Exploring the Latest Techniques to Measure the Effects of Nutrition on the Brain

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Assessing Cognitive Function

• Requires administration of tests
• Tests need to be:
  • Practical to administer
  • Relevant to everyday behaviour
  • Valid
  • Reliable
  • Comprehensive
  • Sensitive
• Automation of testing confers numerous advantages in test conduct & the internet makes the outreach vast
Most Widely used Automated Cognitive Test Systems

CDR SYSTEM
Computerized Cognitive Testing

COGSTATE

CANTAB

WESNES
COGNITION
Criteria for validation and selection of cognitive tests for investigating the effects of foods and nutrients

Celeste A de Jager, Louise Dye, Eveline A de Bruin, Laurie Butler, John Fletcher, Daniel J Lamport, Marie E Latulippe, Jeremy PE Spencer, and Keith Wesnes

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Cognitive Benefits of Breakfast

Brief communication

Breakfast reduces declines in attention and memory over the morning in schoolchildren

Keith A. Wesnes\textsuperscript{a},* Claire Pincock\textsuperscript{a}, David Richardson\textsuperscript{b}, Gareth Helm\textsuperscript{c}, Simon Hails\textsuperscript{d}

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Received 4 August 2003; accepted 6 August 2003
Study Design

• Run in a half-term week
• 30 children aged 9-16
• Day 1: Training on Tests
• Days 2 to 5: Study Days
  • Conditions, counterbalanced over days
    • No breakfast
    • Glucose Drink
    • Cheerios
    • Shreddies
• Each day:
  • Tests - Pre-’Breakfast’
  • 0.5 hours later
  • 1.5 hours later
  • 2.5 hours later
  • 3.5 hours later – midday
Power of Attention

Declines in Concentration

Time

0.5 hour  1.5 hour  2.5 hour  3.5 hour

msec

0  20  40  60  80  100  120  140  160  180

Nothing
Glucose Drink
Cheerios
Shreddies
Cheerios and Squigles have always been good nutritious breakfasts. Well now, new research carried out by CDAB and Reading Scientific Services confirms this. Their series of tests involved children aged 9-16 years old. Over time their concentration dropped markedly. Cheerios and Squigles reduced this decline by up to 50% that’s because the complex carbohydrates released energy steadily, helping to keep the mind active. This was far better than simple carbohydrates, like glucose, or a skipped breakfast.

For further details go to www.Cheerios.co.uk

Giving your family Cheerios for breakfast is a great way to start their morning and help them pace whatever challenges the day may bring.

The tasty, toasted Os with the nutritional goodness of four whole grains makes Cheerios a family favourite.

Cheerios contains B vitamins, iron and calcium to help keep your family strong and healthy!

There’s a whole lot of good in those little Os!
UK Government Nationwide School Based Breakfast Initiative
The Farmhouse Breakfast Week Internet Study

• UK Government Initiative
• Nationwide study run in UK during January 2004 based on findings of previous study
• Children from schools throughout UK logged on to CDR website and performed CDR tests and answered a questionnaire about breakfast
• Total of 2036 individuals logged on and performed tests
• 1386 Children aged 6-16 logged on before 12.30 pm
Research report

Breakfast is associated with enhanced cognitive function in schoolchildren. An internet based study

Keith A. Wesnes a,b,*, Claire Pincock c, Andrew Scholey b

a Bracket Global, Gatehampton Road, Goring-on-Thames, RG8 0EN, UK
b Centre for Human Psychopharmacology, Swinburne University, Melbourne, Australia
c Quintiles, Reading, UK

Fig. 1. Differences in cognitive function between children who reported having breakfast and those who did not (least squares means with standard errors). Poorer scores are plotted to descend.
Size of effects directly comparable between internet & laboratory based studies

Power of Attention

![Graph showingPower of Attention over time with different treatments: Nothing, Glucose Drink, Cheerios, and Shreddies. The graph compares the Power of Attention across different time points (0.5 hour, 1.5 hour, 2.5 hour, 3.5 hour). The x-axis represents time in hours, and the y-axis represents milliseconds (msec). The legend indicates the treatments: Nothing in blue, Glucose Drink in red, Cheerios in yellow, and Shreddies in brown. The graph shows a significant difference in Power of Attention between NO BREAKFAST and BREAKFAST conditions, p=0.007.}
Survey Run on Pharmaton Website

• Run over 12 months 2011-2012
• Four tests from the CDR System, were internet enabled:
  • Simple reaction time
  • Choice reaction time
  • Digit vigilance
  • Picture recognition
• 5 language versions were available: English, Greek, Hungarian, Portuguese & Spanish
• 120,171 individuals logged on to a website, entered their age and gender, and performed the tests on-line
• Male to female ratio 41% v 59%
The role of human cognitive neuroscience in drug discovery for the dementias
Keith A Wesnes\textsuperscript{1,2,3} and Chris J Edgar\textsuperscript{4}

Current Opinion in Pharmacology 2014, 14:62–73

Figure 3

Illustration of cross-sectional declines in normal ageing for a measure of focused attention and information processing gathered recently from individuals who logged onto a website and performed 12 min of cognitive testing.

