



BRAINnet

Brain Research And Integrative Neuroscience Network

BRAINnet Standardized Methods



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Details of the BRAINnet standardized assessments

Clinical information

(disorder specific; example for schizophrenia provided)

- SCID structured interview⁷
- DSM-IV criteria for diagnosis (inter-rater reliability established)
- PANSS ratings of psychosis symptoms⁸
- Calgary Depression Scale⁹
- Young Mania Scale¹⁰
- Functional outcome (SOFAS, WHOQOL-BREF, GAF, Premorbid Adjustment, Role Functioning)¹¹⁻¹⁵

WebQ (Web Assessment Questionnaire)

Demographics

Disposition: Personal Details

- Demographics, (10 questions on DOB, sex, country of birth, marital status, height, weight, occupation, education x 2, ethnic origins)
- Handedness (Annett's Handedness Inventory, including items from Edinburgh Handedness Inventory, 15 questions)^{16,17}

Medical history and psychological measures

Disposition: Medical

- Vision, hearing, mobility/dexterity, mobile phone use, learning/dyslexia, psychiatric/psychological, neurological, sleep x 2, eating, tobacco, alcohol, marijuana, recreational drugs, surgery, physical trauma) (16 trigger questions for optional sections 1 to 15)¹⁸
- Axis-I symptoms (SPHERES and PHQ; 34 questions)^{19,20}
- Caffeine, Alcohol, Addictive Drugs (3 questions for harmful use)¹⁸
- Prescription medications (5 questions x max. of 3 medications)¹⁸

Feeling and Self Regulation: Wellbeing and Personality questions

- Depression Anxiety and Stress Scale-21 (21 questions, validated with PHQ-9, Beck Scales)²¹
- Schizotypy Questionnaire (12 questions)²²
- Paranormal Belief (5 questions)³³
- BRIEF (Brain Resource Inventory of Emotional intelligence Factors; 14 questions)²³
- NEO-FFI (NEO-Five Factor Inventory, 60 item)²⁴
- BRISC (Brain Resource Inventory of Social Cognitions; 45 questions)^{5,6,25,26}

Environment: Stressors

- Early Life Stress (19 questions)^{27,28}
- Traumatic life events (11 trigger questions for optional sectional 16 on DSM trauma criteria)²⁹



Additional section (based on trigger questions)

Disposition: Medical (expanded from 16 trigger questions)

- Vision (2 questions)¹⁸
- Hearing (2 questions)¹⁸
- Mobility/Dexterity (2 questions)¹⁸
- Mobile phone (4 questions)
- Learning (difficulties/dyslexia; 5 questions)¹⁸
- Psychiatric/Psychological (8 questions)¹⁸
- Neurological (8 questions)¹⁸
- Sleep (Multi-variable Apnea Sleep Symptom Frequency Questionnaire; MAP; plus brief survey screen for prediction of Apnea, 16 questions)³⁰
- Eating (disordered eating, Patient Health Questionnaire, 7 questions)²⁰
- Tobacco-Smoking (Fagerstrom Test for Nicotine Dependence, 6 questions)³¹
- Alcohol (AUDIT – WHO Alcohol Use Disorders Identification Test, 10 questions)³²
- Marijuana (3 questions)¹⁸
- Recreational Drugs (2 questions)¹⁸
- Surgery (3 questions)¹⁸
- Physical Trauma (7 questions)¹⁸
- Traumatic experiences (DSM-IV Criterion A trauma, 30 questions)²⁹

IntegNeuro and WebNeuro

A computerized assessment of cognition using a Touchscreen format. WebNeuro is an equivalent assessment battery enabled in a web format. The validation between formats has been published²⁸.

Thinking tasks for General Cognition:

- Motor Tapping
- Choice Reaction Time
- Verbal Memory Recall (including delayed conditions)
- Spot The Real Word
- Word Generation
- Span Of Visual Memory
- Digit Span (Forwards and Reverse)
- Verbal Interference (Parts 1 & 2)
- Switching of Attention (Parts 1 & 2)
- Executive Maze
- Go/NoGo
- Continuous Performance Test (n-back)

Emotion tasks for Emotional Cognition

- Emotion Identification (explicit)*
- Emotion Recognition (implicit, delayed)*

* Using stimuli from Gur et al (2002) series



Example of how the tasks have been validated for disorder-specific use; in this case relative to the MCCB for the MATRICS domains in schizophrenia)^{61,62}

