IntegNeuro™
Installation & user manual

Brain Resource®

IntegNeuro is a Brain Resource product

▶ QEEG ▶ Cognition ▶ fMRI ▶ Genetics ▶ ERP ▶ rTMS

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DIAGNOSTICS

THE Personalized Medicine Resource

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IntegNeuro™ User Manual Version 3

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Roy Sugarman PhD

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Introduction

In essence, there is no such thing as a direct test of brain function or dysfunction. The testing of brain function dates back to WWI, and some of those tests, or derivatives of them, are still in use today. These were originally designed as broad psychological tests, and as the science of neuropsychology emerged, scientists began to infer the nature of brain-behaviour relationships from the results of these tests. In essence, these tests measure the speed and accuracy of the brain's information processing capacity, the 'power' of the cognitive engine. To this, we have added the concept of emotional cognition. The basic format of the IntegNeuro tests creates a platform which can easily be expanded to include other assessment tools such as BRISC, a behavioural health measure, and tests of negative response bias, which assess motivation to present a biased profile to the examiner.

The Brain Resource Company ('BRC') has taken the science of inference one step further, by administering unique computerised versions of these tests while subjects are monitored by a myriad of neuroimaging and psychophysiological devices, drawing together aspects of body and brain normally examined in isolation. This allows a series of objective, informed inferences to be made about the underlying brain-behaviour relationships with unprecedented validity and reliability: the combination of cognitive and psychophysiological measures enhancing both specificity and sensitivity. Using the methodology of integrated neuroscience, 16 000 datasets now exist, with reliable markers of dysfunction for various conditions now being identified. Hundreds of scientific journal articles in peer-reviewed journals attest to the value of this integrative approach to neuroscience, emanating from the Brain Dynamics Centre, and our laboratories and clinicians in over 100 centres around the world in ten countries.

The result is IntegNeuro, a 50-60 minute, IBM Touchscreen-interfaced, objective computer-based toolkit designed to deliver markers of general and social cognition that alert clinicians of the need to further assess and intervene in various conditions, in young and old, such as ADHD and the dementias. Unique to IntegNeuro is the addition of tests of social and emotional cognition, with markers for affective disorders such as mood variants, a neglected tradition in cognitive assessment, as well as the possibilities of other applications in industry, sport, Wellness and so on.

An intuitive IBM Touchscreen computer interface combined with simple task instructions allows the test to be undertaken across a wide range of ages, 6-90 with no limitation imposed by the user's computer proficiency. The IBM Touchscreen provides for comprehensive analyses in that each touch provides important supplementary information about clients' variable response patterns. Automation thus allows for consistency in administration, response and reporting. In addition, the use of global standardisation allows for validation in a wide variety of settings worldwide.

Thus IntegNeuro is a comprehensive but not exhaustive battery, a focussed and researched set of tools designed to provide meaningful diagnostic information to the clinician about sensorimotor, attentional, memory, executive planning, emotions and aspects of language function as well as social cognition. Despite its brevity, the clinician can validly and reliably evaluate the subject against thousands of others in the population database. The variety of available reports allow clinicians and clients both to track the outcome trajectory as clinical interventions take hold or are changed. Whilst IntegNeuro, a more sensitive toolkit, requires a touch screen and some set up costs, the alternative, but less exhaustive WebNeuro requires simply

the possession of a PC and Windows/Vista software. WebNeuro thus provides an inexpensive method to evaluate treatment before, during and after intervention, in key areas of general and social cognition, but IntegNeuro is designed to be part of more site-dependant clinical practice, and has more tests.

IntegNeuro follows the credo that personalised medicine begins with a baseline assessment. This baseline allows the test-taker to then undergo repeated evaluations that chart their progress across time; using themselves as a control mitigates the questionable value of their comparative position in the norm tables. Personalised treatment can thus be measured in terms of efficacy and efficiency without concerns about how they fare against their peers, as wide variance is a regular feature of normal profiles (Matarazzo 1990) as well as pathological.

Computer-driven performance batteries thus have the capacity to maintain a running profile of the individual's scores over time, facilitate empowerment and feedback, and quite dramatically reduce the cost of expensive re-assessments over time, as well as highlighting those who need more face-to-face assessment. In addition, the use of computerised screening batteries allows for data to be presented in a consistently objective manner and can provide ready databases for multi-subject and multi-centre studies. Again, repeated testing at fairly frequent intervals is a sensitive means of comparing treatment and underlying illness interactions.

In summary, the specific strengths and advantages of IntegNeuro are:

- The standardised presentation of stimuli and recording of responses
- Use of minimal equipment in terms of the IBM Touchscreen and amplifiers
- Efficient and accurate, rapid collection of detailed data
- The collection of more precise visuomotor and psychomotor function than is usual in a qualitative cognitive exam
- Comprehensive analysis of data which is quickly accessible to the clinician within a short turnaround time
- The ease of compiling data across subjects and centres and by illness cohort
- The repeated evaluation of the subject's performance against baseline across time using the same log-ins.

For more detailed assessments by the clinician, the use of IntegNeuro is recommended. See www.brainresource.com

Note: Further information is available at the above link, by clicking on http://www.brainresource.com/products/index.php?id=83 or in the case of ADHD http://www.brainresource.com/features/ Information on the normal curve and other issues for clinicians and end users is also available there. Clinicians can purchase blocks of logins online by registering with, or inquiring at info@brainresource.com A list of FAQ's is also accessible on http://www.brainresource.com/clinical_management/index.php?id=40

The Test Administration

Administration of the tests is completed using an IBM touchscreen, set up and calibrated at one of our clinics or partner clinics.

The core battery requires approximately 50-60 minutes to complete.

Responses are automatically uploaded for scoring and analyses on completion. Scoring of responses is conducted using an automated software program at BRC. Once internet connection is established, the screen will run serial assessments until it needs to upload them by Internet re-connection

Reports are provided within a day or so to the individual clinician. Given the limitations of the interface, results should always be seen as tentative: negative results should always be discussed with a clinician with expertise in such psychometrics. Further information for clinicians and users can be obtained by visiting ***www.brainresource.com*** and other links on our site. There is an extensive range of IntegNeuro products for many applications in clinical, scientific and commercial/business applications. Also contact ***support@brainresource.com*** for any technical enquiries.

Minimum System Requirements

To run IntegNeuro you need a standard PC with Windows 2000 or Windows XP, with at least 256MB RAM.

Other requirements installed and necessary for running the IntegNeuro toolkit:

- Internet Explorer 5 or above
- Windows Media Player
- Available hard disc space: 150MB for installation and 6MB for each session's data you acquire
- High Speed Internet access is required for authentication at the beginning of the day's sessions, and when uploading data to BRC at the end of the day, but not for running the IntegNeuro toolkit on clients in between these tasks
- No screen saver or power saver that will activate in less than 20mins, as the keyboard and mouse may not be used for up to 20mins at a time
- No unnecessary background tasks running such as virus scans
- No sharing of the hard disks over the network
- No high priority tasks running
- Proxy server settings on networks and intranets may cause error messages

Setting up the hardware

Identifying all the Parts:

1. Keyboard
2. Touchscreen
3. Computer
4. USB cable
5. Monitor cable
6. Power cable for Touchscreen
7. Y-connector
8. Power cable for Computer
9. Headset

The Touchscreen comes with 3 cables and 3 ports (shown).

USB cable
Monitor cable
Power cable (2 parts)

2. Locate the monitor cable. On each end is a male 15 point D connector.

Thread one end through the bracket and connect to the middle socket of the Touchscreen (see first picture).

Connect the other end to the standard monitor connector on the computer. Take care to ensure that the pins are lined up to the holes on the computer port. Do not force the pins. The monitor connector looks like this:

3. Locate the power cable. Note that it comes in two parts, one that goes from the Touchscreen to the power pack and the other from the power pack to the power source.

Note: The power plug on the "Mickey Mouse" cable (see shape) is different for every country.

Connect the two parts together.

Thread Touchscreen end through the bracket and attach to the Touchscreen.

Plug into power source. When the power is switched on, the power indicator light in the corner of the touchscreen turns on.

Turn your attention to the computer. It should have a keyboard attached. (A mouse may also be attached, but is not necessary).

You have been provided with a headset (headphone and microphone) which you can attach to the computer now. The two jack plugs are clearly labelled showing which plug is for the microphone e.g. and which one is for the headphone e.g. .These need to be attached to the corresponding plugs on your computer (which may be located at the front or the back of the computer).

Turn the power on and start the computer.

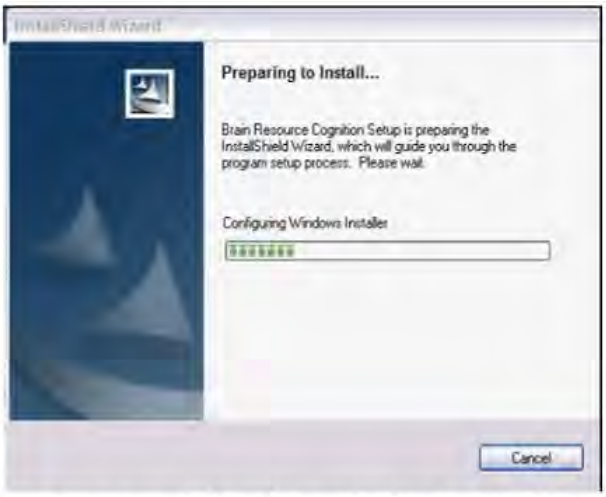
Test the Touchscreen now. The pointer prompt on the Touchscreen should follow your finger as you tap around the surface of the screen.

Setting up the software

You are going to be installing an application on your computer. You will need to have administrator rights. If you do, you or your system administrator will now have to do the following:

1. With the keyboard attached, log into the compute using the Windows administrator logins provided with your computer.
2. Insert the BRC COGNITION installation CD into the disk drive, or if you do not have a CD drive, ask your BRC representative to provide another method to do this, such as a removable disk drive.

The screen below will appear and the installation process will start automatically.



This process may take a few minutes and is then automatically followed by the following screen:

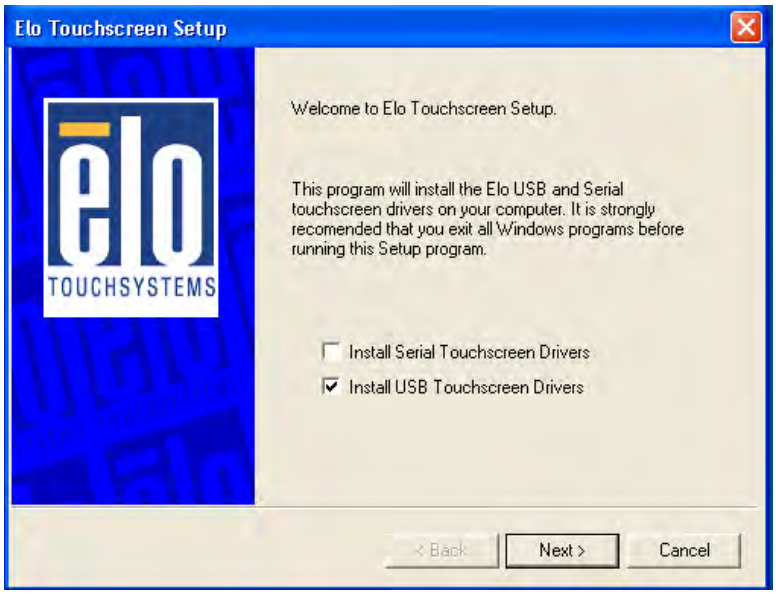
3. Follow the prompts in the installation program. Just press “Next” until completion.
4. The Cognition software should now be installed.
5. Don’t forget to remove the installation disc from the CD –drive and store in a secure place.

Installing the touch screen Driver

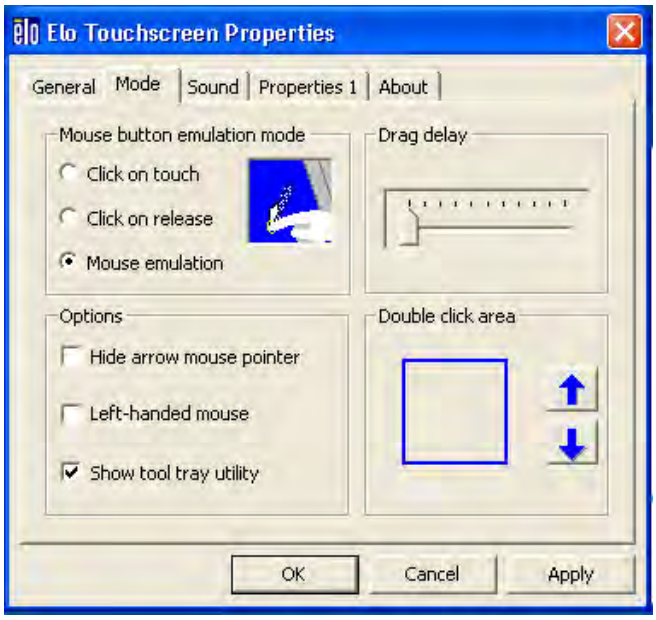
NOTE: please follow these steps after you installed the IntegNeuro software!

To ensure a good reliable signal from your touch screen you need to install the touch screen driver. Follow the steps below.

1. Browse on the provided CD to IntegNeuro\Touch screen driver and double click on the Icon **EloSetup**
2. Install the driver by following the steps that appear on your screen.
3. Make sure you set it up for USB Touch screen



4. Finish the complete process and the touch screen driver is installed.



5. When the touch screen is attached to your computer, the **ELO Icon** will appear in the right corner of the toolbar. Double click to open.

6. Go to the 2nd tab "**Mode**" and make sure that the Mouse button emulation mode is marked on "**Mouse Emulation**". Click **Apply** and **OK**.

7. Your touch screen is now ready to be used for IntegNeuro.

Checklist before seeing the first subject:

We recommend that the test administrators familiarize themselves with the IBM Touchscreen before testing the first Subject using demonstration logins. This will allow you to run through the toolkit without generating a report. You may prefer to record the details of your organisation on a sticker attached to the computer.

Setting up the room for IntegNeuro

Follow the instructions in the next section: "Administering the Test" using this information: BRC around the world is strictly standardized.

Room Checklist:

- **LIGHT**

Preferably no fluorescent lights overhead to reflect on the screen. Minimise such reflection: a room lamp is often a good alternative to overhead lighting if the installation is likely to be permanent.

- **PHYSICAL DISTRACTIONS**

Clocks, books, paintings, toys, mobile phones, telephones, fax machines, photocopiers, printers, etc are distracting and should be avoided.

- **NOISE DISTRACTIONS**

BRC recommends background noise no louder than 30db (quiet library) for sounds ranging from 500Hz to 20kHz. Acoustic barriers may help to minimize ambient noise. See FAQ for more tips on minimizing distracters.

- **CHAIR HEIGHT**

An adjustable chair should allow the subject to look downward on the screen.

- **HELP or BREAK required?**

If the subject requires attention or needs to take a break, there should be an arranged method, such as a bell push or agreed on signal.

- **VOLUME**

Instructions need to be delivered by headphone, at a clear volume, adjusted from the toolbar on the bottom right hand side of the Windows page, see FAQ below. Make sure the microphone and speakers are working before starting!

- **TOUCH**

Users of the Touchscreen should tap firmly with the fleshy pad of the pointing finger of the dominant hand, avoiding clothing, jewellery and other items touching the screen. Hovering above the screen should not be allowed, as this may set off the screen. Some subtests are more likely to receive tentative taps from the subject when they are unsure, and this may lead to false omissions or other errors. See test description for warnings in this regard.

NB: Watch out for dangling bracelets, sleeves, chains, and other items that may set off the touch screen, or trailing fingers hovering around.

NB: Push firmly and deliberately on the screen, especially during CPT and Visual Memory. Other fingers can set off the touch screen on Vis Mem!

NB: Park your hand when not busy: DO NOT hover over the screen as this may set it off. Keep hand away from touch area unless ready to tap.

Handleiding bij het gebruik van de internet vragenlijst (demografische gegevens) ten behoeve van IntegNeuro.

Voordat de cliënt komt voor zijn/haar neuropsychologische onderzoek ofwel IntegNeuro, dienen zij **eerst thuis** (of op locatie indien zij geen internet hebben) een internet vragenlijst in te vullen. Hiermee wordt veel aanvullende informatie verkregen die belangrijk is. Waaronder medische geschiedenis, trauma, DASS, Emotionele intelligentie, NEO-FFI en medicatie gebruik.

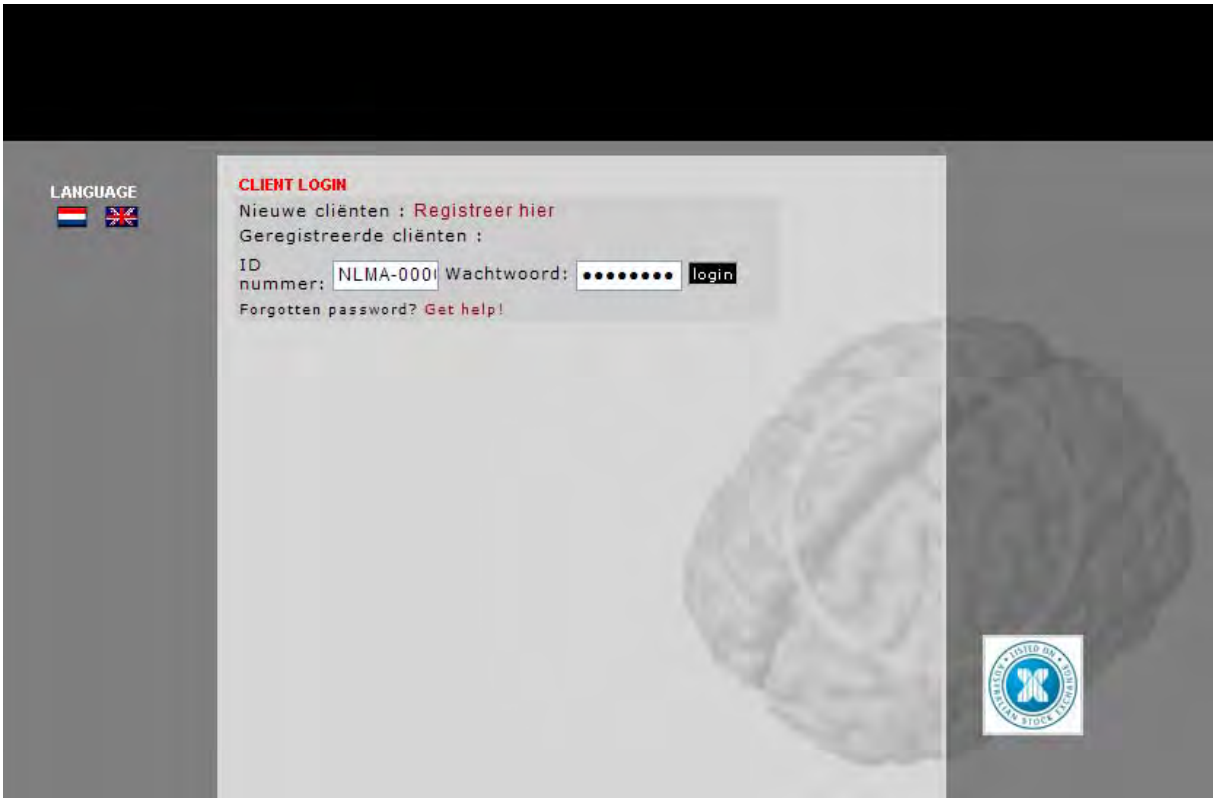
BELANGRIJK: Zorg ervoor dat deze lijst is ingevuld vóórdat de testgegevens van IntegNeuro worden geupload. Anders kunnen de demografische gegevens niet gekoppeld worden aan de testgegevens.

Hiervoor dient de cliënt zijn persoonlijke Login en Password te krijgen, bijvoorbeeld:

Login:	Password:	Org.Code:
DEMO-NLMA-001	GRINJILT	NLMA
DEMO-NLMA-002	SOWNDOVE	NLMA
DEMO-NLMA-003	CLIPUSED	NLMA
NLMA-00001	LIFTMACE	NLMA

In dit geval nemen we Login **NLMA-00001** en password **LIFTMACE**

De cliënt kan inloggen op: https://www.brainresource.com/QUESTIONNAIRE/ (laatste deel is hoofdlettergevoelig) door eerst de juiste taal te selecteren middels de vlaggetjes aan de linkerkant. Daarna dienen de Loginnaam en het wachtwoord ingevuld te worden en kan op Login gedrukt worden.



Voorbeeldbrief aanmelding IntegNeuro

Geachte heer/mevrouw,

Hierbij bevestig ik de afspraak die met u is gemaakt voor **dinsdag 2 december** om **13:00u.** voor een neuropsychologisch onderzoek.

Ter voorbereiding op het onderzoek verzoeken wij u vriendelijk een vragenlijst op internet in te vullen. Bij voorkeur vóór u de afspraak bij ons op de praktijk heeft. Heeft u geen beschikking over internet of lukt het thuis niet, neem dan even contact met ons op. Dan kunt u, in overleg, deze lijst op de praktijk invullen.

U kunt de vragenlijst vinden op de link https://www.brainresource.com/QUESTIONNAIRE/ (hoofdlettergevoelig). Selecteer dan eerst door middel van het vlaggetje de juiste taal.

De inlogcode/het ID nummer waarmee u zich kunt registreren bij de internetvragenlijst is:

NLMA-00001 *(Operator: vul hier de ID code en wachtwoord in van de ontvangen pdf met Client_Login)*

Het wachtwoord is

LIFTMACE

Het invullen van de vragenlijst zal ongeveer **één uur** in beslag nemen. Er zullen vragen in staan die mogelijk niet op u van toepassing zijn. Probeer toch alle vragen zo goed mogelijk in te vullen.

Gelieve bij verhindering dit tenminste 24 uur van te voren aangeven, omdat wij anders genoodzaakt zijn de kosten bij u in rekening te brengen.

Ik hoop u hiermee voldoende geïnformeerd te hebben. Mocht u vragen hebben, neemt u dan contact met ons op.

Met vriendelijke groet,

Administering the IntegNeuro Test

Running a BRC Cognitive Assessment or other application

All of the following steps may be completed without a keyboard and mouse. However, the keyboard may remain connected and stowed out of the way.

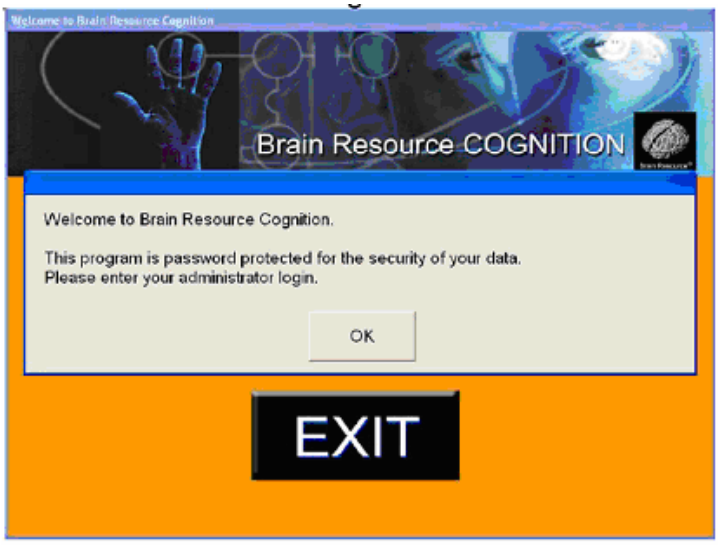
There are TWO modes of running an assessment:

- Internet Mode – connected via high-speed broadband preferably
- Temporary Stand-alone Mode – plugged into power but no internet connection, although you have to connect at the start of the day, and later again. There is no backup of the data until it is uploaded eventually. In between two sessions with the same login, the data has to be uploaded or the second session will NOT start

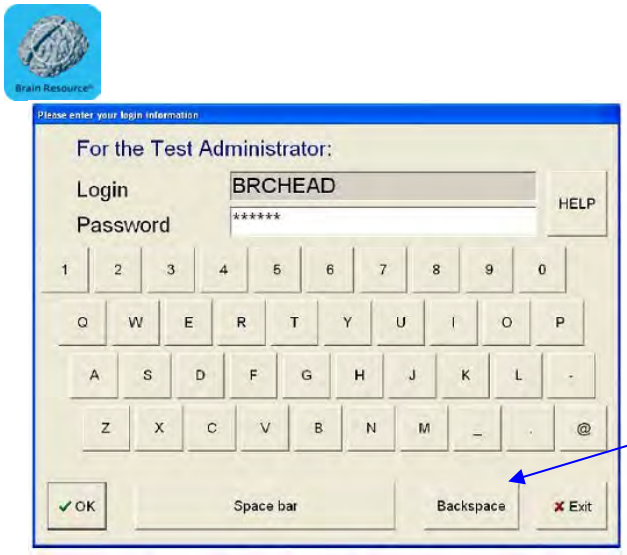
NB: The first time you use the BRC toolkit you must be in Internet Mode. This verifies your administrator authority and "caches" the subject logins for your site.

After that, you may acquire subject data in temporary Stand Alone Mode, testing as many people as you like one after the other. To upload the data to BRC at the end of that time, you must be in Internet Mode: it is recommended you do this at the end of every day of testing to upload results and then receive reports in time, especially when .wav files have to be scored at BRC in another time zone.

1. Start the BRC Cognition software from the desktop shortcut on your screen. Look for the BRC Cognition Icon (right) on your screen and either double-tap on it or single tap on it and press Enter using the keyboard. You will be greeted with another screen (below), tap **OK** to proceed with your administrator's code ready to hand. *(If you use the Y-Connector supplied, you can disconnect this and reconnect your keyboard and mouse now without disrupting anything)*

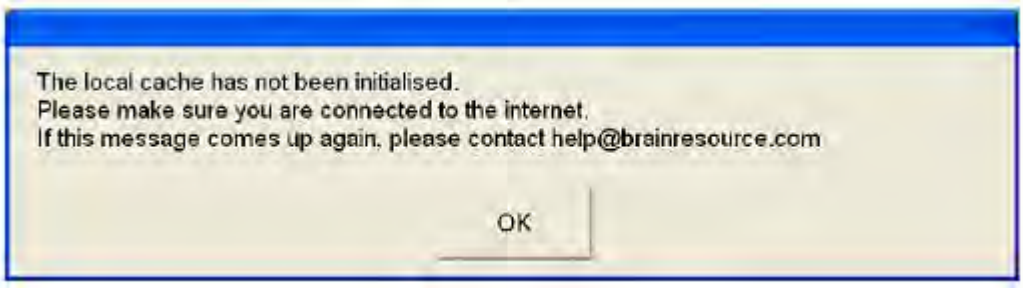


2. You will then see the following screen:

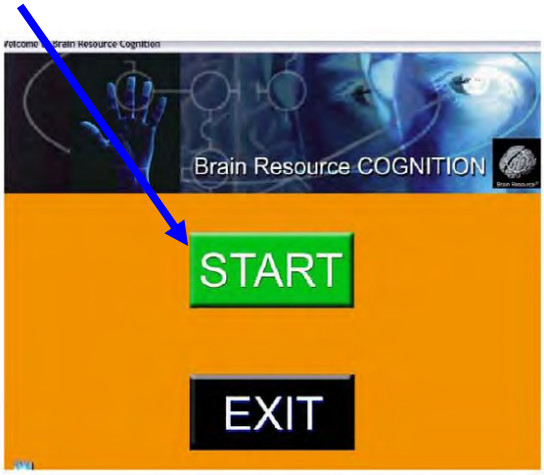


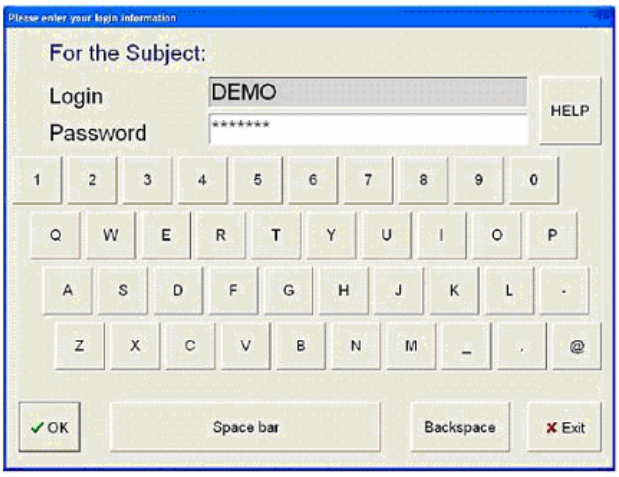
3. Enter the administrator's login and password you were provided with by BRC, by tapping the onscreen keyboard. Press backspace at the bottom of the screen if you make a mistake. After one login, you can test as many subjects as you like.

The following message will displayed <u>the first time</u> BRC Cognition is run on any computer: Make sure you are connected to the internet, and then tap **OK.**

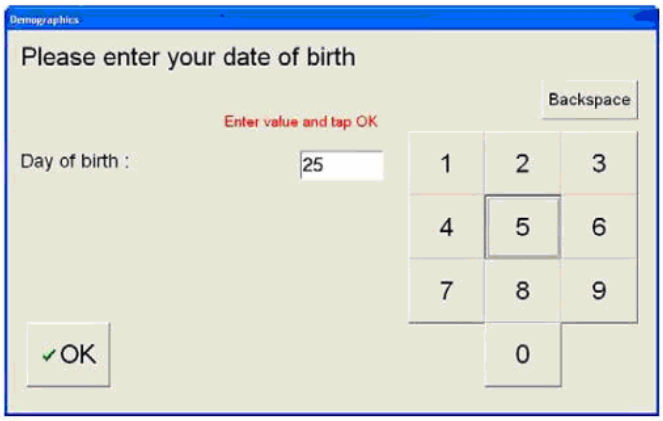


4.Tap the START button on the welcome screen:

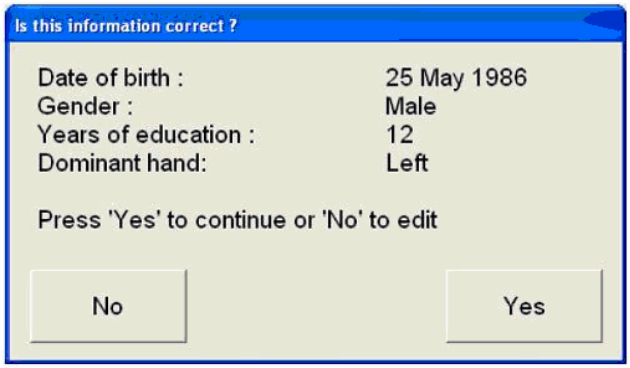




5. Enter the subject's login code as above. This is done for each subject, using their unique login code. The test Administrator needs to keep a record of which subject this applies to, as BRC is unable to identify subject's data as the reports are de-identified. When the same login code is used for retesting, an alternative but parallel version of the test will automatically run. Tap **OK** to continue.
6. The subject will now be required to enter their age, gender and education details as prompted. Note: Years of education includes all schooling from Grade 1/Year 1, not Kindergarten or pre-school, reception year, and so on, to the year the subject finished school, college or university e.g. 12 years to the end of high school plus 3 years undergraduate = 15 years of education.



Tap inside the field or touch "OK" to get a prompt, and enter the required response. I you make an error, just use the backspace button and re-enter the information. After you have entered the information you will be asked to verify that it is correct by tapping "Yes":



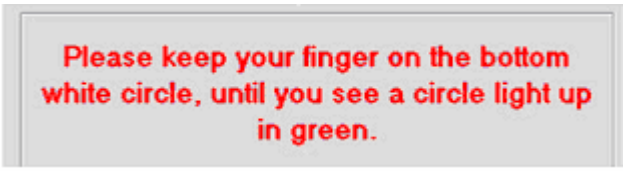
7. This screen below signals the start of the test toolkit sequence:

Once ready to begin, tap on “continue” and follow the detailed instructions for each test paradigm.

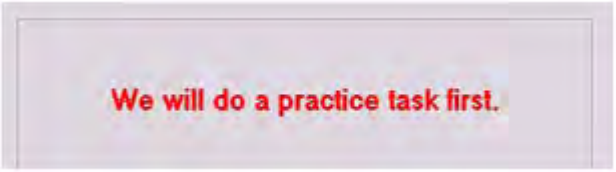
Each test in the toolkit will be introduced as follows:

The test title is as the top of the screen and there is a progress bar near the bottom to indicate which test the subject is up to and how many remain. Each test consists of the following forms:

A: test instructions are provided:



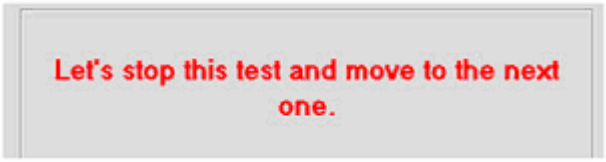
B: A practice task is offered:



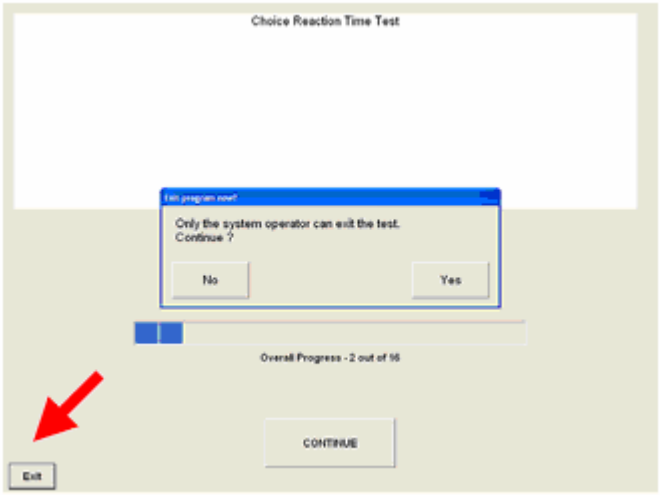
C: If the practice is successful, a prompt is provided to let you know when the real test will start:

D: If there was a problem understanding the practice task, the instruction will be played again:

E: The test will time out or move on if it is obvious that the instructions cannot be understood.

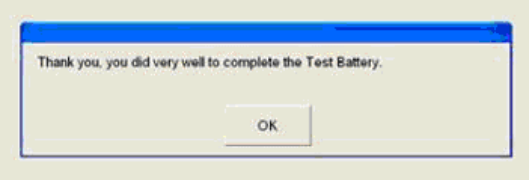


8. It is only possible to exit the test battery BETWEEN tests. That is, from the Progress screen as shown below. The TEST ADMINISTRATOR is the only person who can exit a test. To exit, simply tap the “Exit” button in the bottom left-hand corner of the progress screen. The TEST ADMINISTRATOR will be required to enter their login and password

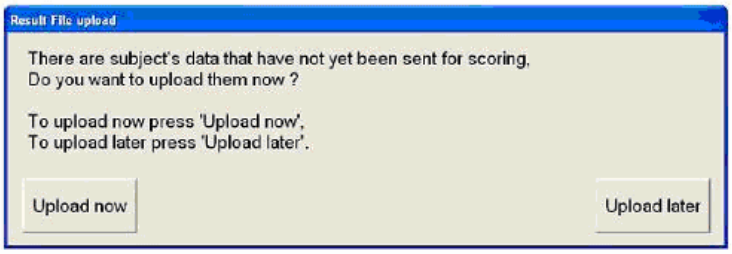


The system saves the data so far acquired, and provides the following options: The subject log in and password will restart the test where it was halted in order to finish the tests, or secondly, the data will be packaged for uploading to BRC in its incomplete form.

9. Once the subject has completed the entire toolkit, they will be presented with the following message on the screen: Tap **OK**

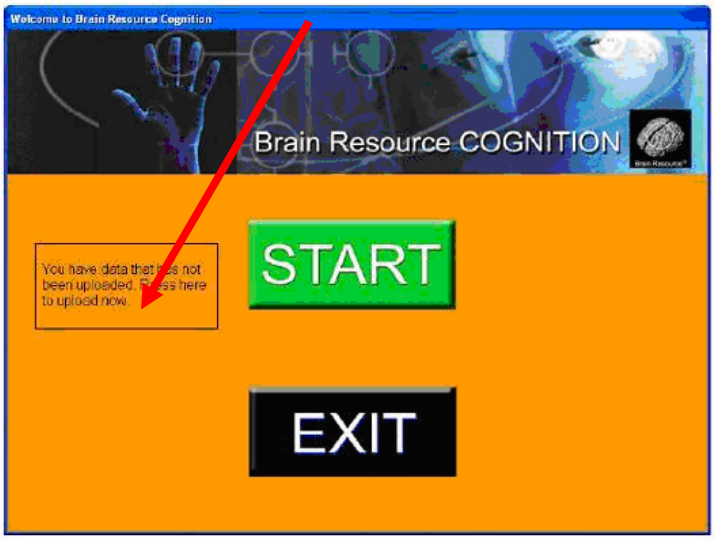


You will now be offered the choice to upload data collected from the test at this time, or later on if you choose:



If you are in internet mode, you would probably upload immediately. If you are in stand-alone mode, you would probably upload later.

If you select to upload later, you will return to the welcome screen and there will be an upload reminder displayed in a box to the left of the 'START' button. This reminder will appear on the welcome screen each time you run BRC cognition, until the data has been uploaded, either on this screen, or manually. It won't run the same login code twice unless you do!



Uploading the IntegNeuro Test Data

There are two options again to upload the date depending on whether you are connected or stand alone. All files are encrypted to protect the privacy of the subjects' data.

Internet Mode:
If you are connected, the cognition software will prompt you to upload any data that has not already been sent to BRC for analysis. The upload count for each assessment is about 5-6MB. ON a fast data line, this takes around 30secs.
Without Live Internet Connections:
As long as you log in on the first day when connected, you do not have to be connected to acquire data, as these are stored on your hard drive. When you do connect, the files can be uploaded. BRC recommends this be done after each day of testing, if not more often. The upload provides a backup to your computer files.

If for any reason you cannot connect, the files can be sent manually. A USB flash memory stick can be used to transfer to a computer that has email.

Open "My Computer" from the Start Menu or icon on your desktop. Browse the 'Data' subfolder of the directory where you stored the BRC Cognition on your computer:
Usually this is: C:\Program Files\BRC\BRC Cognition\Data
The data files will all have the extension .pmb Copy and paste all selected .pmb files to you flash memory card, or click and drag them onto the card.

The files should then be emailed to ***cognitionupload@brainresource.com***
BRC will provide a regular summary of the reports we have received which you can cross-check with your own.

The protocol to follow with each subject

The IntegNeuro toolkit has been designed scientifically so that it tests all people in exactly the same standardized way across the world. This standardization is critical for objective, evidence-based reporting. It makes it possible for someone who is not a psychologist to oversee test administration, and removes the human error associated with clinical settings in which timing, test instructions and other critical test material can be corrupted. A consortium of psychologists and other professionals around the world spent two years on designing every aspect of the toolkit delivery, and nothing should be altered. Comments on difficulties that emerge will always be welcome and should be delivered to clinical@brainresource.com

The administrator must ensure that the conditions of toolkit delivery are standardised:

1. The physical location of the Touchscreen with regard to the room, seating, lighting and screen angle, based on the mounting cradle
2. Preparing the subject for the experience.

1. **The Room:**
    - Free of visual distractions
    - Facing a plain wall

- Well lit but avoiding screen reflection
- Free of auditory distractions
- Sit directly in front of it looking down on the screen
- Use the cradle to keep the screen angle standard
- Bring the screen to the edge of the table and adjust chair height
- Switch the screen on before the client enters the room
- The screen should be free of fingerprints
- The administrator should have logged in already
- The headset should be plugged in and adjusted

2. **Preparing the subject for the experience:**
   - Orientate the to the coming task and the time taken
   - Sit them comfortably looking down on the screen
   - Vary the lighting to eliminate glare
   - Adjust clothing and jewellery to avoid screen contamination
   - Adjust hair away from the face so they do not have to do so at times
   - They should use their dominant hand
   - You can assess this by how they enter their subject login and details
   - Stay in the room until sure they are comfortable with the situation
   - They can double tap in the bottom right hand corner of the screen **or**
   - Use a bell push or signal to alert you of the need to help them
   - They need to understand this is a cognition toolkit, and that there is a predictable structure to the tests.
   - Use the following as a standard introductory script:

"This is a test of cognition, a test of your memory, attention, sensory motor and problem solving skills. Your aim is to do each test as well as you can, following the instructions that are given to you exactly. Remember, the same tests have been used around the world to test people of all ages and abilities, so we expect there to be a wide variety of responses, Just do the best that you can, there is no pass or fail.

There are many tests that make up this toolkit. They are numbered so you can see where you are up to as you go along.

Some of the tests will ask you to speak into the microphone. Let's make sure you have that positioned correctly now.

Before each test you will be given instructions through the headphone and on the screen for that task and you will be given an example of what to do.

To make sure that you have understood the instructions, you will get a chance to practise the task. If you get the practice test right, you will continue with the real test. If you don't understand the instructions then the system will repeat them to you. If you don't understand how to perform the test after a few repetitions, you might be moved directly to the next test.

Once you have heard the instructions and done the practice tasks correctly, you will then start the real test. Listen for the prompts about how to start the actual test.

Make sure you only use the index (pointing) finger to touch the screen. "Tap" the screen with the tip of your finger, not the nail. Do not "push" the screen to register your response. You can rest your palm on the edge of the frame, but not the screen itself. If you accidentally touch the screen with your whole hand instead of just the pointing finger, you will be told.

All the tests are timed and are designed to be completed in around an hour. Sometimes you will be moved on to the next task.

If at any time during the test you really feel you need to stop, please call me (the administrator).*

Do you have any questions before we start?"

*(*The test administrator may choose to tap twice at the bottom right hand corner of the screen, as you would double-click a mouse, to skip any of the 16 subtests of the toolkit. See the FAQ for more information.)*

Frequently asked questions:

What is my Login code? Where do I get Logins?

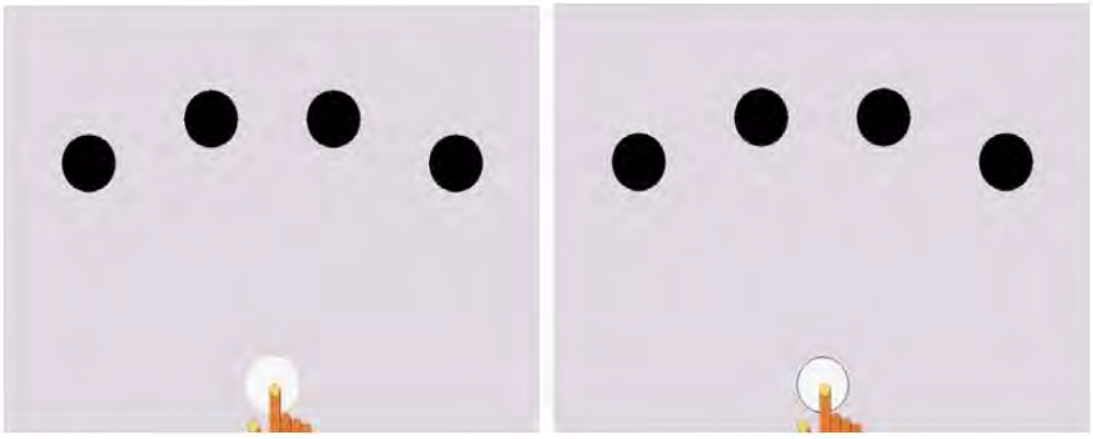
There are 2 different Login codes. One for the Test Administrator and one for each Subject doing the tests. The codes come from Brain Resource.

How do I move around a Touchscreen?

Using the pointing finger on your dominant hand, tap the field where you want to enter a response.

What do I do if the screen is not responding to my touch?

The program provides some feedback to tell you that it has registered a touch. There is usually a black circle around the button or it changes color. If there is no feedback, check that the cable connecting the touchscreen to the computer is in place.



Can I go back and do a test again?

If you pause or skip a test you cannot go back and start that particular test again. You will be presented with the next test in the battery. If you use the

same login on a separate occasion, you will be presented with a different version of the test.

What happens if the power fails or there is some other interruption?

Your data is continuously saved to the hard disc of your computer so if there is any interruption, and you will be able to start again where you left off. You use the same login code, and the test will continue as usual.

Do I need a high bandwidth connection for IntegNeuro?

You can use a slower connection, but the upload of the .wav (voice) files takes some time. Testing can recommence though during uploading

How long does it take to complete the entire IntegNeuro toolkit?

IntegNeuro takes on average an hour, but some manage it in 50minutes depending on how tests are done, completed, or missed.

Does the test administrator need to be present during the session?

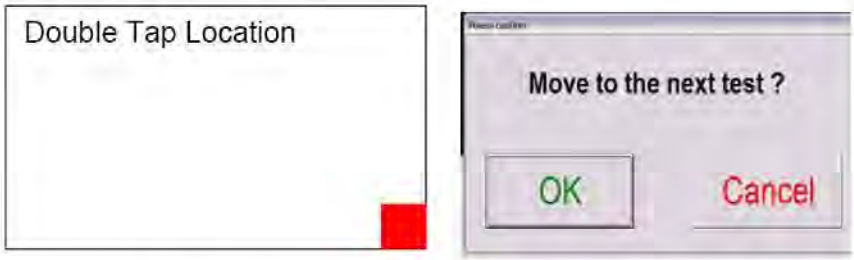
The BRC Cognition methodology has been designed to be run automatically. If the subject is struggling with the test, they should be instructed to ask for help. The individual subtests do time out if the subject cannot complete a task. There are pauses between tests where it is possible to ask for assistance. Combined with the deliberately simple task instructions, this means that in the vast majority of cases, the Brain Resource Cognition can be used with minimal supervision (at the beginning of the test to demonstrate to the subject how it works).

Nevertheless, for very young children, children with ADHD or elderly people who have cognitive impairment, some supervision may be prudent.

What if the subject needs to stop during the test? Can they pause the test?

The Subject cannot pause for a break in the middle of a test – only between tests.

It is possible to stop the test you are in by double-tapping in the bottom right-hand corner or the touchscreen. It is much like a double-click on a mouse except you "double tap" with your index finger. A dialog box pops up which asks if you would like to move on to the next test (or continue).



It is up to the Test Administrator whether they show this to the Subject or not. However if the Subject is in distress it can be used to initiate exit from the system.

You can practice finding the right spot using your demo login.

Can I continue the test on another day?

If the subject needs to stop the test half way through the battery they can do so (see above). The program will automatically save the data up to that point on the hard disk and offer the Test Administrator the choice of uploading that data or continuing the test later. When the Subject returns to the test battery and enters the SAME LOGIN code, they will automatically be presented with the next test in the battery, allowing them to resume the test from where they left it. Any time interruptions longer than 5 minutes should be logged with support@brainresource.com.

Do I need to keep the keyboard of the computer connected during the test?

Neither the Test Administrator nor the Subject has a need for the keyboard during the test. You can detach a USB connected keyboard at any time while the system is running. PS/2 keyboards like to remain attached once the system is running. They should be just taken out of the way.

Can I change the angle of the screen?

No. The screen angle is standardized and must remain the same for all subjects. However, if the Subject has difficulty using the screen, we suggest that the chair height be adjusted and the unit brought closer to the Subject. The Subject should be able to comfortably look down on the screen.

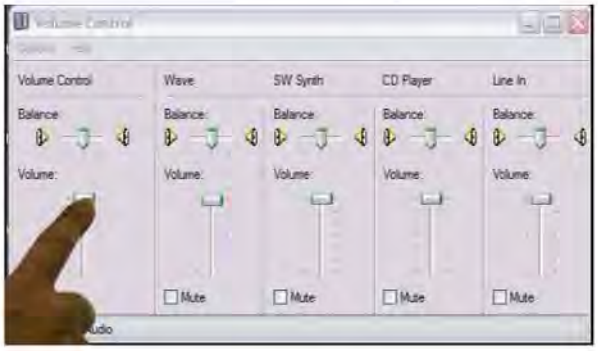
I can't differentiate colors on the screen – what do I do?

This is typically due to the angle of the screen, (see above) or light reflecting on the screen. The Subject should be made aware of this possibility and adjust the chair height and posture accordingly. If this continues to be a problem, then it should be reported as a technical issue.

How do I adjust the volume for the headsets?

The volume can be adjusted from the Windows Volume control. You can access this program from your desktop, (click on the speaker icon in the bottom right-hand corner)

or *from the Control panel (Click START, Control Panel, Sounds and Audio devices).*



How do I know if my microphone works?

You can test your microphone in Sounds and Audio devices. See the Voice tab for "test hardware" and follow the directions.

What are the minimum hardware requirements for the PC to run the BRC application?

Windows 2000: PIII, 128MB RAM
Windows XP: PIII, 256MB RAM

Other requirements:
Internet Explorer 5 or above installed.
Windows Media Player installed.
Available HDD space: 150MB for installation & 6MB per acquisition.

Can I use the computer for other applications?

Yes you can, however the more "stand-alone" the Cognition system is, the less support is required for the system. If you do use it for other applications, we recommend you create a separate profile with separate support protocols.

What is the recommended Windows profile in which to run BRC Cognition?

One that switches off screensavers, automatic security updates and other automatic programs which might interrupt a test. The BRC Cognition software comes with the recommended profile.

How do I access the Brain Resource Web Questionnaires?

The steps to log in are as follows:
1) Go to the Brain Resource website www.brainresource.com
2) Click on 'Client login GO' on the left side
3) Enter the client login and password provided to you for the Brain Resource Cognition test and follow the prompts.
Do not register for new users.

How do you minimise the impact of noise in the testing environment?

BRC recommends that subjects undergo BRC testing in as quiet environment as possible to minimise the risk of distractions, which might impact test performance. Taking into consideration the need for a quiet environment, balanced with the practica limitations of typical testing centres, BRC recommends that background noise levels b no greater than 30dB (a quiet library) for sounds ranging from 500Hz to 20kHz, as measured using a SLM.

This level is after consideration of the effect of intermittent loudness and the use of acoustic barriers to minimise the impact of noise have been implemented. The discret and judgement of the administering clinician should inform final decision-making as to the suitability of the test environment for different test purposes.

Acoustic barriers minimise ambient noise. Acoustic barriers include:

- *Structural Design Measures, which reduce sound by reducing reverberation ar shielding the subject from the noise source. For example:*
  - *testing room location away from environmental noise such as traffic, waiting rooms*
  - *use of solid walls, not just partitions*
  - *double glazing for windows/ glass partitions*
  - *sealed rooms/ use of doors,*
  - *irregularly shaped rooms to minimise reverberations*
- *Sound Dampeners, which include furnishings such as:*
  - *cloth covered partitions*
  - *soft furnishings (eg carpet, rugs, cloth wall hangings, heavy fabric curtains)*

- *Environmental Measures (situation specific and temporary)*
  - *noise reducing or noise cancelling headphones,*
  - *signs requesting quiet, closing of windows/ doors,*
  - *scheduling noisy activities to occur outside of critical periods*
  - *staggering test schedules so that audible test responses are delivered at the least distracting times*
  - *alerting people that some noise can be expected during the tasks but ask that they ignore them as much as possible. In this way, the presence of noise becomes an expected rather than unexpected phenomenon and is therefore less distracting.*

These measures will reduce noise levels as well as the impact of this noise and help ensure the most conducive environment for testing purposes.

My client has some concerns about the privacy of their data and how the data can be used by the Brain Resource Company.

