Introductory Guide to CANTAB Tests

V.2.1

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Contents

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1 Introduction

This document gives a brief overview of each of the CANTAB Connect tests, detailing how the task runs and what it measures.

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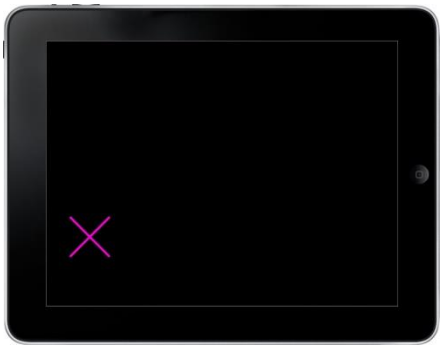
2 Induction

2.1 Motor Screening Task (MOT)

(Approximately 1 minute)



- Participants touch a series of flashing crosses shown in different locations on the screen.
- This brief exercise is designed to familiarise participants with the touch screen interface.

MOT provides a general assay of whether sensorimotor or comprehension difficulties limit collection valid data from the subject.

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3 Visual Memory

3.1 Delayed Matching to Sample (DMS)

(Approximately 8 minutes)

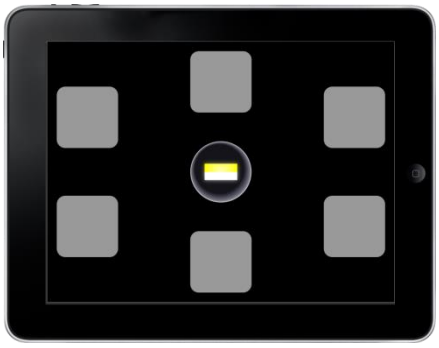
- DMS is a test of simultaneous and delayed matching to sample. This test assesses visual matching ability and visual recognition memory.
- The participant is shown a complex visual pattern and then after a brief delay, four patterns. The participant must touch the pattern that matches the sample. In some trials the sample and the choice patterns are shown simultaneously, whereas in others there is a delay (of 0, 4 or 12 seconds) before the four choices appear.

Many lesion studies, in both humans and non-human primates, have indicated that delayed matching to sample is primarily sensitive to damage in the medial temporal lobes (particularly hippocampus) and frontal lobes (Sahgal & Iversen, 1978).

In a human model of Alzheimer's disease, healthy volunteers who were given an acute dose of the anticholinergic drug scopolamine show significant dose-dependent and delay-dependent deficits on this task (Robbins et al., 1997).

3.2 Paired Associates Learning (PAL)

(Approximately 8 minutes)



- PAL assesses visual associative learning and memory.
- Boxes are displayed on the screen and are automatically opened in a randomised order to show a number of patterns. Participants must learn to associate the patterns with locations on the screen. After all the boxes have been opened each pattern is then shown in the centre of the screen and the participant must touch the box where that pattern was located.
- If the participant makes an error, the patterns are re-presented to remind the participant of their locations. The difficulty level increases with the number of patterns to be remembered. For participants who fail to complete all levels, an adjusted total is calculated that allows for errors predicted in the stages that were not attempted.

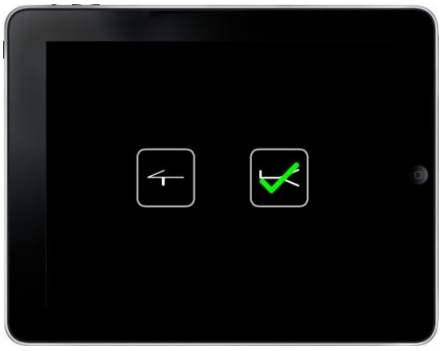
Successful performance of the PAL test is dependent on functional integrity of the temporal lobe, particularly the entorhinal cortex (Owen, Sahakian, James Semple, Polkey, & Robbins, 1995) . PAL is a useful tool for assessing patients with questionable dementia, Alzheimer's disease, and age-related memory loss.

PAL has sound preclinical validation and task performance is sensitive to pharmacological manipulation. For example, scopolamine impairs PAL performance in rhesus monkeys (Taffe, Weed, Gutierrez, Davis, & Gold, 2002).

