Pleased to meet you!

Ed just keeps laughing
- Resilience in what your goals are!

Fleur Howells
Howells Psychosis Translational Research Group
Department of Psychiatry
Faculty of Health Sciences, University of Cape Town

Networking the Brain – Cortex Club Inaugural Symposium, November 2014
First exposure to research

2004 Bsc(Hons) physiology
- Professor Vivienne Russell
- Professor Laurie Kellaway
- Dr Musa Mabandla

Techniques:
- Unilateral PD animal model: **stereotaxic surgery** to produce unilateral Parkinson’s Disease by creating a neurotoxic lesion of substantia nigra
- **Intervention** used voluntary running wheel exposure
- **Behaviour** used to assess this - apomorphine rotations – move towards the side of the lesion as motor neurons as super sensitive in response to lack of DA availability – exercising rats performed fewer rotations
- **Dopamine neuron count**: **Immunohistochemistry** to measure the lesion which supported the behavioural result
MSc (2005) upgraded to Phd (2006)

• 2005
  – Professor Vivienne Russell
  – Associate Professor Alan St Clair Gibson (moved to UK)

• 2006 – through to grad
  – Professor Vivienne Russell
  – Professor Kit Vaughan

Title of Thesis: Attentional and Arousal a human and rat study

Clinical techniques:
Electroencephalography (EEG) - frequency analysis, event-related potentials (ERPs), Electrocardiography (ECG) with heart rate variation, Skin conductance response (SCR)

Questionnaires: a few, to note - mental effort visual analogue and Childhood trauma questionnaire (CTQ)

Subjects: Healthy participants – convenient sample

Basic techniques:
Superfusion: every which way norepinephrine is released in response to glutamate stimulation

Behaviour: open-field, elevated plus maze, novel object recognition

Brain areas: prefrontal cortex, hippocampus, cerebellum

All conventional rat strains depending on the question being asked: Long Evans, Wistar, Sprague Dawley, Spontaneously hypertensive rat, Wistar Kyoto
Research Report

Glutamate-stimulated release of norepinephrine in hippocampal slices of animal models of attention-deficit/hyperactivity disorder (spontaneously hypertensive rat) and depression/anxiety-like behaviours (Wistar–Kyoto rat)

Fleur Margaret Howells, Vivienne Ann Russell

Neuroscience Laboratory, Division of Physiology, Department of Human Biology, Faculty of Health Sciences, University of Cape Town, Observatory, 7925, South Africa

Howells et al. Behavioral and Brain Functions 2010, 6:39
http://www.behavioralandbrainfunctions.com/content/6/1/39

Perceived mental effort correlates with changes in tonic arousal during attentional tasks

Fleur M Howells1,2, Dan J Stein1 and Vivienne A Russell2

Behavioral and Brain Functions 2009, 5:24

Synergistic tonic and phasic activity of the locus coeruleus norepinephrine (LC-NE) arousal system is required for optimal attentional performance

Fleur M. Howells · Dan J. Stein · Vivienne A. Russell

Frontiers in Integrative Neuroscience

Childhood trauma is associated with altered cortical arousal: insights from an EEG study

Fleur Margaret Howells1,2, * Dan J. Stein2 and Vivienne A. Russell1

1 Department of Human Biology, Faculty of Health Sciences, University of Cape Town, Cape Town, South Africa
2 Department of Psychiatry, Faculty of Health Sciences, University of Cape Town, Cape Town, South Africa

Metab Brain Dis
DOI 10.1007/s11011-012-9287-9

ORIGINAL PAPER

Behavioral and Brain Functions

Cross-fostering does not alter the neurochemistry or behavior of spontaneously hypertensive rats

Fleur M Howells, Leander Bindewald and Vivienne A Russell

Address: Neuroscience Laboratory, Division of Physiology, Department of Human Biology, Faculty of Health Sciences, University of Cape Town, Observatory, 7925, South Africa

Email: Fleur M Howells · Fleur.Howells@uct.ac.za, Leander Bindewald · leleskypwking@yahoo.com;
Vivienne A Russell* · Vivienne.Russell@uct.ac.za

* Corresponding author

Published: 21 June 2009

Received: 15 March 2009
Accepted: 23 June 2009

Behavioral and Brain Functions

Co-supervision of students during postgrad yrs

BSc (Med) honours student
2006 Heleen Soeters

DOI 10.1007/s11011-008-9098-1

Methylphenidate does not increase ethanol consumption in a rat model for attention-deficit hyperactivity disorder—the spontaneously hypertensive rat

Heleen Suzanne Soeters · Fleur Margaret Howells · Vivienne Ann Russell
Increased glutamate-stimulated release of dopamine in substantia nigra of a rat model for attention-deficit/hyperactivity disorder—lack of effect of methylphenidate

Fleur L. Warton · Fleur M. Howells · Vivienne A. Russell
Co-supervision of students during postgrad yrs