The Brain Resource Database is deidentified. Only Client ID numbers are used. BRC never has access to patient names. It is the responsibility of the Service Provider to keep track of Patients and their corresponding BRC login number. The following format may be useful for the test administrator.

BRC Client ID number	***Subject's name***	***Age***	***Cognition test date***	***Comments***
*(include test number e.g.TEST-00023-**2***				*Make note if test is interrupted other observations*

Even though there are no personal details provided to BRC, the Client's data is only added to the Brain Resource database with Client consent. Below is a sample consent form which you can use.

Sample IntegNeuro Consent Form

1. About the test
You are about to do an automated test of your thinking. This is a series of tests designed to assess your memory, attention, visual-spatial, language and problem-solving skills. The tests are delivered on a touch screen computer. You will not need any computer skills to complete these tests.

2. What happens to your responses?
Your responses will be sent to the Brain Resource Company for centralized analysis via a secure Internet connection. Your responses will be compared to others of the same age, sex and years of education in the Brain Resource International Database. Brain Resource will provide a report to this clinic.

3. The privacy and confidentiality of your information is assured.
All details that personally identify you will be removed from the data and replaced by an anonymous ID key before transmission. The central processing facility will not receive your name, only your anonymous ID key. Your name will be held in strict confidence here at your local clinic and stored separately and independently of the database.

4. Request permission to include you data in the International database.
With your permission, your de-linked data will be included in the Brain Resource International Database, and may be made available for scientific, clinical and commercial purposes.

I understand and agree that scientists internationally may have access to data from this test at any time in the future and that the information may be used for scientific, clinical or commercial purposes. I understand and agree that **no personal identification information** (i.e. name, address, contact details) will be transmitted to the central international database.

☐ Yes ☐ No (please tick ✓)

Signature..... Date.....

Signature of parent/guardian (if subject is under 18)

..... Date.....

Troubleshooting and Support: support@brainresource.com

Software support issues and questions

1. First check the Frequently Asked Questions in the manual provided.
2. Email support@brainresource.com . Brain Resource will respond to any email within 24-hours.

During the setup period for your site, we recommend scheduling one teleconference with Central BRC Support for a managed, real-time review. Write to support@brainresource.com to arrange a suitable time.

Questions about report interpretation

Brain Resource reports provide indications of brain function and cognition as compared to a normative database. Its only purpose is to act as a screening tool for possible dysfunction. **It is not to be used as a basis for action without consideration by a competent relevant professional.** The report is not intended to diagnose, treat, or cure any health condition.

If a Clinician has any questions about how to interpret a BRC report, they may take advantage of our Report Support service.

1. First refer to the Report manual, available on the BRC website
2. Email reportsupport@brainresource.com . Brain Resource will respond to any email within 24-hours.
   - Clinicians should provide contact details and the best time to schedule a call with one of our Report support consultants
   - They should quote the Client number of the report to be reviewed.

Hardware support:

Please contact Brain Resource for advice. Where there is an obvious hardware problem with the IBM Touchscreen 4820 – 5GN or IBM computer, we can help you to arrange IBM warranty support at the number provided in your hardware manual. Your Brain Resource representative may also be able to assist with a replacement unit in urgent cases.

If IBM warranty service is called upon, they will attempt to resolve the issue by telephone first, then arrange a Customer Replacement Unit as soon as possible.

Contact us

Internet: www.brainresource.com
Email: info@brainresource.com
Mail: PO Box 737, Broadway NSW 2007 Australia
Head Office Switch: +61 2 9211 7120

Test Toolkit description

Neuropsychology Test Battery

The Neuropsychological test battery provides a profile of a participants' core cognitive competencies, namely: sensory-motor-spatial, verbal and nonverbal memory, attention and vigilance, language and planning (executive functions). There are a total of 14 tasks, which take approximately 50 minutes to complete. Tasks marked with * are also used during psychophysiological recordings. The order of these tasks (and the associated times) are as follows:

1) Motor Tapping (2 mins)
2) Choice Reaction Time (3 mins)
3) Timing (2 mins)
4) Span of Visual Memory (5 mins)
5) Spot the Word (2 mins)
6) Digit Span (5 mins)
7) Memory Recall and Recognition (7 mins)
8) Verbal Interference (3 mins)
9) Word Generation (6 mins)
10) Visual Working Memory (Sustained Attention)* (6 mins)
11) Switching of Attention (Trial B) (4 mins)
12) Executive Maze* (8 mins)
13) Go NoGo task (6 mins)*
14) Emotion Recognition Task (10 mins)

See Pages 66 and 67 for Principal Components Analysis of general cognitive factors and cognition-brain construct validity studies

Technical Subtest Descriptions

This section provides you with detail as to what each subtest measures

Note: What now follows is a brief description of each test, and a **general** discussion of the findings in the scientific literature about the constructs that are measured by such tests. Later on in each section we describe what has been measured which is specific to our test and the inter-correlations between our tests, as well as their shared variance with other aspects of our integrative neuroscience database. So if two tests co-vary, as one changes its scores and shares say 46% of the main effects variance with another test, 46% of the change in the second test scores will reflect what the two test measure together. If the probability of that measure is say .001, if you redo the tests 1000 times, they will do that reliably 999 times.

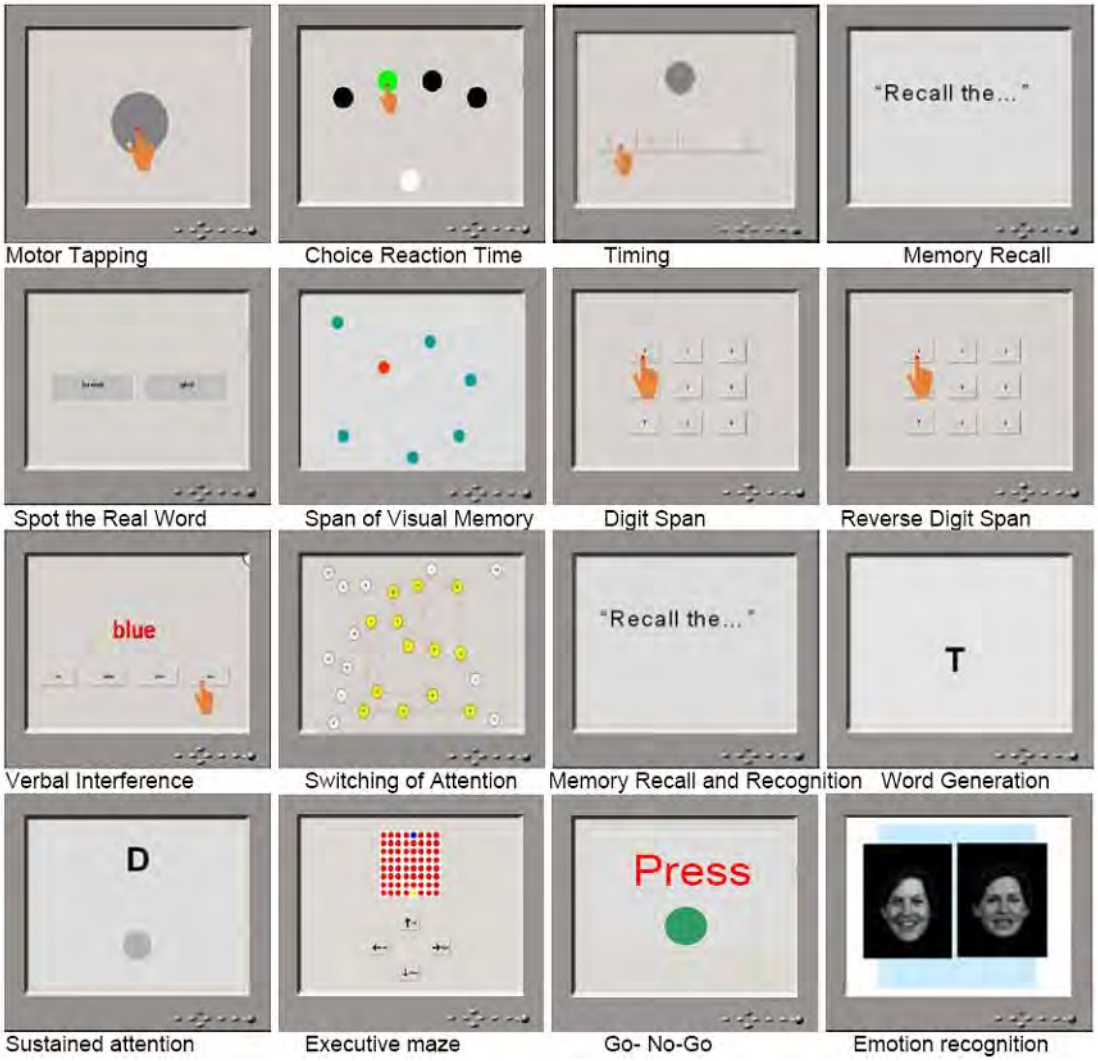
More details of the literature specific to our tests and methodology can be found at: http://www.brain-dynamics.net/

For an understanding of Z scores, Standard Scores and Standard Deviations: http://www.brainresource.com/uploads/Standard_distribution.pdf and ignore warning.

Note: Our computerised tests have been compared to similar and identical tests and found to share common variance within high levels of probability (see http://www.brain-dynamics.net/research/validity.html). Nevertheless, skilled neuropsychological interpretation is the provenance of the experts, as each person responds differently and wide variance in test performance is a feature of normal human individuality, not necessarily of pathology. What might create difficulties in the classroom may advantage the individual working in emergency rooms, or lead to bravery and leadership on the battlefield. Always ask your healthcare professional to interpret results of these and any other test. For a full discussion of this topic, see Matarazzo JD (1990). Psychological Assessment versus Psychological Testing: Validation from Binet to the school, clinic, and courtroom. *American Psychologist* 45(9) 999-1017

Descriptions of the test items and literature related to such tests with the same or similar characteristics

The 14 tests are presented in 16 sequences, as follows



Each of the 14 tests listed above is described in detail below

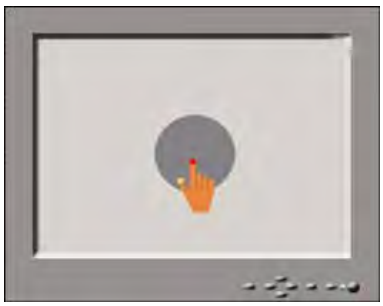
A note on the use of the IBM touch-screen: Keep your palm and fingers clear of the screen, utilizing only your dominant index (pointing) finger as shown in the illustration below:

NB: Watch out for dangling bracelets, sleeves, chains, and other items that may set off the touch screen

NB: Push firmly and deliberately on the screen, especially during CPT and Visual Memory.

NB: Park your hand when not busy: DO NOT hover over the screen as this may set it off. Keep your hand away from touch area unless ready to tap.

1: Motor tapping (*Sensori-Motor*)



What is the test? The test is similar in most aspects of underlying construct to the many versions of Ward Halstead and Ralph Reitan's Finger Oscillation Test, later known as the Tapping Test. Our test however differs in terms of the delivery modality, the single 30-second time trial. As with the original, and in contrast to the WebNeuro test, the index fingers of **both** hands are used. Preferred hand tapping is characterized by a reduced inter-tap interval and a smaller variance in this interval. The original test used a mechanical tapper, with performance scored over ten-second tapping bursts with rest periods intervening, albeit with some confusion in the manuals about the application of these criteria. Newer versions used an electronic tapper, with different norms needed as the technology changed. Computerized versions of the test show high correlation with the original versions, confirming the construct is the same (Christianson & Leathem 2004). See, for this and other tests beneath:
http://www.brain-dynamics.net/research/validity.html

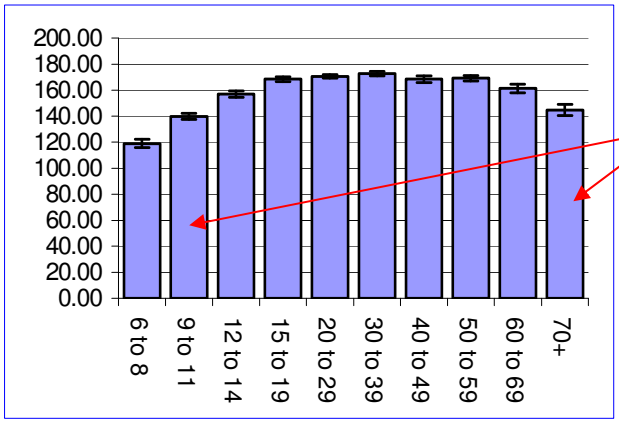
Trials on original equipment that were deviant by 10 taps from the mean were discarded in the original protocol, but the criteria were vague. Traditional cutoff scores have generated unacceptably large numbers of misclassifications. In short, as a screening test, the effects did not appear with enough selectivity or consistency to support its construct validity, and so the greatest utility of the test is gained when it is used in conjunction with other tests, as we do here, or when validated against other measures, as we do.

Testing procedure: Using their dominant hand first participants here are required to tap the circle on the touchscreen with **only** their index *(pointing)* finger, heel of hand on the frame of the screen, as **quickly** as possible for 60 seconds, (our test is longer, as longer tests are more reliable: see Michel 1993). **The other fingers remain inert above the screen surface, palm down.** The dependent variable is total number of taps with the index finger of each hand.

What areas of function are measured by such tests?

- **In Brain Injury:** Prigatano et al (2004) found greater activation on fMRI in the bifrontal brain areas on healthy controls versus patients with TBI, using only the right hand. Brain injury often but not always slows tapping speeds. Lateralised dysfunction usually slows speeds on the contralateral hand. Tapping frequency can distinguish patients with motor dysfunction of cerebellar, basal ganglia, and cerebral origins from normal subjects including those with migraine and with MS (Scherer et al 1997). Diseases of the brain that affect motor capacity all have a significant effect on tapping speed.
- **Gender:** Gender has a strong effect on tapping speed; men are consistently faster than women: both slow with age (Clark et al 2006).
- **In Aging:** Age has a strong effect on tapping speed; overall slowing with age becomes apparent in the fifth decade. Slowing accelerates in subsequent decades. The sensitivity of the Motor Tapping Test to age effects is likely to reflect in part a decline in dopamine brain function, and the strong relationship of tapping tests with D2 receptors indicates that the test may be particularly useful for monitoring dopamine-related function both in the caudate and the putamen (Volkow et al 1998). Arthritic damage appears to not affect the results significantly (Kauranen et al 2000). Education level is also a minor factor in aging, with privileged groups doing marginally better,

Motor tapping: N=1007: Number of Taps by age



but not significantly on our test (Clark et al 2006). Motor Tapping scores increase across age into the 20-29 age range, in keeping with cortical maturation, but then decline slowly after that age range. Declines at around 70 years place the scores back to the preteens; children about 9-11 years old have the same scores as those in their 70's overall.

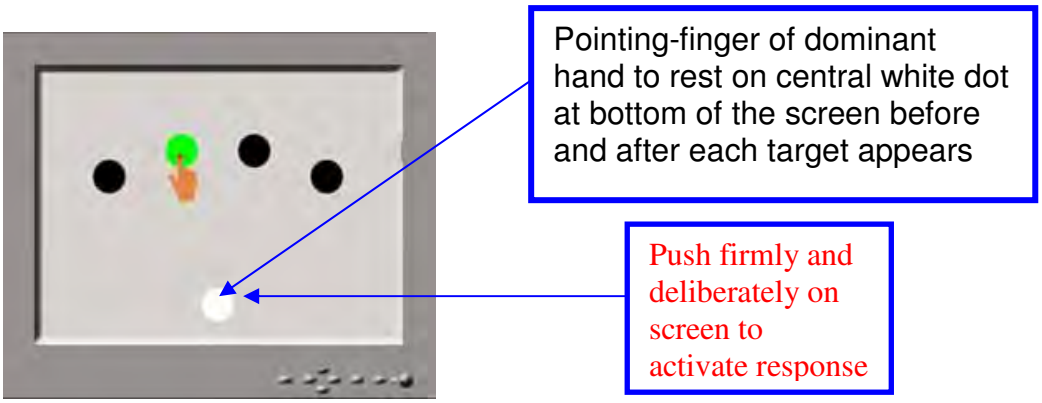
- **Medication in Epilepsy/anti-convulsants:** Epileptic patients generally do poorly, but this may be a medication effect. In this regard, Carbamazepine is the worst, followed by valproic acid, oxcarbazepine, topiramate, lamotrigine and lithium in turn. See http://www.medscape.com/viewarticle/541762_Tables
- **Alcoholism:** Some patients with chronic alcoholism tap slowly, but many do not. Effects may recover with abstinence, and allows monitoring of recovery
- **Cerebellum**: The test discriminates those with olivo-ponto-cerebellar atrophy amongst those with otherwise pure spinocerebellar degeneration.
- **Malingering**: Noncredible ('faking') male and female patients tap slower than their comparison group counterparts. The dominant hand score proves to be more sensitive in noncredible performances than other scores using either hand or the non-dominant hand (Arnold et al, 2005).
- **Mercury toxicity**: Increasing blood mercury levels appear to be correlated with better tapping scores, not worse (Weil et al 2005).

- **After stroke**: Finger tapping scores on the side contralateral to the stroke site initially decline after stroke, as the brain begins compensation, improving as the brain recovers, and is a good measure of recovery of the affected side.
- **EEG/MRI**: In our laboratories, the test correlates negatively with Alpha (peak) activity, and fairly positively with occipital lobe volume on MRI. Earlier P200 Target Latency is equated with faster tapping

Note: Alpha peak frequency has been found to predict performance on memory tests, namely the peak of spectral alpha power of the EEG. Activity in the alpha band has been also associated with higher cognitive functions including attention and anticipation and has been shown to slow with age. Few studies, however, have examined whether there might be a relationship between working memory (WM) decline and alpha peak frequency. Clark et al (2004) specifically investigated this relationship. Digit span was used as the index of WM function. Forward and reverse digit span were found to be lower in older relative to younger age groups. Spontaneous alpha peak frequency slowed with age and more so at anterior than posterior sites. Frontal alpha peak frequency was found to be a significant predictor of reverse digit span, with each 1 Hz increase in frequency associated with a 0.21 increase in reverse digit span score and this was independent of age, indicating a positive relationship between alpha peak frequency and working memory performance

Note: as with all our tests, there is now a gap between this and the next subtest for brief respite, toilet breaks or comments. The test-taker or administrator is prompted to let the computer know when they are ready to begin the next test, giving them time to absorb the test instructions. Impulsive children should be warned to read the test instructions carefully, but this prompt should not be given every time, only once, as their lack of diligence is diagnostic, and should not be removed as a variable by adult scaffolding or surrogacy of control.

2. Choice Reaction Time *(Sensori-Motor)*



What is the test? The Choice Reaction Time Test is a measure of simple reaction time and represents a measure of sensorimotor and information processing speed. As slowed speed of information processing often underlies attentional deficits, such tests serve as a relatively direct means of measuring processing speed.

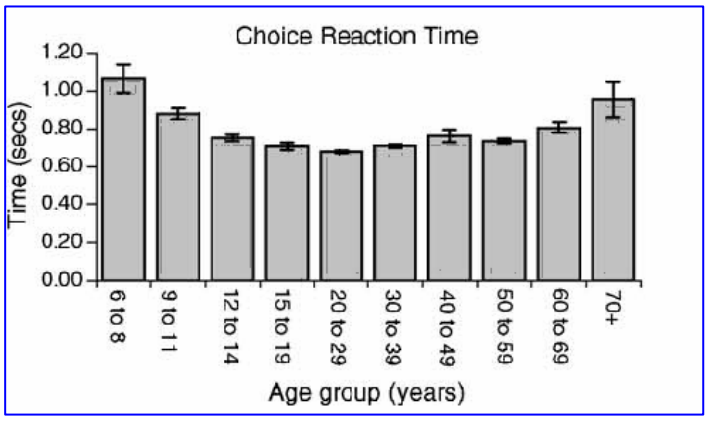
Test procedure: Participants on our unique version of this genre of tests are required to attend to the computer screen, the *dominant hand index finger* resting on

the white central home base circle, as one of four target circles lights up in green on one of four different positions on the screen in pseudo random sequence over a series of trials. For each trial, the subject is required to touch the illuminated green circle as quickly as possible. Twenty trials are administered with a random delay between trials of 2-4 seconds. The dependent variable is the mean reaction time across trials. Speed is greater when the subject sits centrally in front of the screen, dominant hand relaxed on the rest circle.

What areas of function are measured by such tests?

- **In Aging**: The difference between the normal elderly patient and those with dementia is much larger when stimulus choice tests are used (about two standard deviations slower- see Pirozzolo et al 1981), and is independent of gender effects. There is a marked age effect, with reaction time shortening from early childhood into the late twenties, mirroring the myelination of the cortex, and then slowing until the fifth and sixth decades, speeding up the rate and variability of slowing into the 70's and later. Older people may in fact be more cautious, rather than just slower. Older people, facing a distraction, may focus on a single stimulus, ignoring the other more completely than younger adults do. Slower times predict a higher risk of dying in the elderly (Metter et al 2005; Shipley et al 2006). With regard to our version, Clark et al (2006) found a marked peak at 20-29, after gradual improvement, and then not much decline until 59, accelerating in the 6th and 7th decade:

Choice reaction time N=1007



- **In Depression**: Depressed patients also have slowed responses, but still quicker than dementing patients, so the test alone may not be entirely useful when trying to partial out pseudo-dementia from dementia in isolation (Pirozzolo et al 1985). When this is suspected, a close look at Emotional Recognition, later on in this battery, is warranted to evaluate the impact of the emotional valance.
- **Cortical arousal**: Reaction time is fastest with an intermediate level of arousal, and slows when the subject is either too relaxed, or too tense. Mental fatigue has a greater effect than physical fatigue, worse in younger adults. Background noise appears to slow responses. Fitness can affect reaction time, but seldom for long, and not much in the elderly patient. Caffeine in coffee, but not soft drinks, was found to speed reaction times, but amphetamines in the elderly did not.
- **Gender**: As with tapping, males tend to have faster reaction times than females, even when training/practice is given to females: however, as women participate in sport and other activities, the times for visual presentations are

shortening, rivaling male times. This difference relates to muscle contraction rates that improve with exercise.

- **Handedness effects**: Using a computer mouse, left-handers are equally fast with either hand, right-handers only faster with their dominant hand.
- **Intelligence**: Intelligence has a uncertain and variable effect, as there is much variance within the same scored level of IQ group.
- **In Brain Injury**: Concussion with headache appears to also result in slower responses, with brain injury overall represented in respect of severity. (See literature review by Robert J Kosinski on the web at http://biology.clemson.edu/bpc/bp/Lab/110/reaction.htm). Inherently good performance and increasingly shorter reaction times on such tests are linked to cortical white matter supporting visuospatial attention rather than white matter supporting motor or interhemispheric pathways. See Tuch et al (2005): http://www.nmr.mgh.harvard.edu/martinos/publications/posters/ISMRM-2005/Tuch_ismrm-rxn-2005-000.pdf
- **Culture and Race:** Race may be a factor in response times.
- **In Parkinson's Disease:** Parkinson's Disease patients early in their treatment may show improvement, but not veterans of treatment (Muller et al 2004). The slower times in PD relate to cerebral processing deficits rather than in pre-programming (Kutukcu et al 1999).
- **In HIV/AIDS:** Slowed reaction time in AIDS patients is not accounted for by depression, level of intellectual function, age, or education. Psychomotor slowing here is consistent with early AIDS Dementia Complex (ADC) and may herald the onset of cognitive dysfunction in otherwise neurologically healthy patients (Nanceet et al 1990).
- **Hypertension:** CRT may be preserved in hypertensives, whereas simple reaction time may not (Harrington et al 2000).
- **Lewy Body Dementia/Parkinsonism:** Patients with Lewy Body dementia are less impaired when there is less or no parkinsonism, compared to Parkinson's dementia (Ballard et al 2002) but in practice it is almost impossible to find cognitive profiles that distinguish the two conditions otherwise using computerized testing (Corani et al 2006).
- **Lewy Body Dementia vs. Alzheimer's:** discriminating DLB patients from Alzheimer's patients and elderly controls using computer methodology is easier and possible (Bradshaw et al 2006).
- **In Stroke (white matter):** Stroke survivors without dementia do better than aging, matched controls on CRT (Ballard et al 2003). The volume of white matter hyperintensities on MRI in stroke survivors is correlated with CRT performance on a computer battery (Burton et al 2004), and is a predictor of early cognitive impairment in elderly stroke patients (Ballard et al 2003).
- **MRI (gray matter):** In our laboratory, the test also correlates fairly strongly with overall grey matter volume, more strongly with cingulated and temporal volume, and fairly strongly with amygdala volume.
- **EEG:** In our laboratory, earlier P300 equates to faster reaction time on CRT

3. Time Estimation *(Attention and working memory)*

What is the test? The test is a measure of the client's capacity to estimate the duration of time passing between the beginning and end of a signal. Cognitive time management is an important aspect of human cognition that has so far been understudied, and the way we code temporal information is as yet not understood; there is no sensory modality by which time can be directly perceived and experienced (Pouthas & Perbal 2004). Several regions of the frontal lobes, inferior parietal lobes, cerebellum and basal ganglia have been found to be involved in tasks of time estimation (Rubia & Smith 2004).
One component is believed to consist of an oscillatory pacemaker emitting pulses at a mean constant rate. The accumulated storage of this measure is transiently stored in a working memory system for comparison with the content of reference memory, and some mechanism compares the current duration values with those in working or reference memory to decide on a response in time (Church 1984). Any pathology that interferes with this process will lead to a misperception of time and thus mistimed action. The temporal organization of behavior includes preplanning the acts that constitute purposeful behavior, deciding their temporal onset, and monitoring their time course once they have been initiated (Fuster 1985). Perception of time also relies on stored representations of intervals in working memory (Rao et al 2001) and is sensitive to frontal lesions (Mimura, Kinsbourne & O'Connor 2000), with frontal patients estimating times below 28 seconds to be longer than they are (Kinsbourne 2000)

Test procedure: A black circle appears on the screen, turning green for times varying between 1 and 12 seconds in pseudo random order. The subject is required to attend to the screen and estimate the duration of the target trace on the screen, using keys on a fixed display touchpad at the bottom of the screen with the numbers 1-12. The test lasts for about two minutes overall. Test stimuli are in pseudorandom sequence. The dependent variable is the value of the averaged differences between the duration of the stimuli and the user's estimates, weighted by the length of the stimulus in each response.

What areas of function are measured by such tests?

- **ADHD and arousal:** In studies of high versus low arousal, attention-disordered students estimated longer times in the low-arousal condition than normal students but not in the high-arousal condition. This evidence supports the cortical under-arousal hypothesis as the basis for an attention disorder.
- **ADHD and use of time**: Compared to normal students, such children were poorer in use of time (Shaw & Brown (1999) and Rubia and Smith 2001 & 2004.)

- **ADHD, distraction and medication**: Tested for the effects of interval duration, distraction, and stimulant medication on the reproductions of temporal durations in children with ADHD, control subjects were significantly more accurate than ADHD children who were significantly less accurate when distracted. Both groups became less accurate with increasing durations to be reproduced. The result of preliminary studies support the prediction that sense of time is impaired in children with ADHD and does not seem to improve with administration of stimulant medication (Barkley, et al, 1997)
- **ADHD and discrimination threshold**: Children with ADHD were significantly impaired in their time discrimination threshold: on average, time intervals had to be 50 ms longer for the hyperactive children in order to be discriminated when compared with controls. Children with ADHD also responded earlier on a 12-second reproduction task, which however only approached significance after controlling for IQ and short-term memory. No group differences were found for the 5-second time reproduction or verbal time estimation tasks. The findings suggest that children with ADHD may have a perceptual deficit of time discrimination, which may only be detectable in brief durations which differ by several hundred milliseconds. A temporal perception deficit in the range of milliseconds in ADHD may impact upon other functions such as perceptual language skills and motor timing (Smith, et al 2002).
- **ADHD, time estimate and time reproduction:** In a study that compared Hispanic children with combined type and inattentive type attention deficit hyperactivity disorder and a control group on time-estimation tasks. The ADHD groups did not differ in time estimation from the control group. Findings suggest that ADHD is associated with a specific impairment in the capacity to reproduce rather than estimate time durations and that this may be related to the children's deficits in inhibition and working memory (Bauermeister, et al 2005).
- **Developmental Dyslexia and cerebellum:** a time estimation task considered to be a sensitive index of cerebellar function was administered to matched groups of dyslexic and control children. They showed the predicted deficit on time estimation (among the most severe obtained in the research programme) but not on a control task (Nicolson, Fawcett & Dean 1995). Others, namely Ramus, Pidgeon & Frith (2003) found no evidence for the involvement of the cerebellum in time estimation in Dyslexia.
- **Neuroanatomical sites:** Structural and functional neuroimaging findings suggest a dysfunction in fronto-striatal-thalamo-cortical and fronto-cerebellar circuitries as the neural correlate of the disorder (Rubia & Smith, 2001).
- **Inclusion in a performance test battery:** the potential is regarded as unique and is recommended (McCauley, Kennedy & Bittner 1980)
- **Depression:** Among the depressive symptoms, only psychomotor retardation was correlated with the time estimation scores (Kitamura & Kumar 1983). Severely depressed patients over-estimated time when left completely unoccupied or when attending to tasks requiring concentration. Those in remission, but exhibiting signs of psychomotor retardation, selectively over-estimated time when required to concentrate under time pressure. Anxiety disordered patients with an intermediate level of subjective depression and almost normal psychomotor functioning did not over-estimate any of these intervals (Munzell et al 1988)
- **Parkinson's Disease and levodopa:** Patients with PD underestimated the duration of a time interval in the verbal time estimation task. Patients with more severe PD performed worse on the time estimation tasks compared with those with milder disease. Administration of levodopa-carbidopa

(205/25 mg, p.o.) significantly reduced absolute errors in time estimation and reproduction in conditions where time markers were presented at the two faster rates of 5 Hz and 3.3 Hz. Performance in these two latter tests best discriminated patients and controls and had a positive significant association with simple reaction time and movement time. These results lead us to suggest that time estimation is abnormally slow in PD (Pastor et al 1992). L-Dopa administration in PD patients may counteract the slower rate of the internal clock typically reported in non-medicated patients, without restoring all of the memory functions (Pouthas & Perbal 2004). Dopaminergic treatment improves time perception in PD (Rao et al 2001).

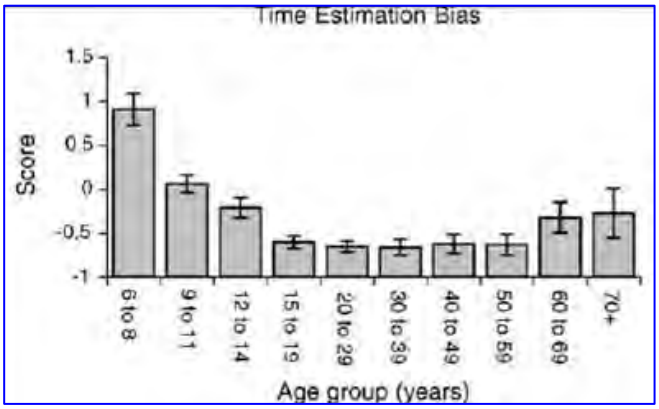
- **Parkinson's disease and short intervals:** are deficient in estimating time intervals in the range of seconds, more severe when subjects are requested to count internally during the demanded intervals, and when the rate of internal counting is fast. This study examined PD patients' processing of short durations (1 sec) and long durations (up to 48 sec). The patients were impaired at discriminating between short intervals. This deficit was independent of task difficulty and appeared to be based on a impairment of divided attention. They estimated time intervals up to 48 s as accurately as the controls. The authors suggest that time estimation, is normal in PD patients despite impaired discrimination of brief intervals in the range of seconds (Riesen & Schnider 2001).
- **Alzheimer's disease and short intervals:** This study investigated the estimation of short temporal intervals in Alzheimer's disease. Results indicated that AD patients show deficits both in the accuracy and precision of time judgments. It is concluded that the estimation of short temporal intervals could be useful as an objective indicator of cognitive decline in AD (Carrasco, Guillem & Redolat 2000).
- **Alzheimer's disease and Executive function:** The authors studied prospective time verbal estimation in AD matched normal controls in two different conditions: during a digit span task and during an attentional task. Results showed that the performance of AD patients was significantly worse than, suggesting a role of attentional-executive functions in time estimation (Papagno, Allegra & Cardaci 2004).
- **Gender and expectancy:** The authors found that males pressed the button more accurately than females. Time estimation performance was affected by gender and expectancy-related motor responses (Dolu et al 2004)
- **Aging and levodopa:** Aged participants show duration-dependent timing errors that are larger than those shown by the young participants. Levodopa administration yielded lengthened time production of both target intervals. The aging and levodopa effects did not interact. Also, aging slowed reaction time (RT) and increased RT variability, but levodopa had no effect on the RT. These results suggest that at this dosage and under these specific conditions, timing is dopamine-mediated but the effect of aging is not. The levodopa timing effect cannot be attributed to the effects of dopaminergic function on psychomotor speed (Rakitin, et al 2006).
- **Age and subjective experience across spectrum:** This study aimed to develop and validate a neuropsychological tool to study time perception with aging. Participants (15-90yrs) had to verbally estimate intervals signaled by auditory beeps, of 7-, 32-, and 58-s duration. Results showed a correlation between estimation and age suggested a faster "internal-clock" in the older participants. However, this finding lost significance when controlled for literacy. The results corroborate the hypothesis of a change in subjective time perception with aging. It was not possible to conclude if this effect was a specific result of aging or biased by the interference of literacy (Coelho et al 2004).

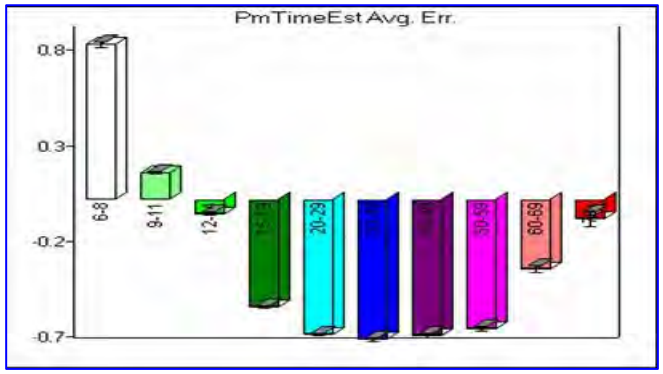
- **Age and stroke:** Another study of 256 subjects (20 to 80 yrs). Among the elderly, a group of patients with cerebral atherosclerosis and a group of apparently healthy persons were selected. The study also involved 48 patients with remaining manifestations of right- and left-sided stroke. The unoccupied time interval and the interval occupied with performance of verbal tasks were estimated. In both cases, interval durations were 45 s. There was an underestimation of the unoccupied interval in the young group and it was overestimated by the elderly group. With the performance of verbal tasks, the age differences were insignificant. Occupied interval vs. unoccupied interval was underestimated to a greater degree. No sex differences were noted. Time estimation in cerebral atherosclerosis without focal disturbances was analogous to the pattern being observed in aging. In left-sided stroke, underestimation of time and estimation accuracy exceeded similar indices in other groups. The relationship was established of the subjective time estimation with non-verbal intellect and several characteristics of brain asymmetry, but not with handedness (Polyukhov 1989)
- **Impulsive adults:** Increasing the number of task alternatives in a match-to-sample problem led to longer decision times in cognitively reflective but not in cognitively impulsive adults. 'Impulsives', as compared to 'reflectives', were found to verbalize less "thinking out loud" coded verbal behaviour, to endorse less motivation for success and more motivation for speed, and to consistently underestimate time (i.e., periods of 10, 20, & 60 seconds). There is a latency-related response inhibition deficit in cognitively impulsive adults (Kendall et al, 1980).
- **Aging and dual task:** Changes in time estimation with aging are related to different cognitive deficits depending on the conditions under which temporal estimations are collected, best explained in older adults by working memory limitations (Pouthas & Perbal 2004).
- **Borderline Personality Disorder:** Patients with BPD performed similarly to controls with orbitobasal frontal lesions in that both had a faster perception of time than healthy comparisons (Berlin, Rolls & Iverson 2005) also (Berlin, Rolls and Kischka, 2004).
- **Temporal lobe lesions (right antero-medial):** Patients with either left or right antero-medial-temporal lobe (MTL) resection were investigated. Patients with right MTL lesions underestimated all three durations, compared with controls and with patients with left MTL resection (Perbal, et al, 2001)
- **Temporal lobe and the WADA:** Patients with unilateral temporal lobe epilepsy either left or right were evaluated against controls following Wada administration and were asked to estimate how much time had passed since administration. Elapsed time was significantly underestimated by both left and right TLE groups following right hemisphere injection. Left TLE patients, consistent with normal controls, made more accurate time estimates when they could anticipate the estimation task following the second amobarbital administration. More accurate time estimates, however, occurred only when left hemisphere injection was second in sequence. Right TLE patients did not improve regardless of the order of injection. Right hemisphere function thus plays a critical role in the accuracy of time estimations of intermediate temporal duration. Inter-hemispheric interaction may be required to make accurate retrospective temporal judgments (Drane et al, 1999). Right temporal lesions systematically underestimate durations resulting from a distorted representation of those time units in long-term memory (Pouthas & Perbal 2004).

- **fMRI and primary time keeper:** This research investigated the fMRI measured brain response and tested for the presence of brain activity reflecting a primary time keeper function, distinct from the brain systems involved either in conscious strategies to monitor time or attentional resource and other cognitive processes to accomplish the task. Results revealed lateral cerebellar and inferior temporal lobe activation were associated with primary time keeping. Behavioral data provided evidence that the procedures for the explicit time judgements did not occur automatically and utilized controlled processes. Activation sites provided indications of the other structures involved in time estimation that implemented task components related to controlled processing. The data are consistent with prior proposals that the cerebellum is a repository of codes for time processing, but also implicate temporal lobe structures for this type of time estimation task (Tracy et al, 2000). Regions of the prefrontal cortex behave as the accumulator (working memory) for an internal clock model, only with durations of more than several seconds (Rubia & Smith 2004).
- **ERP's and timekeeper:** Two event-related potential studies were conducted to investigate timing accuracy, which was shown to be similar for all three target durations. As revealed by current-source density analysis, slow-wave components during both presentation and reproduction were independent of target duration. The present findings support the notion of a general timing mechanism irrespective of interval duration as proposed by scalar timing theory and pacemaker-counter models of time estimation (Gibbons & Rammsayer 2004).
- **Prefrontal cortex:** fMRI and Pet studies have confirmed the predominant role of the prefrontal cortex in cognitive time management. Patients with lesions of the right or left frontal brain regions are impaired in their ability to estimate temporal durations of milliseconds, seconds and minutes (Casini & Ivry 1999; Rubia et al 1997) which may also relate to frontal-striatal dopaminergic connections (Rao et al 2004).
- **Right dorsolateral prefrontal cortex and right inferior parietal lobe:** are critical for time estimation deficits of several seconds (Harrington et al 1998; Kagerer et al 2002).
- **Frontal areas and Korsakoff's:** Findings suggest that both working memory and episodic memory play an individual role in temporal cognition. Turnover within a short-term working memory buffer provides a metric for temporal decisions. The depleted working memory that typically attends frontal dysfunction may result in quicker turnover, and this may inflate subjective sense of time duration. On the other hand, temporal estimation beyond 30 s requires episodic remembering, and this puts Korsakoff patients at a disadvantage (Mimera, Kinsbourne & O'Connor 2000).
- **Supplementary motor area and anterior cingulate:** The ACG may assist the SMA in longer estimation tasks as well (Rubia & Smith 2004).
- **Cerebellum:** the lateral portions and the vermis appear to play a central role in temporal perception especially in times of less than a second (Rubia & Smith 2004) at around 100's of milliseconds (Jueptner et al 1995). Rao et al 2001 did not find compelling evidence for the cerbellar role in encoding time intervals, but was involved in time estimation, but in the vermis, rather than the lateral portions, so damage here will slow sensory acquisition.
- **Basal Ganglia:** lesions in the right supralenticular white matter, namely fronto-striatal fibres, have been observed to be involved in impaired time estimation of several seconds. Left and right putamen and left globus pallidus and caudate nucleus are also activated (Rao et al 1997; 2001). Mostly it's the caudate and putamen involved in time estimation tasks such

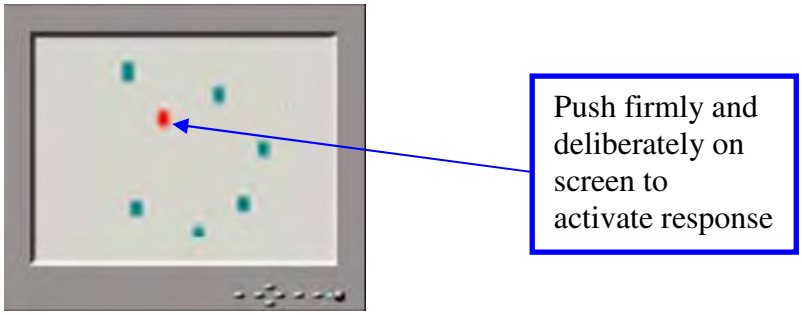
as this, and in millisecond tasks, hence the deficits in Parkinson's Disease. The BG are vital in formulating representations of time, with activation in the right putamen and caudate uniquely associated with encoding time intervals (Rao et al 2001). BG are involved in time estimations from hundredths of milliseconds to tens of seconds (300ms-20sec: Rao et al 2001).

- **Parietal Lobes:** especially in time estimation tasks (Harrington et al 1998) and could be related to sustained attention to time (Ortuno et al 2002).
- **Severe TBI:** Duration judgments are more variable than in normal controls, a very robust finding, higher in frontal patients, related to problems with general attention, working memory and processing speed problems (Pouthas & Perbal 2004).
- **Marijuana:** Perception of time is impaired in normal healthy males after smoking one cigarette (Vachon, Sulkowski & Rich 1974).
- **Reduced body temperature:** There is a positive relationship between oral temperature and speed of internal clock (Baddeley 1966).
- **Cortisol infusion:** slows the internal clock, changing time perception (Kopell et al, 1970)
- **Summary:** Predominantly right hemispheric dorsolateral and inferior prefrontal cortices, anterior cingulate, the SMA, basal ganglia and the lateral cerebellar hemispheres and mostly the cerebellar vermis appear to be involved in time estimation (Rubia & Smith 2004). The basal ganglia are involved across the 300ms-20sec time estimation spectrum, and dopaminergic modulation of the fronto-striatal pathways is critical.





4. Span of Visual Memory (Attention and working memory)

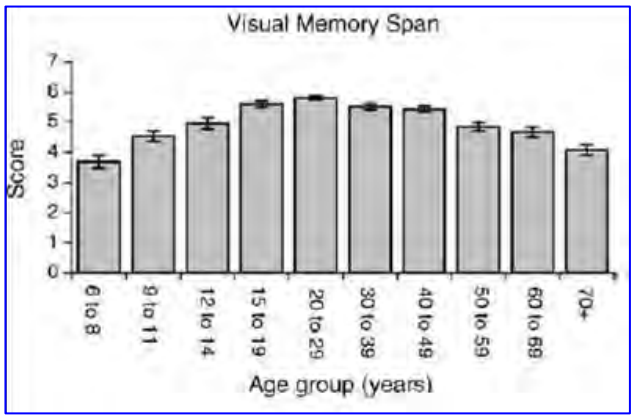


What is the test? The test assesses the aspects of working memory including the capacity to hold and sequence visuospatial information in short- term memory. Mean span capacity increased incrementally and linearly with age, and no gender difference was observed. The increase in performance with advancing age supports the notion that spatial immediate memory capacity increases with maturation throughout childhood. Comparisons indicated that the span capacity of eighth graders (M = 6.9) was not statistically different from that of the young adults (M = 7.1), suggesting an upper developmental plateau for spatial span in early adolescence (Pagulayan et al, 2006). Path length increases with sequence length to avoid the Corsi Block/Dot Location Tests' confounding sequence length and path length.

Test procedure: 9 asymmetrically positioned squares light up on the screen in a pseudo random sequence. Four seconds later, the subject hears a tone indicating they have to reproduce the order in which the squares previously were lit, by touching on each square in sequence order, with only one attempt per trial. Sequence length varies between two and nine, with two trials for each length. The test terminates after two failures of the same length, or when all 18 trials are complete. The dependent variable is the longest sequence length correctly completed (on either of the two trials per sequence length).

What areas of function are measured by such tests?

- **Williams Syndrome:** Spatial memory span is impaired compared to closely matched control subjects, secondary to spatial working memory problems (Pléh, Lukács & Racsmány 2003, and others by these authors)
- **Aging:** The visual working memory span changes with age, independent of processing speed (Beigneux, Plaie & Isingrini 2006).
- **Children with Bipolar Disorder:** were found to be impaired on such measures of spatial memory span (Dickstein et al 2004).
- **Huntington's disease:** Visual memory span is impaired, but not forward digit span or WCST (Brown et al 2001).
- **Schizophrenia and premorbid adjustment:** Scores on visual memory span were reduced in those with poor premorbid adjustment (Levitt et al 1996).
- **Lateralisation of lesion:** 20% of the patients perform in the borderline range on this task, and over 8% have an impaired performance ("retarded"). Right hemisphere patients performed worse than left hemisphere patients. These tests can be effectively used to assess visual memory span in patients with brain damage, and are selective for the side of the lesion (Kessels et al 2000).
- **OCD:** Significant deficits in visual memory span were identified in the patients with OCD compared to normal controls (Zitterl et al 2001).



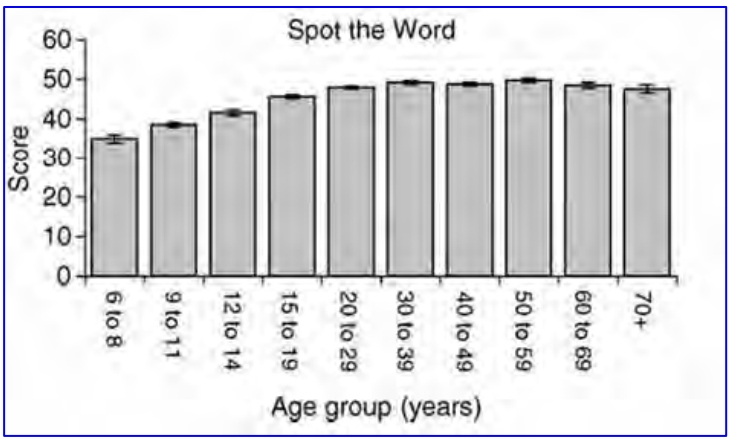
5. Spot-the-Real-Word (Language, estimate of intellectual capacity)

What is this test? This task resembles in some ways the Spot the Real Word Vocabulary intelligence test (Baddeley et al 1993). The total correct score can be entered into a regression formula that factors education and age to render an estimated IQ for those 16 and older (Sullivan, Senior & Hennessy 2000). In this way we have correlated our version (using either Spot the Word or Spot the Real Word as alternative names) against the WAIS III FSIQ (Hermens et al 2005a; Paul et al 2005), and found a significant convergence of shared covariance, namely *r*=.76: other versions correlate against the WAIS III VIQ only.

Test Procedure: Participants are presented with two words simultaneously and side by side on the screen. One of the two words is a valid word in the English language and the second is a non-word foil. Participants are required to identify which of the two words is a real word by touching that word as quickly as possible. The ordering of the words is pseudorandomised over trials. The test has the advantage that no verbal response is required. The total correct score is the dependent measure, namely the number of words correctly selected.

What areas of function are measured by such tests?

- **Anxiety:** Such tests are thought to be resistant to brain anxiety.
- **Brain Injury:** Such tests are thought to be resistant to brain injury.
- **In Aging:** Although thought to correlate well with verbal intelligence scores, this is disappointingly tenuous at best in the elderly (Morris et al 2000). Clark et al (2006) produced a fairly consistent finding with very little decline over age, peaking at 30-39, but then stable, as is IQ:



- **Dementia:** The test is also sensitive to early mild dementia because it should not decline with normal aging (Beardsall & Huppert 1997).
- **Neural components on EEG:** A higher score is associated with lower parietal amplitude of Go No-Go ERP P300 components and greater frontal amplitude of the Oddball Target N200 component.
- **Psychophysiology and EEG:** A better Choose the Word score is associated with a higher task heart rate, lower HR variability in an emotion task, and less SCRs in oddball.
- **MRI:** In our laboratories, the test correlates fairly positively with cingulate size, and very positively with frontal size. More gray matter is associated with higher spot the word variability of reaction times.

6. Digit Span: Forward *(immediate memory recall) and Reverse Span (simple mental tracking)*

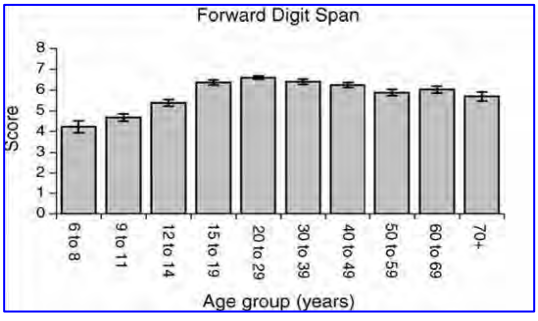
What is this test? The test is a classic as used in IQ tests from the original Stanford-Binet to the Wechsler's, but this version, as with Point Digit Span, does not require auditory capacity or verbal response. The test measures immediate verbal recall, and the forward and reverse formats comprise testing of two separate modalities, hence are affected differently when the brain is compromised. Most normal subjects have forward spans in the 5-8 digit range, and the correlation with other cognitive measures is not robust. It is not really a memory test, and is better correlated with attentional factors, such as freedom from distractibility, a measure of the efficiency of the attentional system. With such tests, practice effects are statistically significant, but of no real consequence, with test-retest reliability good,

but variable with age. The spread of difference between the easier digits forward task the harder reverse task ranges between none, and two. Across the decades, digit span average scores have increased, with education and healthier aging populations, with both spans declining marginally until 70 or so, and then more sharply as verbal working memory declines.

Test Procedure: Participants are presented with a series of digits flashed on the computer screen, separated by a one second interval. The subject is asked to enter the digits immediately in the same order as presented, by pressing on the touch pad that appears. There is then a delay of 5 seconds until the next trial. The test has two parts, and in the **first** part of the test, subjects are required to recall the digits in same order as they were given. In the **second** part, they are required to recall them in the reverse order. In each part, the number of digits in each sequence is gradually increased from 3 to 9, with two trials of the same length at each level. The test terminates when both trials of a single length are failed. The dependent measure for each part is the maximum number of digits the subject recalled without error.

What areas of function do tests such as this measure?

- **In Aging:** Although similar as attentional tests, the two parts, forward and reverse digits remain stably correlated until the seventh or eighth decade of life, but there is some evidence that the reverse span is more sensitive to aging effects while the forward span is minimally affected, although there is some gradual decline from 20-70, and then a sharper trajectory of decline. In our own study (Clark et al 2004) based on 550 normal subjects aged between 11 and 70 years in the Brain Resource International Database, forward and reverse digit span were found to be lower in older, relative to younger age groups. Spontaneous alpha peak frequency slowed with age and more so at anterior than posterior sites.
- **EEG and aging:** Frontal alpha peak frequency was found to be a significant predictor of reverse digit span, with each 1 Hz increase in frequency associated with a 0.21 increase in reverse digit span score and this was independent of age, indicating a positive relationship between alpha peak frequency and working memory performance. Bopp and Verhaeghen (2005) found similarly that simple span, backward span and then mental tracking were loaded in terms of increasing size and age effects. In this way, a slowing in rehearsal capacity in working memory can explain the small changes from ages 20-70, and the steeper decline after 65-70 results from slower motor planning and execution, perceptual degradation, deficient executive control associated with rehearsal and recall, related to more posterior rather than prefrontal decline. See Clark et al (2006), graph below, on our testing.