PAL is sensitive to pharmacological manipulation over short time periods. For example, Greig et al., 2005 showed significant improvement on the PAL after 12 weeks' administration of phenserine in patients with mild Alzheimer's disease.

3.3 Pattern Recognition Memory (PRM)

(Approximately 5 minutes)



- The participant watches a series of 12 patterns appear, one at a time, on the screen. These patterns are designed so that they cannot be easily given verbal labels.
- In the recognition phase, the participant chooses which of two patterns they have already seen before. This is then repeated, with a new set of 24 patterns to be remembered.
- An optional delayed phase tests recognition after 20 minutes.

PRM performance can be enhanced in healthy volunteers using a variety of stimulant drugs and other substances. For example, PRM performance was found to be improved after a single administration of 100 mg or 200 mg modafinil in healthy young volunteers (Randall et al., 2005). PRM performance was also improved in healthy volunteers by administration of Ginkgo biloba supplements (Elsabagh, Hartley, Ali, Williamson, & File, 2005).

4 Executive function

4.1 Multitasking Test (MTT)

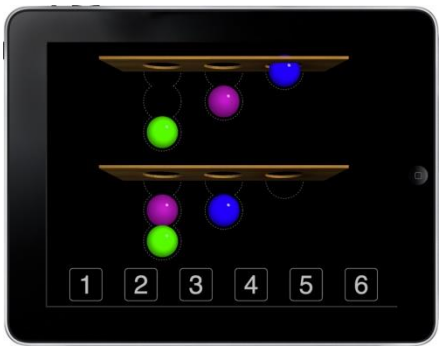
(Approximately 8 minutes)

- MTT is a test of executive function which provides a measure of the costs of multitasking.
- On each trial, an arrow appears on the right or on the left hand side of the screen and the participant is asked to make a right or left response.
- During training stages, participants learn to respond either according to the direction of the arrow, or according to the side of the screen on which it appears.
- During the assessed stage, each trial is preceded by a cue indicating whether the participant should respond according to the direction or side. For some trials the arrow's direction and side are incongruent.
- In some sections of the test the same rule is applied consistently (either side or direction, single task), whereas in others the rules are presented in a randomized order (multitasking).

This task assays two aspects of the cost of processing complex information: it allows detection of both a Stroop-like effect (by comparing response latencies and errors from trials in which arrow direction and location are congruent versus incongruent) and a multitasking effect (by comparing latencies and errors from trials in which participants have to follow the same rule consistently versus trials in which the rules are intermixed randomly). The MTT is recommended for use in studies where cognitive flexibility is to be assessed repeatedly because, unlike many tasks of executive function, it does not depend on novelty. Response time and errors are measured over a large number of trials, providing robust outcome measures.

4.2 One-Touch Stockings of Cambridge (OTS)

(Approximately 10 minutes)

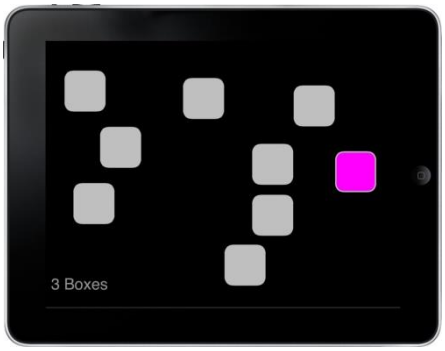


- OTS is a test of executive function, planning and working memory based upon the 'Tower of Hanoi'.
- The participant sees two displays containing three coloured balls and must work out in their head how many 'moves' would be required to make the lower display match the upper display. Latency and accuracy measures are calculated.

OTS is the one-touch version of the CANTAB Stockings of Cambridge (SOC) task. Performance on the SOC task has been shown to be impaired in patients with frontal lobe damage (Owen, Downes, Sahakian, Polkey, & Robbins, 1990). Neuroimaging studies have revealed that SOC performance activates a neural network of structures including the dorsolateral prefrontal cortex (S. C. Baker et al., 1996; Dagher, Owen, Boecker, & Brooks, 1999; Owen, Evans, & Petrides, 1996).