BSc (Med) honours student
2009 Toni-Lee Sterley

Sterley et al. Behavioral and Brain Functions 2011, 7:11
http://www.behavioralandbrainfunctions.com/content/7/1/11

Effects of early life trauma are dependent on genetic predisposition: a rat study

Toni-Lee Sterley¹*, Fleur M Howells² and Vivienne A Russell¹
International Brain Research Organization

School:

Travel Awards to attend and present empirical research:
• International Brain Research Organization Travel Grant Awarded for attendance: International Neuroscience Conference, Al Ain, United Arab Emirates (2005)
• International Brain Research Organisation Travel Grant for the attendance of the 7th Annual World Congress of Neuroscience, Melbourne, Australia (2007)
• International Brain Research Organisation scholarship for attendance to the Marine Biological Laboratory (MBL) summer course: Neural Systems & Behaviour (2008)
• International Brain Research Organisation Travel Grant for the attendance of the 39th annual Society of Neuroscience conference, Chicago, United States (2009)
• Selected for the IBRO alumni symposium and awarded a Travel Grant for the 10th International Conference of the Society of Neuroscientists of Africa (SONA), Topics in Neuroscience: Basic to Clinical. Addis Ababa, Ethiopia (2011)
• International Brain Research Organisation Travel Grant for the attendance of the 10th International Conference of the Society of Neuroscientists of Africa (SONA), Topics in Neuroscience: Basic to Clinical. Addis Ababa, Ethiopia (2011)
• Selected for the IBRO alumni symposium at the 8th IBRO World Congress of Neuroscience, Florence, Italy (2011)
• International Brain Research Organisation Travel Grant for the attendance of the 8th IBRO World Congress of Neuroscience, Florence Italy (2011).
Marine Biological Laboratories (MBL) summer course in Neural Systems & Behaviour attended and completed (Woods Hole, Massachusetts, USA, 2008). Thanks to an IBRO.
Graduation!!!

Pleased to meet you!

7 November 2014
Post-doc in Psychiatry 😊 yay!!! 2009-2013

Mentor: Professor Dan Stein

Funding:
• Brain and Behaviour Initiative Postdoctoral Fellowship, Department of Psychiatry, University of Cape Town (2009 & 2012)
• University Research Committee Postdoctoral Fellowship, University of Cape Town (2010 - 2011)
• National Research Foundation Innovation Postdoctoral Fellowship, University of Cape Town (2010 - 2012)

Mid career award 2013-2016

Mentor: Professor Dan Stein

Funding:
• Hasso Plattner Foundation Mid-Career Development Programme Award from Institute of Infectious Disease and Molecular Medicine (IDM)
New skill set

Working with individuals with severe mental disorders – including schizophrenia 😊 Yay!

Clinical diagnostics and questionnaires

$^1$H-Magnetic resonance spectroscopy, an MRI modality

Mindfulness based cognitive therapy in Bipolar disorder - completed:


Methamphetamine projects, many currently running:


Anxiety disorder project, currently on going:


Couple of book chapters and a patent....
Co-supervision – Toni-Lee Sterley

Research Report

Nicotine-stimulated release of [3H]norepinephrine is reduced in the hippocampus of an animal model of attention-deficit/hyperactivity disorder, the spontaneously hypertensive rat

Toni-Lee Sterley*, Fleur M. Howells*, Vivienne A. Russell*

*Department of Human Biology, Faculty of Health Sciences, University of Cape Town, Observatory, Cape Town 7925, South Africa

Evidence for reduced tonic levels of GABA in the hippocampus of an animal model of ADHD, the spontaneously hypertensive rat

Toni-Lee Sterley*, Fleur M. Howells*, Vivienne A. Russell*

*Department of Human Biology, Faculty of Health Sciences, University of Cape Town, Observatory, Cape Town 7925, South Africa

Maternal separation increases GABA_A receptor-mediated modulation of norepinephrine release in the hippocampus of a rat model of ADHD, the spontaneously hypertensive rat

Toni-Lee Sterley*, Fleur M. Howells*, Vivienne A. Russell*

*Department of Human Biology, Faculty of Health Sciences, University of Cape Town, Observatory, 7925, South Africa

Department of Psychiatry, Faculty of Health Sciences, University of Cape Town, Observatory, Cape Town 7925, South Africa
Full final draft PhD done – hob nobbing in Boston, where he was awarded best young scientist at ToS – Obesity Society! Yay!!! 🎉


Hume DJ, Howells FM, Rauch, Kroff, Lambert EV. Mind the gap: electrophysiological record of brain reactivity and behavioural response to visual food cues are different in weight loss maintaining and weight regained women. *Submitted*

Hume DJ, Howells FM, Rauch, Kroff, Lambert EV. Electrocortical measures of visual food cue processing and executive control in female restrained eaters. *Submitted*
Completed **CIAM**: Cortical inhibition and attentional modulation a study in psychotic disorders
- Schizophrenia, Bipolar I disorder hx psychosis, Methamphetamine-Induced psychosis, and socio-demo controls
- 20-40 years