MATRICES domains	'IntegNeuro' cognitive tasks	References to IntegNeuro Psychometric quality and use in clinical groups
Speed of Processing	<ul style="list-style-type: none"> Switching of attention Part 1 (numbers) & Part 2 (numbers and letters) (assessing constructs equivalent to Trails A &B) 	Psychometric Quality ³⁴⁻⁴⁰ Brain basis established ⁴³⁻⁵² Use in Clinical Groups ⁵³⁻⁶¹
Attention/Vigilance	<ul style="list-style-type: none"> N-Back Continuous Performance Test (assessing constructs equivalent to other n-back & CPT tasks) 	Psychometric Quality ³⁴⁻⁴⁰ Brain basis established ⁴³⁻⁵² Use in Clinical Groups ⁵³⁻⁶¹
Working Memory	<ul style="list-style-type: none"> Span of Visual Memory Digit Span Forwards and Reverse 	Psychometric Quality ³⁴⁻⁴⁰ Brain basis established ⁴³⁻⁵² Use in Clinical Groups ⁵³⁻⁶¹
Verbal Learning	<ul style="list-style-type: none"> Verbal Memory Recall Includes Immediate Recall, Delayed Recall 	Psychometric Quality ³⁴⁻⁴⁰ Brain basis established ⁴³⁻⁵² Use in Clinical Groups ⁵³⁻⁶¹
Visual Learning	<ul style="list-style-type: none"> Maze, errors 	Psychometric Quality ³⁴⁻⁴⁰ Brain basis established ⁴³⁻⁵² Use in Clinical Groups ⁵³⁻⁶¹
Reasoning and problem solving	<ul style="list-style-type: none"> Maze, completion time 	Psychometric Quality ³⁴⁻⁴⁰ Brain basis established ⁴³⁻⁵² Use in Clinical Groups ⁵³⁻⁶¹
Social Cognition	<ul style="list-style-type: none"> Emotion Identification Emotional Intelligence (assessed in Web Assessment Questionnaire) 	Psychometric Quality ^{41,42} Brain basis established ^{59,71} Use in Clinical Groups ^{59,71}



LabNeuro

A computerized assessment of electrical brain function (EEG, ERPs) and concurrent autonomic measures of body function (skin conductance, heart rate/heart rate variability and respiratory rate, plus EMG). Conditions and activation tasks (with primary measures in parentheses) are as follows:

- Resting (Eyes Open, Eyes Closed)
EEG power and asymmetry, autonomic
- Habituation
Autonomic
- Smooth Pursuit Eye Tracking
EMG
- Auditory Oddball
ERPs (P300), autonomic
- Go/No-Go
ERPs (N200), autonomic
- Novelty task
ERPs (Early P300), autonomic
- Continuous Performance Test (CPT, n-back); Working Memory
ERPs (P450), autonomic
- Startle (with Startle and Prepulse Inhibition conditions)
EMG, autonomic
- Facial Expressions of Emotion (unmasked, conscious)
ERPs (P120, N170/VPP), autonomic
- Facial Expressions of Emotion (masked, nonconscious)
ERPs (P120, N170/VPP), autonomic



Summary of the psychometric qualities of these measures and their use in clinical disorders has been established in published studies⁶²⁻⁸⁵,

LabNeuro Task	LabNeuro measures	References to LabNeuro Psychometric quality and use in clinical groups
Resting	<ul style="list-style-type: none"> • EEG power • Skin conductance level • Heart Rate, Heart Rate Variability 	Psychometric quality ⁶²⁻⁶⁶ Use in Clinical groups ^{68-70,72,75,83}
Auditory Habituation	<ul style="list-style-type: none"> • Event related potentials • Skin conductance level • Heart Rate, Heart Rate Variability 	Quantified data available from 2010
Auditory Oddball	<ul style="list-style-type: none"> • Event related potentials • Gamma synchrony • Skin conductance level • Heart Rate, Heart Rate Variability 	Psychometric quality ⁶²⁻⁶⁷ Use in Clinical groups ^{71,78-81}
Go/No-Go	<ul style="list-style-type: none"> • Event related potentials • Skin conductance level • Heart Rate, Heart Rate Variability 	Psychometric quality ⁶² Use in Clinical groups ⁷⁵
Visual Tracking	<ul style="list-style-type: none"> • Smooth pursuit eye tracking 	Use in Schizophrenia ⁷³
Continuous Performance Test (n-back)	<ul style="list-style-type: none"> • Event related potentials • Skin conductance level • Heart Rate, Heart Rate Variability 	Psychometric quality ⁶²⁻⁶⁷ Use in Clinical groups ^{75,77,78,81-83}
Novelty	<ul style="list-style-type: none"> • Event related potentials • Skin conductance level • Heart Rate, Heart Rate Variability 	Use in Clinical groups ^{77,78,81-83}
Maze	<ul style="list-style-type: none"> • Skin conductance level • Heart Rate, Heart Rate Variability 	Use in Clinical groups ⁷⁵
Startle/PPI	<ul style="list-style-type: none"> • Event related potentials • EMG • Heart Rate, Heart Rate Variability 	Use in Sub-clinical groups ⁷⁶
Emotion Processing (unmasked conscious, masked nonconscious)	<ul style="list-style-type: none"> • Event related potentials • Skin conductance level • Heart Rate, Heart Rate Variability 	Psychometric quality ⁶⁸ Use in Sub-clinical groups ⁸⁵