- **In Brain Injury:** With some forms of acquired brain injury, this relationship between forward and reverse span changes and the forward and reverse

spans are dissociated. Initially after concussions or brain surgery, the span may shrink, but over time does seem to recover.

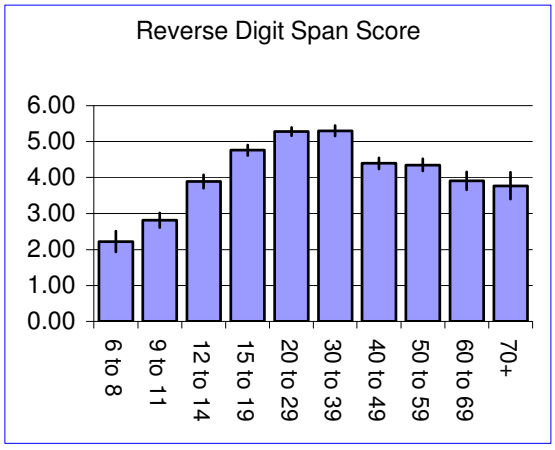
- **Time of day:** Patients do better in the morning than the afternoon (according to reports cited in Franzen 2000) but other studies appear to show that younger adults improve across the day, but older adults decline (see Hasher et al 2005).
- **In Solvent Exposure:** Long-term exposure to solvents may also affect the span.
- **In Dementia:** Although retained in early dementia, shrinkage of a normal forward and reverse span in a healthy individual to below average while dementing is a sign of impending death in the next year or so.
- **IQ, Education, and Culture:** The test is poorly correlated with overall IQ, and affected by education levels, and by culture. In the verbal-auditory versions, Chinese do better than English Americans, since Chinese words for numbers are shorter, but these advantages disappear with our nonverbal format (Hedden et al 2002). Interestingly, older Chinese have no advantage over older Americans on the reverse order task.
- **In Delirium:** The test is sensitive to delirium.
- **Neural substrates:** Patients with lesions in the left hemisphere tend to do poorly on both subtests, but patients with right hemisphere lesions perform poorly only on the reverse subtest (Weinberg et al 1972). Franzen (2000) pointed out the need for the physiological substrates of these tests to be specified. Recently (2000), Mueller and colleagues from the University of Michigan have worked on a computational model, and present data that indicate Digit Span correlates positively with resting metabolism in posterior brain regions, but not in the prefrontal cortex. Their data indicate that the task does not involve simple storage, but rather that it requires complex cognitive rehearsal and recall. This suggests that Baddeley's phonological loop does not work like a 2-second tape recorder, but flexible executive processes manage operation of the loop, and executive processes for performing the task are implemented in the left posterior parietal lobe, not the prefrontal cortex. Stuss and Levine (2002) found similarly that the process is dependent on executive functions, but not necessarily the frontal cortex.
- **In COPD:** Digit span can only marginally distinguish those with COPD from other groups (Incalzi et al 1997).
- **Cocaine abuse:** Prolonged cocaine abuse is correlated with digit span performance (Ardila, Rosselli & Strumwasser 1991).
- **In Schizophrenia:** In Schizophrenia, digit span scores are lower, but there is no differential between forward and reversed, not in a meta-analysis in any event (Aleman et al 1999).
- **In ADHD chromosome research:** In researching the endophenotype in ADHD, Digit Span scores are not sensitive enough for some researchers, who prefer the Go,No-Go tasks below which are reliable and valid for their purposes (Kuntsi et al 2005).
- **In Malingering:** Very low forward scores in otherwise alert individuals are considering sentinel signs of less than honest presentations, as forward span is fairly robust.
- **EEG:** Earlier N200 targets equate with a longer forward digit span.

With regard to the reverse digit span task (not on WebNeuro):

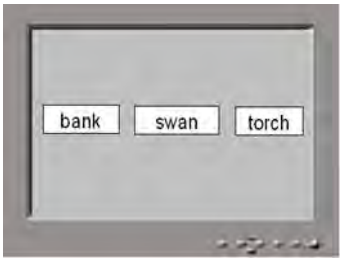
- **Concrete and confused patients:** patients who are extremely concrete or confused may not understand the instruction to reverse the digits by saying the last number first.

- **Mental Tracking:** Compared to the more passive forward span, the holding of information in the brain and the reversal of it before replying on screen requires a more active form of attention, in the realm of mental tracking, in that the memory task and reversing tasks are simultaneous, namely double mental tracking.
- **Impact of visual field deficits:** Patients with visual field deficits do worse on this task as well, suggesting in factor studies that both visual and verbal capacities are utilised in the reverse task, and supporting the role of the visuospatial posterior areas.
- **In Solvent Exposure:** This test is very sensitive to the type of damage that follows prolonged solvent exposure
- **In Dementia:** The test is sensitive to the dementing processes
- **Wernicke's:** The test is robust in the face of Wernicke's encephalopathy
- **Anticholinergic medication:** Thienhaus et al (1990) found that anticholinergic side effects of some medication could also have some (although minimal impact) on the reverse span, mimicking aging, as one would expect.
- **In Ischemia:** Our switching of attention task below may be more sensitive to small vessel ischemic leukoaraiosis than reverse span testing (O'Sullivan et al 2005)
- **Depressed elderly:** Depressed elderly patients have difficulties with the reverse, but not forward span; they are also slower (O'Brien et al 2004).
- **Aging:** Clark et al (2006) using our database found as follows: A peak occurs in the 20-39 year age group, followed by a steady decline in the 40-59 age group, worse after 50+
- **MRI:** More right parietal gray matter predicts longer reverse digit span

Reverse Digit Span by age N=1007



7. Memory Recall and Recognition - Verbal List-learning, immediate recall, and delayed recall and recognition; executive function:



What is the test? The loading of this task is at the *time* of learning, to make possible an association between a to-be-remembered-item and its context: later, this association must be retrieved (Stark & Squire 2000). Several models of recognition memory have proposed that recognition judgements involve a deliberate retrieval of specific trace information as well as an assessment of item familiarity (Madden et al 1999). The test may be useful in determining material-specific deficits in recognition memory as distinct from effortful recall memory, and these deficits may be related to laterality of lesion. Recognition memory for individual items deteriorates in lists that have more items, hence our choice of 24 words in the recognition task (Ratcliff, Clark & Shiffrin 1990). However, in recognition memory there is no effect of the amount of study, so four trials is sufficient. There is a curvilinear relationship between the number of items in the memory list and the time to make the judgement if the word was part of the original list, but only in lists up to 20 items, hence our choice again of 12 for the recall word list, and 24 for the recognition task (Briggs 1974; Burrows & Okada 1975). Glanzer & Adams (1990) described a mirror effect, namely that the more accurately a target is recognised the more accurately the foils are rejected. Consequently we have controlled for concreteness, number of letters and frequency following Shiffrin, Huber and Marinelli (1995) and others. The timing of presentation is based on Baddeley's concept of the phonological loop, namely that the amount of words that the subject can hold in rehearsal is equivalent to the amount that can be rehearse-processed in two seconds (Baddeley 1986). With regard to the underlying neurological processes that we are currently gathering data about, it is clear that words are better remembered than images, both in the long and short term, but the underlying neuronal processes are comparable (Doty & Savakis 1997).

Test Procedure: There are several parts to this test. In the first part the subject is warned to attend to, and then say back in any order what is then presented binaurally by headphone, namely a list of 12 words, one second at a time (Learning trial 1). The procedure is repeated three further times, with the same 12 words (four trials in all). Words are closely matched on concreteness, number of letters and frequency (see Clark et al 2006, pg 452 for details). Their answers are recorded through a microphone into '.wav' files. The subject is then presented with a second list of 12 distracter words (foils) and asked to recall that list. None of the words in the distracter list are phonetically or semantically related to the first list. After this distraction, the subject is asked immediately to recall the 12 words from the original list. By now about 6 minutes have elapsed. About 25 minutes later, the subject is asked to again recall the 12 words from the original list. The total number of words recorded across the four trials is recorded during scoring. The test assesses the effortful declarative recall of the subject.

In the second part of the test* the subject's **recognition** of the previously presented words is tested. The subject is presented with a series of 24 words on the screen in fixed, pseudorandom order, half of which appeared in the original list, half of which are novel, and asked to respond by touching "Yes" or "No" on the screen to indicate whether the word was included in the original list of twelve.

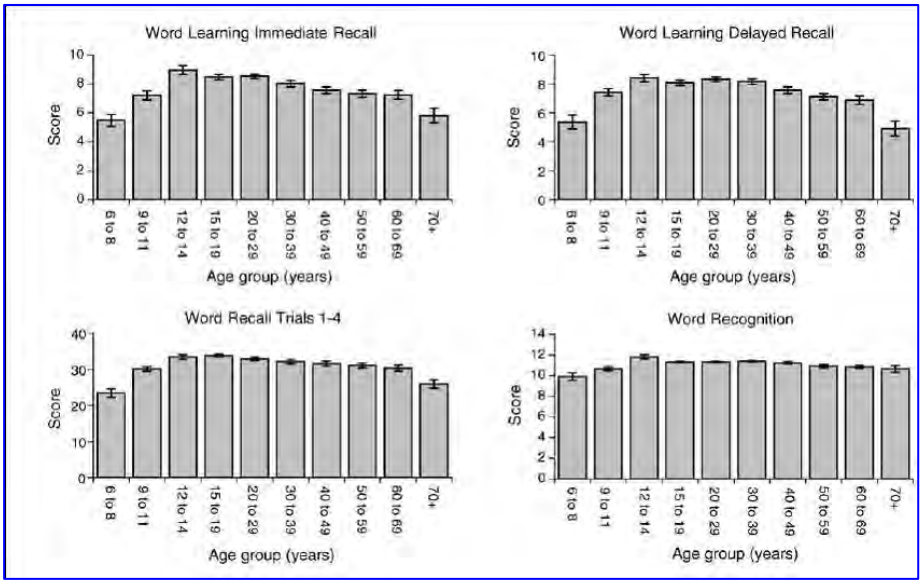
All words are concrete words between four and seven words in length. Executive function is measured by the number of words incorrectly recalled in trials 1-4 (intrusions) and the number of repeats of correctly recalled words during trials 1-4 (repeats) taken as indices of self-monitoring failures.

What areas of function are measured by such recognition tests?

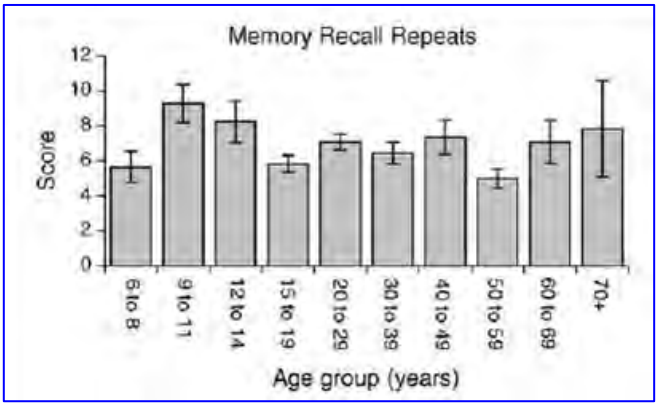
- **In brain injury:** In these populations, such tests may be correlated with duration of amnesia, rather than the GCS (Kelly, Johnson and Govern, 1996).
- **Malingering:** The forced choice methodology might be useful in the evaluation of patients with negative response bias (e.g. Iverson & Franzen 1994, 1998; Millis 1992).
- **Neural pathways:** Some researchers have found that activation of the left inferior parietal area is associated with recollection, but deactivation of the left anterior medial-temporal area is associated with familiarity, and the intraparietal and prefrontal areas respond in detecting the target word (Henson et al 2005). In patients with unilateral temporal white matter abnormalities, ERP studies demonstrate no activity on either verbal or visual recognition memory tasks, whereas in healthy patients, bilateral activation is present on both tasks (Puce et al 1991). Andreasen (1995) and her colleagues found during PET investigation a much wider activation during such tasks. Kim (1999), a member of Andreasen's PET group, showed that the activation sites in word recognition tended to be lateralised to the left hemisphere, distributed as small loci, with particular loading in the left middle and inferior temporal gyri. Kavcic and colleagues (2003) using fMRI found that passive viewing produced small, lateralized islands of activation depending on the nature of the material, but activation became more bilateral when an effort to remember was made. Retrieval activity shifted laterality in quite a major way, so the nature of the to-be-remembered words is clearly a major factor in accord with the asymmetrical lateralization in their basic representation. Buckner (2003) took this further: he showed that there is a posterior-to-anterior gradient within the prefrontal cortex, with posterior regions participating in domain-specific processes (verbal-visual), and more anterior-prefrontal regions participating in less domain-specific, high-level control tasks. Frontal-polar regions participate in maintaining context-appropriate mental sets during recognition and remembering. This may explain age-related changes in the recruitment of frontal regions that then change the capacity for recognition memory by changing the way the brain approaches the task. This work is supported by the findings of Casasanto et al (2002), using fMRI to evaluate verbal encoding and recognition tasks: Neocortical activations associated with later successful and unsuccessful recognition memory were found to differ in magnitude and hemispheric laterality. Performance-related activation during encoding showed both neocortical and medial temporal activation. Clearly, not all studies show hippocampal-temporal activation. Stark and Squire (2000b) took up this issue. They reported robust hippocampal activity for targets relative to foils-distracters when single words were used, with activation left-lateral for words,

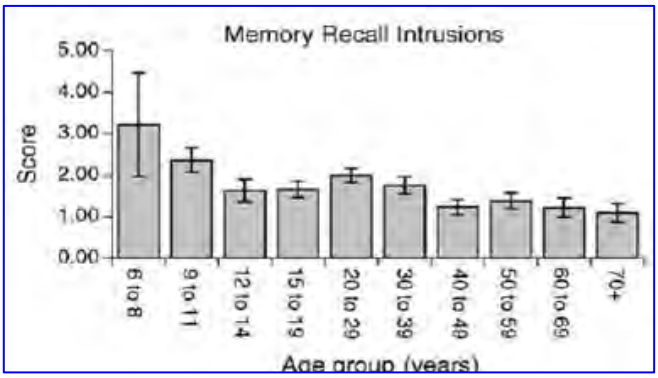
and bilateral for objects, as suggested before, elsewhere, observed at two separate MRI facilities. Opposed to Casasanto's later work in prefrontal areas, they found recollective success was not consistently localised to either the more anterior or posterior hippocampus. The failure of other studies to image hippocampal activity thus relates to the size of the area and its proximity to the sinus cavity, and secondly, as in our test, the activity around encoding the foils masks the difference in activity around target words and foils. This is because the mesial temporal lobes are automatically activated when unfamiliar words appear, and so the problems are operational. It can be thus said with some assertion that the test lateralizes quite reliably, and that there is a frontal gradient during exposure, encoding, and later recognition/differentiation from foils. If the foils are familiar, this effect decreases, hence our control of the foils in our test, and we did not need to use cross-modal or visual items in our test (Stark and Squire 2000b). At the same time, Grunwald et al (1999) were showing that hippocampal glutamate (NMDA) receptors in the hippocampus were involved in this process, as Eric Kandel had shown, and for which he was awarded a Nobel Prize in 2000. This led Wais and colleagues (2006) to show that the hippocampus supports two aspects of recognition memory: namely recognition and a sense of familiarity. Baddeley et al (2001) had in fact shown similarly in a single patient with lifetime amnesia that the recollective process is not necessary for either recognition or for acquisition of such tasks. Kuchinke et al (2006) have shown different areas of activation depending on the emotional valence of the words used, enhancing the idea of modality.

- **Benzodiazepines:** Munte et al (1996) have shown that benzodiazepines can impair recognition memory functioning.
- **In Stroke:** In stroke, a left thalamic infarct in a patient led to selective verbal memory impairment, implicating the thalamus as well as the cortex generally (Schott et al 2003).
- **In Aging:** In aging populations, Madden et al (1999b) have shown that older adults recruit additional neural systems compared to younger adults, reflecting a more continual allocation of attention to support task performance in both encoding and retrieval in verbal recognition memory tasks. Recall tasks are more sensitive than recognition tasks.
  However: on our tests, Clark et al (2006) found very little age effect on effortful recall until age 61+, after which the falloff is pronounced:



- **Alcoholism vs. Polysubstance abuse:** In alcoholics contrasted with polysubstance abusers, there are differences on free recall, but not on recognition, typically reflecting on subcortical dysfunction (Bondi et al 1998) and the loading of effortful memory in recall tasks.
- **OCD:** The position in OCD is similar (Savage et al 1996) to that of subcortical dysfunction, reflecting on the feedback loops involved (see Carlson 2000) in Obsessive Compulsive Disorder.
- **Schizophrenia:** The above localisations don't hold true in Schizophrenia. Despite having intact performance in word recognition, patients in remission, on fMRI scanning, have less activation of the right dorsolateral and anterior prefrontal cortex, right anterior cingulate, and left lateral temporal cortex during word encoding compared with healthy matched controls. During word recognition, impairments in activation of the bilateral dorsolateral prefrontal and lateral temporal cortices (Hofer et al 2003a) appear. The same authors, using un-medicated subjects during an acute episode, found intact recognition again, but reduced activation of the anterior prefrontal, posterior cingulate and retrosplenial areas relative to controls during encoding and during recognition, as well as reduced activation in dorsolateral prefrontal and limbic/paralimbic regions. On the other hand, higher metabolism in the bilateral anterior prefrontal cortices was then noted (Hofer et al 2003b) perhaps related to increase effort or loss of frontal efficiency and underlying gray matter.
- **MRI:** More limbic gray matter equates with less recall intrusions, in keeping with the cognitive reserve hypothesis.





*Notes on delayed memory recognition task

What areas of functioning do tests such as this measure?

- **Parkinson's Disease:** patients with Parkinson's Disease were worse than controls on delayed recognition memory (Stebbins et al 1999). Higginson et al (2005) found that this problem was related to prefrontal dysfunction, not a retrieval deficit.
- **Geriatric Schizophrenia:** In geriatric patients with schizophrenia, a more subcortical pattern of forgetting collapsed any difference between recognition memory and recall memory: the older the patient, the worse this effect (Putnam & Harvey 1999) and findings are similar in schizophrenia (Myung-Sun et al 2004). However, in subjects who smoke, recognition memory is better than average for schizophrenia patients (Myers et al 2004) indicating some role for nicotinic receptors.
- **In Aging:** The data on delayed recognition provide evidence of intact rapid and impaired delayed recognition memory in aging. Alternations in frontal cortical control of posterior and limbic regions may contribute to the memory changes observed in aging (Nielsen-Bohlman & Knight 1995).
- **Effects of cholinesterase inhibitors:** Cholinesterase inhibiters improve delayed recognition memory in those with Alzheimer's relative to those who are medication naïve (Crowell et al 2006).
- **Underlying glutamate/acetylcholine physiology:** With regard to long-term potentiation and recognition memory, both kainate and NMDA play separate roles in the underlying plasticity of the perirhinal area (Barker et al 2006). Turchi et al (2005), in collaboration with Mortimer Mishkin, have shown in an animal model that cholinergic activation of the rhinal area was essential for storage, and thus delayed recognition.
- **Normal children vs. Down's Syndrome Children:** Using toddler subjects, normal infants showed superior recognition memory compared to toddlers with Down Syndrome (Miranda & Fantz 1974).

8. Verbal Interference *(Part 1: Attention and working memory; Part 2: executive function)*

What is this test? As a measure of cognitive flexibility, in its many variations since 1935, the Stroop task existed for years as a measure of the human capacity to suppress an over-learned response in favour of a novel task. It accomplished this by moving from an everyday task (reading aloud the names of three colours printed in black), to a second everyday task (naming the colours of the ink X's printed on a sheet), to a novel third task which requires the subject suppress the pull to read the name of the colour as in the first task, but rather *naming the colour of the ink* in which the contrasting name of the colour was printed (as in the second part). This meant saying "blue" to the word "red" printed in blue ink and so on. Research showed that

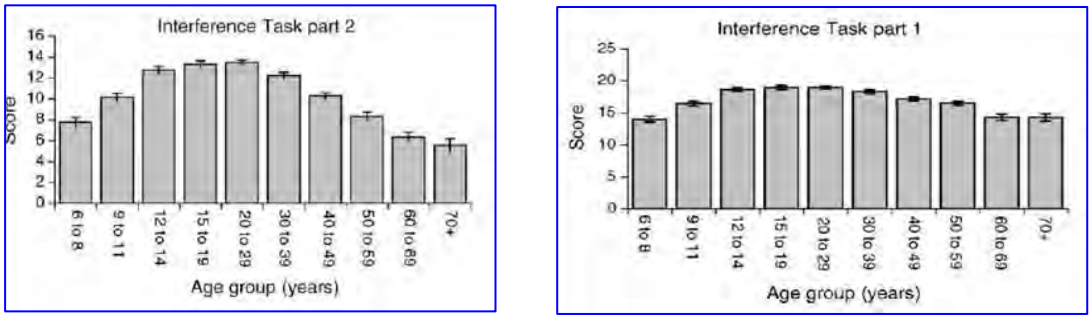
just using the last of the three sheets was sufficient, and jumbling the order made no difference (Taylor 1998). In any event the test demand is commonly thought of as obeying a visual demand while fending off conflicting demands that are typically over-learned in English readers (other languages mean less conflict for the reader). This makes it a test of concentration effectiveness more than anything else, hence its enduring appeal in neuropsychology.

Test Procedure: In our test the subject is presented with four coloured words, one at a time. Each word is drawn from the following set of four colours: red, yellow, green and blue. Below each coloured word is a response pad with the four possible names of the colours displayed in black and in fixed format. Our test has two, not three parts. **In part 1**, the subject is required to read the name of each coloured word as quickly as possible and touch on the appropriate matching tab. **In part 2**, the subject is required to name the contrasting colour of the ink in which the word is printed, as quickly as possible and click on the appropriate tab. Each of the two parts lasts for 1 minute. Responses are made on the screen by pressing on the appropriate word on the bottom screen tab. The dependent variable in each part is the number of words correctly matched with the name of the colour in part one, and the colour of the ink in which the word is printed in part two. Care should be taken in younger pre-teen children to emphasise the test instructions, or they do not easily notice the switch from colour naming to the interference task.

What areas of functioning do such tests measure?

- **Age and IQ:** The test is sensitive to both age and intellectual level.
- **In Aging:** Aging adults present with slowing of colour naming in part one, and with an increase in the colour-word interference effect provided in part two. There is an emerging consensus that the effect in aging is due to generalised slowing (e.g. Verhaeghen and Meersman 1998), rather than a specific loss of prefrontal capacity: however these findings are challenged by real-time correlation with frontal activation changes as measured by EEG during the interference phase of the test. Slowing may thus affect the colour naming first part, but frontal activation correlates with the interference effect of part two. In any event, age over 50 suggests caution against false positive determinations, taken care of by our norms. Peaks occur at 15-29 in our database, suggesting interactions with cortical maturity and myelination.

Interference scores N=1007



- **Anaesthesia and sentinel events:** Sentinel life events such as anaesthesia may contribute to slower performances, mimicking aging effects (Houx et al 1993 & Dijkstra et al., 1999).
- **Neural substrates in aging:** An fMRI study by Milham et al (2002) found areas subserving attentional processes in the dorsolateral prefrontal and parietal cortices. This suggests possible impairments in the implementation of attentional control in older participants. Older participants exhibited more extensive activation of ventral visual processing regions (i.e. temporal cortex) and anterior inferior prefrontal cortices, reflecting a decreased ability to inhibit the processing of conflicting information. Also, the anterior cingulate cortex, involved in evaluatory processes at the level of response showed age-related increases in its sensitivity to the presence of competing colour information. In a recent, large study, Van Der Elst et al (2006) found that the *time* to complete a subtest rather than the *accuracy* measures were affected by the demographic variables of age and education, in addition to the main effects of the demographic variables. This suggests that executive function declines with age and that the decline is more pronounced in people with a low level of education. This is consistent with the reserve hypothesis of brain aging. With regard to the 'slowness' controversy, Troyer at al (2006) have found that increased interference effects with age is **not** accounted for by simple cognitive slowing and more likely reflects other cognitive changes, such as decreased response inhibition. Amieva et al (2004), in studying 7 reviews of patients with Alzheimer's, found similarly that the deficits on this task were not purely related to slowing, and more related with the putative interference effect.
- **Neural Substrates:** A PET study by Pardo et al (1990) found the most robust responses to the test were in the anterior cingulate cortex, supporting data that implicate this area in the selection and recruitment of the processing areas in attention, namely the left premotor cortex, left postcentral cortex, left putamen, supplementary motor cortex, right superior temporal gyrus, and bilateral peristriate cortices.
- **White matter disease:** Jokinen et al (2005) found correlations between white matter intensities on MRI and the test results. O'Sullivan et al (2004) found correlations with executive dysfunction and diffuse tensor-imaging MRI correlates; the test correlated well with measures of leukoaraiosis.
- **Gender effects and aging:** The Van Der Elst et al (2006) study did not confirm that females may be quicker, but if the test situation doesn't arouse anxiety, men do the same or perhaps a little better than women. However, in the older aged, over 85, women are significantly faster than men (van Exel et al 2001).
- **Laterality of lesion:** Patients with left hemisphere lesions take approximately twice as long as controls on some versions of the test, but left and right hemisphere damaged patients perform similarly on both trials.
- **Closed Head Injury:** Overall, the effect of closed head injury is measured some months after seeming recovery. Local research points to a factor of generalised slowing in CHI (Ponsford and Kinsella 1992), but this again, as with aging, may be an over-simplification.
- **Test-retest Reliability:** Test retest reliabilities are in the .70-.90 in various studies, and about 89% of normals and 85% of brain- injured patients are correctly diagnosed. Older adults demonstrate the same practice effects as younger adults.
- **In Discriminating ADHD in adults from depressives:** In its various forms, the Stroop tests have not had good discriminatory capacity in ADHD adults and those with attentional problems in depression, or

- **Alzheimer's versus Frontotemporal Dementia**: In its various forms, the Stroop tests have not had good discriminatory capacity between Alzheimer's versus Frontotemporal Dementia
- **Discriminating Normals from others:** Local research shows the test can discriminate between normals, those with Schizophrenia, Huntington's and Parkinson's disease, and in these populations, the test correlated well with executive function measures (Hanes et al, 1996) but didn't discriminate the groups from each other, which is understandable. The test may be related to frontal circulation and prefrontal function in younger people, so the construct being measured may change from cohort to cohort.
- **Effect of Culture:** In African-Americans, women may be faster than men.
- **In Small Vessel Disease:** Prins et al (2005) found that slowing in small vessel disease as assessed by lesion on MRI affected scores in information processing speed in the elderly (60-90y, over 5-6years of assessment).
- **Use of the test as a stressor:** Šiška (2002) shows data on the use of such tests as stressors in research on heart rate variability, subjects showing evident changes in the autonomic modulation of heart rate (predominance of sympathetic activity over parasympathetic), making the test useful in psychophysiological medicine. Hayashi et al (2006) showed that the computerised version causes vasoconstriction in visceral arteries, with the implication that it induces differential blood flow and vascular responses in visceral arteries.
- **Correlation with Homocysteine levels:** Interestingly, such tests are highly correlated with homocysteine levels in the cognitively normal, healthy, elderly, with interference scores worsening as homocysteine levels rise over a short period of time. Elevated blood levels of homocysteine have been associated with cerebrovascular disease and cognitive impairment, so the test is an important marker for risk of cerebrovascular disease (Garcia et al 2004). High homocysteine level in turn is an independent marker for poor memory in the elderly both cross-sectionally and longitudinally.
- **In CADASIL:** Nurk (2005) and Peters et al (2005) found significant correlations between patients with CADASIL, with accelerating scores when timing the colour naming and interference performances, as well as the time for Part B of the Trails Test (see switching of attention below), when comparing healthy subjects, those with mild impairment and those with severe impairment.
- **In Hypoglycaemia:** Dantz et al (2002) found that hypoglycaemia measures were correlated with the number of correct responses, which could be attenuated with vascular endothelial growth factor.
- **In cardiac catheterisation:** Lund et al (2005) used the test to show cognitive falloff after left heart transradial artery catheterisation, after microembolic damage.
- **MRI/EEG:** In our laboratory, there is moderate activation of total gray, cingulate, frontal, temporal and amygdala areas, as well as milder activation of occipital, parietal and hippocampal areas. There is fairly weak delta activity and stronger theta activity over the parietal-occipital areas, predominantly right-sided, and some posterior alpha activity, stronger on the right again. Alpha peak in the same areas is noted, with some more left-sided theta/beta activity in the left posterior mostly.

9. Word Generation (Language: letter fluency, verbal fluency)

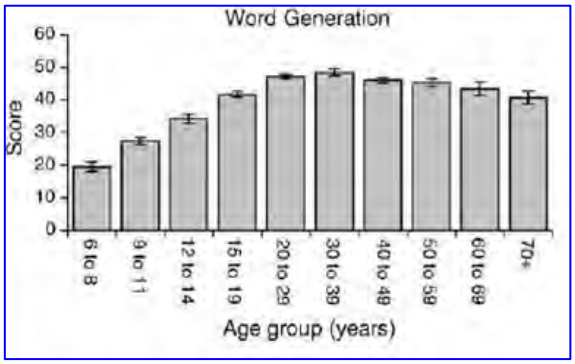
What is the test? The test involves being presented with a stimulus letter of the alphabet, and then saying as many words as one can in the space of one minute. Originally designed by Arthur L Benton and referred to as the Controlled Oral Word Association Test, (COWAT), the capacity to generate words to the prompt of F, A and S, or alternatively C, F, and L is believed to indicate the capacity to search verbal lexicons and fluently produce words in a category. A wide variety of syndromes are assessed by this task (Bruggemans et al 1997). FAS and CFL are equivalent (Lacey et al 1996), and most normal people produce more words in the beginning of the test (Crowe 1998). It is the standard for verbal fluency evaluations.

Test procedure: A letter of the alphabet is flashed on the screen, and the subject has to say out loud words that begin with each of F, A and S in that order, with a minute for each trial respectively. Verbal production is recorded in '.wav' files as before. The dependent variable is the number of words produced across the three trials in total.

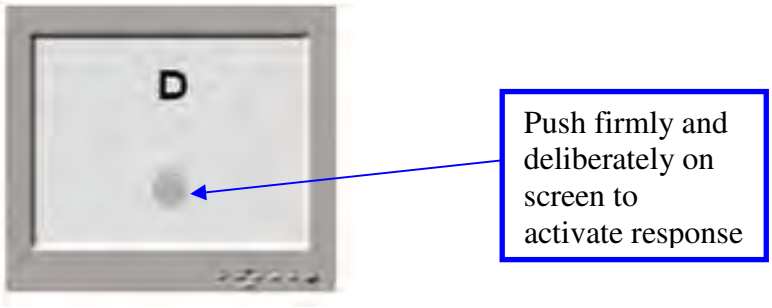
What areas of function are measured by such tests?

- **Depression**: decreases scores and adds to the variability (Veiel 1997)
- **OCD**: Patients with poor verbal fluency also had high mean obsession scores compared to those without verbal fluency problems (Fontenelle et al 2001).
- **Fluoxetine non-responders**: Non-responders to Prozac tend to have worse FAS scores (Barclay & Lie 2006) related to psychomotor speed as well as low scores on the Verbal Interference task.
- **Alzheimers vs Parkinson's**: AD patients are worse than PD on FAS but not on animal categories (Fama et al 1998).
- **Alzheimer's Disease vs normals, Huntington's and Parkinson's**: AD sufferers give largely nouns, normal aging include verbs and adjectives too, (Suhr & Jones 1998) found no difference between HD, PD, AD and normals. 67% of AD show preference for categories over FAS fluency (Sherman & Massman 1999)
- **Advanced Parkinson's Disease**: verbal fluency is impaired together with list learning and Verbal Interference Test Vingerhoets et al 2003).
- **Site of lesions**: Relationship of scores on test may be to site of lesion. Superior medial frontal lesions are correlated with poorer performance on the COWAT, less clear in animal category (Stuss et al 1998)
- **Laterality**: performance is apparently not sensitive to laterality (Loring et al 1994)
- **Testosterone supplementation in Klinefelter Sydrome**: a history of testosterone supplement appeared to be correlated with higher verbal fluency scores (Patwardhan 2000).

- **Executive function:** without using integrative neuroscience, the test relates better to EF with more categories given to perform on (Hanes et al 1996)
- **Frontal functioning:** Baldo & Shimamura 1998 reported frontal patients impaired on both forms CFL and FAS suggesting that the frontal lobes have more general role in fluency overall, and the premotor cortex shows up on fMRI on Brodmann areas 44 and 6 (Condon et al 1997)
- **Education vs Age:** FAS is more sensitive to education than age (Franzen 2000).
- **Mild TBI:** In mTBI, subjects produce fewer words on both FAS and Animal Naming, and more errors of perseveration and out of category names (Cohen et al 1999).
- **Severe TBI:** Correlations between conventional measures of executive function (e.g. verbal fluency) and WAIS-III were of comparable magnitude to the correlations between new, ecologically valid executive tests and WAIS-III (Wood & Liossi 2007).
- **Aging:** In our laboratories, peaks occur after a gradual increase in numbers of words until 20-29, stable till about 70, whereafter it declines gradually.
- **Independence in ADL's in aged:** verbal fluency performance and Trail Making Test performance made significant independent contributions to the prediction of independent activities of daily living as reported by a caregiver (Stuss et al 2002).
- **Schizotypal Personality Disorder:** No deficits were found by Diforio et al 2000.
- **Anesthesia:** up to 60 minutes after propofol-based anaesthesia, deficits in verbal fluency are still seen (Munte et al 2001).
- **fMRI:** A relationship between the pixel count and the total number of words was found for the left, but not right hemisphere. In the left middle frontal region, pixels correlated significantly with the second, but not the first, 30-s fluency epoch. By contrast, the first epoch, but not the second, correlated significantly with the pixel count within the left inferior frontal region. This suggests differential involvement of dorsolateral and ventrolateral prefrontal cortex (Wood et al, 2001).



10. Continuous Performance task (Sustained Attention and visual working memory)



What is this test? CPTs are tools that yield valuable and unique information, easily integrated into a wide range of assessments and treatment monitoring (O'Laughlin and Murphy 2000). Computerized Continuous Performance Tasks (CPTs) are becoming increasingly popular as an additional source of information regarding the ability to maintain attention and inhibit impulsive responding over time. **Omission errors** are defined as a failure to respond to target stimuli and thus reflect inattention whereas **commission errors** are responses to non-target stimuli and are thought to reflect impulsive tendencies. Three of the primary criticisms of the use of CPTs in the diagnosis of ADHD involve (1) ecological validity (2) a high rate of false negatives, and (3) the limited ability of CPTs to discriminate between ADHD and other clinical disorders (O'Laughlin & Murphy 2000). The presence of an examiner can result in higher than average performance for children who respond well to the attention and reinforcement provided by a set of 'surrogate frontal lobes". The novelty and attractiveness of a computer-based task may also result in performance that is an overestimation of the child's typical ability to maintain attention, hence the WebNeuro application which may exclude an examiner being present. The essence of the task is to be boring, so retesting may be more valuable in that regard as a true indicator. BRC have taken this into account, and have matched scores on this CPT with a host of psycho-physiological and neuroradiological data to scaffold the ecological validity. Without such convergent data, various versions of CPTs have yielded false negative rates from 20% to 37% or worse (Greenberg, 1993; Barkley, 1991). As noted above, the ability of these tests to be repeatedly used in a single subject to assist in monitoring medication dose effectiveness may be particularly useful given the findings from the NIMH multi-modal treatment study (Pelham, 1999) that note the need to repeatedly test to examine the optimal stimulant medication dosage in ameliorating ADHD symptoms.

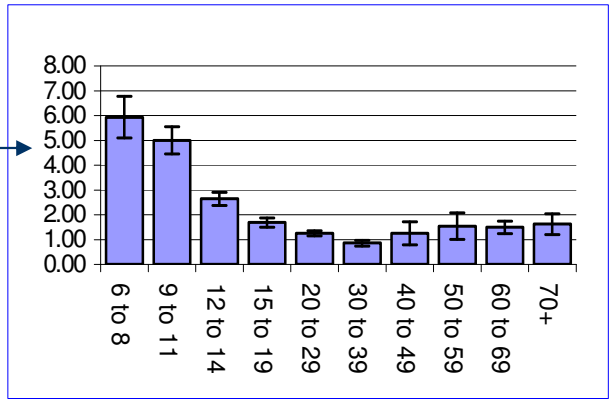
Test Procedure: To tap sustained attention on our task, a series of similar looking letters (B, C, D or G) are presented to the subject on the computer screen (for 200ms), separated by an interval of 2.5 seconds. If the same letter appears twice in a row, the subject is required to press the response button on the screen. Speed and accuracy of response are equally stressed in the task instructions. There are 125 stimuli presented in total, 85 being non-target letters and 20 being target letters (i.e. repetitions of the previous letter). The dependent variables are reaction time, and the number of false positive responses, and the number of false misses.

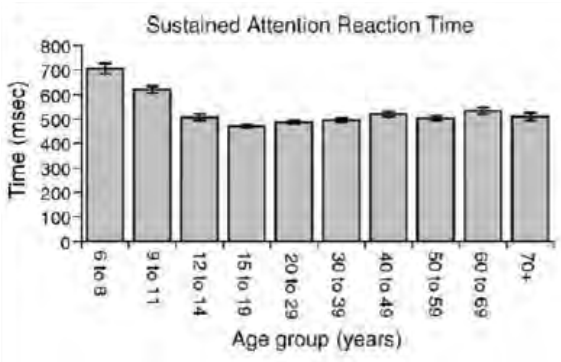
NB: Make the instruction clear: Watch for CONSECUTIVE presentation of the same letter, so A….B….C….B….C….C (TAP)!

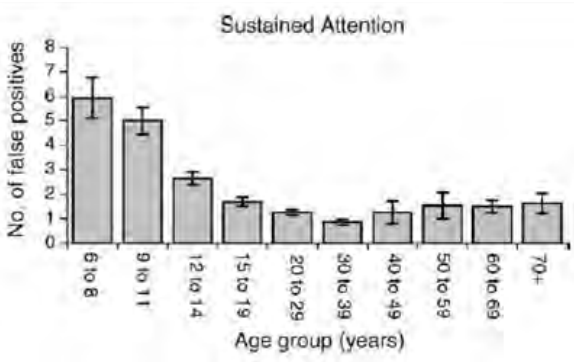
What areas of functioning do such tests measure?

- **Children with ADHD:** CPT omission and commission variables have been found to discriminate between children with ADHD and normal controls (Losier, McGrath & Klein 1996). In summary, the deficits noted in ADHD appear to revolve around inefficient allocation of attentional resources (Gualtieri & Johnson 2006).
- **In Traumatic Brain Injury:** Naito et al (2005) found that traumatic brain injury also resulted in the same pattern of omission errors emerging. In mild traumatic brain injury, in the presence of the Dopamine D2 T-allele influences CPT errors (McAllister et al 2005). Gale et al (2005) found correlations between gray matter concentrations and CPT performance after TBI.
- **False negatives in high IQ:** Those with high IQ's may manage the task despite their attentional problems.
- **Underlying neuronal pathways:** By 1998, SPECT, PET and fMRI studies proposed the existence of a distributed large-scale attentional network, mediated by the dorsolateral prefrontal and mesial frontal cortex, thalamus, basal ganglia and posterior parietal and superior temporal lobes (Hager et al 1998).
- **Correlation with maternal anxiety in-utero:** Recent studies on in-utero stresses have however contributed to a growing body of evidence that performance into adolescence may correlate with maternal anxiety during pregnancy (12^{th}-22^{nd} week: van den Bergh et al 2004).
- **Aging:** Mani et al (2005) found that increasing age in adults resulted in more commission errors, and the test is sensitive to aging, more so than other tests such as the Stroop (Rush et al 2006). Decline in reaction time is however marginal beyond age 39 (Clark et al 2006).

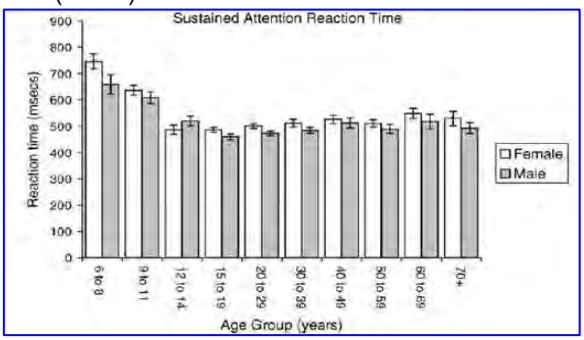
Continuous Performance Task by age: False Positives N=1007





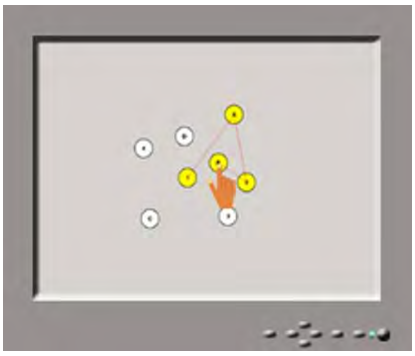


- **Findings in other patient groups:** In adolescents, errors of commission are correlated with other measures of executive control only in patients with a variety of disruptive behaviours (Dougherty et al 2003).
- **Toxins:** Commission errors on a CPT are also highly correlated with *in utero* exposure to PCB (polychlorinated biphenyl) toxins, and since it is connected to PCB exposure, to the size of the corpus callosum, well into the late childhood years (Stewart et al 2005).
- **Effect of stimulants:** Riccio et al (2001) showed that CPT performances are improved by stimulants of any kind.
- **Findings in Adults:** Riccio (2001) found the test sensitive to attentional problems in adults. Li et al (2004) have shown a correlation with noradrenergic modulation during sustained attention in adults.
- **Studies in Mania:** CPT studies in adult mania correlate with prefrontal volumes Sax et al (1999).



- **Gender:** In our study, females made fewer errors but were slower in reaction times overall despite being more accurate (Clark et al 2006). Females peak earlier than males on reaction times, at age 12-14.
- **Education:** Reaction time on this task is covariate with education on our test (Clark et al 2006), but does not reliably differentiate groups (non-linear effect).
- **MRI:** In our laboratory, the test correlates mildly with hippocampal and amygdala size. More frontal grey matter was equated with more variable working memory reaction times
- **EEG:** Earlier P300 Target Latency equated with greater underestimation of time (see above). Later P200 background (and earlier target) equates with faster Working Memory.

11. Switching of attention (Part 1: Attention and working memory; Part 2: Executive function)



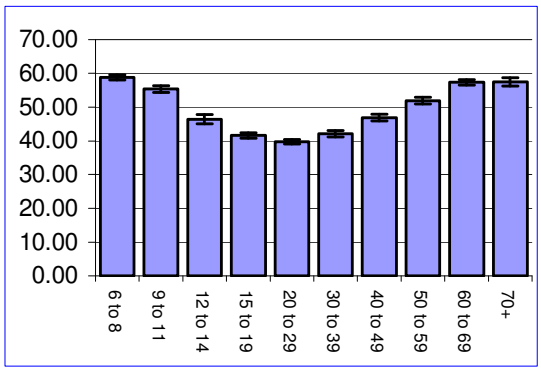
What is this test? One of the most sensitive though non-specific tests in any battery is one that assesses the capacity to switch mental set from one over-learned task to another. We have designed a computerized adaptation similar to the Trail Making Test introduced by Ralph Reitan in 1958, now in the public domain. On the original, the subject would be confronted with Parts A and B, the former with the requirement to join the numbers beginning with 1, using a pencil, and not raising the point off the paper. The demands of the second part change the task, and now requires the subject to begin with a number as before, but change to a letter of the alphabet, then back to the next number in the sequence, then back to the alphabet again in the sequence 1-A-2-B- and so on. The test is thus loaded on complex visual scanning with the motor component of the original removed to a large extent. The motor component was correlated with motor nerve end plate activity, thus outside of the central nervous system (Tarter, Kirisci & Clark, 1997). The computerized formats do not appear to affect the sensitivity (Mercer et al 1997; Paul et al 2005).

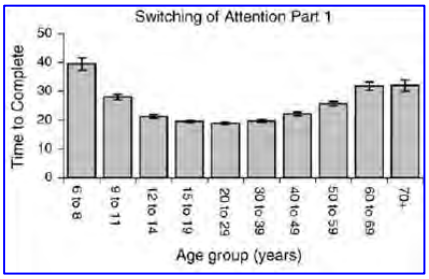
Test Procedure: In Part 1, the subject is presented with a display of 25 numbers and asked to touch the numbers in ascending numerical sequence (1,2,3..) while the computer draws lines connecting the correct numbers as they are touched. The screen will not allow a wrong connection and resets to the last correct number. The dependent variable is the time taken to complete the task. In Part 2, the subjects are presented with a pattern of 13 numbers (1-13) and 12 letters (A-L) on the screen. They are required to press on the number-letters alternatively in a somewhat similar manner as with Part B of the Trail Making Test, in ascending sequence (1-A-2-B and so on). The computer then draws a fine line to connect each number or letter to the preceding number or letter in the sequence. This allows the subject to visualize the path that they have touched. The test has some benefit over the paper and pencil version in that the hand of the test taker is not blocking the view. The dependent variable is time to completion. An erroneous attempt to join, say, 1-B, is met with a "wrong" signal appearing briefly on the screen. This eliminates the problem with the paper and pencil version where the tester has to intervene, introducing a variable that is hard to standardize. The dependent variable is again time to completion.

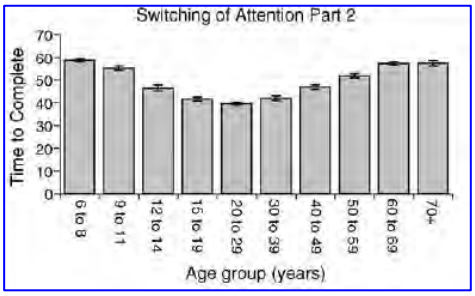
What areas of functioning do such tests measure?

- **In Aging:** Results of studies show a significant decline in performance over each decade of age, but not if the education level of the subjects is high, again showing the value of reserve brain capacity, especially with Part B. In our studies (Clark et al 2006), a peak was noted in the 20-29 age group, with smooth improvements from 6 years on, and then declines from 30 years onward, flattening out in the 60's and 70's.

Aging and switching of attention and mental set
N=1007

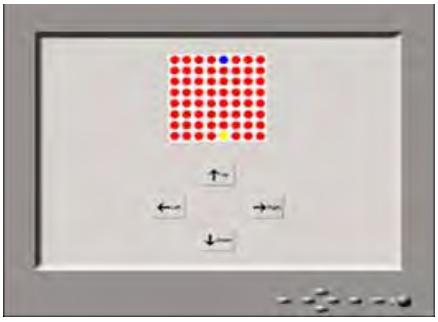






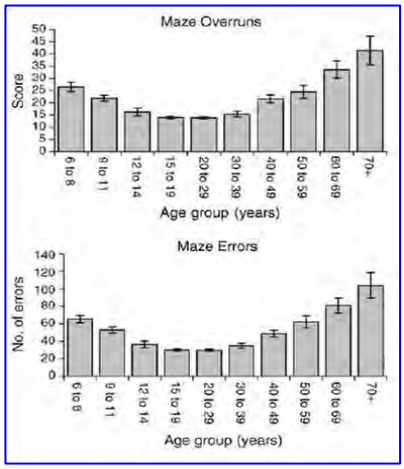
- **In Dementia:** The test is sensitive to dementia, with Part B correlated at 0.80 with caudate atrophy in Huntington's (Starkstein et al 1988).
- **Lateralisation of lesion:** Hundreds of studies have shown that the relationship of Trail Making Part A to B has no cortical lateralising value.
- **Psychological vs. Neurological:** The test is too sensitive to discriminate psychologically from neurologically impaired patients.
- **Hypoxia and COPD:** The test can reliably distinguish controls from patients with mild hypoxia and COPD, being sensitive to arterial oxygen pressure and arterial carbon dioxide pressure (Stuss et al 1997),
- **In Mild TBI:** The test is not sensitive to mild TBI (Cicerone 1997).
- **In Learning Disability:** Young adult learning-disabled patients also show lowered scores.
- **In Aphasia:** Performance on this test is independent of aphasia.
- **Culture:** The test may lose ground with the failure of many schools to teach the English alphabet.
- **Education:** Performance is covariate with years of education (Clark et al 2006).
- **Localizing of lesions:** Because of its sensitivity, the test is unlikely to match to finite areas of the brain. Activation on EEG shows multiple areas of the brain involved.). Poorer performance was associated with smaller cerebral hemisphere volumes and larger volumes of peripheral CSF, lateral ventricles, and third ventricle (Coffey et al 2001), as well as in changes in the healthy elderly (Cook et al 2002).
- **MRI:** In our laboratory, the test correlates fairly strongly with overall gray matter, cingulate, temporal and hippocampal volume, strongly with occipital and parietal volume, and mildly with amygdala volume. More parietal gray matter equates to a higher switching of attention score.

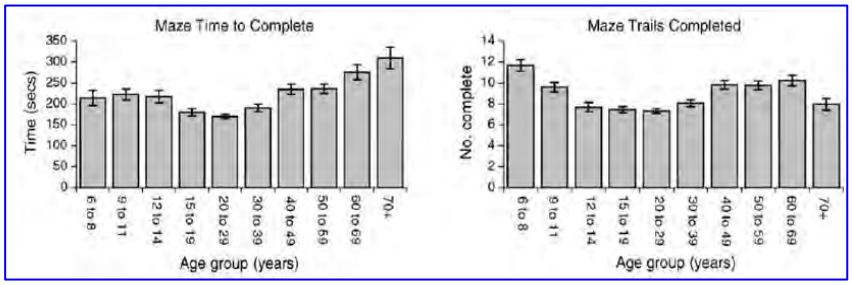
12. Executive Maze *(Learning and memory; executive function)*



What is this test? This task is a computerized adaptation of the 10x10 matrix maze tests such as those created by Porteus (1959), and more closely, by Milner (1970) and others, commonly used by about 54% or more of neuropsychologists (Sullivan and Bowden 1997). Morrison (1988) found that computer versions of the test were equivalent in construct and test demands. The test is used to assess high level mental functions, such as planning, foresight and self-monitoring during the course of learning and remembering a complex pathway through a visuospatial array.