4.3 Spatial Span (SSP)

(Approximately 6 minutes)



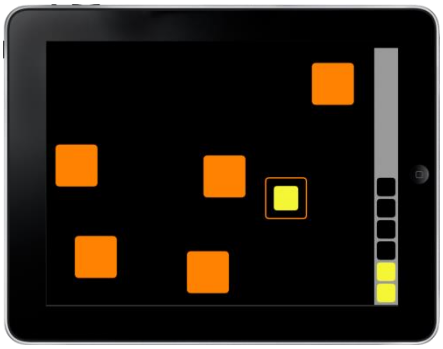
- SSP is a test of working memory capacity.
- In this test, based on the Corsi block tapping task, white squares briefly change colour in a variable sequence. The participant must remember the sequence and then touch the squares in that same order. The sequence length increases through the test. There are up to 3 attempts at each sequence length and the test terminates if all three are failed.

Patients with major unipolar depression are impaired on SSP. For example, medicated patients with severe unipolar depression showed significantly reduced spatial span compared to age and IQ matched healthy controls (Elliott et al., 1996). Reduced spatial span has also been recorded in unmedicated subjects with bipolar disorder (Roiser et al., 2009).

Span length is sensitive to drug manipulations. For example, an acute dose of the DRD2 agonist bromocriptine enhanced spatial span length in healthy young volunteers (Mehta, Swainson, A D Ogilvie, Sahakian, & Robbins, 2001).

4.4 Spatial Working Memory (SWM)

(Approximately 8 minutes)



- SWM measures the ability to retain spatial information and manipulate it in working memory. It is a self-ordered task that also assesses the use of strategy.
- Participants must search for blue tokens by touching the coloured boxes to open them. The task becomes more difficult as the number of boxes increases. The critical instruction is that the participant must not return to a box where a token has previously been found.

SWM performance is impaired by damage to the prefrontal cortex, especially the dorsolateral prefrontal cortex (Manes et al., 2002; Owen, Downes, Sahakian, Polkey, & Robbins, 1990). Similarly, in neuroimaging studies in healthy volunteers, SWM performance is associated with activations in the dorsolateral and mid ventrolateral prefrontal cortex (Owen, Evans, & Petrides, 1996).

SWM is sensitive to differential effects of pharmacological compounds. For example, the stimulant methylphenidate significantly improves SWM performance in healthy volunteers as well as various patient groups (Kempton et al., 1999; Mehta et al., 2000; Turner, Blackwell, Dowson, McLean, & Sahakian, 2005).

5 Attention

5.1 Rapid Visual Information Processing (RVP)

(Approximately 10 minutes)

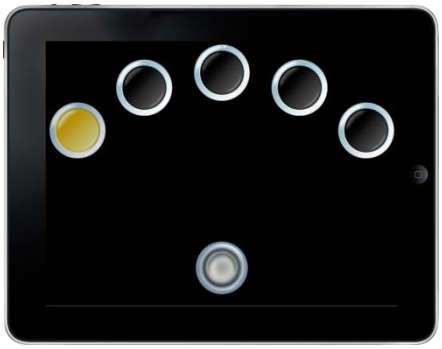
- RVP is a test of continuous performance and visual sustained attention.
- In a white box in the centre of the screen, single digits appear at a rate of 100 digits/ minute. Participants must detect a series of target sequences (for example, 2, 4, 6; 4, 6, 8; 3, 5, 7) and register responses by touching the blue button. Nine target sequences appear every 100 numbers.
- Measures include reaction time and accuracy scores derived from signal detection theory.

Performance of the RVP task is associated with activation in a network of brain structures including the frontal and parietal lobes (Coull, Frith, R. S. Frackowiak, & Grasby, 1996).

RVP is sensitive to the effects of many pharmacological compounds, particularly monoamine manipulations, including clonidine (Coull, H C Middleton, Robbins, & Sahakian, 1995). Dietary depletion of the dopamine precursor tyrosine impaired RVP performance in recovered depressed patients compared to patients treated with a balanced amino acid mixture (Roiser et al., 2005). While stimulants can increase the rate of commission errors on this task, methylphenidate has been found to improve performance in adults with ADHD (Turner, Blackwell, Dowson, McLean, & Sahakian, 2005), and nicotine improves performance in healthy volunteers and patients with Alzheimer's disease (G. M. M. Jones, Sahakian, Levy, Warburton, & Gray, 1992; Sahakian, G. Jones, Levy, Gray, & Warburton, 1989).

