvulsants</td>
<td>2%*</td>
<td>5%*</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>Antiparkinsonian</td>
<td>2%</td>
<td>4%</td>
<td>24*</td>
<td>36*</td>
</tr>
</tbody>
</table>

*p < 0.05
## Benzodiazepine Exposure, Doses and MCI

<table>
<thead>
<tr>
<th></th>
<th>Normal N = 511 (%)</th>
<th>MCI N = 280 (%)</th>
<th>Normal Median dose (Dz equiv)</th>
<th>MCI Median dose Dz equiv</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzodiazepine 2 years pre-baseline</td>
<td>27%</td>
<td>37%</td>
<td>1500</td>
<td>1562</td>
</tr>
<tr>
<td>Benzodiazepine 2 years post baseline</td>
<td>27%</td>
<td>32%</td>
<td>1250</td>
<td>2250</td>
</tr>
</tbody>
</table>

Exposure to benzodiazepines before baseline increases risk of MCI at baseline. Benzodiazepine users with MCI have significantly higher dosage in the 2 years post baseline than normals.

\[ *p < 0.005 \]
## Costs of Psychotropic Use and MCI

<table>
<thead>
<tr>
<th></th>
<th>Normal mean $ Benefit Used</th>
<th>MCI mean $ Benefit Used</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Psychotrophic (Sed Hyp/Antidep/Antipsych)</td>
<td>228*</td>
<td>329*</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>425</td>
<td>478</td>
</tr>
<tr>
<td>Sedative/hypnotics</td>
<td>34*</td>
<td>65*</td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>19*</td>
<td>1144*</td>
</tr>
<tr>
<td>Anticonvulsants</td>
<td>715*</td>
<td>260*</td>
</tr>
<tr>
<td>Antiparkinsonian</td>
<td>1336</td>
<td>2174</td>
</tr>
</tbody>
</table>

*p < 0.05
Conclusions

• Benzodiazepines are associated with increased risk of MCI and possibly conversion to dementia in older people

• Antipsychotic drugs are also associated with MCI & while used less frequently have disproportionately higher costs

• Longitudinal prospective studies might help disentangle the extent to which the drugs are causing cognitive decline or are used to treat associated symptoms
Thank you…….

Any questions?

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