Measuring key components of executive function in Down syndrome

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Dementia in Down syndrome

• Individuals with Down syndrome (DS) are at a greatly increased risk of developing dementia, specifically early onset Alzheimer’s disease (AD), (Crayton et al., 1998)

• The onset of dementia can occur exceptionally early in DS
Chromosome 21

• Estimated 1.5-2% of humans’ genetic material found on chromosome 21

• Including the amyloid precursor protein gene (APP)

• Amyloid-beta forms the plaques seen in the brains of people with Alzheimer's disease
Chromosome 21

• The gene DYRK1A is also located on chromosome 21

• DYRK1A adds phosphate groups to tau: this has a role in producing the tangles seen in the brains of those with AD

• Amyloid-beta leads to more activity of DYRK1A. As people with Down syndrome produce more amyloid-beta, DYRK1A will become more active
Dementia in Down syndrome

• Neuropathological signs of AD, are thought to be present in the brains of all individuals with DS beyond the age of 40 (Cork, 1990)

• Clinical signs of AD are present in only a proportion of these individuals
Alzheimer’s disease: Behavioural traits

• Individuals without DS who have AD display various cognitive difficulties, such as memory and attentional problems.

• AD also affects their behaviour and mood, with some individuals experiencing depression, among other symptoms (Hodges, Salmon, & Butters, 1992; Perry & Hodges, 1999; Rovner, Broadhead, Spencer, Carson, & Folstein, 1989).
Executive function (EF)

- EF decline is one of the most consistent early signs of dementia in individuals with Down syndrome (Ball et al., 2006; Das & Mishra, 1995).

- A number of different tasks are used to test the various components of executive functions; such differences can lead to different results.

- Findings mixed (e.g., Borella et al., 2013; Lanfranchi et al., 2010; Pennington et al., 2003; Rowe et al., 2006).

- Verbal vs visual particularly relevant.
• It is vital to obtain reliable baseline measures of executive functions for individuals with Down syndrome such that it is possible to determine meaningful decline
Components of Executive function

- There are various components of executive function, e.g.,

  - Updating in working memory
  - Inhibition of prepotent responses
  - Shifting between different tasks

- Other perspectives linked to EF’s such as proactive and reactive control
Methodology to extract measures of 3 components of EF using one simple framework

Allowing for controlled comparisons of performance across different components of EF

Memory: maintain the task goals/rules

Inhibition: prevent inappropriate responses to external stimuli

Temporal aspect: Moving from reactive control to proactive control over time (anticipating change).
Updating in working memory

No load
Updating in working memory

Low load
Updating in working memory

High load
Inhibition of prepotent responses

Low load: congruent location
High load: incongruent location
• Delay between the onset of the stimuli and the appearance of the response buttons
• Able to respond immediately (Reactive)
• Or forced to delay response (proactive)
Research Questions

- Can individuals with Down syndrome complete this task?
- Does this task obtain independent measures of each component?
- Differences between those with vs without Down syndrome?
- Are these measures reliable for assessing changes over time in the Down syndrome population?
Down syndrome group aged 25-45, N = 16

Retest to determine reliability of measure as baseline

Mental age matched control group aged 6-11, N = 16

4 weeks
Results: Accuracy

Immediate responses

Proactive responses

Memory: $p < .01$, Inhibition: $p = .051$, population: $p = .230$; Delay: $p < .01$; Memory x population: $p < .01$; Memory x delay x population: $p < .01$
Results: RTs

Immediate responses

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Proactive responses

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Mean DS  | Mean TD

Memory: $p < .01$, Inhibition: $p < .05$, Delay: $p < .01$, Population: $p = .085$;
Memory x delay: $p < .01$, Population x delay: $p < .01$
• Are these measures reliable for assessing changes over time in the Down syndrome population?
Test-Retest Reliability

\[ r = .83, \ p < .01 \]
Test-Retest Reliability

$r = .62, p = .01$
Test-Retest Reliability

$\text{No delay - delay cost}$

\[ r = .48, \ p = .06 \]
Summary (1)

• Individuals with Down syndrome are able to complete this task

• Overall difference between populations does not reach sig.

• Increases in memory load, inhibitory load, and temporal demands, lead to significant increases in RT and decreases in accuracy, for both populations

• Thus, the expected effects of each of these manipulations can be detected with this framework
Summary (2)

- Memory does not appear to be independent from the temporal manipulation, with memory load influencing the extent to which individuals experienced accuracy and RT benefits from the preparation time.

- However, inhibition did appear to be an independent component.

- Most importantly: Framework appears to capture reliable individual differences in those with DS for each measure extracted.
Conclusion

These findings so far suggest these measures have the potential to capture reliable individual differences in executive function. This framework could be further adapted to provide a simplified, fast baseline screening measure to assess decline in executive functions in those with DS.