5.2 Reaction Time (RTI)

(Approximately 6 minutes)



- RTI is a measure of simple and choice reaction time, movement time and vigilance during simple and 5-choice reaction time trials. This task also permits measurement of anticipatory/premature responding and perseverative responding.
- The participant must hold down the blue button until a yellow spot appears on the screen, and then touch the yellow spot. The spot appears in a single location during the simple reaction time phase and in one of five locations in the 5-choice reaction time phase.

The CANTAB RTI test shows differential pharmacological sensitivity; for example clonidine, but not guanfacine, impairs five-choice reaction time performance in young healthy volunteers (Jäkälä et al., 1999).

6 Semantic / Verbal Memory

6.1 Verbal Recall/Recognition Memory (VRM)

(Approximately 7 minutes)

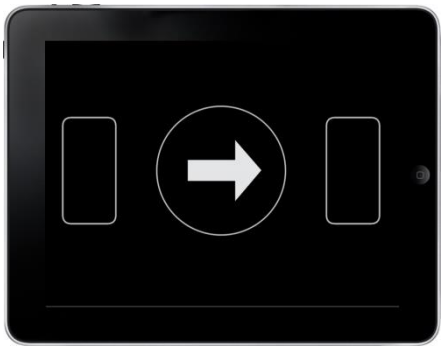
- VRM measures the ability to encode and subsequently retrieve verbal information. Twelve words are presented and participants are subsequently asked to recall them. Twenty minutes later a recognition test is carried out. Measures include reaction time and accuracy scores.

Recall performance on tests of this type depends on fronto-temporal networks (Fletcher & Henson, 2001), while the recognition phase depends on the functional integrity of the hippocampus (Dobbins, Kroll, Tulving, Knight, & Gazzaniga, 1998; Henson, Homberger, & Rugg, 2005).

7 Decision-Making and Response Control

7.1 Stop Signal Task (SST)

(Approximately 15-20 minutes)



- SST is a classic stop signal reaction time test which measures the participant's ability to inhibit a response.
- Arrows appear on the screen and the participant learns to press the button corresponding to the direction in which the arrow points. If a stop signal – an auditory tone – is presented, the participant must inhibit their response. A stop signal occurs on 25% of trials.
- At the end of every assessed block, a graph shows the participant's performance and the participant is encouraged to go faster on the next block.

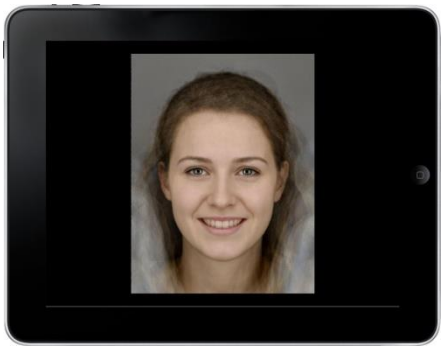
SST performance is associated with integrity of the right inferior frontal gyrus (Aron, 2003).

SST is sensitive to pharmacological manipulation in patients and healthy volunteers. The stimulant drugs methylphenidate and modafinil significantly improve performance on SST (Aron, 2003; Turner, Clark, Dowson, Robbins, & Sahakian, 2004), as does the selective noradrenergic reuptake inhibitor atomoxetine (Chamberlain et al., 2007).

8 Social Cognition

8.1 Emotion Recognition Task (ERT)

(Approximately 10 minutes)



- ERT assesses social cognition and measures the ability of the participant to identify emotions in facial expressions.
- The participant is shown a series of computer generated faces expressing different degrees of emotion and asked to identify the emotion (happiness, sadness, anger, disgust, surprise, and fear).

Those who suffer from depression have been shown to provide more negative ratings of emotional expression (Kellough et al 2008, Linde et al 2015, Grady & Stahl 2013). This reflects the well-known negative bias seen in depression, where positive or neutral stimuli are seen as more negative. The brief presentation encourages implicit processing, as opposed to conscious appraisal of the faces.

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