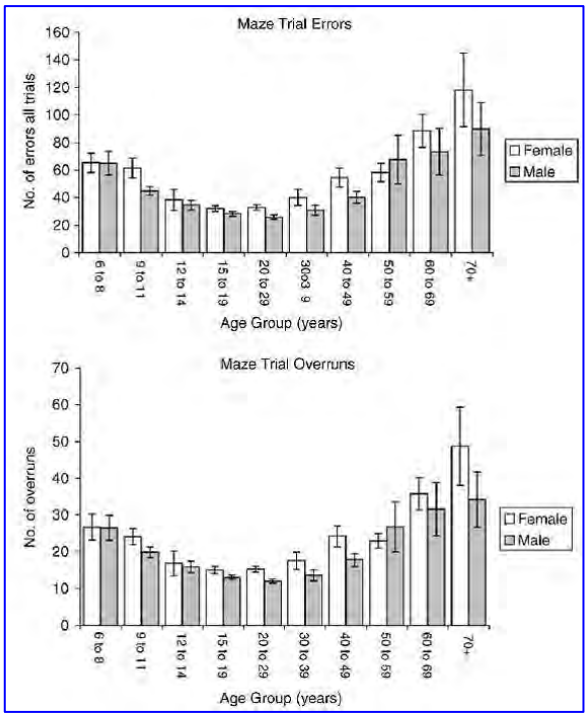
Test Procedure: In our version of an electronic maze, the subject is presented with a grid (8x8 matrix) of circles on the computer screen. The object of the task is to identify the fixed, hidden path through the grid, from the beginning point circle at the bottom of the grid in yellow, to the end point circle at the top in blue. The subject is able to navigate around the grid by touching the arrow keys on the directional button box. A total of 24 consecutive correct moves are required to complete the maze. The subject is presented with an X on the screen and the sound of a tone if they make an incorrect move, and a ✔ and a different tone if they make a correct move. The task measures how quickly the subject learns the route through the maze and their ability to remember that route. Only one maze is presented across trials. The test ends when the subject completes the maze twice without error or after 7 minutes have elapsed, whichever comes first. The dependent variable is total number trials completed, or trials completed until timed out, and the time to finish. Age is a marked covariate in overruns and number of errors (Clark et al 2006). Unlike the original tasks, the subject is unable to make the forbidden diagonal moves. As in the originals, the maze wind its way back and forward, up and down, and has a ceiling effect which further differentiates it from the Austin or Porteus mazes. Executive function is measured by the total number of off-path moves (errors) and the total errors which involve the failure to turn at that point (overruns)





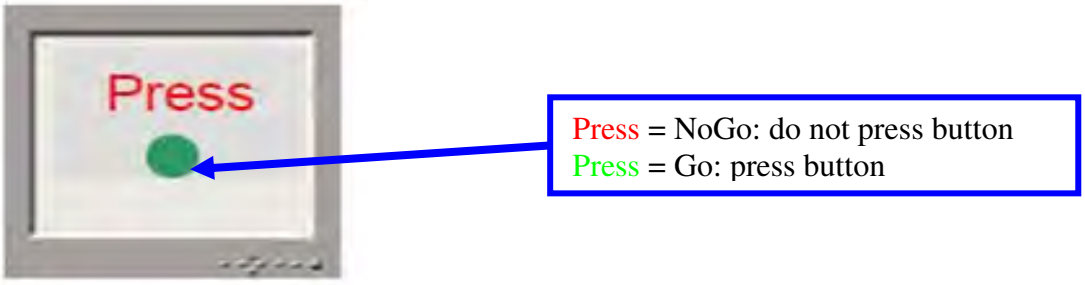
What aspects of functioning do tests such as this measure?

- **Visuospatial:** Crowe et al (1999) found visuospatial and then visuospatial memory skills to be necessary, but not executive function and working memory, in solving the 10x10 version of the Austin maze in the 10-15 trials a normal bright individual would require. However, our more integrated neuroscience evaluations find the executive dimensions as vital, hence the term we use in naming the test.
- **TBI and OCD:** Coetzer et al (2001) found those with TBI did worse than controls, and those with OCD better, but not significantly.
- **Aging:** In our database, peak performance occurs in the 15-29 age group, followed by a gradual decline, and therefore representing, in the teens to young adult group, a parallel with normal cortical maturation and myelination (see bar chart above). Consequently time to complete mazes only improves marginally 6-29, with diminishing errors, and with a clear peak time at 20-29, which then declines steeply. Time to completion in older groups >70 is marred by time-out at 5 minutes. 50-59 years olds perform at the six to eight year old levels. Maze overrun scores are similar in age effects. Overall, Maze overruns and errors, as well as trials completed decline markedly with age
- **Gender effects:** Females make more errors and overruns than males; females however peak earlier in their performance than do males, at 15-19 whereas males peak at 20-29, suggesting earlier maturation in females. There is a moderate effect on time to complete the maze.
- **Education:** Completion time is affected by years of education.
- **MRI:** In our laboratory, the test moderately correlates with total grey matter, cingulate, frontal, occipital, temporal, parietal, hippocampal and amygdala areas equally.



- **EEG:** there is moderate delta and theta activity (strongest over right frontal areas), as well as theta/beta activity, mostly right-sided but including left occipital activity overall.

13. Go, No-Go Task



What is this test? This task measures target detection rate, response time, errors of commission and errors of omission. It is used to assess cognitive inhibition, the capacity for suppressing well-learned, automatic responses. In essence, executive functions require the individual capacity to initiate correct responses, continue with the correct response, suppress incorrect responses (prepotent responses), and change habitual responses when the evidence is that they are incorrect. Luria described this as the verbal regulation of motor activity, using frontal lobe capacity. Response inhibition on this task entails emitting a simple motor response to one cue (PRESS written in green, so press) while inhibiting the response in the presence of another cue (PRESS is written in red, so don't press). Such tests have been effective in demonstrating impulsivity (elevated commission error rates) or inattention (omission error rates) in those with attentional problems (Trommer et al 1988). Trommer et al (1988) found that within the ADD-ADHD group, the non-hyperactive subjects were characterized by a high number of commission errors early, and significant improvement with practice ($p < 0.01$). In contrast, the hyperactive ADD subjects did not differ from control subjects in number of early commission errors, but differed from both control subjects and those without hyperactivity subjects in their failure to improve with practice. In addition, the incidence of omission errors was highest in the ADD/H group. Many studies have found reaction time to be normal, but errors of omission distinguish ADHD from controls and other diagnosis patients (e.g. Rubia et al 2001).

Test Procedure: The colour of the word 'PRESS' is frequently presented in green (Go) and infrequently in red (No Go). The object of the test is to press the button once each time the word PRESS appears. The subject is required to inhibit button-press responses when PRESS appears. **It is important with younger children** to reinforce for them that they should press ONCE for each time PRESS appears, as this may happen rapidly in the beginning, and that the word may repeatedly appear in green, requiring a tap each time.

What areas of function do tests like this measure?

- **Response to stimulant medication:** In children, even small doses of stimulant medication improve their go, no-go performance, and hence these tests monitor their response to such therapy (De Wit et al 2002; Koschack et al 2003; Trommer et al 1988, 1991). There is recent evidence that intermediate target doses may be the most effective, suggesting the need for repeated testing using such tests to determine the efficacy of stimulants in improving cognition in adults (Fillmore et al 2006). The test is thus a

measure of the low extracellular dopamine in such children, and the extent to which stimulants can block the reuptake of dopamine.

- **In Gaba activity:** Dr James Bjork at Texas Medical Centre is currently using a computer version of this test to examine impulsivity, and the neurotransmitter Gamma-Amino-Butyric-Acid.
- **In Bulimia and Anorexia Nervosa:** Rosval et al (2006) have recently found motoric indicators of impulsivity in women with Bulimia or Anorexia Nervosa on such tests.
- **In Alcohol:** Alcohol appears to reduce impulsivity on measures of errors of omission, errors of commission and response time in normals (Ortner et al 2003) but the situation is the reverse in those with low capacity in working memory (Finn et al 1999). The implication is that alcohol reduces the capacity of working memory to modulate response inhibition. The development of this interaction between working memory and inhibition of impulse is regarded as crucial in the underpinning of executive functions in children (Brocki & Bohlin 2004). Across several studies, M.C. Olmstead has found that alcohol is thought not to increase motor impulsivity, as cocaine does. In normal individuals the P300 waveform in the 'Go' condition is larger than in the 'No-Go' condition for this task, similar to results of the "oddball" task described previously. In contrast, subjects who are alcohol dependent do not show any increase in the P300 waveform in the 'Go' condition, and they have lower P300 amplitudes overall (Taber et al 2000). Alcoholics with Cluster-B personality disorders showed poor inhibitory control on a Go, No-Go task (Dom et al 2006) compared to those without the personality problems.
- **In Cannabis:** McDonald et al (2003) found no errors on these tasks in the presence of Cannabis use (see also Director's report to the Drug Advisory Committee, NIDA 2003, USA).
- **In Ecstasy:** In a paper presented at the 9th European Congress of Psychology in 2005 http://www.ugr.es/~jcesar/Manuscritos/Communications/ECP05.pdf Perales and Verdejo demonstrated that stimulant users were significantly worse than opioid users as measured by omission errors, and severity of ecstasy use was significantly correlated with commission errors, the test overall being the most sensitive in discriminating these groups. De Win (2006) had found no changes in low-level ecstasy users.
- **ERP components of optimal attention in children:** Using evoked potentials and a Go, No-go test, Lutsyuk et al (2005) found that optimum characteristics of attention were found in children with high amplitudes of the P2 component, P300 component, and contingent negative variation, low amplitudes of the N2 component, and small values of the latencies of the P1-N1-P2 complex.
- **Site of lesions:** Drewe (1975) found evidence in studies of patients with frontal lobe lesions and a Go, No-Go task that errors are more likely to emerge in those with mesial-frontal lesions.
- **In Endophenotype studies:** Kuntsi et al (2005), looking for reliable and valid measures of individual differences for endophenotype studies in ADHD, found Go, No-Go tasks to be valuable.
- **Genetic factors related to impulsivity:** Heiser et al (2006) have found no genetic factors related to impulsivity in a twin study.
- **Narcissistic Personality Disorder:** Vazire and Funder (2006) have analysed studies using the paradigm and showing high correlations with Narcissistic Personality Disorder (see Alcohol studies above). All of these studies, as well as animal studies in the rat show that distinct aspects of

impulsiveness and hyperactivity can be expressed based on large inter-individual differences that vary from poorly to highly adapted behaviours. Inhibitory deficit is related to a higher response to psychostimulants, a characteristic of rats predisposed to amphetamine self-administration, and related to higher limbic dopaminergic activity. Working memory capacity appears to be only related to level of hyperactivity. This approach allows for the identification of particular individuals presenting distinct behavioural characteristics of impulsive-related psychopathologies (Dellu-Hagedorn 2006). Likewise, there is wide support for such measures in the evaluation of prefrontal inhibition mechanisms and test batteries (e.g. Spinella 2004).

- **Aggression and Executive cognitive functions:** Executive cognitive function is related to aggression and impulsivity on Go, No-Go functioning, but again unrelated to set times or gender (Hoaken et al 2003).
- **Neurofeedback:** Kaiser (2003) found the test useful for monitoring the efficacy of EEG neurofeedback training in adults with ADD.
- **In Compensated Hypothyroidism:** A recent study of children with compensated hypothyroidism found omission errors constant across short-term medication regimes (Aijaz et al 2006).
- **MRI:** In our laboratory, the test correlates mildly with cingulate size.

14. Emotional Recognition Test and Delayed Recall

What is this test? This is test of emotional recognition based on one developed at the University of Pennsylvania. It has been adapted to a Microsoft Windows environment by the Brain Resource Company (BRC). BRC also uses the faces in this test in its MRI and Electrical Brain Function evaluations for its international database. Facial expressions of emotion are increasingly being used in neuroscience as probes for functional imaging and as stimuli for studying hemispheric specialization for face and emotion processing. These photographs of real faces can be administered as a measure of individual differences in facial emotion processing. The emotional expressions data can be used as a standard for comparison with clinical populations. While correct recognition of emotion is usually above chance, it varies significantly across emotions**.** Happiness is the most easily identified facial expression and anger the least. Raw scores and times are provided in the report.

Test Procedure: Subjects are presented with a series of faces with different emotional expressions (fear, disgust, happy, neutral). Subjects are required to press on the prompts on the bars on the screen that correctly identify the emotional valence presented by the face. The dependent variable is the total correct. Delayed

recall test memory for prior targets against foils. Delayed recall shows previously seen faces against foils. Raw scores and times are provided in the report.
NB: Children may not understand "Neutral" in some countries: Explain the term means "No Emotion at all"

What aspects of functioning do tests such as this measure?

- **Problems with 'disgust':** In some studies, there is confusion about the identification of disgust (Gur et al 2002).
- **Aging:** There is some evidence for decline in recognition of negative emotion (anger, sad) with older age (Sullivan & Ruffman 2004). Sullivan and Ruffman (2004) found the elderly were impaired when recognizing anger and sadness, and when judging which of two faces was more angry, sad, or fearful, but they were not impaired when judging other emotions. The elderly were also impaired when matching emotion sounds to angry, sad, and disgusted faces. Overall, the results provide support for an age-related decline in the recognition of some emotions that is independent of changes in perceptual abilities, processing speed, fluid IQ, basic face processing abilities, and reasoning about non-face stimuli. Regions of the brain that are independent from those associated with a more general cognitive decline might mediate recognition of emotion stimuli.
- **Anxiety and Mood disorders:** In anxiety and mood disorders there is a bias to misinterpret the facial expressions of peers as angry (McClure et al 2003) and especially in negative emotions during depressive episodes (George et al 1998).
- **In Schizophrenia:** In Schizophrenia, findings show the condition is associated with general difficulties in emotion recognition, which are in turn associated with general cognitive difficulties. There is some evidence these difficulties are greater for negative emotions (Edwards et al 2002; Sachs et al 2004) and in confusion for fear and disgust (Kohler et al 2003). In the same sufferers, their difficulties increase with the difficulty of the task, and may not be seen in simple forced-choice tasks (Loughland et al 2002). These deficits are also seen in first-episode schizophrenia, suggesting their trait-like nature - particularly for fear and sadness (Edwards et al 2001). In Schizophrenia, affect recognition deficits may lead to more problems in social behaviour (Hooker & Park 2002). However, perception of emotion (POE) in schizophrenia is influenced by ethnicity, and the ethno-cultural mechanisms influencing POE transcend the shared variation of POE and neurocognition (Brekke et al 2005).
- **Temporal Lobe Epilepsy:** In temporal lobe epilepsy impaired emotion recognition (especially for fear) is related to age of seizure and epilepsy onset (Meletti et al 2003).
- **Body Dysmorphism:** Body dysmorphic disorder groups also are prone to misidentify emotional expressions as angry (Buhlmann et al 2004).
- **Turner Sydrome:** In Turner syndrome subjects show impairments in fear recognition (Lawrence et al 2003). Frontotemporal dementia subjects demonstrate impairments in facial emotion recognition but not in facial identity recognition (Keane et al 2002).
- **OCD and Huntington's:** In OCD and Huntington's disease, both are associated with specific impairments in disgust recognition (Sprengelmeyer et al 1996).
- **Paediatric Populations:** Easter et al (2005) have found that paediatric populations with anxiety struggle with adult, but not child facial recognition. Children struggle with the concept, "neutral'. **(TOOLKIT ENDS HERE)**

Principal Components Analysis of General Cognition Factors

Rowe et al 2007, Journal of Integrative Neuroscience (in press)
(This page and p67)

PCA was first undertaken with n=410, and then a confirmatory PCA with n=891. PCA for the first subgroup revealed 7 factors with eigenvalues of 1.0 or greater and which together accounted for 60.1% of the variance in test scores:

1. **Information Processing Speed:** (Includes Verbal Interference (p 49), Switching of Attention (p 57) and Choice Reaction Time (p30)
2. **Verbal Memory:** immediate recall, short and long delay recall and recognition memory from Verbal Memory and Learning (p 45)
3. **Working Memory Capacity:** Forward and Reverse Digit Span (p 41)
4. **Vigilance and Sustained Attention:** Continuous Performance Task (p 54)
5. **Sensorimotor Function:** pauses between taps on Motor Tapping Test (p 28)
6. **Verbal Processing:** Word Generation (p 53)
7. **Executive Function:** Maze (p 60) Visual Interference (p 49) Switching of Attention (p 57)

In addition, the first unrotated component extracted from a PCA was included a general cognitive factor 'g' as a measure of overall cognitive performance. This overall solution accounted for 20.35% of the variance.

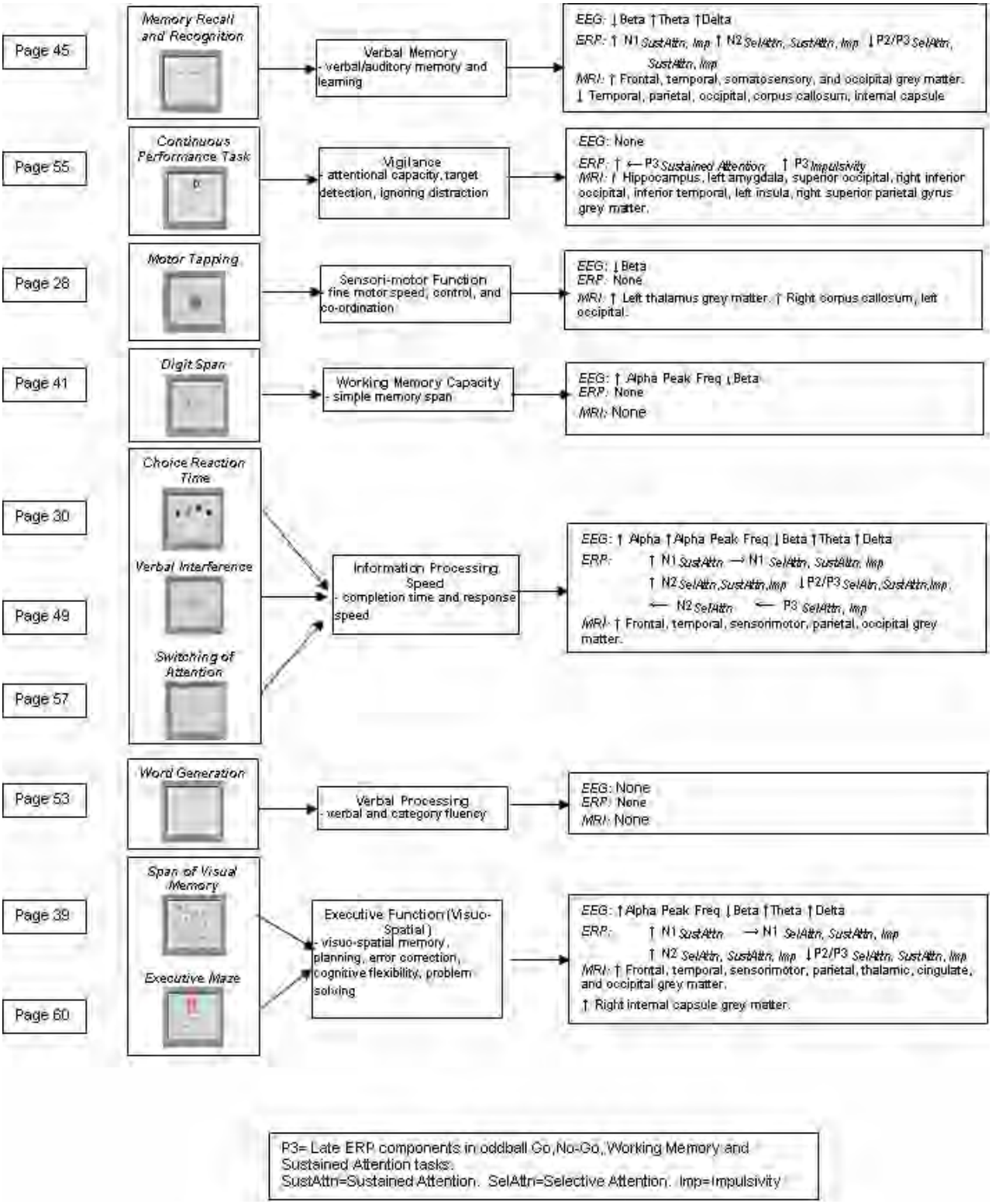
Table 1. Bolded loadings (>0.7) followed by italicized loadings (>0.5) are the highest within a column and were used in the interpretation of the factor identify.

Measure	Information Processing Speed	Verbal Memory	Working Memory Capacity	Vig. & Sustained Attention	Sensori-motor Function	Verbal Processing	Executive Function (vis. spat.)
VI Word Naming Score	*0.68*	0.15	0.04	-0.04	0.00	-0.03	-0.05
VI Color Naming Score	*0.65*	-0.03	-0.10	0.01	-0.05	-0.08	-0.27
SOA: Part 1 Completion Time	*-0.65*	-0.01	-0.16	0.02	0.00	-0.05	-0.03
SOA: Part 2 Completion Time	*-0.59*	-0.12	-0.31	-0.16	-0.04	-0.03	0.11
Choice Reaction Time	-0.49	0.06	0.08	0.41	-0.04	-0.22	-0.01
VML Recognition Accuracy	-0.01	**0.76**	0.07	0.08	-0.02	-0.34	0.03
VML Rejection Accuracy	-0.04	0.44	-0.21	-0.11	-0.04	0.30	-0.03
VML Long Delay Recall	0.12	**0.79**	-0.06	-0.04	0.01	0.12	0.02
VML Total Recall Trials 1-4	0.06	**0.74**	0.05	0.00	0.00	0.16	-0.03
Reverse Digits Trials Correct	0.16	0.05	*0.67*	0.10	-0.10	-0.02	-0.06
Forward Digits Trials Correct	0.10	-0.09	**0.71**	-0.04	-0.08	0.13	0.03
Sustained Attention WM RT	-0.15	0.03	0.19	**0.78**	0.11	0.13	-0.03
Sustained Attention WM Errors	0.26	-0.12	-0.38	*0.64*	-0.02	-0.01	0.11
Dominant Hand Finger Tapping	-0.09	-0.01	0.02	0.04	**0.77**	0.05	-0.02
Nondominant Hand Finger Tapping	0.13	-0.01	-0.15	0.03	**0.73**	-0.05	0.03
Letter Fluency (FAS) Average	-0.01	0.02	0.39	-0.08	0.10	*0.68*	0.04
Animal Category Fluency	0.08	0.10	-0.04	0.18	-0.11	**0.71**	-0.11
SVM Trials Correct	0.02	0.09	0.30	-0.19	0.15	-0.15	-0.47
Maze Completion Time	-0.22	0.06	0.13	-0.02	0.08	-0.01	**0.82**
Maze Overruns	0.07	0.02	0.03	-0.04	0.01	-0.10	**0.91**

* Abbreviations include Switching of Attention (SOA), Verbal Memory and Learning (VML), Working Memory (WM), Span of Visual Memory (SVM), Vigilance (Vig.) and Visual Spatial (vis. spat.).

Cognition-Brain Construct Validity

Tests with Face Validity **Test Factors** **Brain Relationships providing Construct Validity**
(page numbers refer to this manual)



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Note: The references used above are all accessible in mainstream journals, and we have chosen those that have the best relevance for the tests involved. There are countless others, but few of them have been replicated, or are from well-known or peer reviewed journals. Many are out of date, or reflect data from tests foreign to ours in many ways. Where we have used unpublished data, it is from sources known to have a good scientific tradition, such as leading authors or universities with longstanding reputations. There are further references below after the Dr Donald Rowe article (unpublished) for you to pursue (page 87).

That is the end of IntegNeuro testing. Your reports, when generated, will look, to a certain extent, as the case examples below, depending on the application you use.

Remember, this is a brief screening test. Despite the science of reliability and validity behind IntegNeuro, this does not replace a lengthy and complex assessment by a trained Clinical Neuropsychologist.*

If there are any concerns raised by the screening protocol, you should contact your Primary Care Physician/General Practitioner for advice and referral, or contact us at info@brainresource.com

Clinical Neuropsychologist: This is a psychologist who has specialised at the post-graduate level in the role that the brain plays in producing human behaviour. By assessing this behaviour, Clinical Neuropsychologists can tell a great deal about the underlying processing of information in the brain. Most Clinical Psychologists have some knowledge in this area, but not in the professional interpretation and understanding of advanced neuroscience principles necessary for diagnosis and treatment of the sequelae of neurological insult. Some neuropsychologists specialise in the diagnosis and treatment of paediatric conditions, some in the aging adult. Remember, as a consumer, you need to ask questions and find out who is right for you.

For an understanding of the report examples that follow, in following the scoring system which we use, if you are unsure of the values of Z and Standard Scores, or the Standard Normal or Gaussian Distribution, please review:

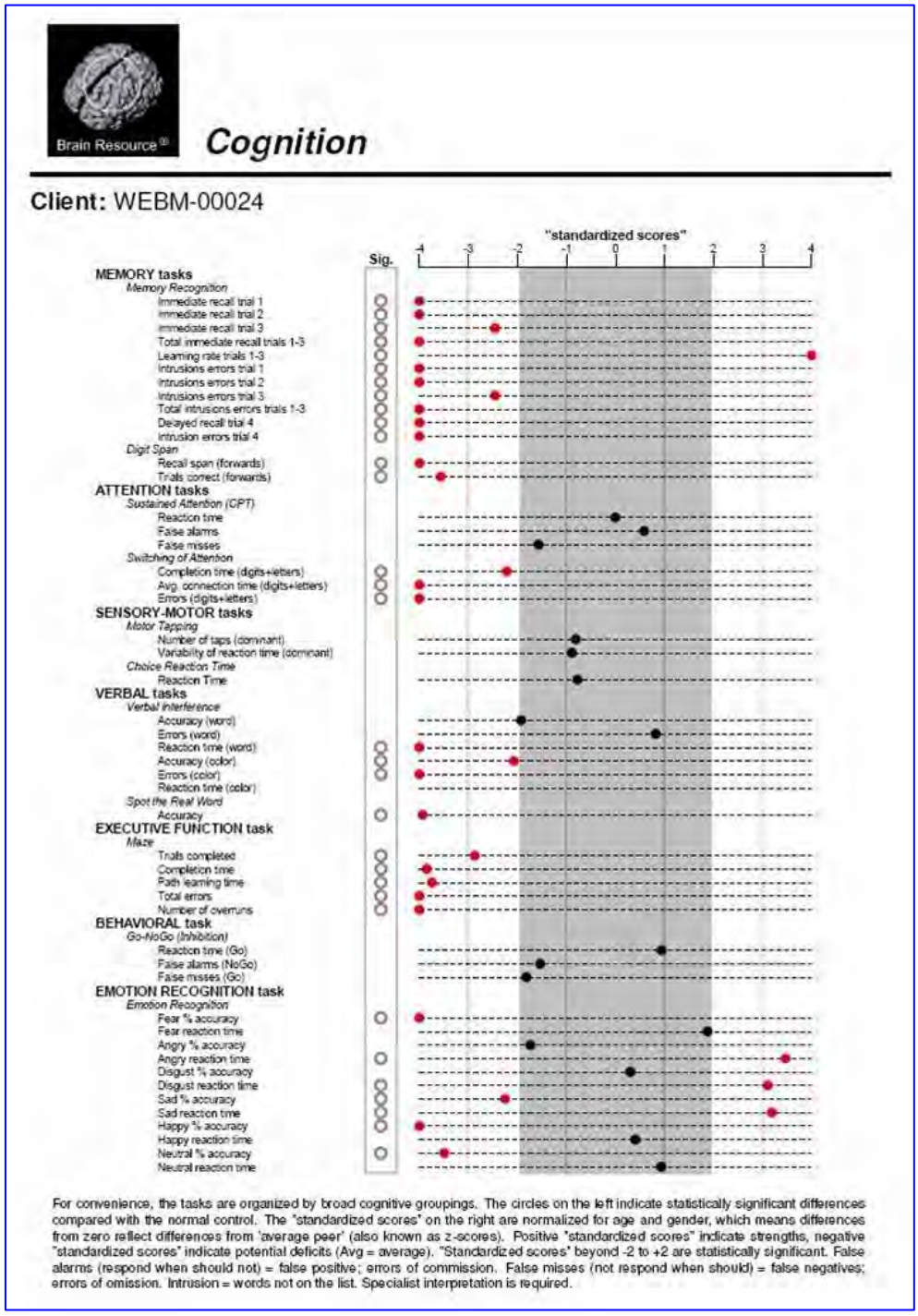
http://www.brainresource.com/uploads/Standard_distribution.pdf

Case Examples

Case Example 1: Interpretation in an elderly adult (from WebNeuro: the principles remain the same)

Mr. XX (below) is a 75-year old male with complaints of forgetfulness and disorientation. Dr Smith referred him for a cognitive assessment to objectively assess his complaints, and a suspected primary dementing process.

Step One in evaluation: Look at the profile



1. The obvious areas of concern are illustrated by the red dots to the left of the report, but there are many areas of strength as well.
2. Areas of no concern, and gratifyingly within the normal range, are in the shaded area.
3. Z-Values at the top are equivalent to standard deviations from the mean. One standard deviation is represented by a z-score of 1, so in the above report, his number of taps is at the z=-1, which means he is at one standard deviation *below* the mean. This is still in the normal range, whereas other scores in red, far to the left, are four standard deviations off the mean, and worse than 99.9% of others comparable to him in demographic terms: see http://www.brainresource.com/uploads/Standard_distribution.pdf

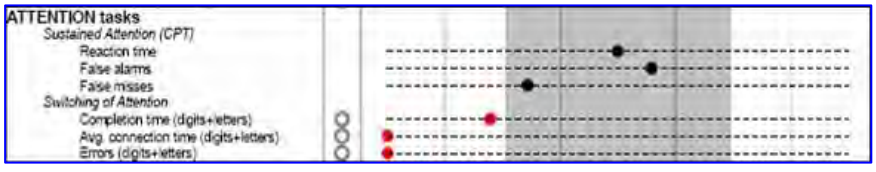
Step Two in evaluation: What might be his baseline IQ?

1. Look at his Spot the Word score as an estimate of his prior IQ score. It is low, suggesting perhaps he has poor education or literacy, or struggled with interference. Since he has 16 years of education, this is not the former, so he is thus struggling with interference. This test is correlated well with Full Scale IQ, about 57% of the variance is shared, so his drop in Spot the Real Word is likely to reflect other factors that vary with the other 43% of the main effect variance. He is thus struggling to exert his intellect in the face of cognitive drop-off. This test is resistant to brain injury and anxiety, and although correlating well with intelligence, this is tenuous with age. Importantly, the test is sensitive to early mild dementia. Note the correlates of neuronal activation are frontal and cingulate on the MRI data supplied in the manual.

Step Three in evaluation: What are his motor-related scores?

1. His tapping speeds are normal. This is a test sensitive to normal aging, and correlated with Peak Alpha and working memory.

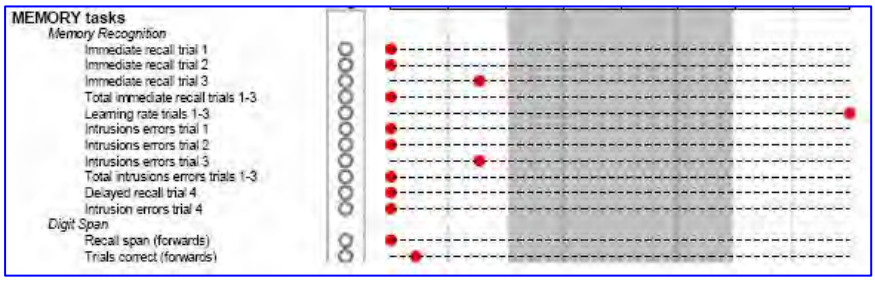
Step Four: Look at components related to attention more closely:



On the Attention tasks Mr. XX' reaction times and accuracy scores were good as components of sustained attention, but he showed impairments in switching attention, which is really executive functioning rather than attention at a lower level, with many mistakes in terms of errors. This indicates that Mr. XX can sustain attention, but struggles from one task to another. Consequently he requires additional time as compared with his normal peers to complete such tasks accurately. The underlying cause is likely to be a problem with cognitive flexibility. This is the ability to switch between two different pieces of information. Mr. XX's short-term memory deficit (see below) and susceptibility to interference (see below) is also likely to contribute to his slower performance during this task. Mr. XX's

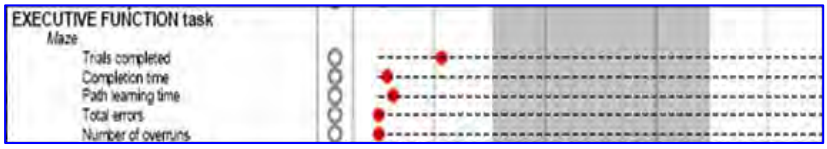
performance on the Sustained Attention (CPT) task was within normal limits suggesting good sustained attention and vigilance over time.

Step Five: Look at performances related to learning:



Looking at his immediate and short-term memory, there is clearly a problem, and the vast population does better than he does on trials 1 and 2 as he tries to learn the words. This is WebNeuro, with only recognition memory, and recognition memory is relatively impervious to age until at least age 60, so his scores are poor even for a 70 year old. His performance did not improve with practice, and by trial three he was a little but not very much better at recognising the correct words. His immediate and delayed recalls are therefore unlikely to be reasonable and in the normal band, so he didn't manage to learn and retain, and errors and intrusions along the way did hamper his encoding of this information. This disorganisation is likely to reflect on his executive functions as well.

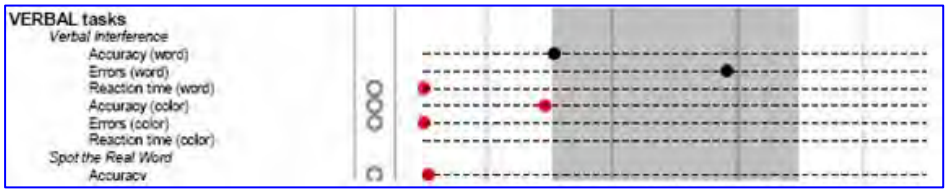
Step Six: Look at tasks requiring executive functions on the Executive Maze Test and the Go,No-Go Test



As can be seen from the above, he has not completed the right number of trials, and his completion time, path learning time, total errors and number of overruns place him low on the percentile tables, on a Maze task.

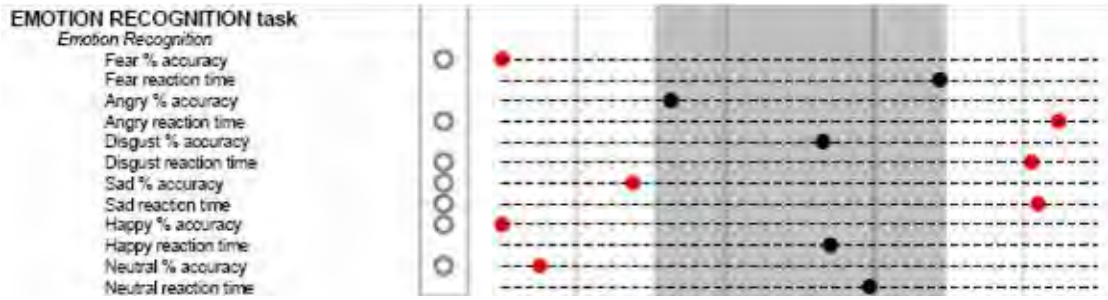
However, on the Go, No-Go inhibition task below, he did well, since his reaction time on the tasks and his number of responses to go and no-go signals was good.

Step Seven: Look at Language-based functions



As can be seen, he has read the words well, and made no errors, but the rest was done poorly. His reaction times were slow, his colour accuracy problems showed he could not release from over-learned mental set, and thus was inaccurate, not for reasons of language, but for executive functioning in managing the novel task. His accuracy and errors for the colour task are all poor, and thus he shows a loss of cognitive flexibility.

Step Eight: Look at Emotional Functions



From the above, it is clear that his accuracy in responding to fear is low, but his reactions times are good, and they are for anger as well. He is inaccurate with regard to sadness, but is quick to respond. Again, he is inaccurate with regard to happy stimuli, but his times are normal, and again with neutrality, the same is seen. Speed is thus overall preserved but his recognition is only accurate for anger and disgust, which are usually harder to recognise than happiness. These results suggest an abnormal pattern, expected of depression and of difficulties in social situations.

Step Nine: Conclusions that could be drawn from this

The major issue to be addressed is that this man is 75 years old. He is complaining of confusion and memory problems. His profile on WebNeuro indicates that overall decline is affecting his executive control of the way he processes information, and his subjective complaints are supported by the objective test results. These difficulties are making him depressed, and he is withdrawing a little from social settings that he is finding difficulty in interpreting. This may lead him to be angry at times, and combative in everyday discussions. He is capable of normal motoric responses, but his strengths there do not help him with more cortical activities, and he struggles with learning and responding to novel or complex situations. Possessed of a good IQ, he cannot apply this flexibly. This profile will present as a stubborn and confused individual, who may misinterpret information and frequently be angry and difficult to reason with. Unable to trust his own information processing, he will find it hard to maintain his confidence and motivation. Pointing out his many lapses in orientation and memory will further anger him, and lead to catastrophic responses in time. He requires a health professional such as a psychologist or occupational therapist to set up an invariant daily schedule for him, with support from errorless learning techniques so he can recall the day, date and so on. His information processing centres in his brain cannot easily deal with error, so he needs to be fed information, rather than be asked to guess. Scaffolding and vanishing cues may help him get through a simplified environment that is constructed for him so as to maintain some independence and manage his disability related to organisation and recall. If the load on his information systems is reduced, he should do better then he is now.

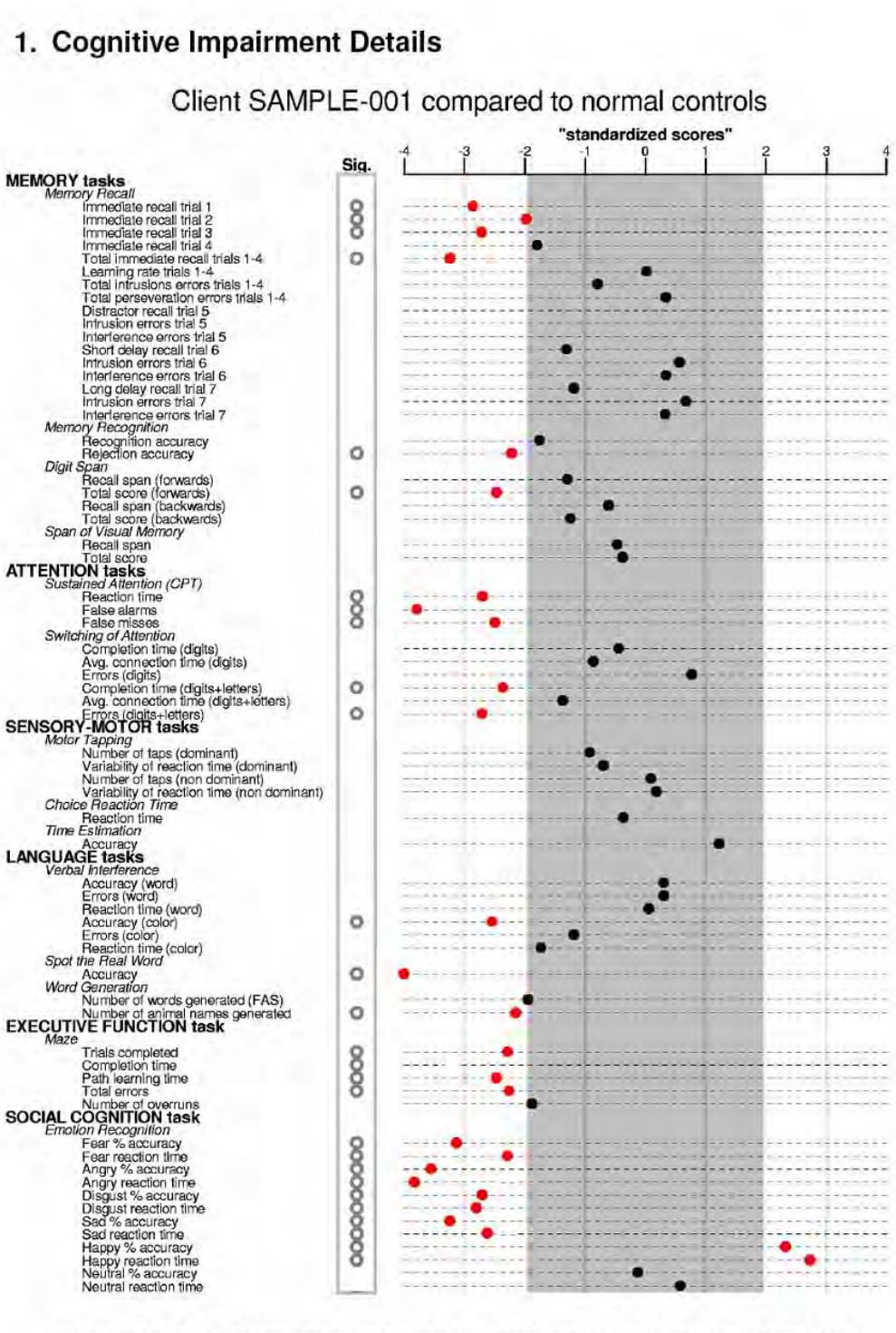
Feedback to the client could look something like this:

Mr XX: the test confirms what you suspected, that you are finding it a little hard to cope with a very busy world, and you need to simplify your life a bit. Your motor and reaction time skills are all still normal, but the volume of things you can take in is a little down. It's as if you are in a hailstorm under a tin roof, and trying to listen to the radio: too much noise is making you feel you can't cope. People like yourself often find it useful to see a doctor who can give you medication to help your brain cope. I also have a list of things here that you might want to chat about, including getting some help planning your day so you can be more organised and then not be so forgetful. Some people move to a place with more support, so that they can preserve being independent. Some folks also get grumpy and miserable when they aren't coping, so you might find you are enjoying things more if you are getting some assistance when and where you need it. Planning and organising things might take some help, but once you are in routine, you won't need too much assistance after a while.

Case Example 2: Another adult with emerging cognitive impairments at risk for Alzheimer's Disease on IntegNeuro

In the case below, another client is struggling in a similar way, but at an earlier stage, with better memory performances on more effortful recall and recognition, since this is IntegNeuro, which has both. With greater insight, he is struggling with emotions, and again, as with Mr XX, his sensory motor capacity is a relative strength. His Spot the Real Word score is likewise depleted, despite adequate education and career, and as with Mr XX, he can no longer apply his inherent IQ capacity and deal with his environment effectively, hence his emotional difficulties. His Digit Span forward score is good, but he fails a one of the two trials on each, so his total forward score is poor, even if the span is okay. Reversed span is good, as this is more arousing, and his cortex responds better than to a simple, no-real-load task such as forward span. Visual memory span confirms this. Sustained attention (CPT) and switching of attention (Trails) are very poor, making errors on Part 2 especially. Combined with poor emotional recognition, his attentional capacity is severely compromised. This is likely to represent a more frontal focus than the previous case, and with a more attentional and cortical arousal problem, a high loading on verbal skills and overall executive function. A frontal-temporal dementia is another risk here.

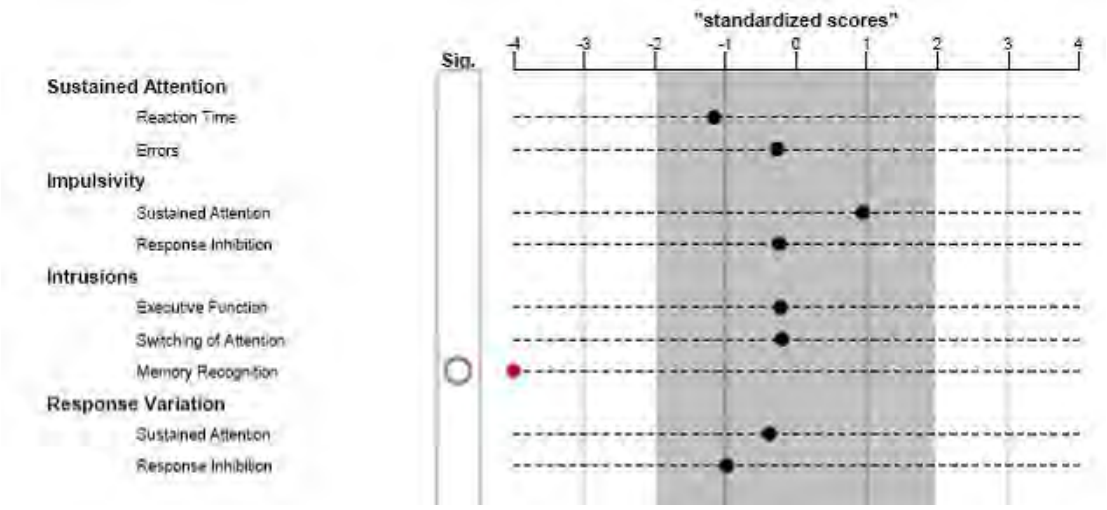
Case Two: MCI-at risk for dementia, report example on IntegNeuro



Case Example 3: Interpretation in a child with attentional problems on WebNeuro

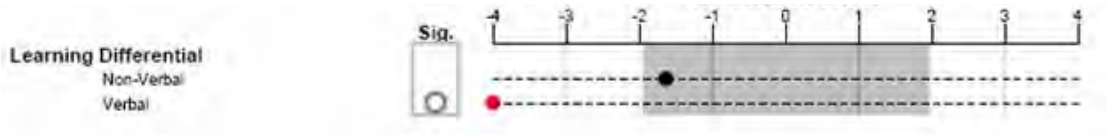
A ten-year-old girl is referred with a suggestion that she is under-performing at school. Her teacher and parents want to know if she is has any learning or other cognitive issues related to her schoolwork.

Her focus profile looks like this:



Question One: Are there any flags she is struggling to learn?

A difference between verbal and nonverbal learning of more than a single standard deviation could suggest we need to test her further. Verbal learning represents what she has accomplished so far, and nonverbal, what her active capacity might be. In this case, the profile below:



shows that the Z-scores between the two capacities are discrepant by a factor of two, namely a normal nonverbal capacity at about z=-1.66 compared to a verbal capacity at about z=-4, which is 2.34 standard deviations. In other words, her fluid capacity for learning is not resulting in a crystallised result in her verbal capacity, so she would be flagged as possibly having problems learning that need further investigation.

Question Two: are there markers for ADHD or other problem that require us to take further action?

Her detailed profile from WebNeuro reads as follows (as with IntegNeuro):

Raw scores of the Client findings (* = statistically significant; Std. Dev = standard deviation; Int = international).
1 = Sustained Attention, 2 = Impulsivity, 3 = Intrusions, 4 = Response Variation.

Measure	Client	Int. Brain Database Average	Int. Brain Database Std. Dev	Standardized Score	Percentile
Sustained Attention					
Reaction time [1,2]	679*ms*	555*ms*	107*ms*	-1.16	12th
False alarms [1,2]	1	4.1	3.2	0.94	83rd
* False misses [1]	7	0.9	1.8	-3.41	< 1st

As can be seen, on sustained attentional tasks, she has a relatively high rate of spotting false alarms, but her false miss rate is bettered by 99% or more of her peers.

Response Inhibition					
Reaction time [4]	267*ms*	291*ms*	66*ms*	0.36	64*th*
False alarms [5]	5	4.3	3	-0.23	41*st*
False misses	9	4.3	4.9	-0.96	17*th*

On response inhibition, she is pretty good, with some solid performances.

Switching of Attention					
• Completion time (digits+letters)	120*s*	64*s*	24*s*	-2.35	1*st*
• Avg. connection time (digits+letters)	6960*ms*	2354*ms*	467*ms*	-9.87	< 1*st*
Errors (digits+letters) [3]	1	0.8	1.1	-0.2	42*nd*

Switching of attention provides further evidence of good responses of her capacity to switch mental set, but her completion time and her average connection time on the task is again bettered by more than 99% of children her age, suggesting she has the capacity for the task, making few errors, but her accurate performance costs her in terms of speed, and she is slow to make the switches, so she may not keep up in class.

Measure	Client	Int. Brain Database Average	Std. Dev	Standardized Score	Percentile
Memory Recognition					
Immediate recall trial 1	18	19.35	0.91	-1.48	7*th*
• Immediate recall trial 2	15	19.58	0.95	-4.79	< 1*st*
• Immediate recall trial 3	9	19.43	0.66	-15.28	< 1*st*
• Total immediate recall trials 1-3	42	57.9	2.1	-7.46	< 1*st*
• Learning rate trials 1-3	-4.5	-0.03	0.52	-8.59	< 1*st*
Intrusions errors trial 1	2	0.65	0.91	-1.48	7*th*
• Intrusions errors trial 2	5	0.44	0.95	-4.79	< 1*st*
• Intrusions errors trial 3	11	0.57	0.66	-15.28	< 1*st*
• Total intrusions errors trials 1-3 [1]	18	2.1	2.1	-7.46	< 1*st*
• Delayed recall trial 4	10	19.25	0.99	-9.31	< 1*st*
• Intrusion errors trial 4	10	0.75	0.99	-9.31	< 1*st*

Question Three: How does she do on a learning task?

Looking at her recognition learning performances above, her initial attempt at the words is borderline, but her subsequent trials are even poorer, as the number of intrusions increasingly interferes with her accuracy. Again, nearly all of her performances are then bettered by more than 99% of children who compare in age. Is this part of an executive problem? This material is organised for her, so it is hard to say, so looking at the Mazes:

Executive Function					
Trials completed	13	10.5	4.5	-0.55	29*th*
Completion time	317*s*	242*s*	102*s*	-0.73	23*rd*
Path learning time	285*s*	214*s*	102*s*	-0.7	24*th*
Total errors [3]	62	56	27	-0.22	41*st*
Number of overruns	47	21	20	-1.32	9*th*

Looking at her Maze performance, it is not the case in the visual domain that she has struggles with the material, as she is well into the normal range with again a low score in errors, but again not as good as she could be, with time sacrificed for accuracy. She is achieving well, but slowly. In other words, she is making more

effort than other children to achieve a normal result. This effort may tire her, and result from a need to exert effort to focus. As she tires, her concentration and attentional skills will wax and wane. So the executive system is working hard, but finding no way into the pathways in the rest of her brain.

Digit Span					
Recall span (forwards)	3	5.3	1.3	-1.77	4th
Trials correct (forwards)	1	5.5	2.3	-1.93	3rd

Looking at simple tests of concentration (forward digits) she is at the borderline of normal, with a struggle to manage her attentional skills, in the normal range, but only just, with about 96-97% of her peers doing better than she can. Motor speed is good:

Motor Tapping					
Number of taps (dominant)	156	146	19	0.51	69th
Variability of reaction time (dominant)	13ms	39ms	11ms	2.29	99th

as is her reaction time:

Choice Reaction Time					
Reaction time	408ms	390ms	93ms	-0.2	42nd

But although she makes virtually no errors in colour responses on the verbal interference task, her accuracy in reading, and her accuracy in colour were poor, as we see below.

Measure	Client	Int. Brain Database Average	Std. Dev	Standardized Score	Percentile
Verbal Interference					
Accuracy (word)	6	18.2	3.8	-3.17	< 1st
Errors (word)	2	0.14	0.35	-5.31	< 1st
Reaction time (word)	1803ms	1064ms	248ms	-2.98	< 1st
Accuracy (color)	10	13.7	3.3	-1.13	13th
Errors (color)	0	1.15	0.84	1.36	91st
Reaction time (color)	1966ms	1307ms	297ms	-2.22	1st

In her performance on choosing the real word from the foils, she was again bettered by 98% of her peers.