MRI-Neuro

Structural MRI, Functional MRI. DTI also available in subset of subjects (pre-2009, and with all MRI-Neuro assessments from 2009 onwards)

Uses standardized battery of structural and functional magnetic resonance imaging sequences.

MRI-Neuro sequence	MRI-Neuro measures	References to MRI-Neuro Psychometric quality and use in clinical groups
High resolution T1-weighted structural sequence for grey and white matter volume	<ul style="list-style-type: none"> Data available in numeric form for both grey and white matter for 106 brain regions based on standardized atlas 	Psychometric quality – changes over age ^{63, 85-87} Effects of early life stress ^{76,88} Use in clinical groups ^{76,86-96}
DTI	<ul style="list-style-type: none"> Fractional anisotropy 	Psychometric quality – changes over age and correlates with cognition ⁹⁷⁻¹⁰⁰
Auditory Oddball (functional MRI sequence)	<ul style="list-style-type: none"> Data available for image analysis 	Psychometric quality – validation in controls ¹⁰¹ Use in clinical groups ¹⁰²
Go/No-Go (functional MRI sequence)	<ul style="list-style-type: none"> Data available for image analysis 	Use in clinical groups ¹⁰³
Continuous Performance Test (CPT, n-back): Working Memory (functional MRI sequence)	<ul style="list-style-type: none"> Data available for image analysis 	In analysis
Facial Expressions of Emotion (unmasked conscious, masked nonconscious) (functional MRI)	<ul style="list-style-type: none"> Data available for image analysis 	Psychometric quality – validation in controls and changes over age ⁹⁸⁻¹⁰¹ Use in clinical groups ¹⁰⁴⁻¹⁰⁹



Molecular-Neuro

Genomics have been acquired using cheek swabs in the first cohorts, and subsequently saliva samples and blood samples. An initial set of 20 candidate SNPs were targeted (below). **A further 759 have also been genotyped.**

The table below summarizes the first 20 SNPs currently available, and the findings from these SNPs:

Gene	References to Molecular-Neuro
Apolipoprotein E, APOE	Integration with age and brain function ¹¹⁴
Brain derived neurotrophic factor (val66met), BDNF	Integrative analyses for subclinical depression, obesity and selective information processing ¹¹⁵⁻¹²⁰
Cathepsin D (224C>T) (A58V), CTSD	In analysis
Catechol-O-methyltransferase (val108/158met), COMT	Integrative analyses of emotional brain function and early life stress and personality ^{121,122}
Dopamine receptor type D2 (-141C Ins/Del), DRD2_1	In analysis
Dopamine receptor type D2 (957C>T), DRD2_2	In analysis
Dopamine receptor D4 (-521C>T), DRD4_2	In analysis
Dopamine beta hydroxylase (-1021C>T), DBH	In analysis
Dopamine transporter (40-bp VNTR), DAT1	In analysis
Dopamine D4 receptor (48-bp VNTR), DRD4	In analysis
Histamine N-methyltransferase (314C>T), HNMT	In analysis
Monoamine oxidase A (30-bp VNTR), MAOA	Emotional brain function and antisocial traits ¹²³
Serotonin receptor 1A (-1019C>G), HTR1A	In analysis
Serotonin receptor 2A (-1483A>G), HTR2A_1	In analysis
Serotonin receptor 2A (H452Y), HTR2A_2	In analysis
Serotonin receptor 3A (C178T), HTR3A	With emotional brain measures of susceptibility to depression ¹²⁴
Serotonin transporter (44-bp DIP), 5HTT-LPR	Emotional brain function and negativity bias ¹²⁵
Succinate-semialdehyde dehydrogenase (538C>T) (H180Y), ALDH5A1	In analysis
Abnormal spindle-like, microcephaly-associated (A44871G; amino acid change is S2562G), ASPM	In analysis
Microcephalin (G37995C – ref to DNA seq; amino-acid change is D219H), MCPH1	Effects on brain volume ¹²⁶



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WebQ (* indicates those publications that are BRAINnet outcomes)

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Use in Clinical groups

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DTI

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