Techniques
- EEG (frequency, ERPs)
- Cortical Inhibition – Electromyography with transcranial magnetic stimulation
- Brief repetitive transcranial magnetic stimulation (20Hz)
- MRI modalities included: anatomical, resting state fMRI, DTI, and of course MRS

Prelim findings are novel – the questions have not previously been asked before
Integration of modalities will take place in the New Year 😊 Yay!!!!
Currently writing up her PhD! Yay!! 😊

The neurobiology of methamphetamine induced psychosis

Jennifer H. Hsieh, Dan J. Stein and Fleur M. Howells
Department of Psychiatry and Mental Health, University of Cape Town, Western Cape, South Africa

Chronic methamphetamine abuse commonly leads to psychosis, with positive and cognitive symptoms that are similar to those of schizophrenia. Methamphetamine induced psychosis (MAI) can persist and diagnoses of MAI often change to a diagnosis of schizophrenia over time. Studies in schizophrenia have found much evidence of cortical GABAergic dysfunction. Methamphetamine psychosis is a well studied model for schizophrenia, however there is little research on the effects of methamphetamine on cortical GABAergic function in the model, and the neurobiology of MAI is unknown. This paper reviews the effects of methamphetamine on dopaminergic pathways, with focus on its ability to increase glutamate release in the cortex. Excess cortical glutamate would likely damage GABAergic interneurons, and evidence of this disturbance as a result of methamphetamine treatment will be discussed. We propose that cortical GABAergic interneurons are particularly vulnerable to glutamate overflow as a result of subcellular location of NMDA receptors on interneurons in the cortex. Damage to cortical GABAergic function would lead to dysregulation of cortical signals, resulting in psychosis, and further support MAI as a model for schizophrenia.

Keywords: schizophrenia, cortex, GABA, neurotoxicity, sensitization, neural circuits

Abductor pollicis brevis muscle

APB
• Chair: Fleur Howells (howellsfleur@gmail.com)
• Secretary: Sian Hemmings (smjh@sun.ac.za)
• Treasurer: Musa Mabandla (mabandlam@ukzn.ac.za)
• Media Officer: Jennifer Hsieh (jennifer.hsieh@uct.ac.za)
• Co-opted executive committee member: Laurie Kellaway (lauriston.kellaway@uct.ac.za)
• Co-opted executive committee member: Vivienne Russell (Vivienne.Russell@uct.ac.za)
• Co-opted executive committee member: Susan Janse van Rensberg (sjvr@sun.ac.za)
• Co-opted executive committee member: Siyabonga Goodwill Sibiya (macyaah@gmail.com)
Starting with a full translational study in Schizophrenia 😊 Yay!!!

Starting 2015: STAR – Schizophrenia Translational Action Research

Hypothesis driven questions that will be asked, which address cognitive disturbances in schizophrenia using both clinical and basic study data:

1. Thalamo-cortical gating system function
   - This system controls the processing of relevant sensory information
   - Cognitive defragmentation in schizophrenia is suggested to result from sensory overload

2. Locus-coeruleus norepinephrine system function
   - This system controls the ability to maintain and control attention
   - Inability to maintain attention in schizophrenia is suggested to result from a mismatch between tonic and phasic activity of the locus coeruleus.

(Javitt, 2009; McCormick and Bal, 1994; Patterson et al., 2008; Szulc et al., 2007; Kraguljac et al., 2012; Clark et al., 2011; Phillips et al., 2011; Powell et al., 2002; Lei et al., Lee and Sherman, 2012; Howells et al., 2012; McLean et al., 2010; Laurens et al., 2005)
STAR research TEAM

Dr Fleur Howells (clinical & basic)
Professor Dan Stein (clinical & basic)
Professor David Kingdom (clinical)
Dr Henk Temmingh (clinical)
Professor Katherine Narr, UCLA (clinical)
Professor Brian Harvey, N-WU (basic)
Professor Vivienne Russell (basic)
Dr Pete Milligan (clinical)
Dr Goodman Sibeko (clinical)
Dr Katherine Sorsdahl (clinical)
Dr Sharon Klientjes (clinical)
Dr Katya Mauff (clinical & basic – stats consultant)

Postgraduate student capacity within STAR

4 doctoral students:
Confirmed - Dr Nico Badenhorst (basic)
Confirmed – Katie Atmore (basic)

4 x clinical neuroscience – needed for late 2015/beginning 2016

8 honours students (2016 & 2017):

4 x basic
4 x clinical

There are also many other projects on the go – if you like the techniques and would like to apply them or join a project which use them do email to find out more....... howellsfleur@gmail.com
I pretty much acknowledge every person I have mentioned from mentor to student – Neuroscience is fun and we can make a difference by asking the right questions!

Yay!!!! 😊

howellsfleur@gmail.com