Spot the Real Word					
Accuracy	26	35.7	4.8	-2.04	2nd

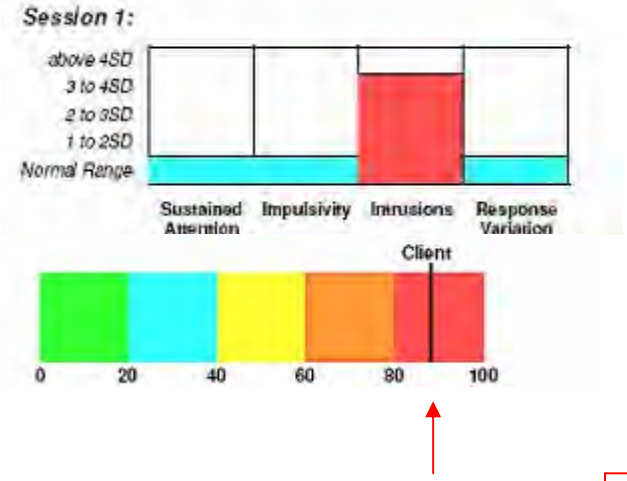
Question Four: How is she doing emotionally?

Emotional response was normal for most items, apart from slow times in responding to fearful and neutral images, with some problems in fear accuracy as well, suggesting anxiety is creeping in to her responses, but it is not the defining issue in her difficulties. She may also not understand what is meant by “neutral”. In any event we are not concerned with her emotions necessarily, although she is showing signs of being miserable.

Emotion Recognition					
• Fear % accuracy	38	76	14	-2.79	$< 1^{st}$
• Fear reaction time	5768	2337	910	-3.77	$< 1^{st}$
Angry % accuracy	63	50	14	0.86	81^{st}
Angry reaction time	3157	2259	715	-1.26	10^{th}
Disgust % accuracy	38	41	16	-0.22	41^{st}
Disgust reaction time	2816	1984	629	-1.32	9^{th}
Sad % accuracy	75	70	23	0.2	58^{th}
Sad reaction time	3134	1967	728	-1.6	5^{th}
Happy % accuracy	100	98.1	4.1	0.46	68^{th}
Happy reaction time	1604	1466	338	-0.41	34^{th}
Neutral % accuracy	100	86	14	0.96	83^{rd}
• Neutral reaction time	3462	1797	613	-2.71	$< 1^{st}$

Summary:

From the Focus report comes the following summary:



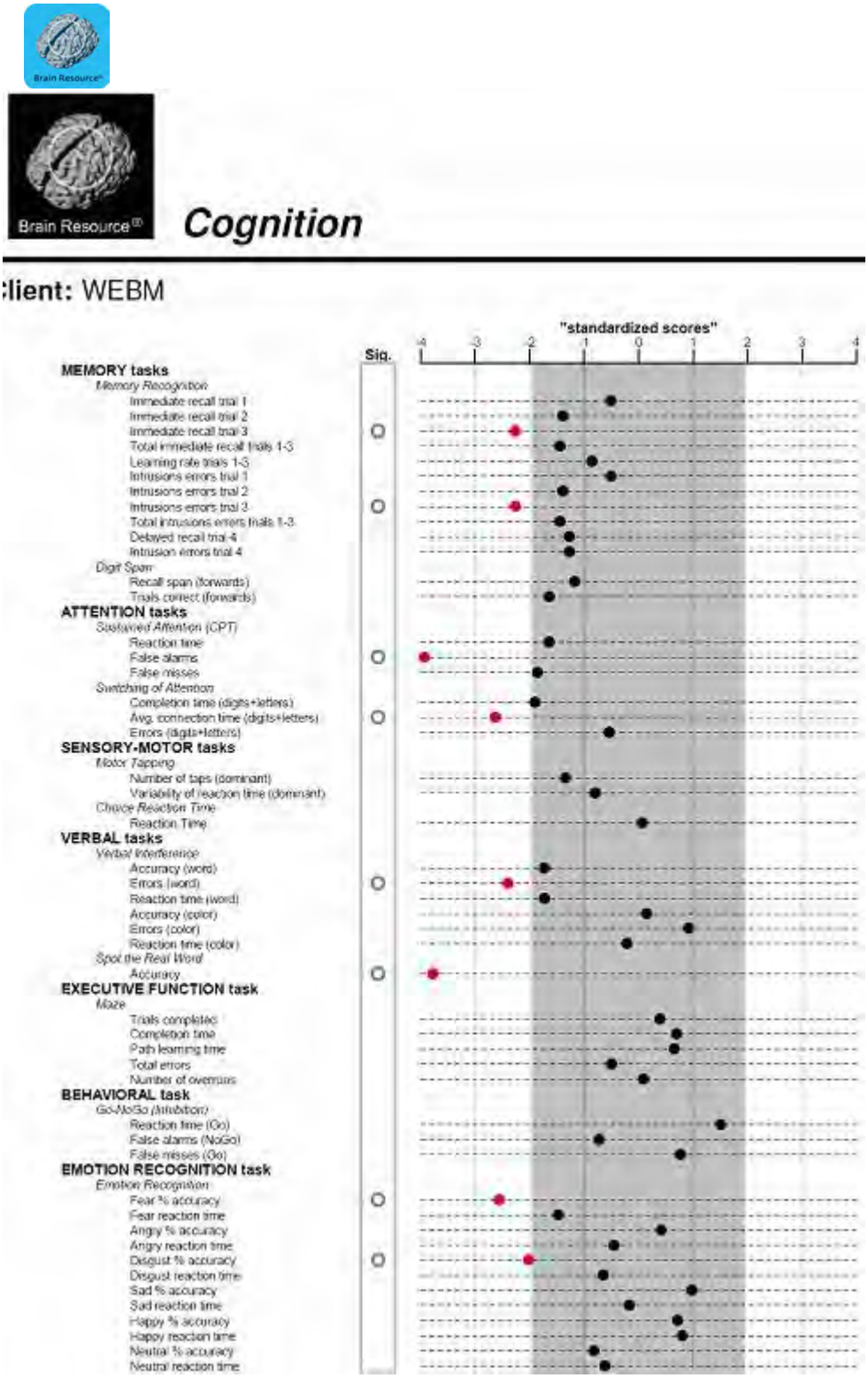
The red column indicates a score 3 standard deviations off the mean, light blue is one standard deviation off the mean

Her severity profile is thus at the 88/100 level, which is a high level of disability compared to her peers, using markers of attentional problems

So from all of this, we can conclude: This little girl does well on many tasks, but struggles to utilise her innate capacity as she is slowed down by the need to be accurate, which then comes at a price. Most of her difficulty is in the verbal domain, suggesting she has a learning problem that will have to be elucidated using a more extensive psycho-educational assessment battery. She would thus appear to have the problems one would expect in a child with attentional difficulties who is struggling with keeping focussed and ignoring intrusions. In summary, she is unlikely to do better at school unless her problems with inattention and are addressed, despite utilising her executive capacity to its limits, and hence being unable to screen out distraction. Her memory could be further investigated with IntegNeuro or the CVLT for children, or a similar list learning, or narrative memory paradigm, and a full educational assessment might also now be warranted after this baseline screening. She should be followed up in 6 months after treatment begins, to assess her improvement with treatment and monitor her development.

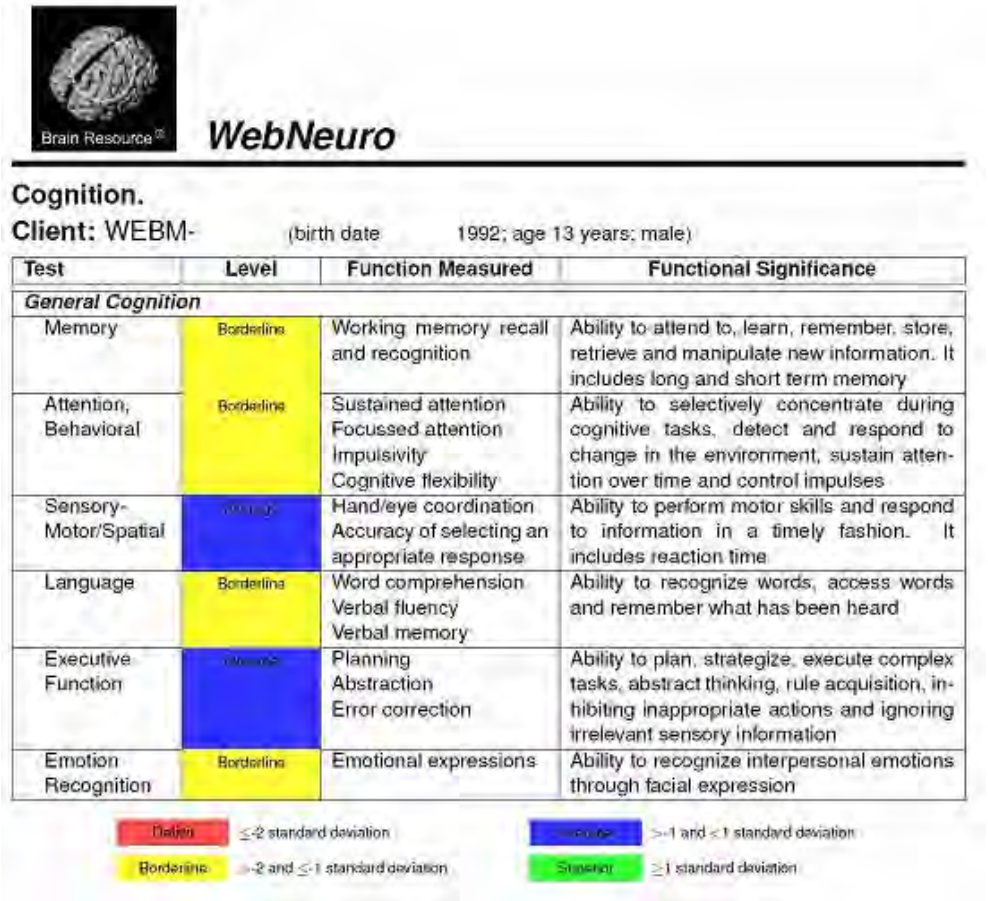
Case Example Four: A teenager with attentional problems, scored pre- and post-methylphenidate on WebNeuro

A 13 year old teenager, about to turn 14, is assessed before placing him on a psychostimulant, methylphenidate. His profile and summaries are as below:

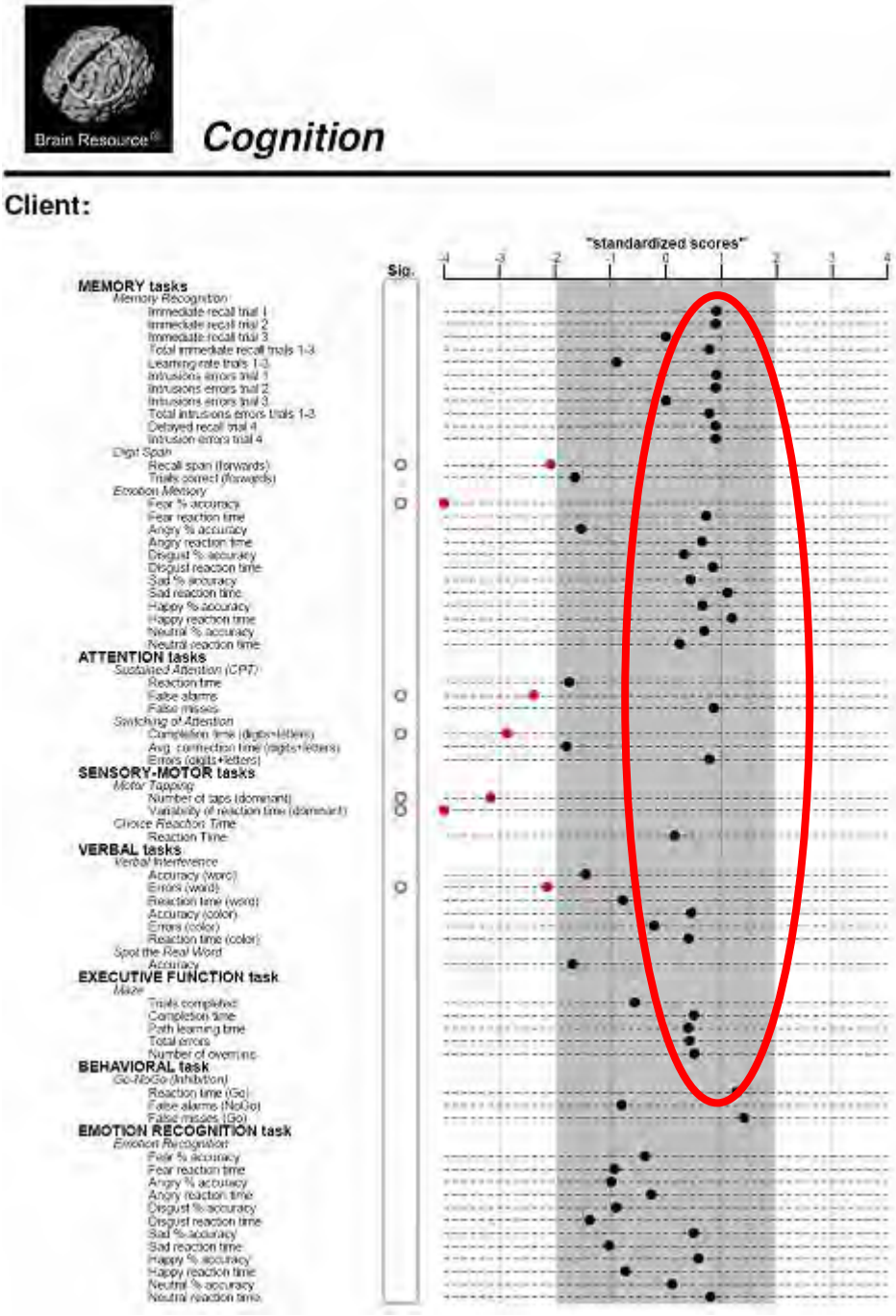


As can be seen from the 'landscape' above, his scores are scattered across a wide range. Although the IQ is likely to be normal, as there are so many scores in the normal range, his spot the real word score is dismal, with 98% of his peer group doing better than he does. A Z-score of -4, would indicate he is four standard deviations off the mean, at the second percentile, hence the comment about his being bettered by 98% of his peers. His immediate recall on trial three of the recognition memory test shows how he loses concentration, despite doing better on the first two trials, owing to intrusions that occur when he tries to partial out essential words (correct words) from the non-essential foils. Sustained and switching of attention are poor, with very little breadth to his performances, as the other scores are only just over the z=-2 scores, two standard deviations off the mean. Switching

attention, namely changing mental set on the task takes him longer, as he struggles to use his working memory to underpin the executive task of fluid changes of mental set: it is effortful for him. His performance on the emotional recognition task suggests he is only just coping emotionally. Consequently, his summary profile is flagging his emerging disability against the normative database for teenagers his age on WebNeuro (in this case):

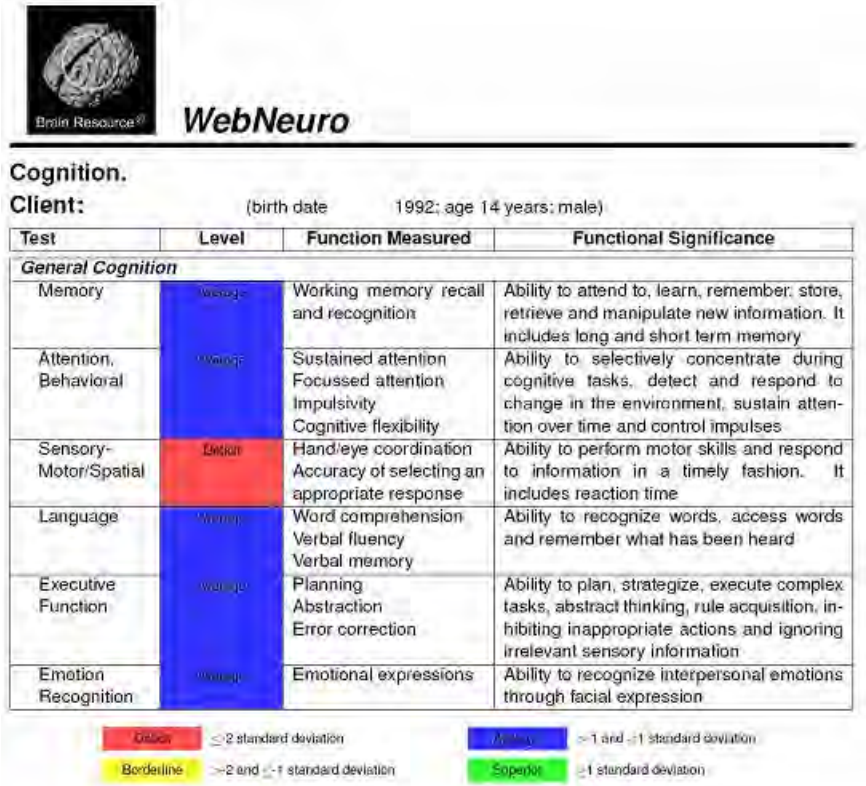


After Medication: As he turns 14, he is placed on methylphenidate. Six months after his personalised baseline, he scores as follows below: As can be easily seen, his problems are resolving in the memory recognition trial, beyond that of retest effects: his scores are now comparable with the best of his peer group, and he is virtually perfect. More importantly, the rows of black dots are almost vertically linear (see red oval above), as he hits the ceiling for many scores. His spot the real word score has moved from a z=-4 to z=-1.5. This does not mean a change in IQ, it just means he can now utilise his IQ capacity more efficiently, and lower the load on his frontal lobes.



Consequently, his post-treatment summary profile is as below: The sensory motor problems we now see are largely on the tapping test, and this may reflect on the medication and a change in Peak Alpha, which is negatively correlated with tapping: a trial of reducing his medication after retesting him may be warranted, as too high a dose can affect his tapping. Overall, the boy and his family would agree this is a good outcome. However, his executive functions were good pre and post medication, better after medication, suggesting myelination of the cortex is proceeding well, but he may be struggling with a poor response to his schooling over the years, and learning problems secondary to his cognitive problems. The intervention is timely however, as the use of stimulants has probably assisted in normalising the comorbid anxiety and depression, and might assist in keeping him out of trouble in society, and off street drugs. One can only imagine what might have happened had this young

man discovered street methamphetamine, with the subsequent rush of normal cognitive control it brought, taking him into a world of addiction, crime, and school drop out.



WebNeuro

Cognition.

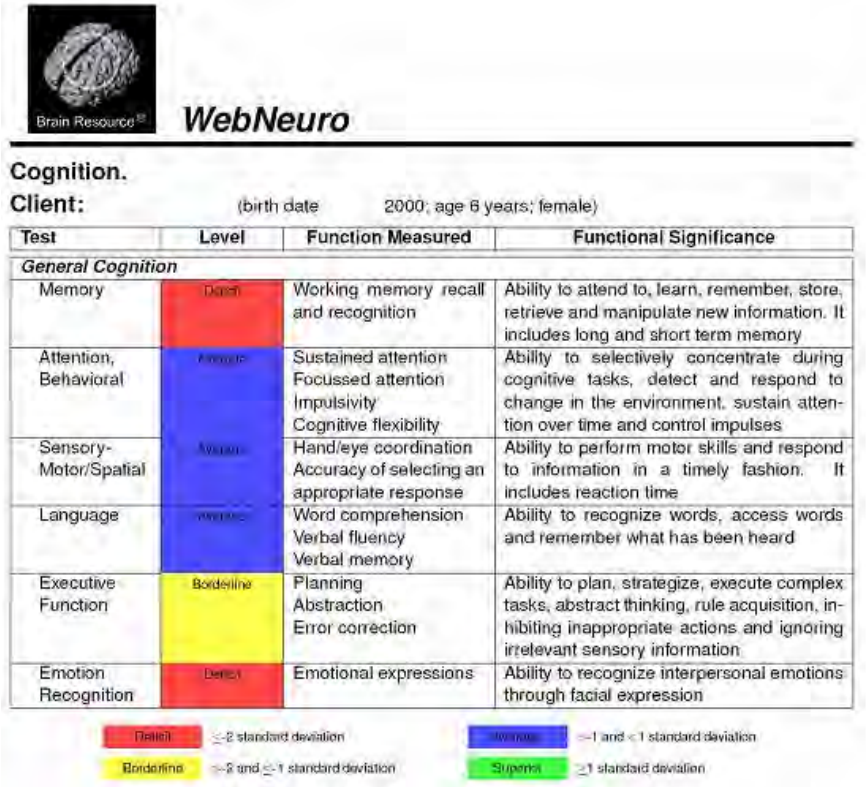
Client: (birth date 1992; age 14 years; male)

Test	Level	Function Measured	Functional Significance
General Cognition			
Memory	Average	Working memory recall and recognition	Ability to attend to, learn, remember, store, retrieve and manipulate new information. It includes long and short term memory
Attention, Behavioral	Average	Sustained attention Focussed attention Impulsivity Cognitive flexibility	Ability to selectively concentrate during cognitive tasks, detect and respond to change in the environment, sustain attention over time and control impulses
Sensory-Motor/Spatial	Deficit	Hand/eye coordination Accuracy of selecting an appropriate response	Ability to perform motor skills and respond to information in a timely fashion. It includes reaction time
Language	Average	Word comprehension Verbal fluency Verbal memory	Ability to recognize words, access words and remember what has been heard
Executive Function	Average	Planning Abstraction Error correction	Ability to plan, strategize, execute complex tasks, abstract thinking, rule acquisition, inhibiting inappropriate actions and ignoring irrelevant sensory information
Emotion Recognition	Average	Emotional expressions	Ability to recognize interpersonal emotions through facial expression

Deficit ≤-2 standard deviation
Average >-1 and <1 standard deviation
Borderline >-2 and ≤-1 standard deviation
Superior ≥1 standard deviation

Case Example Five: A six year old who appears to have severe problems

The little girl, who is just six, produces the following profile summary:



WebNeuro

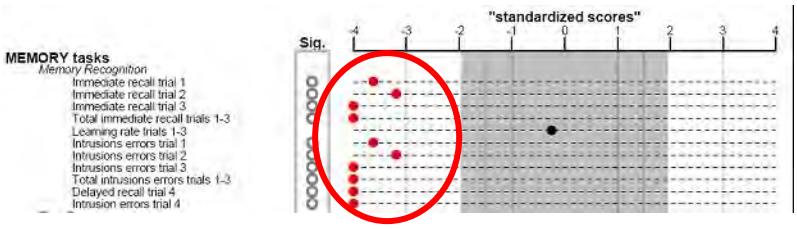
Cognition.

Client: (birth date 2000; age 6 years; female)

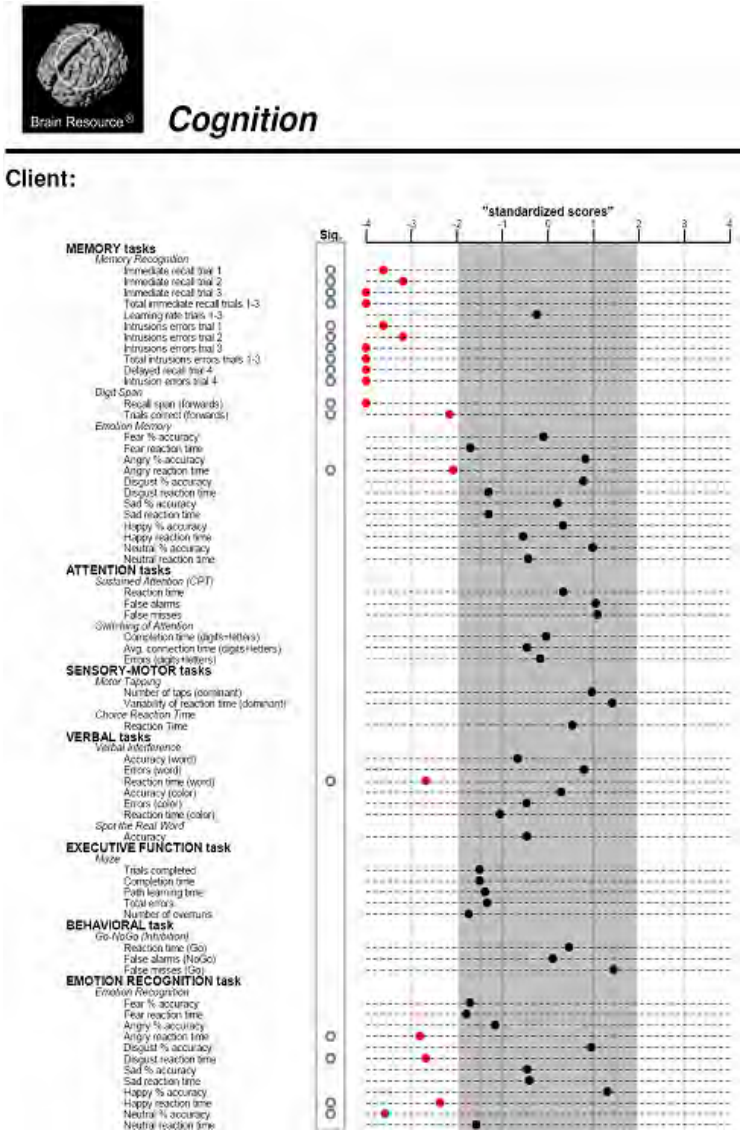
Test	Level	Function Measured	Functional Significance
General Cognition			
Memory	Deficit	Working memory recall and recognition	Ability to attend to, learn, remember, store, retrieve and manipulate new information. It includes long and short term memory
Attention, Behavioral	Average	Sustained attention Focussed attention Impulsivity Cognitive flexibility	Ability to selectively concentrate during cognitive tasks, detect and respond to change in the environment, sustain attention over time and control impulses
Sensory-Motor/Spatial	Average	Hand/eye coordination Accuracy of selecting an appropriate response	Ability to perform motor skills and respond to information in a timely fashion. It includes reaction time
Language	Average	Word comprehension Verbal fluency Verbal memory	Ability to recognize words, access words and remember what has been heard
Executive Function	Borderline	Planning Abstraction Error correction	Ability to plan, strategize, execute complex tasks, abstract thinking, rule acquisition, inhibiting inappropriate actions and ignoring irrelevant sensory information
Emotion Recognition	Deficit	Emotional expressions	Ability to recognize interpersonal emotions through facial expression

Deficit ≤-2 standard deviation
Average >-1 and <1 standard deviation
Borderline >-2 and ≤-1 standard deviation
Superior ≥1 standard deviation

At first glance, she appears to have severe problems in memory, executive functioning and emotional recognition. It appears that intervention for this severely disabled child is necessary. That is wrong however. A look at her landscape shows clues to why the test is not contributing to her assessment in a diagnostically meaningful way: Firstly, her scores on recognition memory are clustered on the floor to the left: the only assumption one can make it that the test is too difficult for her to engage with, and thus she is not being measured at all: Follow up with a CVLT-II or similar task is advised.



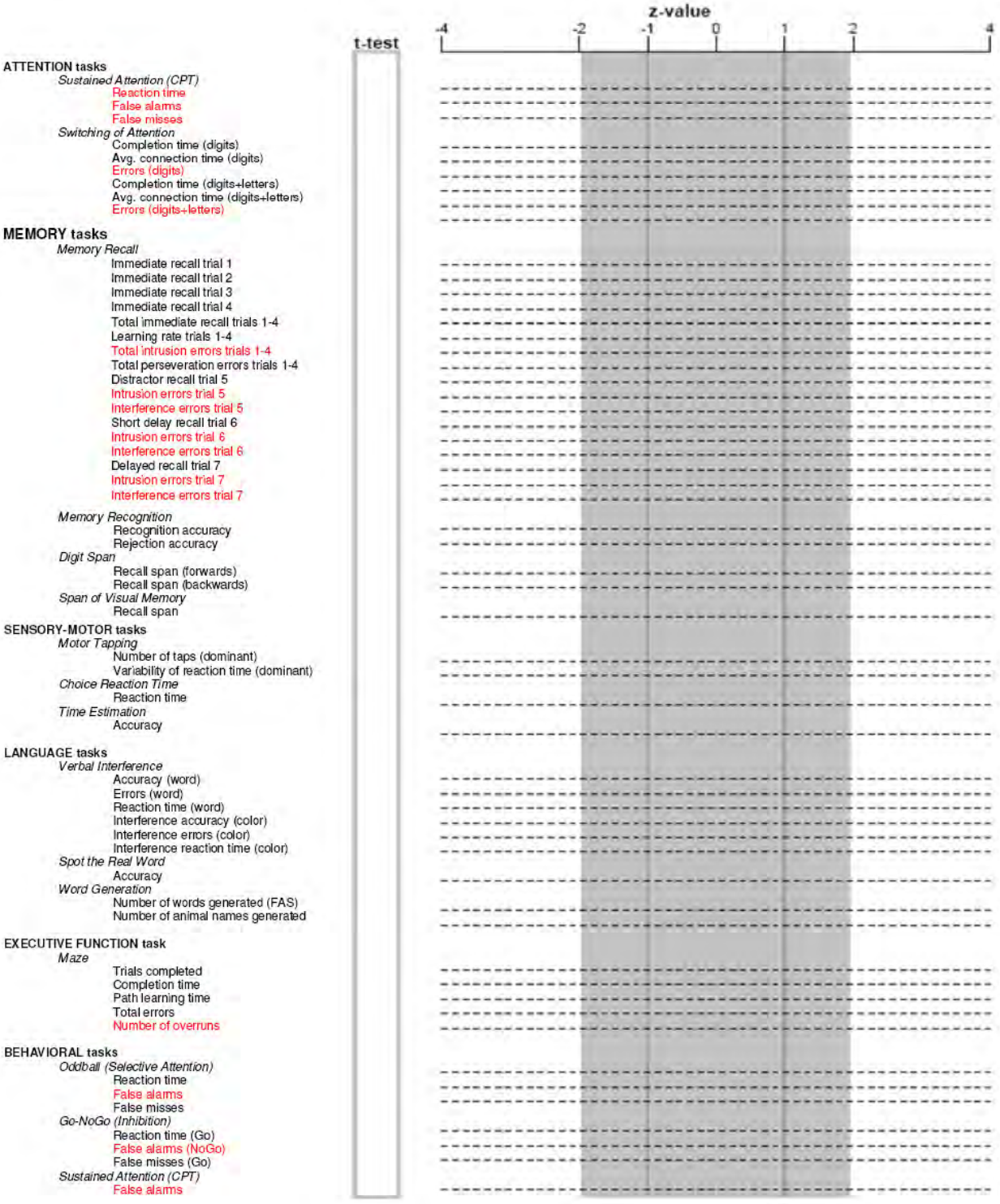
As one can see on the full profile to the right, the executive function is otherwise within the normal range on the mazes, so the loading is coming from her performances elsewhere, and on the mazes she is also clustering in a straight line, suggesting her development is just entering the range for the test. At the bottom limits of the normal curve, and at the upper, psychometric testing is least able to discriminate very tightly, even with large numbers, so caution is necessary. . The emotional recognition test is difficult and variable for her age, she is struggling with the concept of 'neutral', and although she manages 'disgust', a very difficult one to recognise, it only slows her down, but she manages. A young, slightly immature little girl, who needs to be retested a year later, but nothing to worry about! ☺ However, since she is being tested against other little girls her age, why is she not reading as well as they are? There is normal variance perhaps at play here, and her digits forward span, and reaction time are a little suspicious, warranting further review at 6 months, again with WebNeuro or IntegNeuro: the latter requires no reading skill for memory recall and recognition.



What to look for in various conditions when examining the 'landscapes' produced by IntegNeuro:

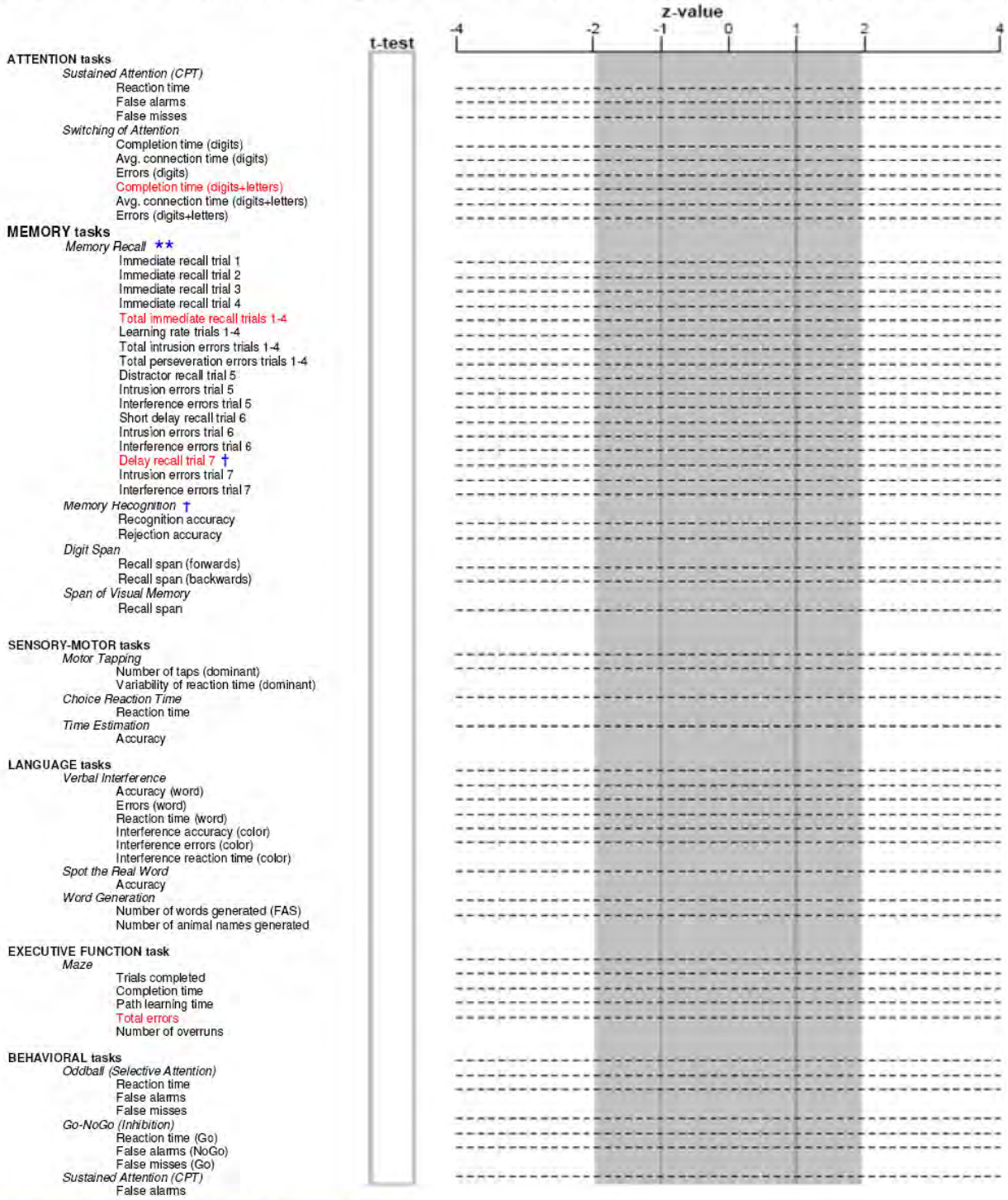
1. ADHD

Possible Cognition deficits in ADHD (in red) from the Brain Resource Database



2. Mild Cognitive Impairment

Possible deficits in Amnestic Mild Cognitive Impairment Cognition results (in red) from the published scientific literature and what experienced clinicians have indica they would anticipate (although clinicians emphasize individual subject variability)

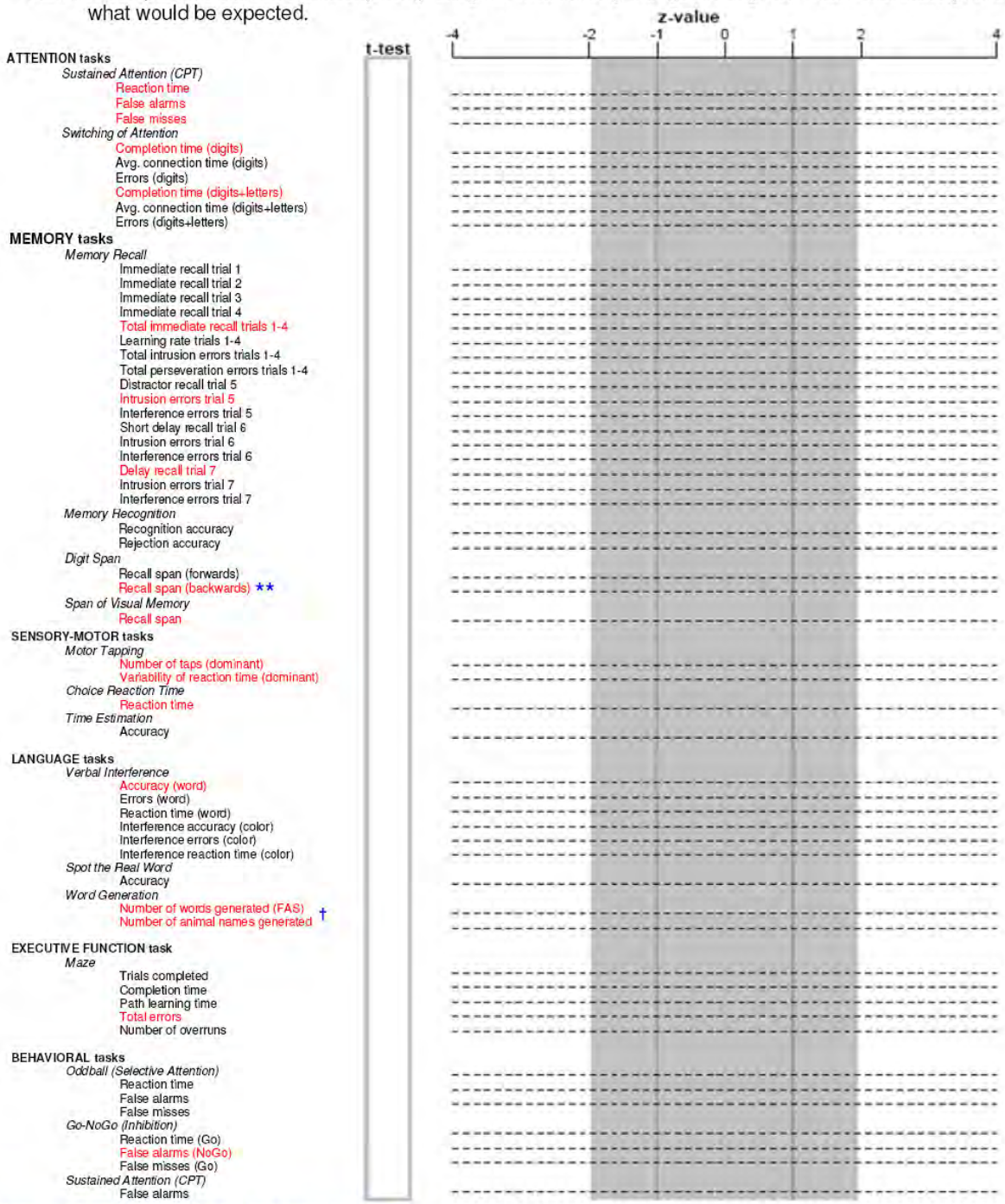


Notes: ** It is predicted that this will be the dominant finding.
† It is important that impairments are present on this measure (in addition to Recognition 'hits' minus 'false alarms' (index to be introduced to the Reports in June 2005).

3. Alzheimer's Dementia

Possible deficits in Alzheimer's Dementia Cognition results (in red) from the published scientific literature and what experienced clinicians have indicated they would anticipate (although clinicians emphasize individual subject variability)

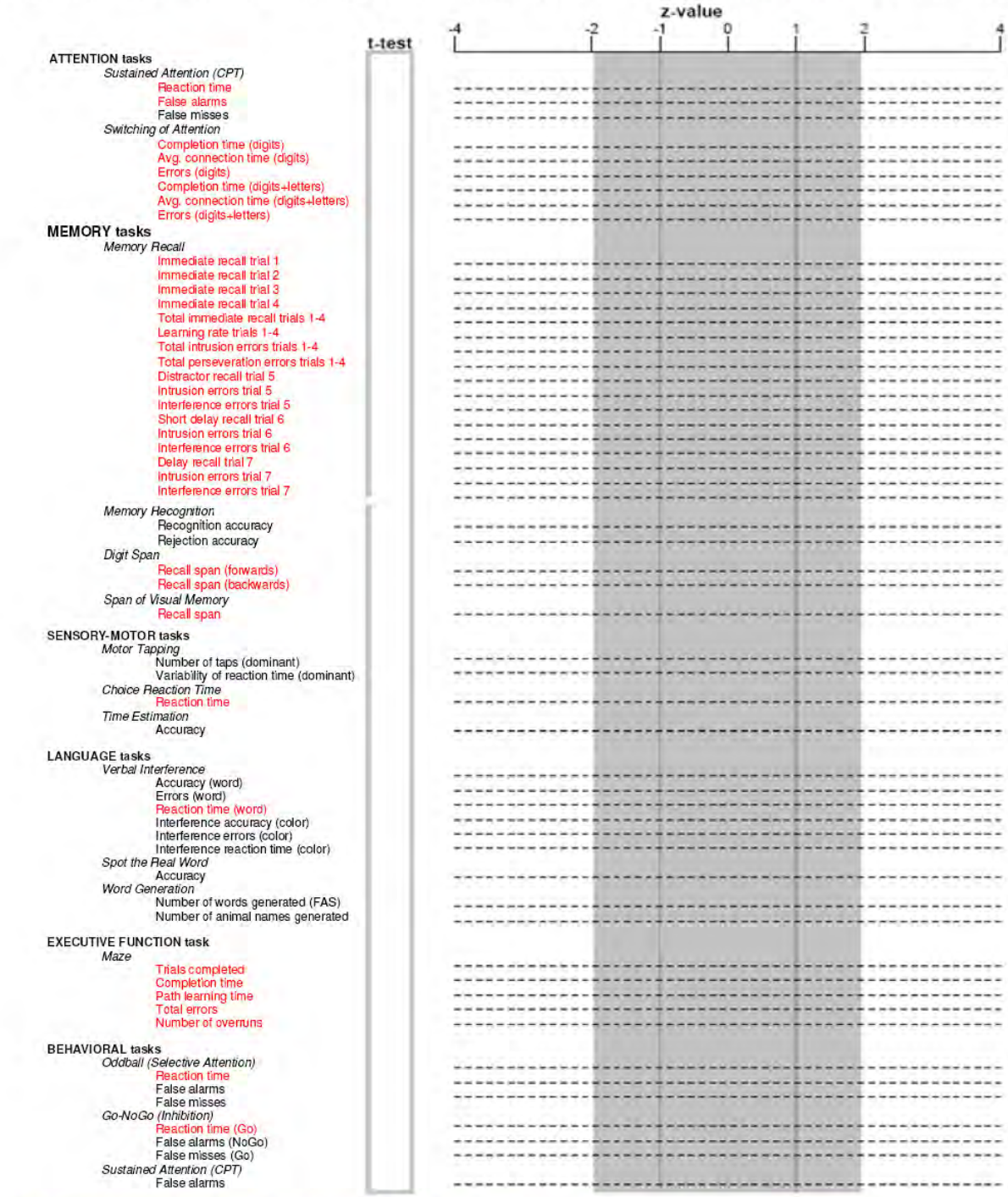
* Note: These patients will have difficulty completing the tests. If they can get through the entire test battery, this is what would be expected.



Notes: ** It is predicted that this will be the dominant finding.
† It is predicted that the score for Animal names < FAS score.

4. Post Traumatic Stress Disorder

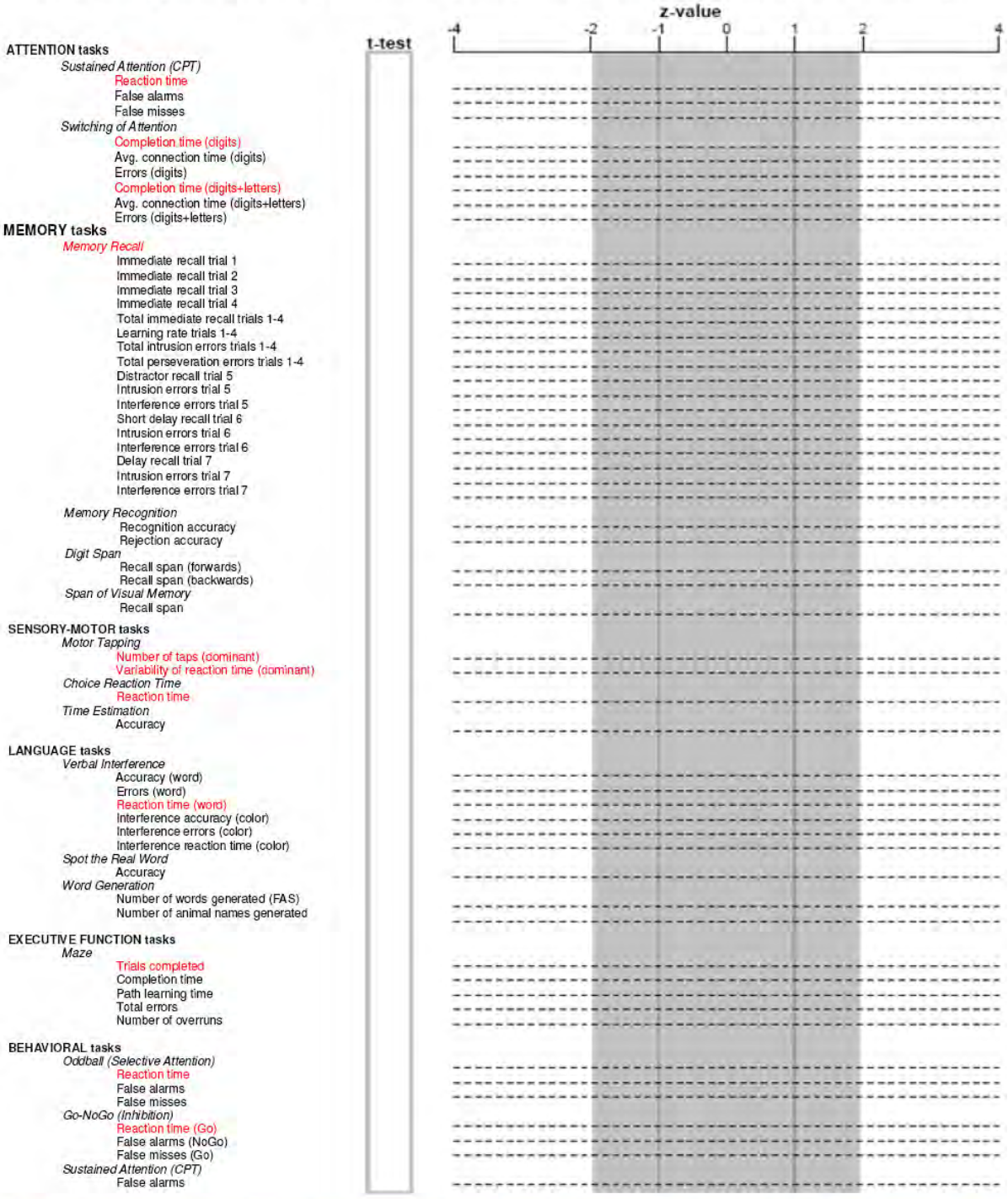
Possible deficits in Post-traumatic Stress Disorder (PTSD) Cognition results (in red) from the published scientific literature and what experienced clinicians have indicated they would anticipate (although clinicians emphasize individual subject variability)



** Note: In conjunction with these findings, high measures of anxiety, stress and depression (as measured by BRC Web Questionnaires).

5. Traumatic Brain Injury

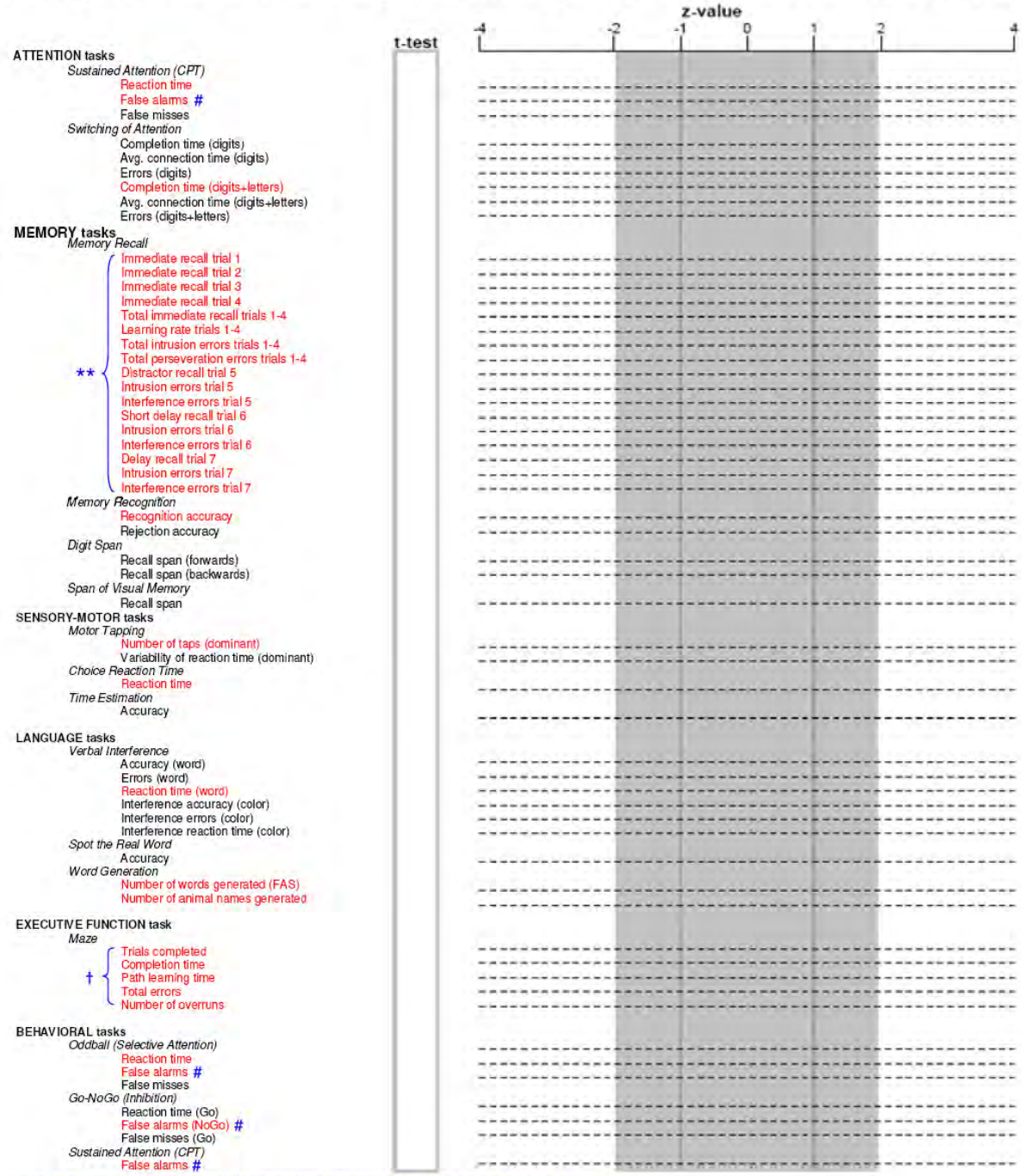
Possible deficits in Traumatic Brain Injury (TBI) Cognition results (in red) from th
published scientific literature and what experienced clinicians have indicated the
would anticipate (although clinicians emphasize individual subject variability)



** Note: In conjunction with these findings, high measures of anxiety, stress and depression (as measured by BRC Web Questionnaires).

