Use of a Modified Hidden Pathway Maze Test in Patients with Alzheimer's Disease Dementia

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Background

Maze tests have a long history as measures of visuospatial learning and executive function. The importance of impairments in both visuospatial and executive function has been increasingly recognized in early AD. In contrast to presented mazes, hidden pathway mazes use underlying rule sets to create decision points meaning additional data, such as different types of error, are obtained and can be used to more fully characterize performance and cognitive impairment. Computerized versions (e.g. the Groton Maze Learning Test [GMLT]) provide even greater analytical scope than manual tests. However, use of extensive rule sets may prove challenging in AD dementia. Here we present basic psychometric analyses for a simplified GMLT in mild-moderate AD dementia.

Methods

The modified GMLT uses a 28-step pathway hidden in a 10x10 tile grid. The pathway is found by selecting one tile at a time revealing a green checkmark which remains visible if correct. A more limited set of instructions is given compared to the usual test, removing instructions regarding going back to the last correct box and guessing again if a red X is shown. Five trials are given, with the number of errors recorded ("Total Errors"). A single, reverse recall trial is also given after a short delay ("Reverse Maze"). Data were collected in a Plb clinical trial in mild to moderate AD patients with MMSE 12-24. Analyses were performed for missingness of data, presence of floor and ceiling effects, test retest reliability and learning/practice effects.

Results

Data were analyzed for 53 AD patients at the baseline assessment (mean age 72.5 [SD 7.23]; 73.6% female) (Table 1).

Table 1: Demographics and clinical characteristics at baseline

		N	Mean	SD	Min	Max
N		53 (100%)				
Sex	Male	14 (26.4%)				
	Female	39 (73.6%)				
Age			72.5	7.23	54	85
MMSE			20.6	2.84	14	24
NPI-12			5.1	6.3	0	26
Years since diagnosis			3.2	2.17	0.3	9.7
Stage of disease	Mild	31 (58.5%)				
	Moderate	22 (41.5%)				

"Find the Hidden Pathway"

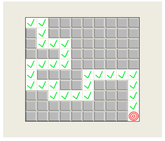


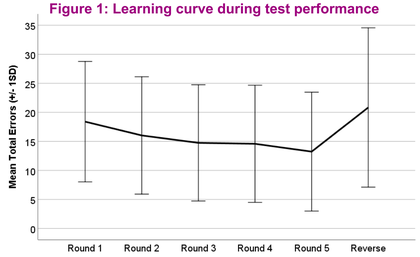
Table 2: Maze performance at baseline

Baseline	N	Mean	SD	Min	Max	Incomplete	Ceiling	Floor
Total Errors	53	77.0	45.86	21	224	10 (18.9%)	0	0
Reverse Maze	53	20.8	13.72	8	66	4 (7.5%)	0	0

Table 3: Reliability from practice 2 to baseline

	N	Practice 2		Baseline		Test-retest
		Mean	SD	Mean	SD	
Total Errors	41	72.2	31.22	77.0	45.86	0.49**
Reverse Maze	41	19.32	12.85	20.8	13.72	0.40*

Figure 1: Learning curve during test performance



- An expected pattern of reduced errors over the 5 repeated rounds of the test was observed (Figure 1)
- 10/53 (18.9%) of test instances were incomplete for total errors
  - 4 of these individuals (7.5%) also failed to complete the reverse maze (reverse maze data were excluded from analysis for all 10 in case this had impacted performance)
- The 10 patients failing to complete the maze had lower mean MMSE (17.3), were more likely to have moderate disease (90%) and more likely to be female (90%)
  - Female patients were a higher proportion of the sample (73.6%) and also a slightly higher proportion of moderate (77.3%) versus mild (71.0%) disease
- Performance was not at ceiling (zero errors) for either outcome measure
- Minimal change was evident between the second practice assessment and the baseline
- Although there is not a theoretical floor (maximum errors) a number of outliers were evident in the data for total errors
- A log transform of the data for total errors increased test-retest reliability to 0.59**

Table 4: Known groups validity

		Age		GMLT Total Errors			
	N	Mean	SD	M	SD	t, p-value	Cohen's d (95% CI)
AD Patients	43	72.28	7.60	76.98	45.86	t = 5.24 p <.0001	0.87 (0.53, 1.20)
Healthy Controls	117	72.68	6.40	49.06	23.56		

			Baseline		Difference			
		N	Mean	SD	Mean	SD	t, p-value	Cohen's d (95% CI)
Total Errors	Moderate	13	83.8	46.85	9.8	15.46	t = 0.64 p =.531	0.21 (-0.44, 0.86)
	Mild	30	74.0	45.90				
Reverse Maze	Moderate	13	23.9	16.22	4.42	4.56	t = 0.97 p=.34	0.32 (-0.34, 0.97)
	Mild	30	19.5	12.55				

Table 5: Construct validity

	Total errors	Reverse maze	MMSE	NPI
Total errors		0.800**	-0.014	0.015
Reverse Maze			-0.064	-0.007
MMSE				
NPI				

- A large effect size impairment was evident for total errors versus healthy age matched controls (d 0.87, Table 4)
  - Normative data were not available for the reverse maze
- A clear difference in the predicted direction was evident between the mild and moderate AD dementia groups, with a small effect size for total errors and reverse maze
  - This did not reach statistical significance
- A strong correlation was seen between total errors and reverse maze supporting construct validity (Table 5)
- No clear association was evident with MMSE and NPI scores for either outcome measure (r<0.1) (Table 5)

Conclusions

Hidden pathway maze learning may be a valuable probe of short-term memory and executive function in AD. Whilst the removal of complex rule sets may make the test more feasible in the dementia stages of the disease, increasing severity of disease may limit utility for some patients.

- The test is acceptable to AD dementia patients and could be completed by moderate patients with MMSE as low as 17
- Test retest reliability was weak to moderate for both the total error and reverse maze scores, which is a common finding in the literature for executive function tests
- Construct validity was evident between the two maze outcomes (total errors and reverse), but only limited evidence was seen for a clear association to global cognition (MMSE) and neuropsychiatric symptoms (NPI), which may be in part related to the distribution of MMSE and NPI data in this population
- Known groups validity was evident versus age matched healthy controls for the total error score and there was evidence for poorer performance on both outcome measures in the moderate versus the mild AD dementia groups
- The total error score may be adversely affected by small numbers of outlier values
  - N=4 had >150 total errors at baseline
  - N=6 had >120 total errors at baseline
- This may impact reliability, variance and other metric properties
- Correlation did not support a clear association between very high error rates and clinical status (MMSE or NPI), but errors during practice were typically also high for these patients
- Assessment of executive processes may be highly feasible in mild AD dementia, but may be more challenging in some moderate dementia patients
- For the total error score, a cap on maximum errors may improve psychometric properties and if applied during test performance could reduce patient burden, whilst still reflecting 'maximal impairment' on the test
  - This is a common approach applied to other tests of executive function used in AD and dementia research e.g. Trail Making Test Part B is usually discontinued after 300 seconds and this applied as the achieved score

Alzheimer's Association International Conference; July 2019; Los Angeles, USA

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