Neural correlates of Trail Making Test performance in older adults: the Lothian Birth Cohort 1936

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Introduction

Part B of the Trail Making Test (TMT-B) is widely used as a quick and easy to administer measure of executive dysfunction (Spreen & Strauss, 1998).

Both neuropsychological (e.g., Stuss et al., 2001) and neuroimaging (e.g., Zakzanis et al., 2005) data have identified the role of the prefrontal cortex in TMT-B performance.

Performance on Part B of the Trail Making Test (TMT-B) declines with age and this is thought to be due to age-related deterioration of prefrontal structures (e.g., Rasmussen et al., 1998).

However:

- Some patient studies have found both frontal and non-frontal patient groups performing poorly on the task (e.g., Chan et al., in press).

- Neuroimaging data indicates that age-related decrements in TMT-B performance might be symptomatic of global age-related brain changes of either cortical regions (e.g., Pa et al., 2010) or the white matter (WM) tracts (e.g., O’Sullivan et al., 2001) that connect anterior and posterior brain regions.

Purpose

To investigate the relationships between TMT-B performance and quantifiable measures of cortical volume AND WM characteristics in a large sample of older participants.

Participants

- 368 members of Lothian Birth Cohort 1936 (Deary et al., 2007)
- Aged 76 +/- 1 year at time of cognitive testing
- Non-demented, non-depressed, community dwelling
- 1.5T scan (resolution 2x2x2mm), 1.5T clinical GE clinical scanner
- DTI scan (resolution 2x2x2mm), 1.5T clinical GE clinical scanner

Cortical Volumes

- FreeSurfer whole-brain volumetric segmentation and cortical reconstruction conducted using the default parameters and the Desikan-Killiany atlas (Desikan et al., 2006).

Tractography

- DTI data pre-processed using FSL (Smith, 2002).

- Major pathways segmented using probabilistic neighbourhood tractography implemented in the TractoR package for fibre tracking and analysis (https://github.com/jonclayde/tractor) (Bastin et al., 2010).

Cognitive Tasks

- Participants performed:
  - Trail Making Test-B
  - WAIS III Digit Symbol Coding ~
  - WAIS III Symbol Search ~
  - Inspection Time ~
  - Simple Reaction Time ~

  - Used to derive latent processing speed factor based on first unrotated principal component analysis: 52.22% variance

Correlational Analyses

- Cortical Volume (corrected for intracranial volume) & TMT-B

<table>
<thead>
<tr>
<th>Lobe</th>
<th>Completion Time (s)</th>
</tr>
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<tbody>
<tr>
<td>Frontal</td>
<td>-0.15*</td>
</tr>
<tr>
<td>Temporal</td>
<td>-0.10</td>
</tr>
<tr>
<td>Parietal</td>
<td>-0.13*</td>
</tr>
<tr>
<td>Occipital</td>
<td>-0.04</td>
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</table>

<table>
<thead>
<tr>
<th>Frontal Region</th>
<th>Completion Time (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right Dorsolateral</td>
<td>-0.14*</td>
</tr>
<tr>
<td>Left Dorsolateral</td>
<td>-0.10</td>
</tr>
<tr>
<td>Right Inferior Frontal Gyrus</td>
<td>-0.13*</td>
</tr>
<tr>
<td>Left Inferior Frontal Gyrus</td>
<td>-0.13</td>
</tr>
<tr>
<td>Right Orbitofrontal</td>
<td>-0.14*</td>
</tr>
<tr>
<td>Left Orbitofrontal</td>
<td>-0.13</td>
</tr>
<tr>
<td>Right Anterior Cingulate</td>
<td>-0.06</td>
</tr>
<tr>
<td>Left Anterior Cingulate</td>
<td>-0.08</td>
</tr>
</tbody>
</table>

- Tractography (fractional anisotropy) & TMT-B

<table>
<thead>
<tr>
<th>Tract</th>
<th>Completion Time (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genu</td>
<td>-0.18*</td>
</tr>
<tr>
<td>Sphenium</td>
<td>-0.18*</td>
</tr>
<tr>
<td>Anterior thalamic radiation</td>
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</tr>
<tr>
<td>Cingulum</td>
<td>-0.06</td>
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<tr>
<td>Uncinate</td>
<td>-0.16*</td>
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<tr>
<td>Arcuate</td>
<td>-0.10</td>
</tr>
<tr>
<td>Inferior longitudinal fasciculi</td>
<td>-0.10</td>
</tr>
</tbody>
</table>

  # Controlling for processing speed

Discussion

- In older adults, performance on TMT-B is related to the cortical volume of both frontal and parietal regions even when speed of processing is controlled for.

- In the frontal subregions, TMT-B performance is related to the cortical volume of the dorsolateral prefrontal cortex, inferior frontal gyrus and orbitofrontal cortex.

- WM integrity of the corpus callosum is significantly related to TMT-B completion time beyond speed of processing.

References

- Deary et al. (2007) BMC Geriatrics, 7, 28.