6. Depression

Possible patterns of Cognition results in Depression from the published scientific literature and what experienced clinicians have indicated what they would anticipate (although clinicians emphasize significant heterogeneity of findings in Depressive subjects



Notes: ** It is predicted that there will be significant impairment in immediate and delayed recall.
† It is predicted that there will be significant impairment in these measures.
# It is predicted that Depressives will have a liberal response style for these measures.

Summary of Scientific data supporting Brain Resource Methodology

Methodology

Gordon E (2003). Integrative Neuroscience and Psychiatry. **Neuropsychopharmacology**, 28, 2-8

Gordon E (2003). Integrative neuroscience in psychiatry: the role of a standardized database. **Australasian Psychiatry**, 11, 156 – 163

Gordon E, Cooper N, Rennie C, Hermens D & Williams (2005). Integrative neuroscience: the role of a standardized database. **Clinical EEG and Neuroscience**, 36, 64-75.

Test-Retest Reliability

Williams LM et al. (2005). The test-retest reliability of a standardized neurocognitive and neurophysiological test battery: 'NeuroMarker'. **International Journal of Neuroscience**, 115 (12), 1605-130.

Cross-site Reliability/Consistency

Paul RH et al. (2006). Cross cultural assessment of neuropsychological performance and electrical brain function measures: additional validation of an international brain database. **International Journal of Neuroscience** (in press).

Validity (convergent and divergent)

Paul RH et al (2005). Preliminary validity of 'IntegNeuro™': A new computerized battery of neurocognitive tests. **International Journal of Neuroscience**, 115 (11), 1549-1567

Norms

Clark CR et al (2006). Cognitive functioning in development and ageing. **Archives of Clinical Neuropsychology,** 21, 449-467

Validation of application in clinical and treatment trials

Steven M. Silverstein[1], Sarah Berten[1], Robert Paul[2], Nicholas Cooper5 Leanne Williams[3-4] & Evian Gordon[3-5] (in press). Development and Validation of a World Wide Web-Based Neurocognitive Assessment Battery: WebNeuro™· **Behavior Research Methods,** ,

Cooper N, Debrota D, Keage H, Hermens D, Williams LM, Clark CR, Gordon E. (2005). The dose-dependent effect of methlyphenidate on performance, cognition and psychophysiology. **Journal of Integrative Neuroscience,** 4, 123-144

Hermens DF Cooper N, Kohn M, Clarke S, Gordon E, Williams LM (2005). Predicting stimulant medication response in ADHD: Evidence from an integrated profile of neuropsychological,psychophysiological and clinical factors **Journal of Integrative Neuroscience**, 4, 107 – 121

Hermens DF, Clark S, Kohn M, Williams LM & Gordon E (2005). Responses to methylphenidate in adolescent AD/HD: evidence from concurently recorded autonomic (EDA) and central (EEG and ERP) measures **International Journal of Psychophysiology**, 28, 21 - 33

Validation of application to clinical groups - ADHD

Hermens DF Cooper N, Kohn M, Clarke S, Gordon E, Williams LM (2005). Predicting stimulant medication response in ADHD: Evidence from an integrated profile of neuropsychological, psychophysiological and clinical factors. **Journal of Integrative Neuroscience**, 4, 107-121. PDF (234 KB)

Keage HAD, Clark CR, Hermens DF, Kohn MR, Clarke S, Williams LM, Crewther D, Lamb C & Gordon E (2006). Distractibility in AD/HD Predominantly Preattentive and Combined Subtypes: The P3a ERP Component, Heart Rate and Performance. **Journal of Integrative Neuroscience**, 5, 139 - 158

Hermens DF, Soei E, Clarke SD, Kohn MR, Gordon E & Williams LM (2005). Resting EEG theta activity predicts cognitive performance in ADHD. **Paediatric Neurology**, 32, 248-256. PDF (KB)

Hermens DF, Kohn M, Clarke S, Gordon E & Williams LM (2005). Sex differences in adolescent ADHD: Findings from concurrent EEG and EDA **Clinical Neurophysiology**, 116, 1455-1463. PDF (142 KB)

Hermens D, Williams LM, Lazzaro I, Whitmont S, Melkonian D & Gordon E (2004). Sex differences in adult ADHD: A double dissociation in brain activity and autonomic arousal? **Biological Psychology**, 66, 221-233. PDF (197 KB)

Cognitive Decline and Age-related cognitive change

Alexander DM, Arns MW, Paul RH, Rowe DL, Cooper N, Esser AH, Fallahpour K, Stephan BCM, Heesen E, Breteler R, Williams LM & Gordon E (2006). EEG Markers for Cognitive Decline in Elderly Subjects with Subjective Memory Complaints. **Journal of Integrative Neuroscience**, 5, 49 – 74

Paul RH, Haque O,Gunstad J, Tate D, Grieve S, Hoth K, Brickman A, Cohen R, Lange K, Jefferson A, MacGregor K, Gordon E (2005). Subcortical hyperintensities impact cognitive function among a select subset of healthy elderly. **Archives of Clinical Neuropsychology**, 20, 697 - 704

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Williams LM, Brown KJ, Palmer D, Belinda BJ, Kemp AH, Olivieri G, Peduto AS, Gordon E. (2006). The 'mellow years': Neural basis of improving emotional stability over age. **Journal of Neuroscience**, 26, 6422 – 6430

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Grieve S, Clark CR, Williams LM & Gordon E (2005). Preservation of limbic and paralimbic regions with aging. **Human Brain Mapping**, 25, 391 – 401

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Kemp AH Stephan BCM, Hopkinson P, Sumich AL, Paul RH, Clark RC, Bryant RA, Gordon E, Williams LM (2005). Toward an Integrated Profile of Depression: Evidence from the Brain Resource International Database. **Journal of Integrative Neuroscience**, 4, 95 – 106

Sumich AL Kumari V, Heasman BC, Gordon E,Brammer MJ (2006). Abnormal asymmetry of N200 and P300 event-related potentials in subclinical depression. **Journal of Affective Disorders**, 92(2-3):171-83

Cohen RA, Paul RH, Stroud L, McCaffrey J, Sweet L, Hitsman B, Gunstad J, Niaura R, McFarlane A, Bryant RA, Gordon E. (2006). Early life stress and adult emotional experience: an International Perspective. **The International Journal of Psychiatry in Medicine**,36, 35-52

Cohen RA, Grieve S, Hoth K, Paul RA, Sweet L, Tate D, Gunstad J, Stroud L, McCaffrey J, Hitsman B, Niaura R, Clark R, MacFarlane A, Bryant RA, Gordon E & Williams LM (2006). Early life stress and morphometry of the adult anterior cingulate cortex and caudate nuclei
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McFarlane A, Clark CR, Bryant RA, Williams LM, Niaura R, Paul RH, Hitsman BL, Stroud L, Alexander D & Gordon E (2005). The impact of early life stress on psychophysiological, personality and behavioral measures in 740 non-clinical subjects. **Journal of Integrative Neuroscience**, 4, 27 – 40.

Hoth K Paul RH, Williams LM, Dobson-Stone C, Todd E, Schofield PR, Gunstad J, Cohen R, Gordon E (2006). Associations between the COMT Val/Met Polymorphism, Early Life Stress and Personality among Healthy Adults. **Neuropsychiatric Disease and Treatment**, 2 (2) 219-225.

Schizophrenia

Whitford TJ, Grieve SM, Farrow TF, Gomes L, Brennan J, Harris AWF, Gordon E, Williams LM (2006). Progressive grey matter atrophy over the first 2-3 years of illness in first-episode schizophrenia: a tensor-based morphometry study.
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Anxiety (PTSD)

Veltmeyer MD, McFarlane AC, Bryant RA, Mayo T, Gordon E & Clark CR (2006).Integrative Assessment of Brain Function in PTSD: Brain Stability and Working Memory. **Journal of Integrative Neuroscience**, 5, 123 – 138

Williams LM, Kemp AH, Felmingham K, Barton M, Olivieri G, Peduto AS, Gordon E & Bryant RA (2006). Trauma modulates amygdala and medial prefrontal responses to consciously attended fear. **Neuroimage**, 29, 347 – 357

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Obesity

Gunstad J, Paul R., Cohen R. Tate, D. & Gordon, E. (2006). Obesity is Associated with Memory Deficits in Young and Middle-Aged Adults. **Journal of Eating and Weight Disorders/ Studies on Anorexia, Bulimia, and Obesity,** 11(1), e15-19.

Gunstad J, Schofield P, Paul R, Spitznagel M, Cohen R, Williams LM, Kohn M & Gordon E (2006). BDNF Val66Met polymorphism is associated with body mass index in healthy adults. **Neuropsychobiology**, 53, 153 – 156

For a summary of BRC Products, visit:
http://www.brainresource.com/uploads/BRC_product_summary_table.pdf

To comment on this manual, or for any general enquiries, contact the author, Dr Roy Sugarman

clinical@brainresource.com
info@brainresource.com

Cognitive Correlates of EEG

EO – Eyes Open EEG Task
EC – Eyes Closed EEG Task

	δ	θ	α	β	α (Peak)	α (Hz)	θ /β
Motor Tapping					EC		
Choice Reaction Time							
Time Estimation							EO EC
Span of Visual Memory							
Spot the Real Word							
Digit Span							EO EC
Memory Recall	EO		EO		EO		EO
Verbal Interference	EC	EO EC	EO EC		EO EC		EO EC
Word Generation		EO					
Visual Working Memory							
Switching of Attention							
Go No-Go							
Executive Maze	EC	EC					EO EC

Cognition:
Biological correlates

	EEG Theta:Beta	ERPs: Working Memory N-Back*	Autonomic: HR variability	MRI: Frontal Grey Matter
Motor Tapping		N2 Latency		
Choice Reaction Time		P3 Amplitude		
Time Estimation				
Span of Visual Memory				
Spot the Real Word				
Digit Span				
Memory Recall				
Verbal Interference		N2 Amplitude		
Word Generation				
Working Memory N-Back		P3 Amplitude Latency		
Switching of Attention		N2 Amplitude		
Go No-Go		P3 Amplitude		
Executive Maze		N2 Amplitude		

*ERP tasks
Assessed Updating of Working Memory

Negative Correlation
(poorer Cognition relates to lower Brain Function/less Grey Matter)

Correlation Legend

Positive Correlation
(better Cognition relates to higher Brain Function/more Grey Matter)

Cognitive Correlates of ERPs

WM = Working Memory ERP
ODDB = Oddball ERP
GNG = Go No-Go ERP
A = Amplitude, L = Latency
B = Background, T = Target
G = 'Go', N = 'No-Go'

Decrease in amplitude/latency associated with better performance

Increase in amp/lat associated with better performance

	ODDB Early	ODDB Late	WM Early	WM Late	GNG Early	GNG Late
Motor Tapping	N1 BT A	N2 P3 T L L T		N2 B L		N2 G L
Choice Reaction Time	P2 T L		N1 B A	P3 T A	N1 G A	N2 G A
Time Estimation					P2 G A	N2 G A
Span of Visual Memory					P2 N A	
Spot the Real Word		N2 T A				P3 G A
Digit Span		P3 T A	P2 B A			P3 G A
Memory Recall					N1 G A	P3 G A
Verbal Interference		P3 T A	N1 T A	N2 B A	P2 G A	P3 G A
Word Generation	P2 T L	N2 T L				
Visual Working Memory	N1 TB A	P3 T A		P3 P3 TB A L T		N2 P3 B L A TB
Switching of Attention		P3 T A	N1 T A	N2 B A	N1 G A	N2 G L
Go No-Go			N1 B L	P3 T A		P3 P3 T A L B
Executive Maze	N1 B L		N1 B A	N2 BT A	P2 BT A	N2 TB A

Cognitive Correlates of MRI

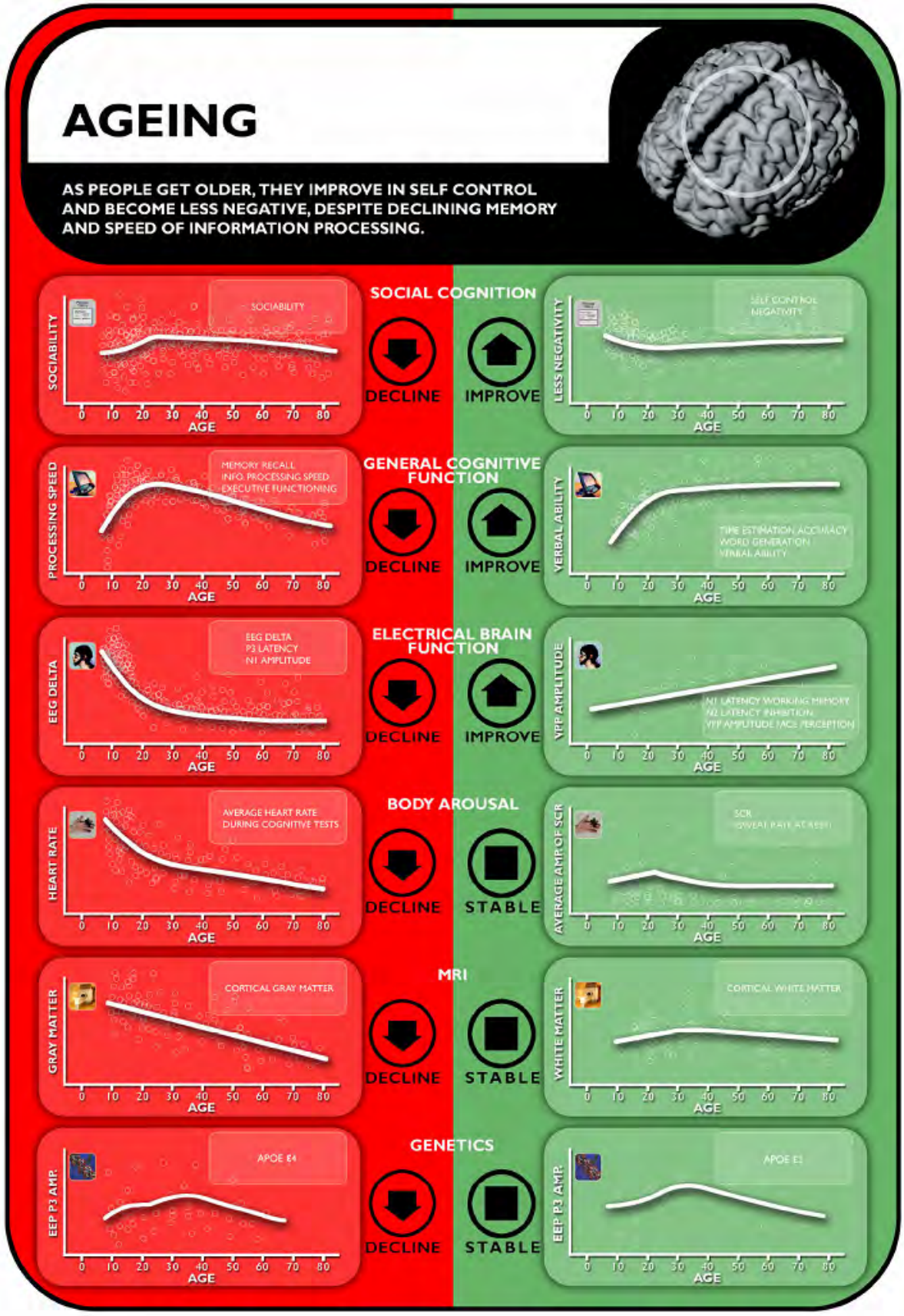
	Total	Cortical					Sub-Cortical	
	grey	Cingulate	Frontal	Occipital	Temporal	Parietal	Hippocampus	Amygdala
Motor Tapping								
Choice Reaction Time								
Time Estimation								
Span of Visual Memory								
Spot the Real Word								
Digit Span								
Memory Recall								
Verbal Interference								
Word Generation								
Visual Working Memory								
Switching of Attention								
Go No-Go								
Executive Maze								

Cognitive Correlates of Heart Rate Variability

Increase in variability associated with a decrease in performance

Increase in variability associated with better performance

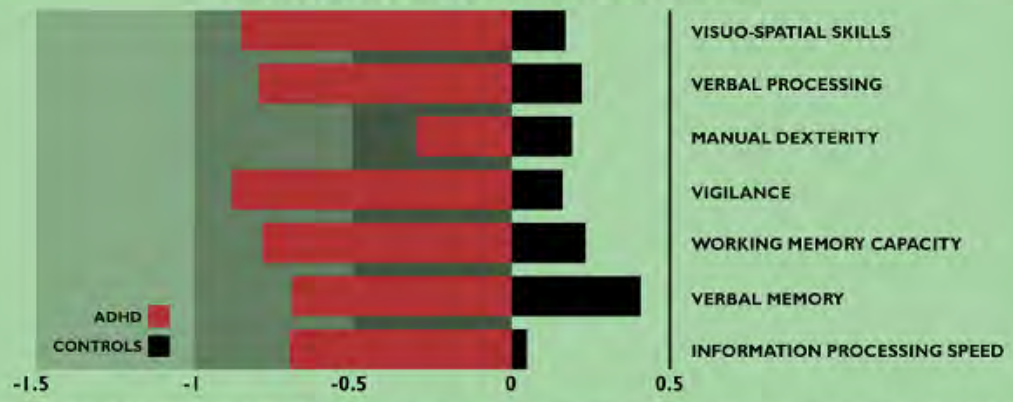
	Resting HR Variability	Task HR Variability
 Motor Tapping		
 Choice Reaction Time		
 Time Estimation		
 Span of Visual Memory		
 Spot the Real Word		
 Digit Span		
 Memory Recall		
 Verbal Interference		
 Word Generation		
 Visual Working Memory		
 Switching of Attention		
 Go No-Go		
 Executive Maze		


AGEING
AS PEOPLE GET OLDER, THEY IMPROVE IN SELF CONTROL AND BECOME LESS NEGATIVE, DESPITE DECLINING MEMORY AND SPEED OF INFORMATION PROCESSING.
SOCIAL COGNITION
SOCIABILITY
SOCIABILITY
AGE
DECLINE
IMPROVE
LESS NEGATIVITY
AGE
GENERAL COGNITIVE FUNCTION
PROCESSING SPEED
MEMORY RECALL
INFO. PROCESSING SPEED
EXECUTIVE FUNCTIONING
AGE
DECLINE
IMPROVE
VERBAL ABILITY
AGE
ELECTRICAL BRAIN FUNCTION
EEG DELTA
EEG DELTA
P3 LATENCY
N1 AMPLITUDE
AGE
DECLINE
IMPROVE
VPP AMPLITUDE
AGE
BODY AROUSAL
HEART RATE
AVERAGE HEART RATE DURING COGNITIVE TESTS
AGE
DECLINE
STABLE
AVERAGE AMP. OF SCR
AGE
MRI
GRAY MATTER
CORTICAL GRAY MATTER
AGE
DECLINE
STABLE
WHITE MATTER
CORTICAL WHITE MATTER
AGE
GENETICS
EEP P3 AMP.
APOE E4
AGE
DECLINE
STABLE
EEP P3 AMP.
APOE E3
AGE

ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD)

A BREAKDOWN IN ATTENTION AND IMPULSE CONTROL LEADS TO THE FAILURE TO PROCESS WHAT IS RELEVANT AND IGNORE WHAT IS IRRELEVANT. THIS IS DUE TO A DYSFUNCTION IN BRAIN-BODY AROUSAL ASSOCIATED WITH A LOSS OF CORTICAL CONTROL OVER SUBCORTICAL ACTIVATING SYSTEMS.

GENERAL COGNITION FACTOR SCORES



COMPARED TO CONTROLS, ADHD SUBJECTS SHOWED DEFICITS ACROSS ALL COGNITIVE DOMAINS

SOCIAL COGNITION

DECLINE

AGREEABLENESS
SELF ESTEEM

GENERAL COGNITION DETAILS

DECLINE

FALSE ALARMS TO MULTIPLE TESTS

ELECTRICAL BRAIN FUNCTION

DECLINE

THETA/BETA RATIO
P3 SELECTIVE AND SUSTAINED ATTENTION
SLOWED N250 TO ANGER FACES

BODY AROUSAL

DECLINE

HEART RATE
SKIN CONDUCTANCE LATENCY

ADHD GROUP FINDINGS OF MARKERS AND CUMULATIVE SNSITIVITY

THESE TEN COMPOSITE SCORES (MARKERS) DISTINGUISH ADHD SUBJECTS FROM HEALTHY CONTROLS

EEG THETA

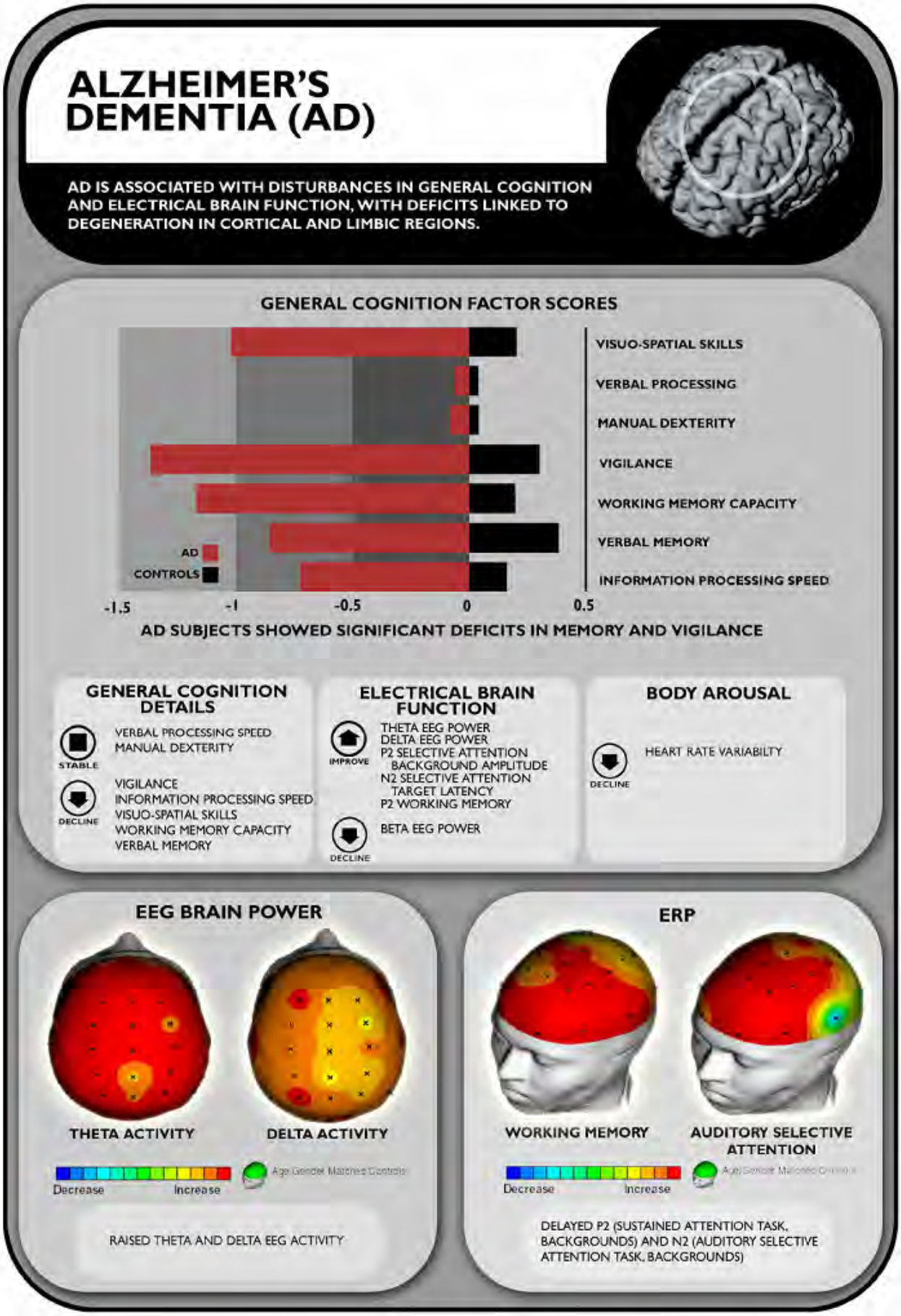
PRE MEDICATION

POST MEDICATION

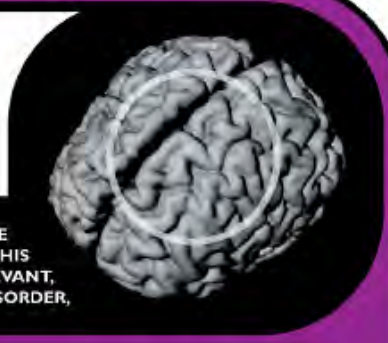
Decrease — Increase

Age/Gender Matched Controls

EXCESSIVE EEG THETA (PRE-MEDICATION) IS NORMALIZED WITH MEDICATION

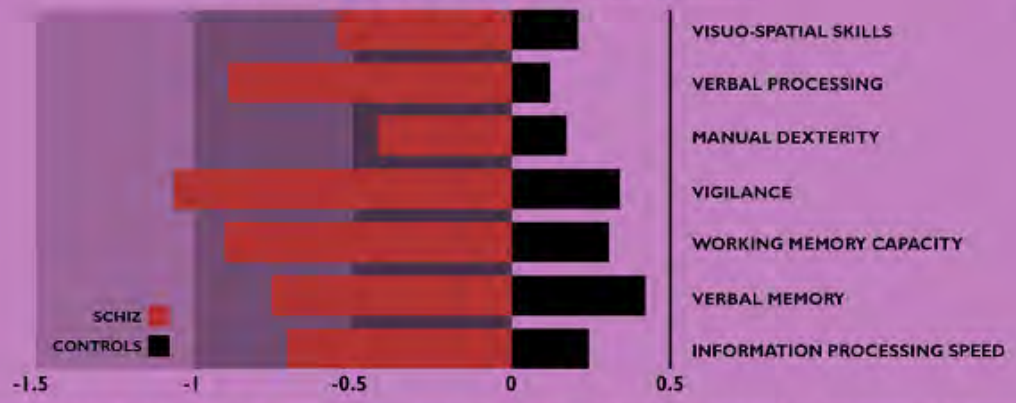

ALZHEIMER'S DEMENTIA (AD)
AD IS ASSOCIATED WITH DISTURBANCES IN GENERAL COGNITION AND ELECTRICAL BRAIN FUNCTION, WITH DEFICITS LINKED TO DEGENERATION IN CORTICAL AND LIMBIC REGIONS.
GENERAL COGNITION FACTOR SCORES
VISUO-SPATIAL SKILLS
VERBAL PROCESSING
MANUAL DEXTERITY
VIGILANCE
WORKING MEMORY CAPACITY
VERBAL MEMORY
INFORMATION PROCESSING SPEED
AD
CONTROLS
-1.5
-1
-0.5
0
0.5
AD SUBJECTS SHOWED SIGNIFICANT DEFICITS IN MEMORY AND VIGILANCE
GENERAL COGNITION DETAILS
STABLE
VERBAL PROCESSING SPEED
MANUAL DEXTERITY
DECLINE
VIGILANCE
INFORMATION PROCESSING SPEED
VISUO-SPATIAL SKILLS
WORKING MEMORY CAPACITY
VERBAL MEMORY
ELECTRICAL BRAIN FUNCTION
IMPROVE
THETA EEG POWER
DELTA EEG POWER
P2 SELECTIVE ATTENTION BACKGROUND AMPLITUDE
N2 SELECTIVE ATTENTION TARGET LATENCY
P2 WORKING MEMORY
DECLINE
BETA EEG POWER
BODY AROUSAL
DECLINE
HEART RATE VARIABILTY
EEG BRAIN POWER
THETA ACTIVITY
DELTA ACTIVITY
Decrease
Increase
Age Gender Matched Controls
RAISED THETA AND DELTA EEG ACTIVITY
ERP
WORKING MEMORY
AUDITORY SELECTIVE ATTENTION
Decrease
Increase
DELAYED P2 (SUSTAINED ATTENTION TASK, BACKGROUNDS) AND N2 (AUDITORY SELECTIVE ATTENTION TASK, BACKGROUNDS)

SCHIZOPHRENIA



THE CORE DISTURBANCE IN SCHIZOPHRENIA IS A BREAKDOWN IN THE CONNECTIVITY OF THE BRAIN'S FRONTAL AND LIMBIC NETWORKS, WHICH ARE REQUIRED FOR APPROPRIATE MOTIVATION AND MEANING OF INFORMATION. THIS RESULTS IN AN INABILITY TO FOCUS ON RELEVANT, WHILST IGNORING IRRELEVANT, INFORMATION. THIS IS REFLECTED IN THE DISASSOCIATIONS OF THOUGHT DISORDER, IN ADDITION TO MULTIPLE COGNITIVE AND EMOTIONAL DISTURBANCES.

GENERAL COGNITION FACTOR SCORES



COMPARED TO CONTROLS, THE SCHIZOPHRENIA GROUP SHOWED DEFICITS ACROSS ALL COGNITIVE DOMAINS

SOCIAL COGNITION

DECLINE — SOCIABILITY

GENERAL COGNITION DETAILS

DECLINE — CONFABULATIONS
VERBAL INTERFERENCE
WORD RECALL

ELECTRICAL BRAIN FUNCTION

DECLINE — N1 ERP LATENCY
P3 SELECTIVE ATTENTION AMPLITUDE
P3 ERP NOVELTY AMPLITUDE
P2 AMPLITUDE FACE PERCEPTION

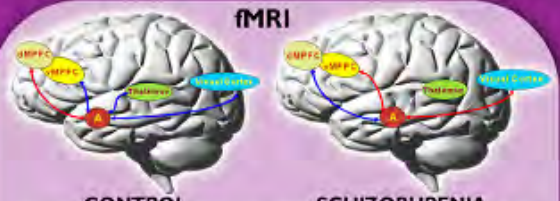
MRI

DECLINE — GRAY MATTER (PREFRONTAL AND TEMPORAL)

BODY AROUSAL

DECLINE — HEART RATE
SWEAT RATE

fMRI

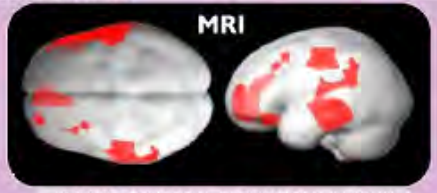


CONTROL — SCHIZOPHRENIA

FEAR PROCESSING: LOSS OF NORMAL FUNCTIONAL CONNECTIVITY (fMRI) IN PREFRONTAL-LIMBIC PATHWAYS IN SCHIZOPHRENIA

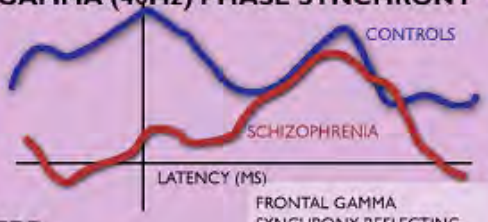
NEGATIVE CONNECTIVITY
POSITIVE CONNECTIVITY

MRI



FRONTO-TEMPORAL REDUCTIONS IN GRAY MATTER IN SCHIZOPHRENIA

GAMMA (40Hz) PHASE SYNCHRONY



FRONTAL GAMMA SYNCHRONY REFLECTING DECREASED INTEGRATION (SELECTIVE ATTENTION TASK)

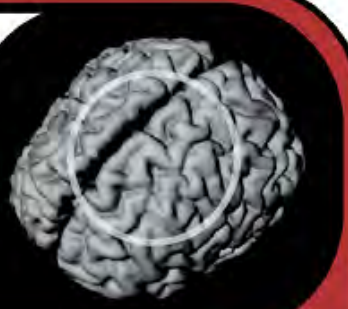
ERP

DECREASE ERP SELECTIVE ATTENTION P3 AMPLITUDE

Decrease — Increase

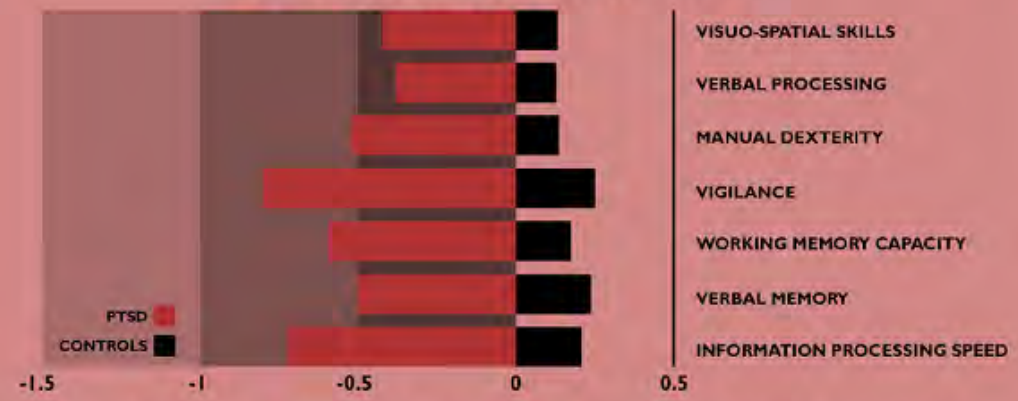
Age/Gender Matched Controls

POST TRAUMATIC STRESS DISORDER (PTSD)



IN PTSD, TRAUMA TRIGGERS A GREATER AUTOMATIC FEAR RESPONSE WITH A LOSS OF REGULATION OF THIS RESPONSE. THESE CHANGES ALSO PRODUCE A DISRUPTION IN WORKING MEMORY.

GENERAL COGNITION FACTOR SCORES



COMPARED TO CONTROLS, THE PTSD GROUP SHOWED DEFICITS ACROSS ALL COGNITIVE DOMAINS

SOCIAL COGNITION

STABLE — SELF CONTROL

DECLINE — NEGATIVITY
SOCIABILITY

GENERAL COGNITION DETAILS

DECLINE — REACTION TIME FOR SELECTIVE ATTENTION
WORKING MEMORY
SPOT THE REAL WORD
SWITCHING OF ATTENTION

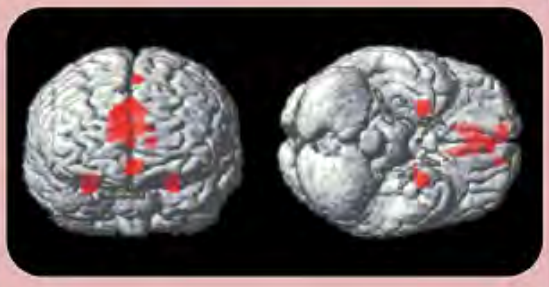
ELECTRICAL BRAIN FUNCTION

DECLINE — P3 WORKING MEMORY AMPLITUDE

BODY AROUSAL

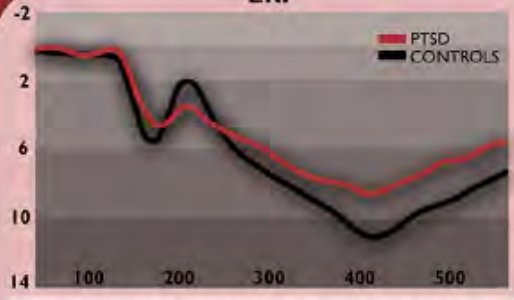
INCREASE — HEART RATE VARIABILITY

fMRI



EXCESSIVE AMYGDALA AND MEDIAL PREFRONTAL RESPONSES TO SUBCONSCIOUSLY PRESENTED FEAR STIMULI

ERP



REDUCED P3 RESPONSES REFLECTS LOSS OF MEMORY UPDATING

BODY AROUSAL

INCREASED VARIABILITY IN HEART RATE

BDNF Genotypes

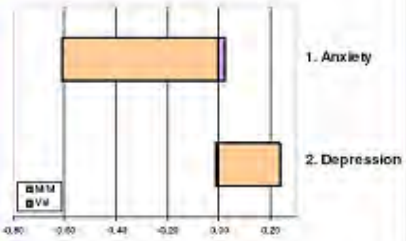
Brain Derived Neurotrophic Factor (BDNF) Val66Met is a genetic polymorphism which affects activity-dependent secretion of BDNF and hippocampal-related functions. In the rare Met-Met genotype, primary deficits in general cognition are associated with some associated problems with depression and social cognition. Val carriers, on the other hand, may have primary deficits in social cognition.

Social Cognition Deficits

Mood

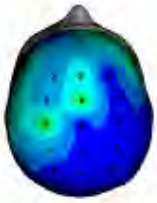
Val (males) = ↑ Anxiety

Met-Met = ↑ Depression



EEG Relative Theta

Val = ↓ Relative Theta Power

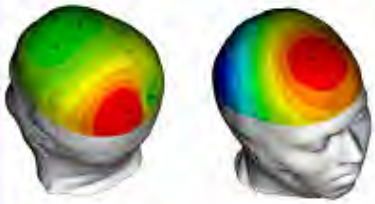


Decrease Increase

Emotion-related ERPs

Met-Met = → Posterior N170 Latency to nonconscious Happy faces

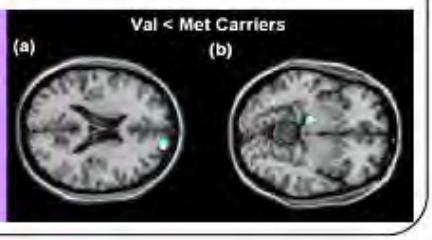
Val = ← Temporal N170 Latency to nonconscious Fearful faces with → Frontal P200 Latency



Earlier Later

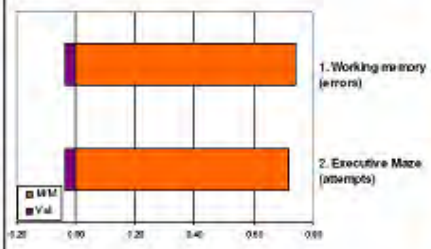
fMRI (Fearful faces)

Val = Decreased (blue) (a) ventral medial prefrontal and (b) subcortical response to nonconscious Fearful faces



General Cognition Deficits

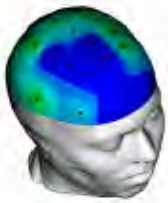
Neuropsychology



Met-Met = Poorer Working Memory (more errors)

Met-Met = Poorer Executive Function (more maze attempts)

EEG Alpha Peak Frequency



Met-Met = ↓ Alpha Peak Frequency

Decrease Increase

Cognitive-related ERPs

Met-Met = → Frontal P300 Latency to Selective Attention

Met-Met = → Posterior P300 Latency to Working Memory Updating

Earlier Later

fMRI (Oddball Selective Attention)

Met-Met = Exaggerated (yellow) hippocampal response to Selective Attention (Oddball task)

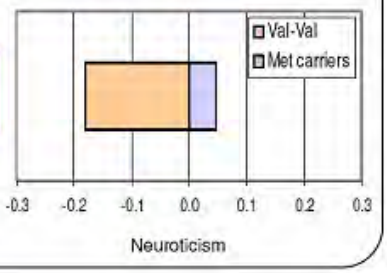
COMT Genotypes

Catechol-O-Methyltransferase (COMT) Val108/158Met is a genetic polymorphism which affects dopamine metabolism in the prefrontal brain. For Val-Val genotypes, deficits in general cognition may be associated with compensatory advantages in social and emotional cognition, while Met-Met genotypes may have deficits in social and emotional cognition.

Social Cognition Deficits

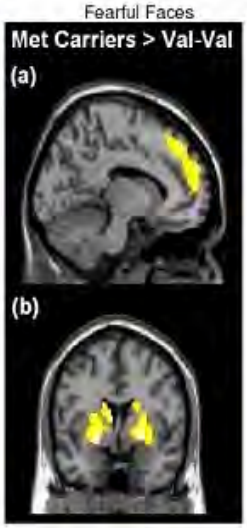
Mood

Met carriers = ↑ Neuroticism

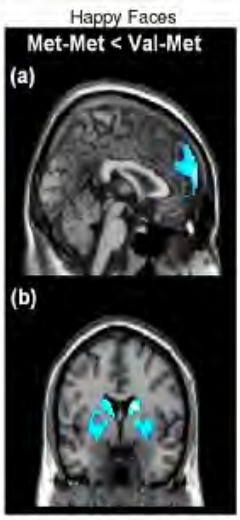


fMRI

Met carriers = ↑ activation (yellow) in (a) frontal and (b) subcortical regions to conscious Fearful faces

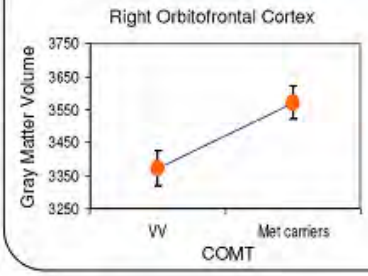


Met-Met = ↓ activation (blue) in (a) frontal and (b) subcortical regions to conscious Happy faces



General Cognition Deficits

MRI

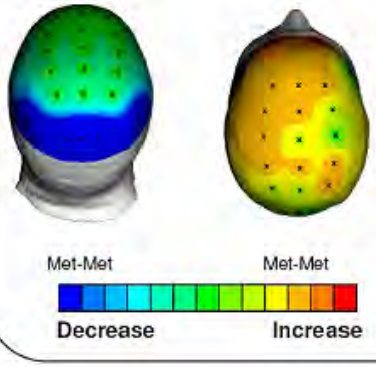


Met carriers = ↑ Frontal Gray Matter Volume

EEG

EEG Theta Power

EEG Delta/Theta Ratio

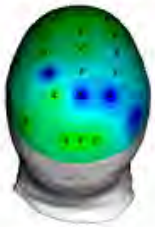


Met-Met = ↓ Resting EEG Theta Power (Eyes Closed)

Met-Met = ↑ Resting EEG Delta/Theta Ratio (Eyes Closed)

Cognitive-related ERPs

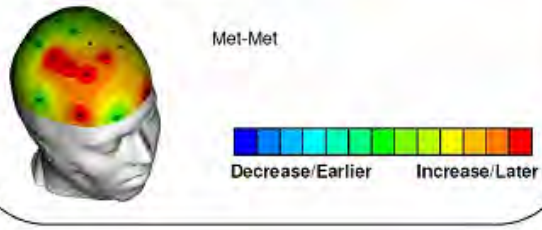
Working Memory: Sustained Attention



Met-Met = ↓ Centroparietal P300 Amplitude for Working Memory Sustained Attention

Met-Met = → Frontal P300 Latency for Working Memory updating

Working Memory: Updating



ADHD: Brain Function - Cognition Profile

	theta	alpha	beta	P3	RT	Time	SoVM	VI	MR	SOA	WG	DS	CPT
2014	↑	↑			→			*				↓	*
2193	↑		↑	→				*		↑		↓	
2306		↑		→			↓	*			↓		
2395		→						*	↓	↑			
2418		↑								↑		↓	
2520		↑		←					↓				
2553	↑	←		→	→	↑	↓			↑		↓	*
2575				←				*			↓		
2744	↑	← ↓	↑	→ ↓	→	↑		*	↓	↑			
2777	↑						↓		↓		↓		*
3149		↑			→		↓	*	↓	↑	↓		*
3251	↑	↑				↑							
3330	↑	↑		↑		↑		*	↓	↑	↓	↓	*
3521								*	↓		↓	↓	
3532				→					↓	↑			
3576	↑	← ↑		→	→		↓	*	↓	↑		↓	
3813		↑						*		↑			*
3846	↑	↑	↑	→			↓	*		↑			*
3824											↓		*
3857	↑	↑		→				*			↓	↓	*
4061					→	↑		*		↑	↓		*
4151	↑		↑	→ ↓	→		↓	*		↑			*
4162	↑	↑	↑	→					↓	↑			
4409	↑			↑							↓		
4397		→	↓					*					
4465								*					*
4476		↑		↑	→				↓				
4487	↑	→ ↑	↑		→			*	↓			↓	*
4926		↑					↓		↓			↓	*
5163		→	↑	→	→		↓	*	↓				*
5118	↑	↑		→ ↓		↑	↓		↓				*
5208		↑			→		↓			↑		↓	
5400	↑	↑											
5411		↑	↑	→ ↓	→				↓	↑			
5422	↑	←	↓	→	→	↑	↓	*	↓			↓	
5332		←					↓	*					

Time	Time Estimation
SoVM	Span of Visual Memory
VI	Verbal Interference (Stroop)
MR	Memory Recall
SOA	Siwtching of Attention
WG	Word Generation
DS	Digit Span (forward or reversed)
CPT	Sustained Attention

Correlations with Psychophysiology: Temporal

Motor Tapping	Earlier P200 Target Latency = faster tapping
Choice Reaction Time	Earlier P300 = faster reaction time
Timing	Earlier P300 Target Latency = greater underestimation of time
Span of Visual Memory	Earlier N200 targets = longer visual memory span
Digit Span Forward	Earlier N200 targets = longer digit span
Reverse Digit Span	Lower P200 amplitude = longer reverse digit span
Memory Recognition	Earlier P200 target = more accurate delayed verbal recall
Verbal Interference	Delayed Background P200 Latency = higher visual interference score
Spot the Real Word	Earlier N2 target = higher spot the word score
Sustained Attention	Later P200 background (and earlier target) = faster Working Memory
Switching of Attention	Earlier Target P300 = more correct in switching of attention
Executive Maze	Lower P300 Target Amplitude = less maze errors

Correlations with Neurocognitive Test Battery

Motor Tapping	More frontal grey matter = faster tapping
Choice Reaction Time	More grey matter in the cerebellum = more variable reaction time
Timing	More parietal grey matter = higher switching of attention score
Span of Visual Memory	More frontal grey matter = longer visual memory span
Digit Span Forward	More frontal grey matter = longer digit span
Reverse Digit Span	More right parietal grey matter = longer reverse digit span
Memory Recognition	More limbic grey matter = less recall intrusions
Verbal Interference	More grey matter = less visual interference errors
Spot the Real Word	More grey matter = higher spot the word variability of RT
Sustained Attention	More frontal grey matter = more variable working memory RT
Switching of Attention	More parietal grey matter = higher switching of attention score
Executive Maze	More grey matter (especially frontal) = faster maze completion

Brain Function Laboratories:
USA – UK – Germany – The Netherlands – South Africa – Australia

Brain Resource®

IntegNeuro Report

Client Assessment (IN-Sample-06)

Birth date withheld (age 13 years; female)

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This report is for clinicians only

The report is provided on pages 1 – 2.

The remainder of the report is score details.

For description of the tests - see http://www.brainresource.com/reportdetails.jsp

For Summary Report Manual - see http://www.brainresource.com/reportmanual.jsp

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Email: info@brainresource.com URL: www.brainresource.com

1. Overall summary of findings

Cognition

Test	Deficit
1. Memory Recall and Recognition	●
2. Digit Span	●
3. Span of Visual Memory	
4. Sustained Attention (CPT)	●
5. Switching of Attention	
6. Motor Tapping	●
7. Choice Reaction Time	●
8. Time Estimation	
9. Verbal Interference	●
10. Spot the Real Word	
11. Word Generation	
12. Maze	

● = deficit compared to matched controls (see Appendix 1.3 for details)

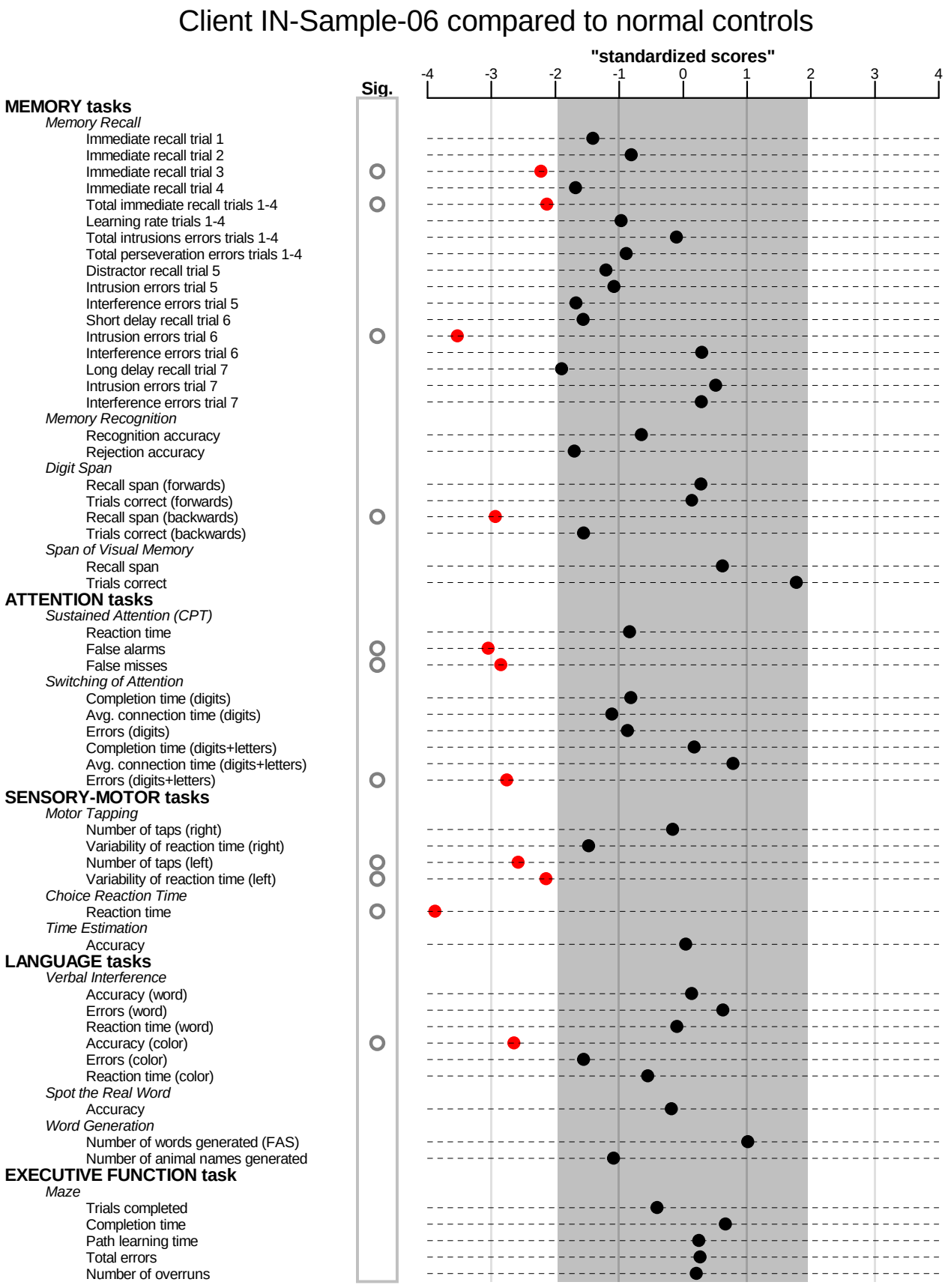
The table above shows deficits found in each test (1–12).

The list below summaries what the practical significance of that deficit is considered to be:

1. Ability to learn and remember new tasks based on verbal information. Critical, central everyday skill.
2. Ability to hold, retain and operate on new verbal information. Skills crucial to most everyday, verbal tasks requiring memory. Everyday examples include remembering telephone numbers and shopping lists.
4. Ability to detect and respond to significant change under conditions requiring vigilance. Fundamental everyday skills e.g. train, plane, automobile, computer and equivalent machine operations.
6. Everyday motor skills such as typing and machine operation.
7. Visual discriminative judgment and response. Examples: visual monitoring tasks requiring choice and reaction such as air traffic control, driving judgement.
9. Part 1: Simple reading ability. Part 2: Ability to control impulses; behavioural control.