Pattern Separation & Neurogenesis
93,087 subjects aged 18-85 assessed via the internet

**Figures expressed as change from 18 to 25 years**

<table>
<thead>
<tr>
<th>Age-Band Years</th>
<th>% Correct Change from 18-25 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>26-30</td>
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<tr>
<td>31-35</td>
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<td>76-80</td>
<td>30</td>
</tr>
<tr>
<td>81-85</td>
<td>35</td>
</tr>
</tbody>
</table>

**Decline in Pattern Separation & Neurogenesis**

93,087 subjects aged 18-85 assessed via the internet

Figures expressed as change from 18 to 25 years
Pattern Separation & Neurogenesis
Internet Children’s Breakfast Study

Original Stimuli Accuracy
LSMeans +/- SEM
Difference $p=0.45$

- No Breakfast
- Breakfast

% Correctly Identified
- No Breakfast: 80
- Breakfast: 82

Neurogenesis Sensitive Stimuli Accuracy
LSMeans +/- SEM
Difference $p=0.0018$

- No Breakfast
- Breakfast

% Correctly Identified
- No Breakfast: 74
- Breakfast: 78
• An online only system
• Based on tests with over 30 years of use in clinical research
• Ability to handle large scale traffic
• Touchscreen enabled
Utility, reliability, sensitivity and validity of an online test system designed to monitor changes in cognitive function in clinical trials

Keith A. Wesnes¹,²,³,⁴,⁵, Helen Brooker¹, Clive Ballard²,⁶, Laura McCambridge⁶, Robert Stenton⁷ and Anne Corbett²,⁶

¹Wesnes Cognition Ltd, Streatley on Thames, UK
²Medical School, Exeter University, UK
³Department of Psychology, Northumbria University, Newcastle, UK
⁴Centre for Human Psychopharmacology, Swinburne University, Australia
⁵Medicinal Plant Research Group, Newcastle University, UK
⁶King’s College London, UK
⁷Manta Software Limited, Cambridge, UK

Correspondence to: K. A. Wesnes, E-mail: keith@wesnes.com

Conclusions: The results of these analyses identify CogTrack™ to be a practical and valid method to reliably, sensitively, remotely and repeatedly collect cognitive data from large samples of individuals aged 50 and over. Copyright © 2017 John Wiley & Sons, Ltd.
Effects of the Red Bull energy drink on cognitive function and mood in healthy young volunteers

Keith A Wesnes¹⁻⁵, Helen Brooker¹, Anthony W Watson⁶, Wendy Bal⁶ and Edward Okello⁵,⁷

Abstract
The present study compared the cognitive and mood effects of two commercially available products, Red Bull energy drink 250 mL and Red Bull Sugarfree energy drink 250 mL, together with a matching placebo 250 mL. Twenty-four healthy young volunteers took part in a randomised, placebo controlled, double-blind, three-way cross-over study. Cognitive function was assessed using an integrated set of nine computerised tests of attention, working and episodic memory. On each study day the volunteers received a standardised breakfast prior to completing a baseline performance on cognitive tests and mood scales, followed by the consumption of the study drink. The cognitive tests and scales were then re-administered at 30, 60 and 90 min post-dose. Red Bull was found to produce significant improvements over both the Sugarfree version and the placebo drink on two composite scores from the six working and episodic memory tests; one combining the 12 accuracy measures from the six tasks and the other the average speed of correct responses from the working memory and episodic recognition memory tasks. These improvements were in the range of a medium effect size, which reflects a substantial enhancement to memory in young volunteers.
Benefits of Red Bull

Memory Capacity Index
Composite score from 6 working & episodic memory tests

Effect Sizes 0.47 & 0.45

Memory Retrieval Speed Index
Composite score from the speed scores on the 4 working memory & episodic memory tasks

Effect Sizes 0.52 & 0.37

Figure 2. Main effects of changes from baseline scores for the memory capacity index (a) and the retrieval speed index (b). Scores are LS Mean changes with standard errors. Descending scores reflect impairments compared to baseline levels, ascending scores improvements. *p<0.01 compared to Red Bull, †p<0.05 compared to Red Bull.
PROTECT
Cognitive health in ageing

UNIVERSITY OF EXETER

KING'S COLLEGE LONDON
Online registration and consent

Completion of Assessments

Collection of DNA sample through postal saliva sample kit

Annual Completion of Assessment

Cognitive Test Batteries:
- PROTECT Cognitive Test Battery
- CogTrack™

Questionnaires
- IQCode (self-report and informant)
- Activities of Daily Living
- Mental Health Questionnaire
  Depression, Anxiety, Stress, Trauma, Alcohol and drug use, Mild Behaviour
- Medical Questionnaires
  Pain, Sleep, Key medical conditions and medications
- Lifestyle
  Physical exercise, supplements, hobbies
- Mood
- Mild Behavioural Impairment Questionnaire (self and Informant)
GLOBAL EXPANSION