The remainder of this report provides the landscape summary and then the details underpinning these results.
For further details or queries not addressed in this report, please email: info@brainresource.com

2. Summary of Cognition results (landscape view)



For convenience, the tasks are organized by broad cognitive groupings. The circles on the left indicate statistically significant differences compared with the normal control. The "standardized scores" on the right are normalized for age, gender and years of education, which means differences from zero reflect differences from 'average peer' (also known as z-scores). Positive "standardized scores" indicate strengths, negative "standardized scores" indicate potential deficits (Avg = average). "Standardized scores" beyond -2 to +2 are statistically significant. False alarms (respond when should not) = false positive; errors of commission. False misses (not respond when should) = false negatives; errors of omission. Memory Recall (Intrusion = words not on the list. Interference = words from the other list. Perseveration = repeat errors). Specialist interpretation is required.

Appendix 1. Details of Cognition

Appendix 1.1 The client's scores

Measure	Client	Int. Brain Database Average	Std. Dev	Standardized Score	Percentile
Memory Recall					
Immediate recall trial 1	4	5.9	1.3	-1.41	8^{th}
Immediate recall trial 2	7	8.3	1.6	-0.81	21^{st}
• Immediate recall trial 3	6	9.6	1.6	-2.22	1^{st}
Immediate recall trial 4	7	10.4	2	-1.68	5^{th}
• Total immediate recall trials 1-4	24	33.9	4.6	-2.13	2^{nd}
Learning rate trials 1-4	0.8	1.39	0.61	-0.97	17^{th}
Total intrusions errors trials 1-4	1	0.9	1.4	-0.1	46^{th}
Total perseveration errors trials 1-4	12	4.3	8.7	-0.89	19^{th}
Distractor recall trial 5	3	5	1.7	-1.21	11^{th}
Intrusion errors trial 5	1	0.26	0.69	-1.08	14^{th}
Interference errors trial 5	1	0.14	0.51	-1.68	5^{th}
Short delay recall trial 6	6	9	1.9	-1.56	6^{th}
• Intrusion errors trial 6	3	0.12	0.82	-3.53	$< 1^{st}$
Interference errors trial 6	0	0.08	0.28	0.29	62^{nd}
Long delay recall trial 7	5	8.7	1.9	-1.9	3^{rd}
Intrusion errors trial 7	0	0.23	0.45	0.51	70^{th}
Interference errors trial 7	0	0.08	0.26	0.29	61^{st}
Memory Recognition					
Recognition accuracy	11	11.56	0.87	-0.65	26^{th}
Rejection accuracy	10	11.8	1	-1.7	4^{th}
Digit Span					
Recall span (forwards)	6	5.6	1.5	0.28	61^{st}
Trials correct (forwards)	6	5.7	1.9	0.14	56^{th}
• Recall span (backwards)	0	3.7	1.3	-2.94	$< 1^{st}$
Trials correct (backwards)	0	2.9	1.9	-1.55	6^{th}
Span of Visual Memory					
Recall span	6	5.1	1.4	0.62	73^{rd}
Trials correct	10	6.6	1.9	1.78	96^{th}
Sustained Attention (CPT)					
Reaction time	$611ms$	$528ms$	$100ms$	-0.83	20^{th}
• False alarms	14	1.6	4	-3.05	$< 1^{st}$
• False misses	12	1.2	3.8	-2.85	$< 1^{st}$
Switching of Attention					
Completion time (digits)	$25.1s$	$21.5s$	$4.5s$	-0.81	21^{st}
Avg. connection time (digits)	$956ms$	$765ms$	$172ms$	-1.11	13^{th}
Errors (digits)	2	0.8	1.4	-0.87	19^{th}
Completion time (digits+letters)	$47s$	$49s$	$11s$	0.17	57^{th}
Avg. connection time (digits+letters)	$1483ms$	$1786ms$	$386ms$	0.78	78^{th}
• Errors (digits+letters)	14	1	4.7	-2.76	$< 1^{st}$
Motor Tapping					
Number of taps (right)	142	146	25	-0.16	44^{th}
Variability of reaction time (right)	$112ms$	$29ms$	$56ms$	-1.48	7^{th}
• Number of taps (left)	67	128	24	-2.58	$< 1^{st}$
• Variability of reaction time (left)	$330ms$	$47ms$	$132ms$	-2.14	2^{nd}

Raw scores of the Cognitive findings (• = statistically significant; Std. Dev = standard deviation; Int = international).

Measure	Client	Int. Brain Database Average	Std. Dev	Standardized Score	Percentile
Choice Reaction Time					
• Reaction time	1486ms	728ms	195ms	-3.88	$< 1^{st}$
Time Estimation					
Accuracy	0.00s	-0.01s	0.18s	0.04	52^{nd}
Verbal Interference					
Accuracy (word)	19	18.7	2.5	0.13	55^{th}
Errors (word)	0	0.23	0.36	0.62	73^{rd}
Reaction time (word)	1026ms	1013ms	140ms	-0.1	46^{th}
• Accuracy (color)	6	12.7	2.5	-2.64	$< 1^{st}$
Errors (color)	3	0.8	1.4	-1.55	6^{th}
Reaction time (color)	1571ms	1425ms	265ms	-0.55	29^{th}
Spot the Real Word					
Accuracy	40	40.8	4.3	-0.18	43^{rd}
Word Generation					
Number of words generated (FAS)	14	11.3	2.7	1.01	84^{th}
Number of animal names generated	17	22.3	4.8	-1.09	14^{th}
Maze					
Trials completed	9	7.7	3.1	-0.41	34^{th}
Completion time	134s	166s	48s	0.67	75^{th}
Path learning time	114s	131s	70s	0.25	60^{th}
Total errors	29	33	13	0.27	61^{st}
Number of overruns	13	14.2	6	0.21	58^{th}

Raw scores of the Cognitive findings (• = statistically significant; Std. Dev = standard deviation; Int = international).

Nominal classification bands	Percentile boundary
Very superior	$\leq 100^{th}$
Superior	$< 98^{th}$
High average	$< 91^{st}$
Average	$< 75^{th}$
Low average	$< 25^{th}$
Borderline	$< 9^{th}$
Extremely Low	$< 2^{nd}$

The test descriptions, selected references and how the scores are derived can be found at http://www.brainresource.com/reportdetails.jsp

Appendix 2. Malingering score

Measures possible deliberate underperformance by the subject.

Details are withheld for reasons of confidentiality.

On a test designed to investigate the validity of responding, there was no suggestion of sub-optimal effort or any deliberate attempt to feign impairment.

Appendix 3. Demographics (summary scores of personal and clinical history)

Personal Details	Client
Date of birth	withheld
Gender	FEMALE
Marital status	Single
Height (cm)	165
Weight (kg)	50
Occupation	CustomerServiceRepresentative
Highest level of education	Secondary/High school
Number of years of education	10
Handedness	Right

Physical/Medical History	Client
Sphere	Fatique and Psychological Complaints
Vision impairment	No
Hearing difficulties	No
Restricted movement	Yes
Mobile phone	Yes
Dyslexia (learning difficulties)	No
Traumatic experience	Yes
Family or personal psychiatric illness	Yes
Family or personal neurological disorder	No
CNS surgery	No
Physical trauma	Yes
Sleep difficulties	Yes
Staying awake difficulties	No
Eating problems	Yes
Number of caffeine beverages per week	14

Substance Used	Client
Tobacco	Yes
Alcohol	Yes
Marijuana	Yes
Non-prescription/recreational drugs	No

Depression Anxiety Stress Scales	Client	Severity Rating
Depression	26	Severe
Stress	24	Moderate
Anxiety	14	Moderate

Emotional Intelligence (EI)	Client	Average	Std. Dev	Standardized Score	Percentile
Empathy/Intuition factor	19	20.41	3.27	-0.43	33^{rd}
Social/Relationships factor	11	13.54	2.63	-0.97	17^{th}
Self Esteem factor	15	13.19	1.91	0.95	83^{rd}

NEO-FFI	Client	T Score	Range
Neuroticism	29	N/A	N/A
Extraversion	36	N/A	N/A
Openness	17	N/A	N/A
Agreeableness	15	N/A	N/A
Conscientiousness	6	N/A	N/A

● = statistically significant (normalized for age, gender and years of education); Std. Dev = standard deviation; N/A = data not available
For the list of questions - see Report Details on http://www.brainresource.com/reportdetails.jsp

Prescription Drugs	Client
Use prescription medications	Yes
Medication 1:	
Name	Ritalin
Reason	ADHD
Dosage	2 mg
Frequency	Many times per day
Medication 2:	
Name	Ritalin
Reason	ADHD
Dosage	10 mg
Frequency	Many times per day
Medication 3:	
Name	Zoloft
Reason	not known
Dosage	1 tablet

Traumatic Experience	Client
Direct combat in war	No
Life-threatening accident	No
Natural disaster	No
Witnessed someone injured or killed	No
Raped	No
Sexually molested	No
Attacked or assaulted	No
Threatened with weapon or kidnapped	No
Tortured or victim of terrorists	No
Extremely stressful or upsetting event	Yes
Shock (happened to someone close)	No

Mobility/Dexterity	Client
Mobility	N/A
Reduced dexterity on hand	N/A

Mobile Phone	Client
Frequency	Many times per day
Duration per call	5-10 minutes
Duration per day	10-30 minutes
Years of usage	1 - 2 years

Psychological History	Client
Diagnosed with psychiatric disorder	Yes
Nature	ADHD
Year	2001
Duration	Ongoing
Treatment	Yes
Treatment type	Pharmaceutical
Family history	Yes
Family condition	ADHD

Eating Habits	Client
Eat within 2 hours	N/A
Vomit	N/A
Laxatives	N/A
Fasted	N/A
Exercise	N/A

Tobacco	Client
First smoking after wake up	6-30 min
Unable to stop smoking	Yes
Unwilling to give up	First in the morning
Amount	11 to 20
Smoke more early	No
Smoke when sick	No

Alcohol	Client
Frequency	Two to four times a month
Amount	7 to 9
Drink six or more	Never
Unable to stop drinking	Never
Morning drinking	N/A
Feel guilty after drinking	N/A
Unable to remember	N/A
Cause injury	N/A
Concerned by others	N/A

Marijuana	Client
Frequency	Occasionally
Duration	Less than 1 year
Amount	Less than 1 per week

Physical Trauma	Client
Area	N/A
Age	N/A
Impact Injury	N/A

Intern. J. Neuroscience, 115:1549–1567, 2005

ISSN: 0020-7454 / 1543-5245 online
DOI: 10.1080/00207450590957890

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PRELIMINARY VALIDITY OF "INTEGNEURO™": A NEW COMPUTERIZED BATTERY OF NEUROCOGNITIVE TESTS

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The purpose of this study was to examine the preliminary validity of a newly developed battery of computerized cognitive measures, IntegNeuroTM. This standardized and semi-automated computerized battery assesses sensori-motor function, attention, new learning and memory, language fluency, executive function, and estimated intelligence. A total of 50 healthy individuals (aged 22–80 years) were included in the study. Correlational analyses revealed highly significant associations between the two cognitive batteries. These results support the use of IntegNeuroTM as a computerized cognitive system. Additional studies are needed to examine the clinical utility of the battery.

Keywords assessment, computerized testing, neuropsychology, validity

INTRODUCTION

Computerized neuropsychological assessment has increasingly received recognition as a valuable research and clinical tool. The American Psychological Association (APA) recognized the value of computerized psychological testing and published guidelines in 1987 (APA, 1987) to assist in the development and interpretation of computerized test results. In this publication, the APA identified six major benefits of computerized assessment including: (1)

automated data collection and storage, (2) greater efficiency of use, (3) release of the clinician from test administration to focus on treatment, (4) greater sense of mastery and control for the client, (5) reduced negative self-evaluation among clients that experience difficulty on the computer, and (6) greater ability to measure aspects of performance not possible through traditional means such as latency, strength, and variability in response patterns.

Despite their promise, initial efforts to computerize cognitive tests focused mainly on individual measures, and the validity of these outcomes varied (for review see Kane & Kay, 1992). Further, many early versions of computerized assessment suffered from poor visual graphics, inadequate sound quality, and inconsistencies in recording of responses. These limitations have been overcome with developments in computing hardware and software. Computer methods now exist that allow for accurate and reliable timing of stimulus presentation, response recording, and multidimensional display of information.

A number of computerized cognitive batteries have been developed in recent years on the heels of the advancements in computerized technology. Three computerized batteries frequently cited in the literature include the Cambridge Automated Neuropsychological Test Battery (CANTAB; Morris et al., 1986), the MicroCog (Devivo et al., 1999), and the Neurobehavioral Evaluation System (Baker et al., 1985). These computerized batteries have provided significant contributions to the research literature. There are, however, aspects of these batteries that restrict their utility, including the absence of language measures on the CANTAB and NES 3, and the assessment of cognitive constructs that differ from standardized clinical assessment (e.g., MicroCog; Elwood, 2001). As such, there is a need for the development of cognitive programs that capitalize on the advancements of computing technology to allow assessment of standard cognitive skills including language and verbal memory.

IntegNeuro™ (Brain Resource Company, Ltd) is a newly developed computerized battery that consists of an automated stimulus presentation protocol, and response recording involving touch-screen and voice recording software. The tests were based on existing paradigms known to be sensitive to brain dysfunction. Attractive features of the battery include standardized instructions using both auditory explanations and visual examples, practice trials prior to test trials, and semi-automated scoring procedures. In addition, the battery include both language and nonlanguage paradigms. The battery was developed by a consortium of scientists involved in the first standardized international brain database (Gordon, 2005). Test-retest reliability for each of the cognitive tests is acceptable for all measures (Williams et al., current volume).

The purpose of the present study was to examine the preliminary validity of IntegNeuro™, via examination of the relationships between performances on IntegNeuro™ and performances on previously developed common tests that tap the same cognitive skills. It was predicted that the individual measures of IntegNeuro™ would correlate strongly with analogous standard measures of cognitive function.

METHODS

Participants

A total of 50 healthy adults (25 females and 25 males, age 22–80) completed the IntegNeuro™ and the standard neuropsychological batteries. Exclusion criteria included any mental or physical condition with the potential to influence cognitive performance, including a personal history of mental illness, physical brain injury, neurological disorder, genetic disorder, or other medical condition (hypertension, diabetes, cardiac disease, thyroid disease), and/or a personal history of drug or alcohol addiction. The computerized Composite International Diagnostic Interview (CIDI, WHO, 1993) was also used to exclude participants if they had a family history of Attention Deficit Hyperactivity Disorder, Schizophrenia, or Bipolar Disorder. The CIDI consists of computer-aided self report endorsement of psychiatric symptoms and diagnoses are determined according to criteria defined in the Diagnostic and Statistical Manual—IV (APA, 1994). The CIDI is both valid and reliability for multi-site and international use (Wittchen, 1991; Wittchen et al., 1999).

Web-based questionnaires were used to acquire demographic data including age, sex, years of education and current mood state in terms of depression, anxiety, and stress (assessed using an abbreviated version of the Depression Anxiety Stress Scale; DASS; Lovibond & Lovibond, 1995). These demographic data are presented in Table 1 for the full sample. All participants voluntarily signed a written informed consent form to participate in the database, according to local Institutional Review Boards.

Procedure

IntegNeuro™ was administered in a sound-attenuated testing room, with participants seated in front of a touch-screen computer (NEC MultiSync LCD 1530V). The cognitive tests were administered using standardized task instructions (via headphones and visual screen display), and the touch-screen

Table 1. Demographic data for the sample

	Mean (SD)
Age	49.2 (18.3)
Education	15.3 (2.0)
DASS depression*	1.9 (1.9)
DASS anxiety*	1.0 (1.3)

*Note that these scores are below recommended cutoffs for clinical significance (i.e., < 4.0; Lovibond & Lovibond, 1995).

computer was used to record nonverbal responses. Examples of the system are provided in Figure 1. The paper-and-pencil tests were administered by a highly trained psychometrician according to standardized manuals. In one half the cases (n = 25), the IntegNeuro™ battery was administered at the first visit, and four weeks later the previously developed standard measures were administered at a second visit. The other half of the cases (25 individuals) first completed the standard measures and subsequently completed IntegNeuro™.

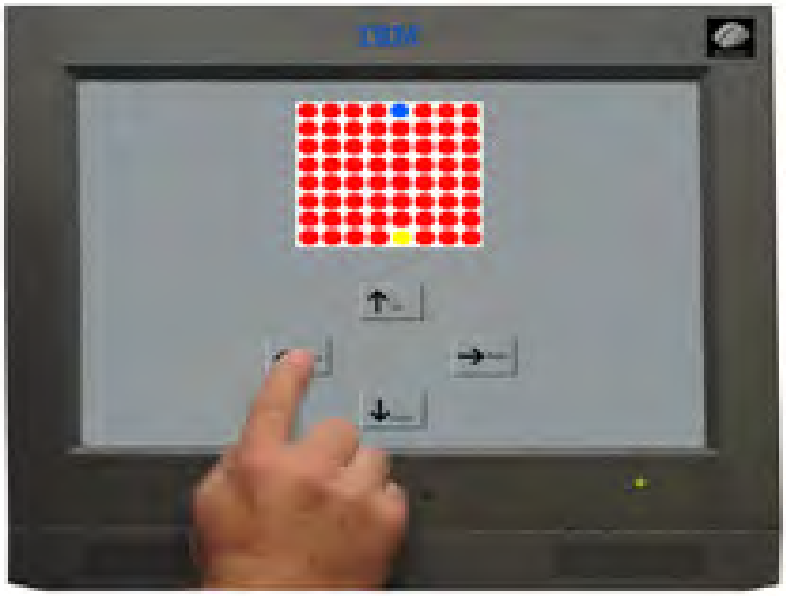

Figure 1. Visual example of the Maze task on IntegNeuro™.

The order of administration (IntegNeuro™ vs. standard measures) was determined by random assignment to avoid an order effect. Each measure of IntegNeuro™ included a practice trial prior to the test trial. Individuals were required to pass the practice trial accurately before completing the test trial. In the event that an individual was unable to perform the practice trial without error, the individual test was terminated and the individual was automatically forwarded to the next test in the battery. In the present study, all participants were capable of passing the practice trials.

Cognitive Tests

IntegNeuro. The battery of IntegNeuro™ tests tapped the following domains of cognitive function: sensori-motor, verbal and language, memory, executive planning, and attention. Scoring of responses was conducted using an automated software program for most tests, and by hand-scoring for .wav files. Hand scoring was required for the two language tests and the verbal memory test. Trained research assistants conducted the hand scoring of the .wav files and oversight was implemented to monitor accuracy. The measures in each of these domains are described in the following.

Sensori-Motor Domains. (i) Simple motor tapping task: Participants were required to tap a circle on the touch-screen with their index finger, as fast as possible for 60 s. The dependent variable was total number of taps with the dominant hand. (ii) Choice reaction time task: Participants were required to attend to the computer screen as one of four target circles was illuminated in pseudo random sequence over a series of trials. For each trial, the subject was required to place their index finger in preparation on a start circle displayed on the touchscreen. On each trial, the subject then had to touch the illuminated circle as quickly as possible following presentation. Twenty trials were administered with a random delay between trials of 2–4 s. The dependent variable was the mean reaction time across trials.

Attention Domain. (i) Span of Visual Memory: This test is a computerized adaptation of the Spatial Span test from the Wechsler Memory Scale (III; Wechsler, 1999b). Participants were presented with squares arranged in a random pattern on the computer screen. The squares were highlighted in a sequential order on each trial. Participants were required to repeat the order in which the squares were highlighted by touching the squares with their forefinger. Both forward and reverse trials are conducted. The total correct

was the dependent variable. (ii) Digit Span: Participants were presented with a series of digits on the touchscreen (e.g., 4, 2, 7, etc., 500 ms presentation), separated by a 1-s interval. The subject was then immediately asked to enter the digits on a numeric keypad on the touch-screen. In the first part of the test, subjects were required to recall the digits in forward order (Digits forwards); in the second part, they were required to recall them in reverse order (Digits backwards). In each part, the number of digits in each sequence was gradually increased from 3 to 9, with two sequences at each level. The dependent measure for each part was the maximum number of digits the subject recalled without error. (iii) Continuous Performance task: To tap sustained attention, a series of letters (B, C, D, or G) were presented to the subject on the computer screen (for 200 ms), separated by an interval of 2.5 s. If the same letter appeared twice in a row, the subject was asked to press buttons with the index finger of each hand. Speed and accuracy of response were equally stressed in the task instructions. There were 125 stimuli presented in total, 85 being non-target letters, and 20 being target letters (i.e., repetitions of the previous letter). The dependent variables were the number of errors of omissions and false positives. (iv) Switching of attention task: this test is a computerized adaptation of the Trail Making test (Reitan, 1958). It consists of two parts. In the first part, the subject was presented with a pattern of 25 numbers in circles and asked to touch them in ascending numerical sequence (i.e., 1, 2, 3, . . .). As each number is touched in correct order, a line is drawn automatically to connect it to the preceding number in the sequence. This allowed the subject to visualize the path touched. This task tests psychomotor speed and the basic ability to hold attention on a simple task. The second part of the test is described in what follows. The dependent variable was time to completion.

Executive Function Domain. (i) Switching of attention task; part 2: In the second part of this task, the subject was presented with a pattern of 13 numbers (1–13) and 12 letters (A–L) on the screen and was required to touch numbers and letters alternatively in ascending sequence (i.e., 1, A, 2, B, 3, C, . . .). This part is harder than the first part and reflects the requirement to switch attention between mental tasks, in this case number and letter sequence checking, and thereby alternate between the respective mental sets induced. The dependent variable was time to completion. (ii) Verbal Interference: This task taps the ability to inhibit automatic and irrelevant responses and has similarities to the Stroop task (Golden, 1978). The subject was presented with colored words presented serially, one at a time. Each word was

drawn from the following set of lower case words: red, yellow, green, and blue. The color of each word is drawn from the following set of colors: red, yellow, green, and blue. Below each colored word is a response pad with the four possible words displayed in black and in fixed format. The test has two parts. In part 1, the subject is required to identify the name of each word as quickly as possible after it is presented on the screen. In part 2, the subject is required to name the color of each word as quickly as possible. Each part lasts for 1 min. Responses are made on the screen by touching the appropriate word on the response pad. The dependent variable in each part was the number of words correctly identified. (iii) Maze Task: This task was a computerized adaptation of the Austin Maze (Walsh, 1985). The subject was presented with a grid (8 × 8 matrix) of circles on the computer screen. The object of the task was to identify the hidden path through the grid, from the beginning point at the bottom of the grid to the end point at the top. The subject was able to navigate around the grid by pressing arrow keys (up, down, left, right). A total of 24 consecutive correct moves were required to complete the maze. The subject was presented with one tone (and a red cross at the bottom of the screen) if they made an incorrect move, and a different tone (and a green tick at the bottom of the screen) if they made a correct move. The purpose of the task was therefore to assess how quickly the subject learned the route through the maze and their ability to remember that route. Only one maze was presented across trials, and the test ended when the subject completed the maze twice without error or after 10 min had elapsed. The dependent variable was the total maze time. It should be noted that although this measure is identified as a measure of executive function, the requirement to retain the maze in memory for two successive trials introduces an added memory component to the task, and therefore this measure taps more cognitive domains than pure executive function.

Language Domain. (i) Letter Fluency: Participants were required to generate by speech words that began with the letters F, A, and S. 60 s were allowed for each letter and proper nouns were not allowed. Responses were recorded via the microphone and hand scored. Intrusive or perseverative responses were not included in the total number correct. The total number of correct words generated across the three trials was the dependent measure. (ii) Animal Fluency: Participants were required to name animals as quickly as possible for 60 s. Intrusions and perseverative responses were not allowed. Total correct served as the dependent variable.

Memory Domain. (i) Verbal List-learning: The participants were read a list of 12 words, which they were asked to memorize. The list contained 12 concrete words from the English language. Words were closely matched on concreteness, number of letters, and frequency. The list was presented orally 4 times (and received by the subject using headphones). On each of the 4 trials, the subject was required to recall as many words as possible by speaking directly into the attached microphone. The subject was then presented with a list of distracter words and asked to recall them after presentation. Immediately following this, the subject was then asked to recall the 12 words from the original list (short-delay recall trial). A long delayed recall trial was completed approximately 20 min later after a number of intervening tasks. A recognition trial was then completed after the delayed trial. The dependent variables were the number of words correctly recalled across the four learning trials, the immediate recall trial and the delayed recall trial, and the total number of correctly identified word on the recognition trial.

Intelligence. (i) Spot-the-Word task: This task is a computerized adaptation of the Spot the Real Word test (Baddeley et al., 1993). On each trial of this task, participants were presented with two words on the touch-screen. One of the two words was a valid word in the English language ("true" target word), and the second was a non-word foil. Participants were required to identify by touching the screen, which of the two words was the true target. The total correct score was the dependent measure.

Standard Neuropsychological Measures.

The standard tests were those developed previously, and described in detail in primary textbooks in the field of neuropsychology (see Lezak, 1995). These tests were selected according to two criteria: (1) the tests putatively measured the same cognitive construct as the tests of IntegNeuro, and (2) the tests were among the most common cognitive measures employed by clinical neuropsychologists (Lezak, 1995). Importantly, all dependent variables for the validity criterion measures were identified a priori. The standard neuropsychological measures were selected by two experienced clinical neuropsychologists based on the presumed overlap in tapping similar cognitive skills (convergent validity) and the lack of overlap in tapping the same cognitive skills (divergent validity).

The individual tests in equivalent domains are described in what follows.

Sensori-Motor Domain. (i) Finger Tapping: On this test participants were required to tap a counter with their dominant index finger as quickly as possible for 60 s. The dependent variable was the total number of taps recorded. Finger-tapping also served as the convergent validity variable for choice reaction time, as this response cannot be accurately captured by paper-and-pencil measures.

Attention Domain. (i) Spatial Span (Wechsler Memory Scale III; WMS-III; Wechsler, 1999b). Spatial Span is the visual analogue to the verbal digit span test. Participants observed the examiner touch a sequence of blocks, and they were required to touch the blocks in the same order. Both a forward and reverse order condition were administered. The dependent variable was the total number of correct trials. (ii) Digit Span test (WAIS-III; Wechsler, 1999a): Participants were administered the Digit Span subtest of the WAIS-III. Participants were presented listened to a sequence of digits (e.g., 4, 2, 7, etc.). The subject was then immediately asked to recall the digits. In the first part of the test, subjects were required to recall the digits in forward order (Digits forwards); in the second part, they were required to recall them in reverse order (Digits backwards). In each part, the number of digits in each sequence was gradually increased from 3 to 9, with two sequences at each level. The dependent measure for each part was the maximum number of digits the subject recalled without error. (iii) Adaptive Rate Continuous Performance Test (ARCPT; Cohen, 1993). This computerized test is based on the standard Continuous Performance Test, which is used to measure vigilance and sustained attention. A series of 1,000 letters are presented on the computer monitor, each for 100 ms. duration. Six out of every 100 letters consists of a target letter combination: "A" followed by "X" (A-X). Subjects respond by pressing the space bar. Accuracy is a function of hits, misses, discrimination ability (d'), and response bias (i.e., beta). Inter-stimulus interval (ISI) becomes shorter or longer on successive blocks of trials based on subjects' accuracy, providing an information processing speed index. Trials are presented in 10 blocks of 100 trials, providing for measures of sustained attention. The dependent variable was the number of errors of omissions and false positives. (iv) Trail Making (Reitan, 1958): The Trail Making Test is a measure of combined visual search and cognitive flexibility. Trail Making A required participants to draw a line and connect 13 numbers (1–13), that are were scattered about the page, in ascending order. In the event that a subject committed an error (incorrect connection between numbers), the computer produced an audible signal and the subject was not allowed to connect additional numbers until

the error was corrected. This process was explained thoroughly to the subject during the practice trial (which included an audible and visual example of an error). The dependent variable was time to completion.

Executive Function. (i) Trail Making (Reitan, 1958): Trail Making B required participants to connect 13 numbers (1–13) and 12 letters (A–L) in an alternating and ascending order. Time to completion was the dependent variable. (ii) Stroop (Golden, 1978): Participants were administered the Golden version of the standard Stroop test. Briefly, participants were required to name color words printed in incongruent ink as quickly as possible. The trial continued for 45 s. The dependent variable was total correct within the time period. (iii) Rey Complex Figure Test: The Rey Complex Figure Test (Meyers & Meyers, 1995) was also administered as a measure of visual learning and retention. Participants were instructed to copy the geometric figure as accurately as possible. Immediately after completing the copy trial, participants were asked to draw the figure from memory. Following a 20-min time delay, participants were again instructed to draw the figure from memory. No time limit was given and the drawings were scored according to standardized criteria (see Lezak, 1995). The dependent measure was the total score on the delayed trial. This dependent measure was selected to examine convergent validity on the Mazes task. While maze tasks are frequently identified as measures of pure executive function, the maze task in the IntegNeuro battery includes a memory component as well, because subjects are required to navigate the maze and retain the maze in memory for two successive trials without error. Due to this added memory component, Rey Delay were elected as the primary measure of convergent validity.

Language Domain. (i) FAS Fluency: Participants were required to generate words from the categories F, A, S as quickly as possible for 60 s on each trial. The dependent variable was total correct across the three letters. (ii) Animal fluency: Participants were required to name animals as quickly as possible for 60 s. The dependent variable was total correct.

Memory Domain. (i) California Verbal Learning Test-Research (CVLT-R; Delis et al., 1987): The CVLT-R was administered in standard fashion. Briefly, the test involves oral presentation of a 16-word list. The list items represent exemplars of one of four categories (fruit, clothing, tools, spices/herbs). Participants were read the list five times and asked to recall as many words as possible from the whole list on each of the trials. Participants were then read

a distracter list, followed by free and cued recalls of the original list. After a 20-min delay, participants were asked to free recall the original list, followed by a cued recall trial, and then a recognition trial. The total number of words recalled across the five learning trials was the dependent measure for verbal learning. The dependent measures included total recall across the learning trials, recall on the short and long-delay free recall, and number of hits on the recognition trial.

Intelligence. (i) Wechsler Adult Intelligence Scale-III (Wechsler, 1999a). The WAIS-III was administered according to standard protocol. The entire battery of verbal and performance measures were administered to yield a full-scale Intelligence Quotient (IQ). The full scale IQ was computed as a reference to the estimated IQ derived from the Spot the Word test.

Data Analysis

The pairing of tests from the two batteries for purposes of validity testing is provided in Table 2. IntegNeuro™ data were scored using standardized and automated algorithms. Performances on the paper-and-pencil tests were scored according to established criteria. Evaluation of test performance on the paper-and-pencil tests was completed without any knowledge of the individual's performance on IntegNeuro™, in order to avoid any potential scoring bias.

Validity was assessed by examining the degree of similarity in performance on the IntegNeuro tests and the paper-and-pencil tests using correlational analyses, as well as predicted dissimilarity between the tests. Correlational analyses were computed for the entire group (50 individuals). Validity was also assessed by examining differences in performances on the individual tests between young individuals and older individuals. The influence of age, education, and sex was examined using correlation analyses and between-group contrasts, respectively.

RESULTS

Convergent and Divergent Validity

The correlational analyses are listed in Table 3 for the entire group of individuals. As evident in the Table, each test of IntegNeuro™ was significantly correlated with the paper-and-pencil measure previously developed to test the same cognitive construct. The correlation between IntegNeuro™ mea-

Table 2. Paired tests administered to assess the validity of IntegNeuro

IntegNeuro test	Convergent validity measure	Divergent validity measure
Digit Span total	Digit Span —WAIS III	Finger Tapping Nondominant
Visual Span total	Spatial Span—WMS III	CVLT-R Recognition
Finger tapping dominant	Finger Tapping Test—dominant	CVLT-R Long Delay
Finger tapping nondominant	Finger Tapping Test—nondominant	CVLT-R Long Delay
Memory recall on the learning trials	CVLT-R Learning Trials	Adaptive Rate Continuous Performance Test—Final ISI
Memory recall on the short delay	CVLT-R Short Delay	Rey Copy Trial
Memory recall on the delay trial	CVLT-R Long Delay Free Recall	Finger Tapping test dominant hand
Letter fluency	FAS	Finger Tapping nondominant
Animal fluency	Animal fluency	Digits Forward
Switching of attention A	Trail Making Test A	CVLT—Recognition
Switching of attention B	Trail Making Test B	Digit Span total
Mazes Time	Rey Complex Figure Test—delay	CVLT-R Short Delay
Verbal Interference	Stroop Incongruence trial	Rey Copy Trial
Choice Reaction Time	Finger Tapping Dominant*	Animal fluency
Working Memory Test	Adaptive Rate Continuous Performance Test	Spatial Span

*Finger tapping dominant hand was included as the convergent validity measure because standardized tests of choice reaction time are not commonly administered as part of paper-and-pencil neuropsychological batteries.

sures and at least one of the target convergent validity measures exceeded .53 in all cases, reflecting a statistically significant degree of overlap between the two variables. As evident in the Table 3, divergent validity was also supported as most of the IntegNeuro™ measures did not correlate with the divergent standard measures. The only exception was Switching of Attention B, which correlated with Digit Span. This is not a surprising finding given the impact of attentional processes on both tasks. Although this does not represent an exhaustive measure of the convergent and divergent validity parameters of the battery, the results provide some measure of specificity in terms of shared variance. Convergent validity was examined between Spot the Word and the Full Scale WAIS III IQ, and these two measures shared a significant amount of variance ($r = .76$). Divergent validity was not examined between the estimated intelligence measure and other cognitive functions as the former would be expected to correlate with most cognitive domains.

Table 3. Correlations between IntegNeuro measures and the paper-and-pencil tasks for all participants

IntegNeuro test	Convergent validity measure	Divergent validity measure
Digit Span	.53*	.20
Spatial Span	.63*	.27
Finger tapping dominant	.55*	.20
Finger tapping nondominant	.60*	.12
Memory recall on the learning trials	.67*	–.26
Memory recall on the short delay	.76*	.14
Memory recall on the delay trial	.63*	.04
Letter fluency	.77*	.07
Animal fluency	.76*	.25
Switching of attention A	.53*	–.19
Switching of attention B	.65*	–.52
Mazes Time	–.65*	–.11
Verbal Interference	.70*	.22
Choice Reaction Time	–.53*	.24
Working Memory Test	.55*	–.00

*Statistically significant association between the two variables.

Relationships to Age, Sex, Education, and IQ

No significant differences were observed between males and females on any of the IntegNeuro™ subtests, although a trend was evident on nondominant finger tapping, with females recording slightly fewer taps compared to males (see Table 4). Correlational analyses were conducted to examine the relationships between age, education, and performance on the individual measures of IntegNeuro™. Results from these analyses revealed that only digit span correlated with number of years of education (r = .44), with higher scores associated with more years of education. More consistent relationships were evident between performance on the IntegNeuro™ tests age and IQ. Age correlated significantly with reverse digit span forward (r = –.56), digit span backward (r = –.44), dominant tapping (r = –.34), nondominant tapping (r = –.31), choice reaction time (r = .31), maze time to completion (r = .54), animal fluency (r = –.61), and FAS fluency (r = –.39).

Full Scale IQ as determined by the WAIS-III was significantly correlated with performance on the IntegNeuro™ digit span test (r = .51), choice reaction time (r = .29), verbal interference test (r = .47), total verbal learning

Table 4. Performance differences between males and females

	Males		Females		
Measure	Mean	(SD)	Mean	(SD)	*F*
Digit Span	11.0	(2.4)	10.0	(3.1)	2.1
Visual Span	7.1	(2.5)	7.2	(2.3)	.04
Finger tapping dominant	157.7	(24.3)	156.7	(33.3)	.01
Finger tapping nondominant	145.41	(18.5)	156.8	(20.2)	3.6 $p = .06$
Learning Trials	29.7	(7.2)	31.6	(5.7)	1.0
Learning Short Delay	6.4	(2.7)	7.2	(2.3)	.28
Learning Long Delay	5.9	(2.8)	6.8	(2.5)	1.2
Letter fluency	47.5	(12.1)	47.5	(13.2)	0.0
Animal fluency	22.9	(6.1)	23.0	(5.6)	0.0
Switching of attention A	24.2	(8.1)	23.4	(8.1)	0.0
Switching of attention B	45.6	(12.1)	46.6	(12.9)	0.0
Mazes time	27.3	(8.0)	28.4	(13.6)	0.0
Verbal interference	19.7	(5.1)	19.9	(4.4)	0.0
Choice reaction time (ms)	757.2	(161.5)	743.3	(147.2)	0.0
Working memory	1.6	(1.1)	2.8	(2.4)	2.7

(r = .50), long delayed verbal recall (r = .39), Switching of Attention 2 (–.42), Mazes time to completion (r = –.46), Animal fluency (r = .43), and letter fluency (r = .63).

DISCUSSION

The results of the study provide preliminary support for the use of IntegNeuro™ to assess cognitive function. The correlational analyses revealed strong relationships between the tests of IntegNeuro™ and standard measures of cognitive function. In addition, divergent validity was demonstrated by the absence of significant relationships between the target measures and cognitive tests believed to tap different underlying constructs on most of the tests. It is important to note that complete divergence is difficult to attain given the dominance of attention and speed factors inherent in the test battery, and the association of these skills with most higher-order cognitive tasks. Nevertheless, the findings provide preliminary support for the convergent and divergent validity of the computerized battery.

It is worth noting that the strongest correlations were observed for the memory measures and the fluency measures, which required subjects to hear

and comprehend accurately verbal instructions and memory lists, as well as provide verbal responses that were subsequently recorded via the attached microphone. A concern regarding these procedures is whether voice activation software is capable of accurately detecting the responses. Although not directly examined in the current study, the strong correlations between verbal fluency and memory scores across the computerized and noncomputerized measures suggest that this is not a significant problem. Overall the findings support the use of language and verbal memory measures in computerized assessment.

IntegNeuro™ may provide clinicians with a sensitive screening of core cognitive abilities that are vulnerable to degenerative disease and other forms of brain injury. Importantly, the battery includes tests that are sensitive to deficits associated with Alzheimer's Disease (AD; long-term recall and recognition memory; Tierney et al., 2001; Bondi & Monsch, 1998), vascular dementia (fluency and recognition memory; Tierney et al., 2001; Collie & Maruff, 2000), and conversion from mild cognitive impairment to probable AD (Trail Making B and verbal learning; Albert et al., 2001; Small et al., 1997). Tests are also included that differentiate AD from probable vascular cognitive impairment (letter fluency and recognition memory; Tierney et al., 2001). As such, the battery is potentially capable of detecting clinically meaningful declines in cognitive function, although this needs to be determined empirically in future studies.

The strength of the correlations appears between the individual tests of IntegNeuro™ and the standard measures appears consistent with the correlations reported between other computerized measures and indices of convergent validity. For example, correlations between measures of the computerized NES 3 and standard paper and pencil measures ranged form .20 to .70 (Proctor et al., 2000), whereas the measures of IntegNeuro™ ranged from .53 to .77. IntegNeuro™ may offer some advantages compared to other computerized batteries concurrently available. Specifically, the inclusion of language-based measures including verbal fluency and verbal memory provide opportunities to assess key cognitive domains most consistent with routine clinical practice, as well as examine cognitive domains that are vulnerable to early degenerative decline. Further, the similar task demands between the computerized tests and the standard measures (e.g., Switching of Attention and Trail Making) allow for a more direct comparison of individual skills.

One area of future research regarding this and all computerized batteries is the issue of computer familiarity. Computer familiarity may account for as much as 40% of the variance in performance on computerized cognitive batteries (Browndyke et al., 2003; Weber et al., 2002). This effect may be

more of an issue for older individuals, who have less personal history working with computers. The methodology incorporated into IntegNeuro™ may reduce the confounding influence of computer familiarity because the apparatus does not require a keyboard or mouse. However, this remains conjecture until studied directly in future investigations.

It is worth noting that participants in the current study reported a high level of education, and this may have influenced the overall findings. Specifically, the higher education values of the sample provide warrants caution in the generalization of the findings to individuals with lower levels of education. Further, it is possible that the restricted range of the education values in this sample constrained the correlation coefficients between education and performance on the cognitive measures. Future studies with less highly educated participants will be an important step in the subsequent validation of the battery. It will also be important to examine relationships between individual tests of IntegNeuro™ and performance on additional "traditional" measures of cognitive function. For example, there are a number of indices that can be derived from the vigilance measure of IntegNeuro™ and the ARCPT (Cohen, 1993), and it would be interesting to examine the relationships between the verbal memory measure and performance on tests of prose passages, as well as other list learning tasks with similar learning and retention requirements (e.g., from the WMS-III, Wechsler, 1999b).

In summary, this preliminary investigation of the validity of IntegNeuro™ provides encouraging evidence for the utility of this measure. The battery appears to capture essential elements of standardized cognitive assessments including language-based measures. The standardization of task procedures and instructions should offer a significant benefit to multi-site studies and research initiatives. Additional information regarding the reliability of the battery, the utility of alternate forms of the tests, the sensitivity of the tests to clinical indications, and differences in education and computer familiarity will be important next steps to determine the broader utility of the battery for research and clinic applications.

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Archives of Clinical Neuropsychology 21 (2006) 449–467

Archives of CLINICAL NEUROPSYCHOLOGY

Standardized assessment of cognitive functioning during development and aging using an automated touchscreen battery

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Accepted 16 June 2006

Abstract

This study examined the effects of age, gender and education on subjects spanning nine decades on a new cognitive battery of 12 tests. One thousand and seven participants between 6 and 82 completed the battery under standardized conditions using an automated, computerized touchscreen. Sensitive indicators of change were obtained on measures of attention and working memory, learning and memory retrieval, and language, visuospatial function, sensori-motor and executive function. Improvement tended to occur through to the third and fourth decade of life, followed by gradual decrement and/or stabilized performance thereafter. Gender differences were obtained on measures of sustained attention, verbal learning and memory, visuospatial processing and dexterity. Years of education in adults was reflected in performance on measures of verbal function. Overall, the test battery provided sensitive indicators on a range of cognitive functions suitable for the assessment of abnormal cognition, the evaluation of treatment effects and for longitudinal case management.

Keywords: Neuropsychology; Development; Ageing; Education; Gender; Cognition

Neurocognitive assessment has continued to serve as a primary method to study both the development and the degeneration of the brain, and improvements in the testing process have helped to solidify its role in the field of neuropsychology. The introduction of standardized methods of test administration, scoring and interpretation represents one of the most important advances in the past century. At present, scientists and clinicians have a remarkable range of standardized tests from which to choose, but individual tests are often constrained by a lack of adequate normative data or limited coverage of domains of function, leaving significant opportunities for further improvement.

This paper reports the development of a cognitive test battery designed to permit measurement across the full lifespan (Gordon, 2003a, 2003b). It has been well reported that cognitive abilities increase with age up until the third or

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doi:10.1016/j.acn.2006.06.005

fourth decade of life (e.g. Anderson, Anderson, Northam, Jacobs, & Catroppa, 2001; Arceneaux, Hill, Chamberlin, & Dean, 1997; Korkman, Kemp, & Kirk, 2002) whereupon they plateau and then gradually decline (e.g. Brabeck, 1984; Compton, Avet-Compton, Bachman, & Brand, 2003; Costa & McCrae, 1993; Herb, 1995; Rabbitt, 2002; Salthouse, 2000, 2001). It is also reported that females develop more quickly in some areas and that, broadly speaking, males develop to perform better on motor tasks and females on some verbal and memory tasks. Further, the relative levels of cognitive performance generally increase with higher levels of education.

Individual studies addressing longitudinal change in cognitive ability tend to focus either on the developmental years or on the effects of aging but not both. The present study used a standardized, computerized test battery with reported reliability and validity (Paul et al., 2005; Williams et al., 2005) to examine healthy participants between the ages of 6 and 82. This battery taps the primary cognitive domains including attention, learning and memory, speed of processing, verbal versus visuomotor ability and executive function. A key aim was to obtain a broad profiling of cognitive ability that considered cross-sectional effects of the full age range within a single study across and to differentiate effects according to gender and years of education. Thus, this study employed the same broad-based, cognitive battery on all participants across the full age range. In particular, the study permitted concurrent assessment of variation in the peaks of the development trajectory across different cognitive domains, the examination of gender differences along these trajectories and examination of the relationship between observed development patterns over time on the various cognitive domains and the subsequent effects of ageing on those domains.

Three methodological issues were also addressed in this study. Firstly, the limitation of small normative samples drawn from a single demographic was addressed by administering the test battery at a number of laboratories to over 1000 individuals. Secondly, the testing environment was tightly standardized. Standardization included the physical environment within which participants are tested (lighting, ambient temperature, visual and auditory distractions), the computerized basis of the control of test delivery and for the measurement of performance and the automation of test instructions. The provision of such controls limited the impact of the environment and human interaction on participant performance. Thirdly, the test battery was constructed to be completed in under an hour, with test order kept invariant. These two controls limited the effects of factors, such as vigilance, motivation and fatigue on test performance, whilst ensuring that the impact of such factors is standardized across tests.

The computerized tests forming the battery were based on existing and well recognized paper and pencil tests known to be sensitive to brain dysfunction. Computerized assessment has increasingly received recognition for use in the research and clinical setting. The American Psychological Association (APA) recognized the value of computerized psychological testing and published guidelines in 1987 (APA, 1987) to assist in the development and interpretation of computerized test results. The APA identified six major benefits of computerized assessment including: (1) automated data collection and storage, (2) greater efficiency of use, (3) release of the clinician from test administration to focus on treatment, (4) greater sense of mastery and control for the client, (5) reduced negative self-evaluation among clients that experience difficulty on the computer and (6) greater ability to measure aspects of performance not possible through traditional means, such as latency, strength and variability in response patterns.

The extent of standardization in the design of the battery used in the present study, together with the relatively large size of the normative database, potentially offers good sensitivity to the measurement of neurocognitive function. This paper specifically addresses the sensitivity of the battery to the effects of age, gender and level of education on cognitive abilities for each cognitive domain across the full age span. A quadratic effect of age was generally expected to reflect improving capabilities over the years of early development followed by decline during old age. No general hypothesis was levied with respect to gender and level of education, with the effects of these variables expected to vary across the measures obtained. The reliability and validity of the battery (published as IntegNeuro: see www.brainresource.com) has been reported recently.

1. Method

1.1. Participants

Participants were 1007 male and female volunteers, spanning nine decades (6–82 years; mean age 28.7). Six laboratories from Australia (Adelaide, Sydney), USA (NY, Rhode Island) and Europe (UK, Holland) participated in the data acquisition in a standardized manner with identical hardware, software, paradigms and experimental procedures. The data from the participants reported in this paper form part of a work in progress related to formation of an

international database of brain and cognitive function (Brain Resource International Database) with final numbers to be spread evenly across age range and gender. A recent comparison of data obtained to date on the battery from the laboratories cited above failed to identify significant differences in cognitive function across the three continents (Paul et al., 2006). All participants completed a screening questionnaire to provide demographic information as well as a self-report of psychological, neurological and physical history. The completion of the questionnaire was overseen by a parent/guardian in the case of participants less than 18 years of age, but with assistance offered to such participants only in relation to specific questions.

Exclusion criteria included a personal history of mental illness, physical brain injury, neurological disorder or other serious medical condition and/or a personal history of sleep disorder, learning disability, or drug or alcohol addiction. Subjects were also excluded if they had a family history of Attention Deficit Hyperactivity Disorder (ADHD), schizophrenia, bipolar disorder or genetic disorder. The SPHERE questionnaire (Hickie, 1998) was used to screen out individuals with a likely anxiety or depressive disorder. Subjects were required to refrain from caffeine-intake and from smoking for at least 2 h prior to testing to standardize the effects of these variables. All subjects (or their guardians for subjects less than 18 years of age) provided written informed consent to participate in the database.

1.2. Materials and equipment

Participants were seated in front of a touchscreen computer (NEC MultiSync LCD 1530 V) located within a sound and light attenuated room with an ambient temperature of approximately 24 °C. The touchscreen was located centrally on a desktop in front of participants with the touch surface subtending an angle of 15°. Task instructions and materials were pre-recorded and delivered in a standardized way using computer 'wav' files presented via headphones and using the visual display of a touchscreen computer. An iterative, automated protocol was used to ensure task comprehension and compliance. This involved a computerized protocol directing the participant through a number of practice trials on each test. If three practice trials were failed on a test, then the participant was taken automatically to the next test in the battery. Task instructions are provided concurrently in verbal form (by headphones) and in written form (on the touchscreen) to increase the accessibility of the test battery to the younger participants in the study, where reading ability may be less well formed.

1.2.1. Integneuro test battery

The test battery consists of 12 tasks that take approximately 50 min to complete. Instruction and practice is completed immediately prior to attempting the task. The tests cover five cognitive domains as follows.

1.2.1.1. Sensori-motor. The Motor Tapping test is a variation of the Finger Tapping test that is considered to provide an index of manual dexterity (Halstead, 1947; Lezak, 2004). The participant is required to place the palm of the hand on the touchscreen and tap with the index finger as fast and as often as possible for a period of 30 s. Measures of tapping frequency from the dominant hand are reported.

The Choice Reaction Time test: four black circles are presented equally spaced along a semicircular arc across the top of the touchscreen, with two circles located to the left of midline and the other two on the other side of midline. The participant is required to rest the pointing finger of the hand with which they write on a white circle positioned on the midline of the screen and located below and equidistant from each of the black circles. Periodically and with equal probability, a black circle is illuminated in green. The participant is required to lift their finger and touch each illuminated circle as fast as they can. A measure of the average speed of response is obtained.

1.2.1.2. Learning and memory. The Memory Recall and Recognition test is a variant of the Rey Auditory Verbal Learning and Memory task (e.g. Geffen, Moar, Hanlon, Clark, & Geffen, 1990; Rey, 1964) commonly used to provide measures of auditory-verbal learning, recall and recognition, as well as indices of self-monitoring ability. The participant is presented with a sequence of 12 words binaurally via headphones, one second at a time (Learning Trial 1). Prior to the reading of the list, the participant is instructed to say back, immediately after the list has been read, as many of the words as they can remember from the list, in any order. This procedure is then repeated three more times, with the same instructions (Learning Trials 2–4). The total number of words recalled during these four trials (Trials 1–4) is recorded. The participant is then presented with a second list of words and asked to say back as many of these as can be remembered (Distractor Trial). None of the words in the second list are phonetically or semantically related to

the words in the first list. Immediately following this trial, the participant is asked to recall as many words as can be remembered from the first list (Immediate Recall Trial). The task takes about 6 min to this point. Approximately 25 min later, after completing a number of other tests in the battery, the participant is again asked to recall as many words as possible from the first list (Delayed Recall Trial). The subject is then presented one at a time with a series of 24 words on the computer screen (Recognition Trial). Half of these words are the words from the first list; the remaining words are new words. The words are in fixed, pseudorandom order. Following each word, the participant is required to touch a "Yes" or "No" button on the touchscreen according to whether or not the word was in the first list.