• PROTECT UK - 2015
• PROTECT - Hong Kong – Nov 2017
• PROTECT Launch – Norway – Nov 2018

Example Imbedded clinical Trials

• A randomized, 12-months parallel-group placebo-controlled online study of anthocyanins in people aged above 60 with an increased risk for dementia
• A self-directed online exercise intervention for people over 50
PROTECT - Baseline Data
Attentional Intensity Index (n=16,635)
Effect Size over Age-Range Cohen's $d= 1.06$
LSMeans with SEM

Age-Group (Years)

- 50 to 54
- 55 to 59
- 60 to 64
- 65 to 69
- 70 to 74
- 75 to 79
- 80 to 96

msec

1280
1300
1320
1340
1360
1380
1400
1420
1440
PROTECT 2017 Full CogTrack System
Quality of Memory (n>2,500)
LSMeans with SEM
Effect Size over Age-Range Cohen's d= 1.1

Overall % Correct

<table>
<thead>
<tr>
<th>Age-Group (Years)</th>
<th>Overall % Correct</th>
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<tbody>
<tr>
<td>50 to 54</td>
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<tr>
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<td>70 to 74</td>
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<td>75 to 79</td>
<td>64</td>
</tr>
<tr>
<td>80 to 90</td>
<td>66</td>
</tr>
</tbody>
</table>
Effects of Diabetes

Responses to the Question: Has a doctor ever given you a diagnosis of, or told you that you have diabetes?

p<0.0001  p<0.0001
Exercise & Neurogenesis

Have you done any physical activity lasting at least 20 minutes that has left you out of breath in the last month?

PATTERN SEPARATION TASK n=15,584

Ability to Correctly Recognise Original Pictures
p=0.15

Ability to Correctly Reject Closely Similar Pictures
p<0.0001
Mental Games & Attentional Intensity

**Word Puzzles**

\[ p<0.0001 \]
\[ d = 0.27 \]

**Number Puzzles**

\[ p<0.0001 \]
\[ d = 0.26 \]

<table>
<thead>
<tr>
<th>How frequently do you engage in word puzzles?</th>
<th>LSMeans +/- SEM</th>
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</thead>
<tbody>
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<td>Occasionally</td>
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<td>1330</td>
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</tbody>
</table>

<table>
<thead>
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<th>How frequently do you engage in number puzzles?</th>
<th>LSMeans +/- SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never</td>
<td>Occasionally</td>
</tr>
<tr>
<td>1330</td>
<td>1335</td>
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</tbody>
</table>

BMI & Attention
n=16,215

Attentional Intensity Index
LSMeans +/- SEM
BMI Quartile

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<thead>
<tr>
<th>Quartile</th>
<th>LSMeans (msec)</th>
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<tbody>
<tr>
<td>1</td>
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<td>2</td>
<td>1340</td>
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<tr>
<td>3</td>
<td>1345</td>
</tr>
<tr>
<td>4</td>
<td>1350</td>
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Sustained Attention Index
LSMeans +/- SEM
BMI Quartile

<table>
<thead>
<tr>
<th>Quartile</th>
<th>LSMeans (%)</th>
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<tbody>
<tr>
<td>1</td>
<td>93.6</td>
</tr>
<tr>
<td>2</td>
<td>93.8</td>
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<td>3</td>
<td>94.0</td>
</tr>
<tr>
<td>4</td>
<td>94.2</td>
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CAN INCREASING THE DIFFICULTY OF A NEUROGENESIS-SENSITIVE TASK ENHANCE ITS SENSITIVITY TO DETECTING AGE-RELATED DECLINES IN VOLUNTEERS AGED 50 TO 96?

Keith Wesnes¹,², Helen Brooker¹, Anne Corbett², Clive Ballard²,³. ¹Wesnes Cognition Ltd, Reading, United Kingdom; ²University of Exeter Medical School, Exeter, United Kingdom; ³King’s College London, London, United Kingdom. Contact e-mail: keith@wesnes.com

- CogTrack data 16,664 PROTECT participants aged 50 to 96
- CDR System data from 34,415 participants over same age range
Results

Increasing the difficulty of the discriminations results in a significant interaction between age groups and test systems (p<0.0001) for the neurogenesis sensitive stimuli, representing a greater effect sized decline over the age-range – 0.96 v 0.62

Conclusions

PROTECT

- A successful example of a remote, large, long-term cohort study
- Incorporating sensitive cognitive test systems
- An engaged cohort for recruitment
- Successful track record of delivering robust trials

Online cognitive testing confers numerous benefits to the field:
- Can be used in laboratory based and remote trials
- Cost efficient way to adequately power trials
- Does not restrict sample size or frequency of study assessments
- Enables international trials to be managed efficiently
- Can be used to engage consumers