All words are concrete words between four and seven letters in length, drawn from the English language. Concreteness was determined from the merged norms of Paivio (Paivio, Yuille, & Madigan, 1968), Colerado (Toglia & Battig, 1978) and Gilhooly–Logie (Gilhooly & Logie, 1980). Using this derivation, only words with a concreteness rating of 538 or more were selected (Paivio et al., 1968). The value of 538 represents the mean concreteness value of the derived list plus one standard deviation. The words in each list are of high frequency, with a value of 50 or more in written frequency (Kucera & Francis, 1967). There are no semantic or phonemic similarities between words either within or across lists. All lists are closely matched on mean concreteness, mean number of letters and mean frequency. Subject verbal recall is recorded in 'wav' files.

The Maze task is a computerized adaptation of the Austin Maze (Walsh, 1985) used to assess high level mental functions, such as planning, foresight and self-monitoring during the course of learning and remembering a complex maze. A computerized format for this task has been shown to be equally as effective as the conventional task design using a light-up circuit board (Morrison & Gates, 1988). An 8×8 grid of red circles (the maze) is displayed across the computer screen in a square array. The maze contains a hidden path commencing at a marked circle (in yellow) on one of its edges and finishes at a marked circle (in blue) on another of its edges. The participant's task is to discover and remember this path. The participant is instructed to move through the maze by touching the up, down, left and right arrows displayed in congruent pattern immediately below it. Each learning trial begins at the yellow start point and is completed once the blue finish button is reached. Participants are required to perform learning trials until they either complete the maze twice in a row without error or 7 min have passed (which ever comes first).

This adaptation of the Austin Maze introduces a number of variations. Firstly, it is not possible for the participant to move diagonally within the maze. Secondly, the maze is smaller, with each side containing 8 rather than 12 grid points. Finally, the duration of the task is limited to 7 min; the original version allowed the participant to perform the task for an indefinite period of time.

This adaptation of the task yields the following measures relevant to visual spatial learning and memory: the number of trials completed or until time out occurred (Trials completed) and the time to task finish (Time to Complete).

1.2.1.3. Language. The Letter Fluency test is a variant of the Controlled Oral Word Association (COWA) test, or FAS, as it is also known (Benton & Hamsher, 1989). The test is used to provide an index of verbal fluency, as measured by the quantity of words produced within given letter categories. This task requires the participant to recall as many words as possible beginning with each of the letters F, A and S, in that order. One minute is allowed for each letter. Subject verbal recall is recorded in 'wav' files. The dependent measure is the number of words recalled across the three letters.

The Spot the Real Word task is a computerized adaptation of the Spot the Word test (Baddeley, Emslie, & Nimmo-Smith, 1993). In each of a series of trials, a pair of words is presented side by side on the computer screen. One of the words in each pair is a real word; the other word is a pseudo word, with the ordering of words pseudo randomized over trials. The words in each pair remain on the screen until the subject indicates by touch which of them is considered to be the real word. The dependent variable reported in this study is the number of words correctly selected. Note the total correct score can also be entered into a regression formula that factors education and age to render an estimated intelligence quotient for those 16 years and over (Sullivan, Senior, & Hennessy, 2000).

1.2.1.4. Attention and working memory. The Span of Visual Memory task is adapted from the Corsi Blocks task (Milner, 1970) and another of its variants, the Dot Location task (Roth & Crosson, 1985). The Corsi Blocks test is used to provide an index of visual short-term memory capacity (Lezak, 2004). The adaptation addresses a noted difficulty with previous versions of the test that confound sequence length with path length. In the present task, path length increases with sequence length. Nine asymmetrically positioned squares are displayed constantly on the computer screen for the duration of this task. The task consists of a series of trials in which a number of the squares flash briefly in sequence, followed immediately by the sound of a tone. The participant is required to touch the squares that flashed

in sequence order, with only one attempt per trial. Sequence length varies between two and nine, with two trials for each length and with trials presented in ascending sequence order. The task is terminated either when the participant fails 2 trials of any sequence length or when all 18 trials are completed. The dependent measure is the longest sequence length correctly completed.

Part 1 of the Switching of Attention (SOA) test is part of a computerized adaptation of the Trail Making test (Reitan, 1955, 1958). Part 1 provides an assessment of visuomotor tracking and motor speed, in which the subject is presented with a display of 25 numbers on the computer screen and asked to touch the numbers in ascending numerical sequence (i.e. 1 2 3 . . .). The numbers are drawn without replacement from the range 1 to 25 and are displayed in a fixed pseudo random pattern. The dependant variable reported is the time taken to complete the test successfully (Time to Completion).

The Time Estimation task consists of a series of trials in which a black circled displayed on the computer screen turns green for a number of seconds. For each trial, the participant is required to indicate the duration in seconds of the colored stimulus. Response is carried out using a fixed display touchpad showing the numbers 1–12 in sequence from left to right across the computer screen. Stimulus duration ranges equiprobably between 1 and 12 s, with order of presentation being pseudo random over trials. Proportional bias in time estimation is estimated from the absolute value of the average difference between the actual duration of the stimulus and the users estimate weighted by the length of the stimulus.

To tap sustained attention, a series of letters (drawn equiprobably from the set of B, C, D and G) were presented to the subject on the computer screen (for 200 ms), separated by an interval of 2.5 s (Sustained Attention task). If the same letter appeared twice in a row, the subject was asked to press buttons with the index finger of each hand. Speed and accuracy of response were equally stressed in the task instructions. There were 125 stimuli presented in total, 85 being non-target letters and 20 being target letters (i.e. repetitions of the previous letter). The dependent variables reported are reaction time (Reaction Time) and number of false positive responses (False Positives).

The Digit Span task is an adaptation of earlier tests of immediate verbal working memory (Lezak, 2004). It consists of two sub-tests. Firstly, a test of Forward Digit Span, which has been used to provide a measure of immediate memory recall. The second is a test of Reverse Digit Span, which has been used to provide a working memory index of mental tracking ability (Lezak, 2004). The Forward Digit Span task consists of a number of trials in which a series of numerals are presented at a constant rate in a box on the computer screen. Immediately after each trial, the participant is required to touch the numerals on a screen keypad, which then appears on the screen, in the order in which they were flashed. There is a 5 s delay between trials. Sequence length varies between three and nine, with two trials for each length and with trials presented in ascending sequence order. The task is terminated either when the participant fails 2 trials of any sequence length or when all 18 trials are completed. The score is the longest sequence length correctly completed. The Reverse Digit Span task is identical to the Forward Digit Span task, except that numbers must be recalled in the reverse order of presentation. The dependent measures reported are the longest sequence length correctly completed in each case (Forward Digit Span score; Reverse Digit Span score).

Part 1 of the Word Interference test is part of an adaptation of the Stroop test (Stroop, 1935). This task consists of a series of colored words presented one at a time on the computer screen. Below the color words are the four words red, yellow, green and blue, displayed permanently in black across the computer screen. The color and name of each colored word is always one of these four colors with the constraints that no colored word has the same color and name but that each name and color is equiprobable. Colored words are presented in pseudo random order. In Part 1 of this test, the participant is required to identify the name of each colored word as quickly as possible after it is presented on the screen. Colored words remain on the screen until the subject responds. This part lasts for 1 min. The number of words correctly identified (Score) is recorded.

1.2.1.5. Executive function/planning. In Part 2 of the Switching of Attention task, the subject is presented with a pattern of 13 numbers (1–13) and 12 letters (A–L) on the screen and is required to touch numbers and letters alternatively in ascending sequence (i.e. 1 A 2 B 3 C . . .). This part is harder than the first part and reflects the requirement to switch attention between mental tasks, in this case number and letter sequence checking, and thereby alternate between the respective mental sets induced. The dependent variable reported is the time to completion (Time Part 2).

Part 2 of the Word Interference test measures the ability to suppress automatic, well-learned responses in the face of competing demands. In this part, the participant is required to name the color of each colored word as quickly as possible after it is presented on the computer screen. Colored words remain on the screen until the subject responds.

This part lasts also lasts for 1 m. The dependent measure obtained is the number of words correctly identified (Score Part 2). It should be noted that this version of the Stroop test differs qualitatively from the original in terms of the nature of response. Instead of verbalizing the name/color, as in the original versions, the subject selects a name/color from a four choice visual array placed below the probe color word on the screen. In principle, this could allow the subject to choose by visual match rather than engaging in mental search before articulation. Nevertheless, the process of suppression of automatic response would still be required. In addition, the task has a fixed duration. This means that absolute and/or relative task performance is not measured in terms of the time to complete a fixed number of trials.

Two measures of executive functioning are also obtained from the Maze task. These include the total number of off-path moves (errors) and the total number of off-path moves made the time a path turn should have been made (total overruns). Two measures of executive functioning obtained from the Verbal Memory Recall task are the number of words incorrectly recalled during trials 1–4 (Intrusions) and the number of repeats of correctly recalled trials during trials 1–4 (Repeats). These were taken as indices of self-monitoring ability.

1.3. Data analysis

The 12 tests yielded 47 dependent variables for analysis, of which 24 are reported in this paper. Scoring of most of these variables is automated. Manual scoring was required for the two tasks involving verbal response (Memory Recall; Word Generation). There were a number of missing values for some participants; however, these data were not replaced.

Data were divided into 10 age groups (age group) as follows: 6–8, 9–11, 12–14, 15–19, 20–29, 30–39, 40–49, 50–59, 60–69 and over 70. These divisions were asymmetrical over the age range to reflect the relatively rapid rates of development during the early years. Data were then analysed in SPSS using a full factorial general linear model (GLM) to investigate the effects on performance measures of the independent variables of age group, gender and years of education.

1.3.1. Analysis of age group and gender

The distribution of participants over the 10 age groupings was as follows: 6–8 years ($n = 57$; female (F): 28, male (M): 29; mean years of education (YOE): 2.7), 9–11 ($n = 98$; F: 46, M: 52; YOE: 5.5), 12–14 ($n = 83$; F: 34, M: 49: YOE: 8.4), 15–19 ($n = 146$; F: 63, M: 83; YOE: 12.3), 20–29 ($n = 254$; F: 130, M: 124; YOE: 13.9), 30–39 ($n = 114$; F: 48; M: 66; YOE: 14.1), 40–49 ($n = 97$; F: 59, M: 38; YOE: 13.4), 50–59 ($n = 83$; F: 49, M: 34; YOE: 13.3), 60–69 ($n = 44$; F: 21, M: 23; YOE: 12.2), >70 ($n = 31$; F: 15, M: 16; YOE: 12.0). Overall, the sample comprised 514 males and 493 females. A GLM was undertaken with age group and gender as fixed factors, with a polynomial contrast for age group and a simple contrast for gender.

1.3.2. Analysis of years of education

Only participants 20 years of age or more were included in this analysis to avoid the confound between years of education and age in younger participants due to the positive correlation of these variables. The participants were assigned to one of four groups representing general level of education: early school leavers (<10 years of education; $n = 82$), high school (10–12 years; $n = 130$), tertiary (13–15; $n = 157$) and postgraduate (>15 years; $n = 254$) level of education.

2. Results

2.1. Age group

Significant linear and/or quadratic main effects of age were obtained on most measures (see Table 1). The only variable that did not differ across age group was a measure of executive function (repeated recalls during the Memory Recall task).

2.1.1. Attention and working memory

All measures of attention and working memory were fitted by a quadratic trend over age group. Figure 1 shows, with minor exception, a graded improvement in performance over all measures through to the middle age bands (15–39) after

Table 1
Statistical effects of age group, gender and years of education on tests of attention and working memory, executive function, language, learning and memory and sensori-motor function

	Age group			Gender	Age × Gender	Education	
	F	Linear (S.E.)	Quadratic (S.E.)	*F*	*F*	*F*	Linear (S.E.)
Attention and working memory							
Time estimation—Bias	3.23***	0.521**	0.513*	1.27	0.91	0.404	NS
Switching of Attention—Time Part 1	7.95***	NS	2508***	2.47	1.13	2.39	NS
Sustained Attention—False Positives	4.29***	1.04***	1.03***	11.42***	1.52	0.135	NS
Sustained Attention—Reaction Time	15.01***	NS	64.21***	28.29***	12.7***	3.08**	NS
Visual Memory Span—Span	4.5***	NS	0.621***	0.024	0.698	1.65	NS
Reverse Digit Span—Score	4.56***	NS	0.802***	0.063	0.948	5.82***	0.157*
Verbal Interference—Score Part 1	6.44***	1.21*	1.19***	0.385	0.26	2.4	NS
Forward Digit Span—Score	3.19***	NS	0.741**	0.784	0.412	5.23***	0.124**
Executive function							
Switching of Attention—Time Part 2	11.97***	NS	4458***	0.054	0.365	3.25*	882.9**
Maze—Errors	14.31***	14.82***	14.6***	30.34***	8.04***	1.66	NS
Maze—Overruns	13.95***	5.79***	5.7***	28.43***	8.85***	2.18	NS
Verbal Interference—Score Part 2	13.05***	1.56***	1.54***	0.004	0.695	0.948	NS
Memory Recall and Recognition—Repeats	1.59	NS	NS	4.76*	1.88	3.15*	1.39*
Memory Recall and Recognition—Intrusions	1.62	NS	NS	1.52	0.53	0.197	NS
Language							
Word Generation—Score	35.74***	2.97***	2.91***	0.064	1.65	5.04**	1.37**
Spot the Real Word—Score	67.86***	0.76***	0.719***	0.001	0.48	8.8***	0.632***
Learning and memory							
Memory Recall and Recognition—Trials 1–4	11.13***	NS	1.28***	6.96**	0.682	1.25	NS
Memory Recall and Recognition—Recognition	7.46***	NS	0.229***	2.23	1.52	1.35	NS
Memory Recall and Recognition—Immediate Recall	10.38***	NS	0.479***	8.72**	0.703	0.386	NS
Memory Recall and Recognition—Delayed Recall	10.68***	0.467*	0.447***	10.41***	1.52	0.205	NS
Maze—Time to Complete	11.66***	18948***	18030***	0.054	1.04	2.74*	1558.47**
Maze—Trials Completed	3.76***	NS	1.89*	0.982	1.8	0.28	NS
Sensori-motor							
Motor Tapping—Taps (dominant)	33.43***	3.68***	3.5***	22.28***	1.25	1.17	NS
Choice Reaction Time—Mean Reaction Time	2.96**	NS	121.04*	1.49	1.74	2.53	NS

NS, not significant.
* $p \leq 0.05$.
** $p \leq 0.01$.
*** $p \leq 0.001$.

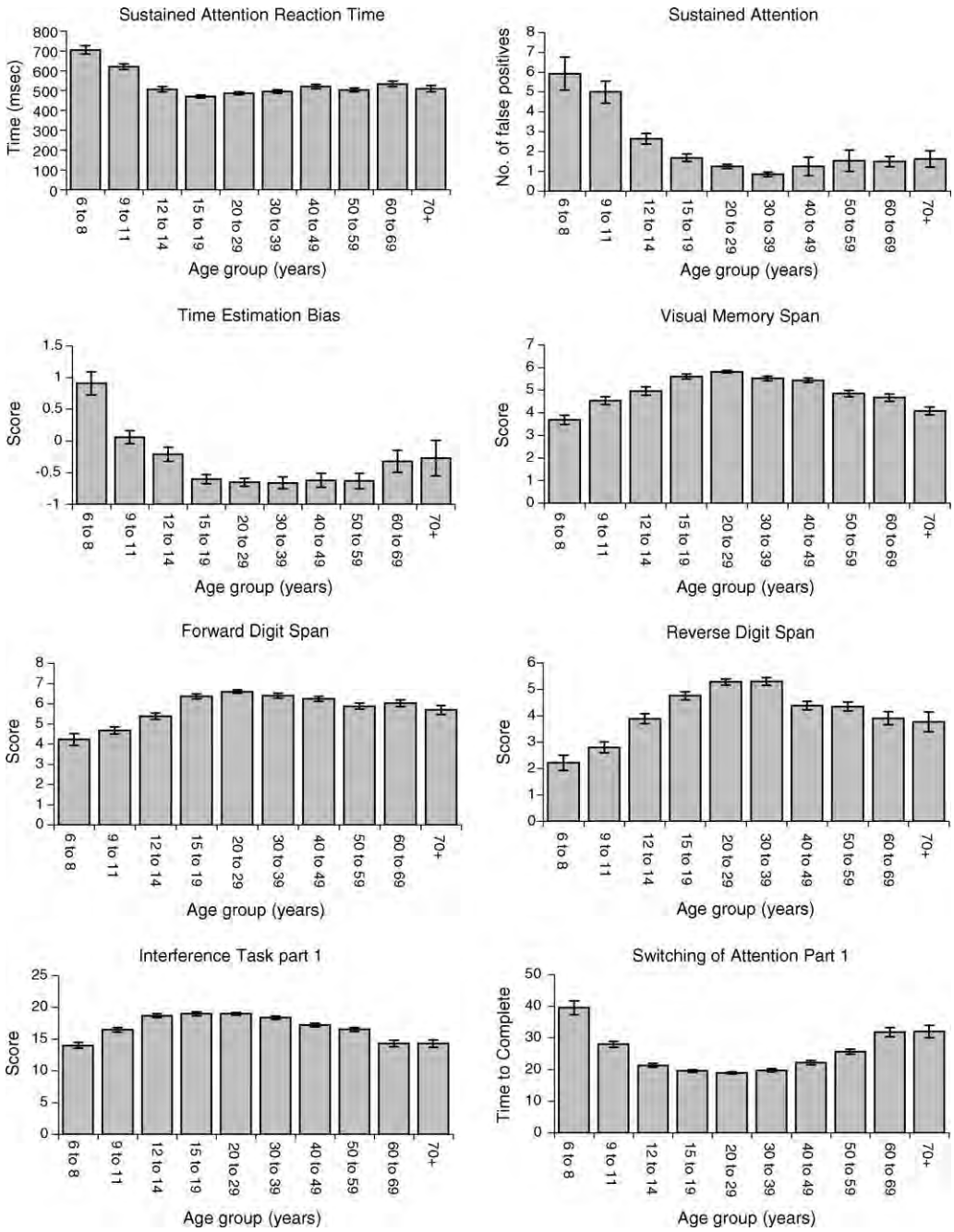

Fig. 1. Means (standard error) by age group on tests of attention and working memory.

which performance gradually decrements. Only Reaction Time asymptotes early (15–19), whilst three measures peak in the 30–39 year age range (i.e. sustained attention target discrimination, Time Estimation and Reverse Digit Span).

2.1.2. Executive function

Performance on four of the six tests of executive function (Verbal Interference Score Part 2, Maze Errors, Maze Overruns, Switching of Attention Score Part 2) was described by a quadratic function over age group with the performance asymptote reached in the 20–29 age group (see Fig. 2). Neither of the measures of self-monitoring from

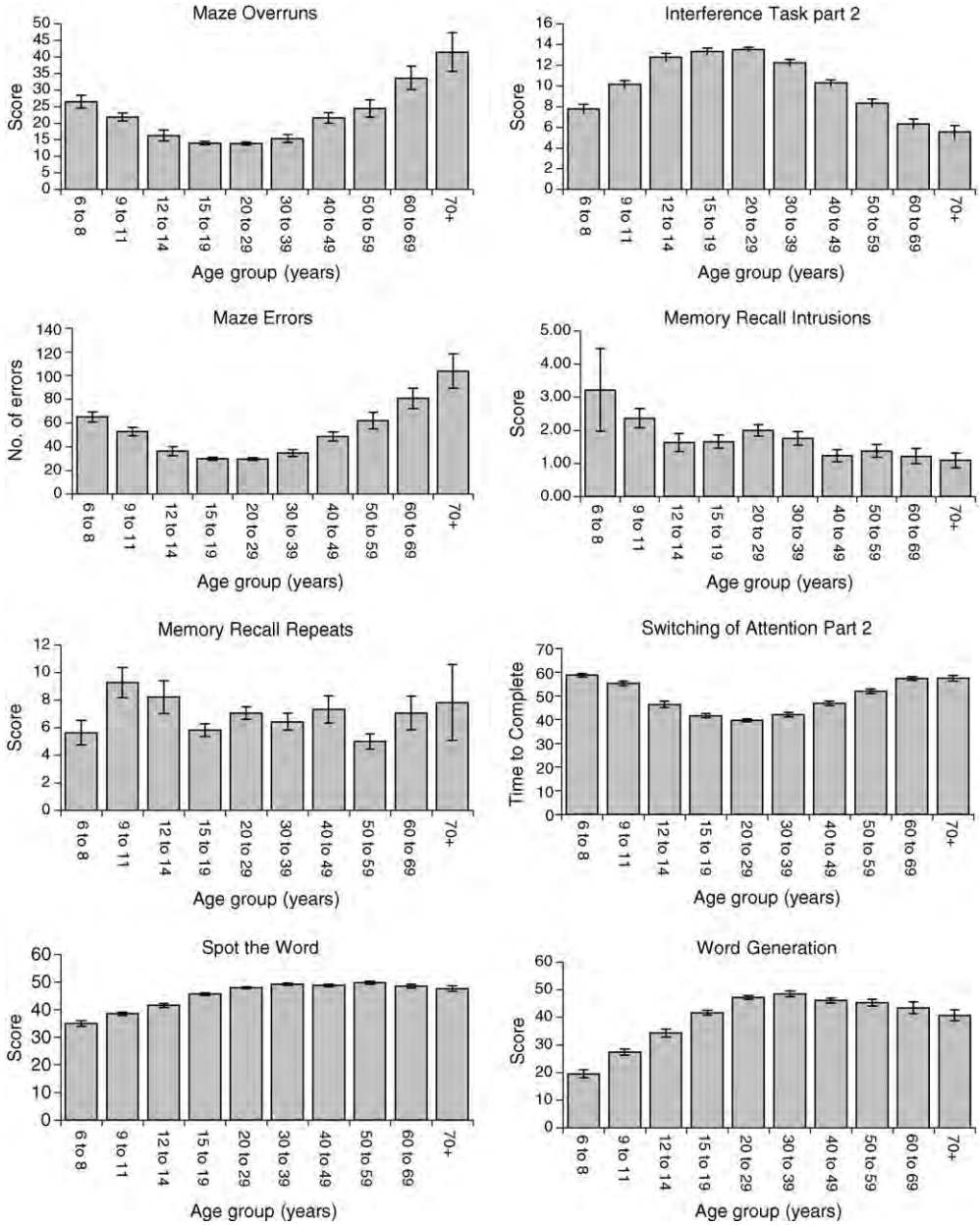

Fig. 2. Means (standard error) by age group on tests of executive function and language.

the Memory Recall test (Intrusions, Repeats) showed robust age effects, despite a small main effect ($p < 0.05$) for Intrusions. The lack of strong effects on these two measures may be related to floor effects over a small scoring range.

2.1.3. Language

A strong quadratic effect of age group was evident for Word Generation (see Fig. 2), with performance increasing linearly through to the 30–39 age group, and declining thereafter. A quadratic effect was also obtained for the Spot the Word Score, though examination of the means over age (Fig. 2) indicates that whilst peak performance is achieved by the 30–39 age group, there is only very minor fall off in performance thereafter.

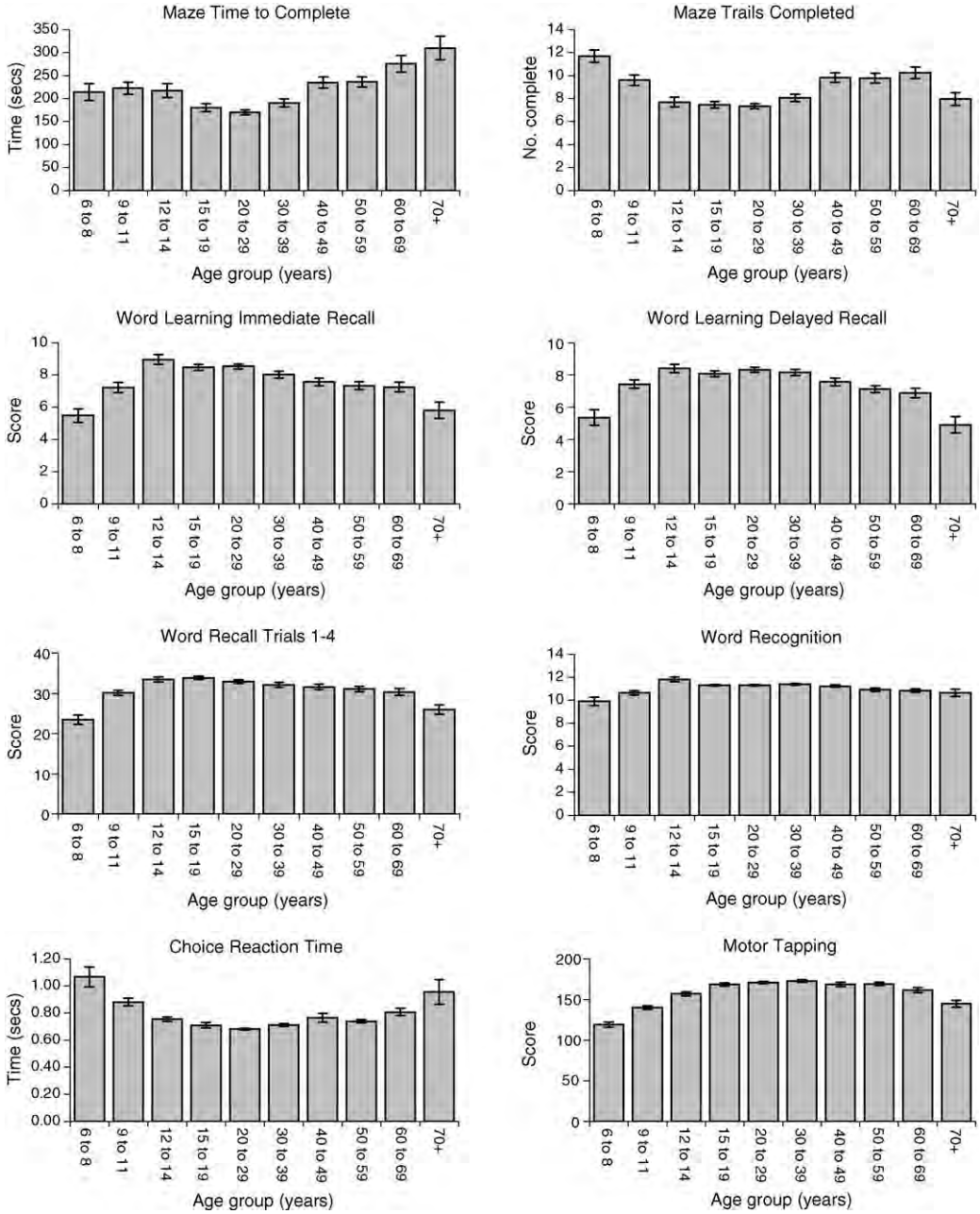

Fig. 3. Means (standard error) by age group on tests of memory and sensori-motor function.

2.1.4. Learning and memory

All six measures were described by a quadratic trend over age group. Measures of verbal learning and memory tended to peak between 12 and 19 years of age, with gradual fall of thereafter (see Fig. 3). By the age of >70, performance level on all four verbal measures approximated that for 6–11 year olds. Learning and memory performance on the maze was also affected quadratically by age group though the trend pattern was more complex. For time to complete (the time taken to learn the maze or until time out), there were only mild improvements between the age range 6 and 29, though with a clear peak in performance in the 20–29 range. Thereafter, performance declined more steeply over the subsequent age ranges. For Maze Trials Completed (the number of trials completed to criterion or until time out), performance improved noticeably through to the 20–29 age group, and declined thereafter through to the 60–69 group.

Table 2
Means and standard deviations by gender on tests of attention and working memory, executive function, language, learning and memory and sensori-motor function

	Gender			
	Males		Females	
	Mean	(S.D.)	Mean	(S.D.)
Attention and working memory				
Time estimation—Bias Score	0.35	1.06	0.51	1.14
Switching of Attention Part 1—Completion Time (s)	23.12	8.27	22.68	8.83
Sustained Attention—False Positives***	2.06	2.77	1.68	3.79
Sustained Attention—Reaction Time (ms)***	501.18	113.21	524.41	112.13
Span of Visual Memory—Score	5.26	1.43	5.21	1.21
Reverse Digit Span—Score	4.49	2.06	4.38	1.82
Interference task—Score Part 1	17.45	3.55	17.93	3.41
Forward Digit Span—Score	6.06	1.60	5.92	1.56
Executive function				
Switching of Attention—Completion Time (s)	46.61	11.60	46.06	11.46
Maze—Error Score***	39.45	41.28	47.01	41.27
Maze—Overruns***	17.22	16.25	20.32	16.00
Interference task—Score Part 2	11.45	4.12	11.28	4.11
Memory Recall and Recognition—Repeats Trials 1–4*	6.93	6.88	7.20	9.14
Memory Recall and Recognition—Intrusions Trials 1–4	2.13	3.77	1.59	2.36
Language				
Word Generation—Words Generated	40.50	13.99	41.74	13.42
Spot the Word—Score	45.67	7.16	46.16	6.56
Learning and memory				
Memory Recall and Recognition—Total Score Trials 1–4**	30.76	6.98	31.78	7.17
Memory Recall and Recognition—Recognition Score	10.96	1.40	11.06	1.30
Memory Recall and Recognition—Immediate Recall Score**	7.52	2.62	8.04	2.60
Memory Recall and Recognition—Delayed Recall Score***	7.34	2.40	7.89	2.52
Maze—Completion Time (s)	201.92	113.45	208.71	109.02
Maze—Trials Completed	7.89	3.56	8.92	4.07
Sensori-motor				
Motor Tapping—Number of Taps (dominant)***	167.00	25.03	158.00	24.49
Choice Reaction Time—Mean Reaction Time (ms)	764.64	250.76	750.90	239.37

* $p \leq 0.05$.
** $p \leq 0.01$.
*** $p \leq 0.001$.

Nominally improved performance in the >70 age group was found to be an artefact of time out effects: an inspection of the scores for this group identified ceiling effects in several subjects who were exceptionally slow at the task and only completed a very small number of trials before the time limit for completion was exceeded. This suggests that the number of trials completed on the task was an inappropriate reference for memory performance in the >70 age group due to the task's time limit.

2.1.5. Sensori-motor

Both measures (Choice Reaction Time, Motor Tapping Score) were described by quadratic trends (see Fig. 3), with performance improving through to the 20–39 age range, and falling thereafter.

2.2. Gender

A main effect for gender was obtained on 9 of the 24 measures (see Tables 1 and 2). On the Sustained Attention task, females made fewer errors but were slower than males. Females made more errors and committed more overruns

than males on the Maze. Their recall of verbal information was better than for males, though they made more repeat errors during recall. They made fewer taps than males on the Motor Tapping task.

2.2.1. Age group by gender

The main effects obtained for age group and gender were modified by interactions on only three measures: Error rate and Number of Overruns on the Maze and Reaction Time on the Sustained Attention task. In each case, the interaction was explained by an earlier peaking over the age range for females than males on the dependent measure. On the Maze, peak performance for females was obtained in the 15–19 age range, whereas for males the peak was obtained in the 20–29 year range. For Reaction Time on the Sustained Attention task, males peaked in the 15–19 years age group; whilst females peaked in the 12–14 year age range albeit at a marginally slower rate that for males (Fig. 4).

2.2.2. Years of education

Level of education affected 7 of the 24 measures assessed. These were Sustained Attention Reaction Time, Forward and Reverse Digit Span, Switching of Attention Part 2 Completion Time, Repeats Score on the Verbal Memory Recall test, Word Generation, Spot the Real Word Score and Time to Complete the Maze (see Tables 1 and 3). All but one of these (Sustained Attention Reaction Time) showed linear improvements in score with increasing years of education. Post hoc analysis of the effects indicated that reaction time during Sustained Attention found no reliable difference between groups.

3. Discussion

The battery used in this study provided sensitive indicators of change in cognition during the years of development of the brain and cognitive system as well as during the years of ageing that follow full development. This outcome was evident for measures of attention and working memory, Word Generation, Verbal Memory Recall, visuospatial learning and memory, executive function and sensori-motor function. In most of these cases, there was improvement in test performance through to some point within the second to fourth decade of life, reflecting the effects of development, followed by gradual decrement or relatively stable performance levels during the subsequent aging years. Age has already been well demonstrated to affect the wide range of higher functions addressed in this study (e.g. Compton et al., 2003; Costa & McCrae, 1993; Rabbitt, 2002; Salthouse, 2000, 2001). The present study, however, considers the full age span in a single study using a single test battery, thereby addressing change over both the developing and declining years.

3.1. Age

One observation of interest is the pattern of change in cognitive performance in the younger age groups. In most tests, performance levels incremented in a graded way from the 6 to 8 age band through, in many cases, to the third and fourth decades of life, pointing to a gradual and graded acquisition of skill during the developmental years. There were only few tests in which the rate of cognitive development was markedly greater for very young children, as has been found in some studies (e.g. Anderson et al., 2001; Archibald & Kerns, 1999), and which might be considered attributable to the delayed myelination of tertiary cortical regions. In the present study, however, an asymmetrically greater development in the 6–8 age band relative to the 9–12 age band was found only for measures of Delayed Verbal Recall, simple visuomotor attention (SOA Part 1) and time estimation. Thus, the view that the rate of cognitive development in children under the age of 9 is markedly greater than that in adolescents (Korkman et al., 2002) does not seem to hold in terms of the age bands tested in this study. One test that conformed to the expected effects of delayed myelination was the delay of improvement in Maze Learning Time (Time to Complete) until the early teen years (12–14). The results of this study also provide clear indicators of cognitive ageing, with clear and gradual decline in performance over the decades of late middle to old age. In some cases, however, the decline was only minimal, such as for recognition memory, word knowledge, vigilance speed (Reaction Time during Sustained Attention), memory span (Digit Span), time estimation, verbal fluency and visual discrimination error (Sustained Attention False Positives). In other cases, decline was particularly marked, such as in some measures of executive function (Maze Overruns, Maze Errors, Interference task Part 2) and in some measures of learning and memory (Maze Trials Completed, Delayed Verbal Recall). The study suggests that tests need to be normed over age to help ensure cross-sectional validity in

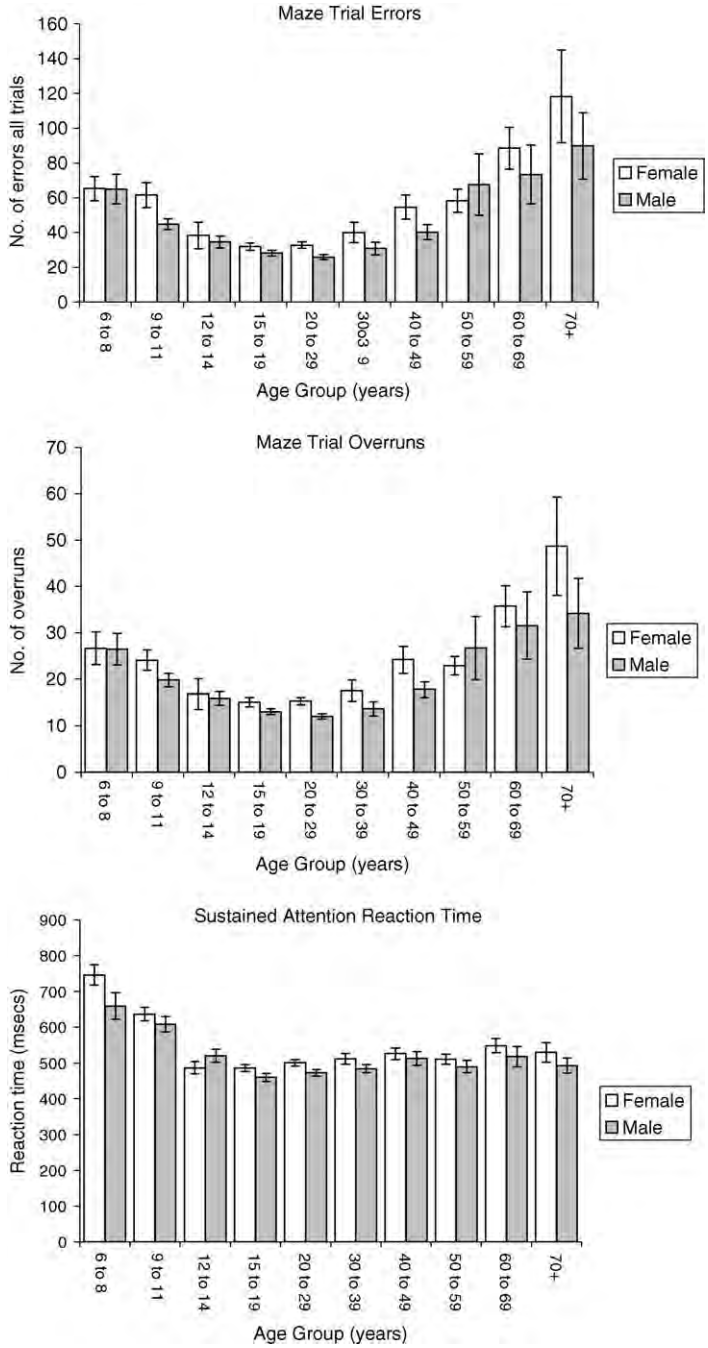

Fig. 4. Means (standard error) by age group and gender on tests of attention and executive function.

clinical assessments, once the utility of this approach has been assessed from appropriate diagnostic and treatment studies. The natural decline in performance with age across many measured functions, as demonstrated in this study, also shows the importance of adequate age norms both during initial assessment in cases of suspected mild cognitive impairment and when following such cases longitudinally over time (see Sarazin & Dubois, 2002). The results from the current study suggest that decline in many cognitive functions from young adulthood into advanced age is quite normal. However, it is likely that some older individuals experience even greater change in cognitive function compared to their peers, such as in cases of mild cognitive impairment and dementia. Our results strongly support the need to

Table 3
Means and standard deviations by years of education (adult participants only) on tests of attention, working memory, executive function, language, learning and memory and sensori-motor function

	Years of education							
	<10		10–12		13–15		>15	
	Mean	(S.D.)	Mean	(S.D.)	Mean	(S.D.)	Mean	(S.D.)
Attention and working memory								
Time estimation—Bias Score	0.07	1.06	−0.51	1.06	−0.65	1.11	−0.62	1.02
Switching of Attention Part 1—Completion Time (s)	27.54	10.73	22.57	8.26	20.65	6.23	21.11	6.66
Sustained Attention—False Positives	3.67	3.96	1.67	3.68	1.29	1.97	1.23	3.04
Sustained Attention—Reaction Time (ms)**	567.67	135.02	487.52	93.95	499.52	100.64	489.87	94.51
Span of Visual Memory—Score	4.59	1.50	5.23	1.32	5.46	1.21	5.59	1.04
Reverse Digit Span—Score***	3.23	1.84	4.29	1.81	4.91	1.64	5.20	1.86
Interference task—Score Part 1	16.63	3.46	17.49	3.76	18.23	3.44	18.30	3.11
Forward Digit Span—Score***	4.98	1.56	5.96	1.38	6.38	1.43	6.58	1.42
Executive function								
Switching of Attention Part 2 Completion Time (s)*	52.51	10.44	46.94	10.52	43.30	11.10	42.98	11.24
Maze—Error Score	49.31	36.27	49.79	55.37	37.91	31.47	39.18	39.02
Maze—Overruns	21.03	14.05	21.56	22.83	16.60	11.20	17.14	14.74
Interference task—Score Part 2	10.35	3.78	11.04	3.99	12.12	4.27	11.86	4.18
Memory Recall and Recognition—Repeats Trials 1–4*	6.36	7.13	7.75	10.84	6.75	9.34	4.76	7.87
Memory Recall and Recognition—Intrusions Trials 1–4	1.43	1.08	1.60	2.20	1.86	2.82	1.49	2.05
Language								
Word Generation—Score**	29.09	12.40	41.51	10.89	45.63	11.38	48.02	11.20
Spot the Word—Score***	38.69	7.32	46.23	5.74	47.94	5.45	50.10	5.39
Learning and memory								
Memory Recall and Recognition—Total Score Trials 1–4	28.27	8.69	30.08	8.18	25.64	10.04	26.51	10.73
Memory Recall and Recognition—Recognition Score	10.97	1.34	10.99	1.46	11.30	1.19	11.32	0.89
Memory Recall and Recognition—Immediate Recall Score	7.29	2.72	7.33	2.30	8.23	2.47	8.03	2.51
Memory Recall and Recognition—Delayed Recall Score	7.00	2.66	7.30	2.17	7.99	2.51	7.95	2.43
Maze—Completion Time*	198.61	94.83	240.60	123.37	194.02	104.38	198.95	112.82
Maze—Trials Completed	9.15	3.97	8.52	3.81	8.02	3.48	8.17	4.08
Sensori-motor								
Motor Tapping—Number of Taps (dominant hand)	144.03	25.34	166.34	21.99	168.54	23.06	169.98	20.66
Choice Reaction Time	874.50	349.73	729.80	159.25	732.11	248.66	699.26	117.20

* $p \leq 0.05$.
** $p \leq 0.01$.
*** $p \leq 0.001$.

represent aging associated cognitive change across a continuum in order to detect sensitively abnormal variation that may occur in such conditions.

One possible concern in the present study is a somewhat skewed distribution of subjects across the age groups. Very young and very old subjects are less easy to acquire than subjects in the middle age bands. As a result, the database tends to contain a relatively larger number of subjects in their twenties and thirties. Fortunately, this age group has reached the full potential in brain functioning and has not yet succumbed to age-related changes that could affect scores on standardized testing. Nevertheless, database numbers are still being increased with an extended effort to elevate numbers and related statistical power in the less well-represented bands. Missing data also presented a minor difficulty, particularly in the youngest age groups but this is not an issue specific to IntegNeuro but rather to the difficulties in testing younger individuals more generally. While this is not so much of an issue within age groups, as variables with large amounts of missing data can be simply excluded from analysis, it can somewhat skew the overall results between age groups.

Another possible concern is that some of the tasks in the battery might have been challenging for the younger children and in particular Verbal fluency, Spot the Real Word, Switching of Attention and Time Estimation. Examination of

the scores on these tests for the youngest age group (6 years old) revealed completion rates of 64% on the Switching of Attention task, 95% for Verbal Fluency and 100% for each of Spot the Real Word and Time Estimation. For 6 year olds that did complete these tests, mean scores were one standard deviation above zero for time estimation and over two standard deviations for the other tests. Thus, it appears that the majority of 6 year olds can complete these tests and evidence of only minimal floor effects for this age. But it should be noted that with one exception, the test battery should pick up any child who finds a test too difficult—by virtue of a practice trial protocol that ensures the test is skipped after three practice test failures. The exception is the Switching of Attention task since, unlike the practice trials, which include only short number letter sequences, the test trials presume knowledge of numbers up to 25 and knowledge of the first 13 letters of the alphabet.

A final concern here is the choice of age bands used in analysis. For example, there are substantial changes in cognitive development between 6–8 and 9–11, with normative datasets for children in these ages usually divided into 6-month periods to capture the rapid maturation for children in these age ranges. Clearly, the number of participant datasets available for the study did not permit finer age divisions. However, the aim of the study was to demonstrate the sensitivity of the battery across the age range rather than provide a definitive set of norms for assessment purposes. With respect to the latter issue, we have recently developed a normalization model based on age regression (Crawford & Garthwaite, 2002; Gordon, Cooper, Rennie, Hermens, & Williams, 2005) that provides precise aged-based normative reference for assessment purposes.

3.2. Gender

The present study also examined the effect of gender on the test battery. Females demonstrated better verbal memory than males, though self-monitoring of retrieval context was poorer than for males. Dextral motor expression was generally slower for females. This was also evident during visuospatial learning and memory, where they were also more error prone than males. They were also slower to react during Sustained Attention on verbal material but were more accurate than males. In some tests, there were indications of females reaching an optimal performance level earlier than males. These results are consistent with earlier studies of verbal memory (e.g. Beatty, Mold, & Gontkovsky, 2003; Ruff, Light, & Quayhagen, 1989) and motor dexterity (Brandon, Chavez, & Bennet, 1986; Coleman, Moberg, Ragland, & Gur, 1997), but failed to find evidence for female advantage on executive functioning (Boone, 1999; Boone, Ghaffarian, Lesser, & Hill-Gutierrez, 1993), verbal fluency (Loonstra, Tarlow, & Sellers, 2001; Ruff, Light, & Parker, 1996; Zappala, Measso, Cavarzeran, & Grigoletto, 1995) or visuospatial memory (Caffarra, Vezzadini, Dieci, Zonato, & Venneri, 2002).

Overall, gender effects were obtained on only a third of the measures reported in the present study. The literature contains many studies reporting a relative lack of gender effects on measures of cognitive functioning. This has been demonstrated in the 4–18 age group, where gender has not been found unrelated to verbal fluency (Regard, Strauss, & Knapp, 1982), executive functioning (Paniak, Miller, Murphy, & Patterson, 1996; Rosselli & Ardila, 1993), sensory and motor functioning (Arceneaux et al., 1997), auditory verbal learning and memory (Van den Burg & Kingma, 1999) or visuospatial construction (Fastenau, Denburg, & Hufford, 1999; Fernando, Chard, Butcher, & McKay, 2003). It has also been demonstrated in the adult age range for attention (Beatty et al., 2003), visuospatial construction and memory (Boone, Lesser, Hill-Gutierrez, & Berman, 1993; Coman et al., 2002 Fastenau et al., 1999; Ruff et al., 1996), visuospatial learning (e.g. Ruff et al., 1996), visuomotor tracking and general attention (Giovagnoli, 1997), visual retention and general memory (Zappala et al., 1995), verbal fluency (Loonstra et al., 2001), verbal naming (Cruice, Worrall, & Hickson, 2000; Kent & Luszcz, 2002), word knowledge (Crowell, Vanderploeg, Small, Graves, & Mortimer, 2002), some tests of attention and working memory (Vlahou & Kosmidis, 2002) and on the Halstead-Reitan Neuropsychological test battery (Elias, Robbins, Walter, & Schultz, 1993).

Overall, the gender findings were of modest magnitude. However, it is important to note that the gender literature would suggest that sex differences are expected only on certain types of task that assess gender-sensitive cognitive functions. Sex differences would not be expected a priori on most tests in this battery.

3.3. Years of education

Finally, the present study examined the effect of years of education on cognitive performance. Most noticeable in this regard was the effect of education on measures of verbal fluency (Word Generation), word knowledge (Spot the

Real Word), verbal memory capacity (Forward Digit Span), verbal working memory (Reverse Digit Span), mental adaptability (SOA Time Part 2), verbal self-monitoring (Verbal Recall Repeats) and visuospatial learning and memory (Maze Completion Time). The effects of years of education on a range of measures of language is perhaps not surprising given the focus of educational systems on linguistic abilities (e.g. Ardila, Ostrosky-Solis, Rosselli, & Gomez, 2000).

An effect of education on cognitive function has often been reported (e.g. Ardila et al., 2000; Bravo & Hebert, 1997; Collie, Shafiz-Antonacci, Maruff, Tyler, & Currie, 1999; Gladsjo et al., 1999; Loonstra et al., 2001; Richardson & Marottoli, 1996; Vlahou & Kosmidis, 2002) though it must be considered that any such relationship would be susceptible to confound by other factors, such as age, intelligence and gender. Ardila et al. (2000), for example, found education effects to be noticeably greater than those of age on a neurocognitive battery assessment of orientation, attention, memory, language, visuoperceptual abilities, motor skills and executive functions. At the same time, there have been studies that reported no effects or only minimal effects of years of education (e.g. Boone, 1999; Fastenau et al., 1999; Jones & Gallo, 2001; Meguro et al., 2001).

The present study differs significantly from many earlier studies of the effect of years of education on cognitive function and this may go some way to explaining some of the differences observed. Firstly, a number of investigations have restricted the age range examined to those 60 years or older, with the specific aim of identifying factors relevant to the onset of age-related cognitive dysfunction (e.g. Bravo & Hebert, 1997; Gontkovsky, Mold, & Beatty, 2002; Rapp, Espeland, Hogan, Jones, & Dugan, 2003; Richardson & Marottoli, 1996). This contrasts markedly with the present study, which examined the full age range. Secondly, several studies have employed only a limited range of measures (e.g. Vlahou & Kosmidis, 2002) or limited testing to only one gender (e.g. Rapp et al., 2003). Again, the present study examined a wide range of measures. Thirdly, assessments of education effects vary in the categorization of level of education. For example, a number of reports have been based on participants with relatively low levels of education (e.g. Ardila et al., 2000; Laks et al., 2003). In the study by Ardila et al. (2000), three of their four education level categories employed involved participants with less than 10 years of education. In contrast, three of the four levels of education categories in the present study encompassed those with 10 years of education or more, and few of those with less than 10 years of education had been at school for less than 8 years. A number of other studies where participant selection has been biased more towards the upper end of the education scale (e.g. Richardson & Marottoli, 1996), which tends to be more strongly populated in western acculturated regions, education has been found to explain only minimal data variance.

3.4. Standardization

The delivery of the best battery in the present study involved standardized conditions in which human contact during testing was minimized, in which test instruction is delivered using pre-recorded audio and video in a two-way interactive setting and in which sound, light and other environmental factors are prescribed. It is suggested that such requirements go a long way towards minimizing variability in test performance that can result across settings due to factors, such as tester bias, variation in test instruction delivery, pace of test delivery (e.g. duration of stimulus presentation and inter-stimulus delays). Nevertheless, some of these same requirements may be seen as a source of weakness when applied to clinical populations. One comment raised often in regard to computerized test batteries is that neuropsychological screening should be supervized by a testing psychologist. The argument is that the psychologist should be able to observe client behavior during test performance, just in case this information might be qualitatively useful in explaining abnormalities in test performance. This would particularly be the case with older groups that might suffer more physical disabilities and who may have more difficulty pressing a touchscreen to register responses.

These are important issues in the case where the test battery used in the present study is applied to the clinical setting. However, the issues are well accommodated by the standardized approach adopted. For example, video monitoring permitted clear observation of test behavior and audio communication allowed contact when and as required. Also, the mode of delivery of instructions was fail-safe and provided an attentional cueing mechanism for test supervision. During instruction delivery, embedded software monitored the client's behavior to ensure that the relatively low demand test trials were performed correctly from a behavioral (i.e. correct response action) and a cognitive (i.e. correct response content) standpoint. Three consecutive failures resulted in a warning being sent to the test supervisor to take note of the failure and to initiate appropriate action with the client. Information about whether a client fails test instructions on none, one, two or three occasions provides useful information analogous to qualitative observation. Further, the highly sensitive, computerized touchscreen allowed quantitative measurement of response behavior. For example, the

touchscreen system used allowed measurement of response variability, such as the standard deviation of the inter-tap interval on the Motor Tapping task. This informs quantitatively about difficulties with motor control, analogous to the qualitative information the neuropsychologist might obtain by observing tapping behavior, but better since the availability of the normative database described in this paper permits statistical assessment of the abnormality of such measures.

3.5. Summary

This study provides insight into the changes of cognitive functions though from the earliest years to the beginnings of decline, and identifies the concomitant contributions of gender and years of education. The test battery that is used is shown to provide a sensitive assessment of cognitive function across the full age range. In this regard, the test battery and its associated database has broad applicability in areas, such as neuropsychological assessment, assessment of treatment effects, longitudinal case management and the assessment of drug efficacy. An important future development using the battery is the collection of data from a wide range of psychopathologies, to permit the development of wide-ranging specificity analysis.

Acknowledgement

We acknowledge and thank the Brain Resource Company (www.brainresource.com) for permission to use the Brain Resource International Database.

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