The RCPsych Gatsby/Wellcome Neuroscience Project

Professor Wendy Burn

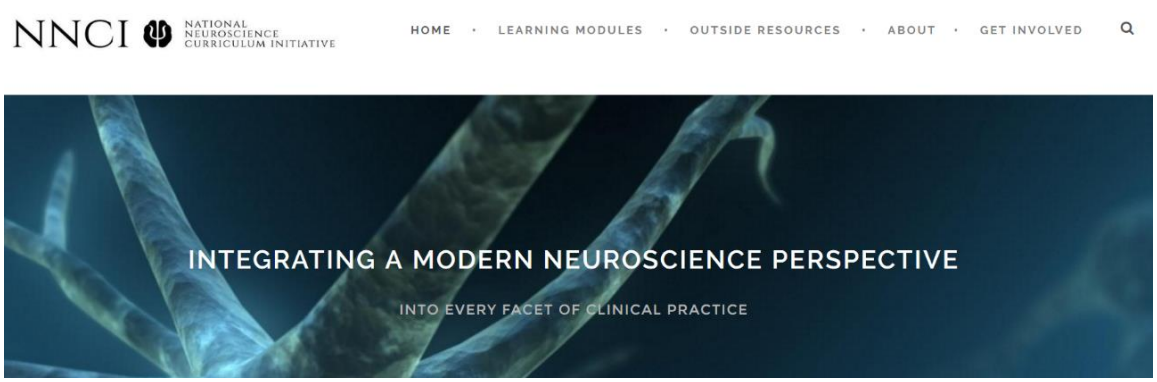
President

Structure of the Project

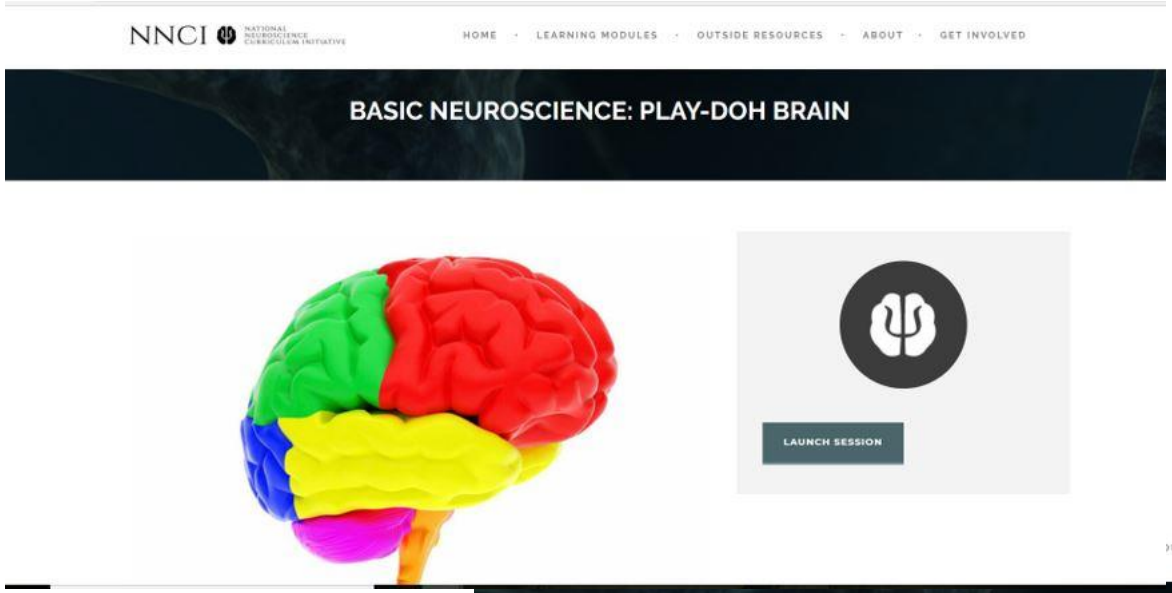
- Initially a 2 year project to introduce a modern neuroscience perspective into psychiatrists' clinical work (summer 2016-18)
- Generously supported by The Gatsby Foundation and The Wellcome Trust
- Based on a USA experience

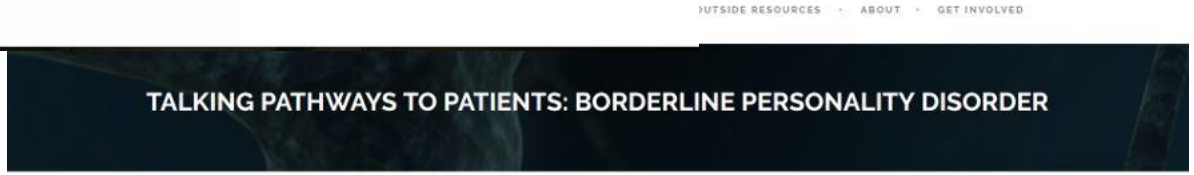
National Neuroscience Curriculum Initiative (USA)

- Making Neuroscience accessible and relevant
- Online, open-access (NIH-funded) learning resource
- www.nncionline.org
- Innovative teaching methods



NNCI Website





NNCI Leadership

- Michael Travis, Pittsburgh

- Melissa Arbuckle, Columbia

- David Ross, Yale

RCPsych Gatsby/Wellcome Neuroscience Project

- Original 2-year project now extended for 3 more years (2018-21)
- Focus on adoption and embedding of new Syllabus for MRCPsych
- Supported by Gatsby Foundation and Wellcome Trust

RCPsych Neuroscience Board

- Oversight of the project
- Will monitor and review:
  - Adoption and implementation of the new Syllabus for the MRCPsych Examination
  - Development of training opportunities, including Brain Camps and a CPD Online module
  - Opportunities for interaction between trainees, psychiatrists and neuroscientists

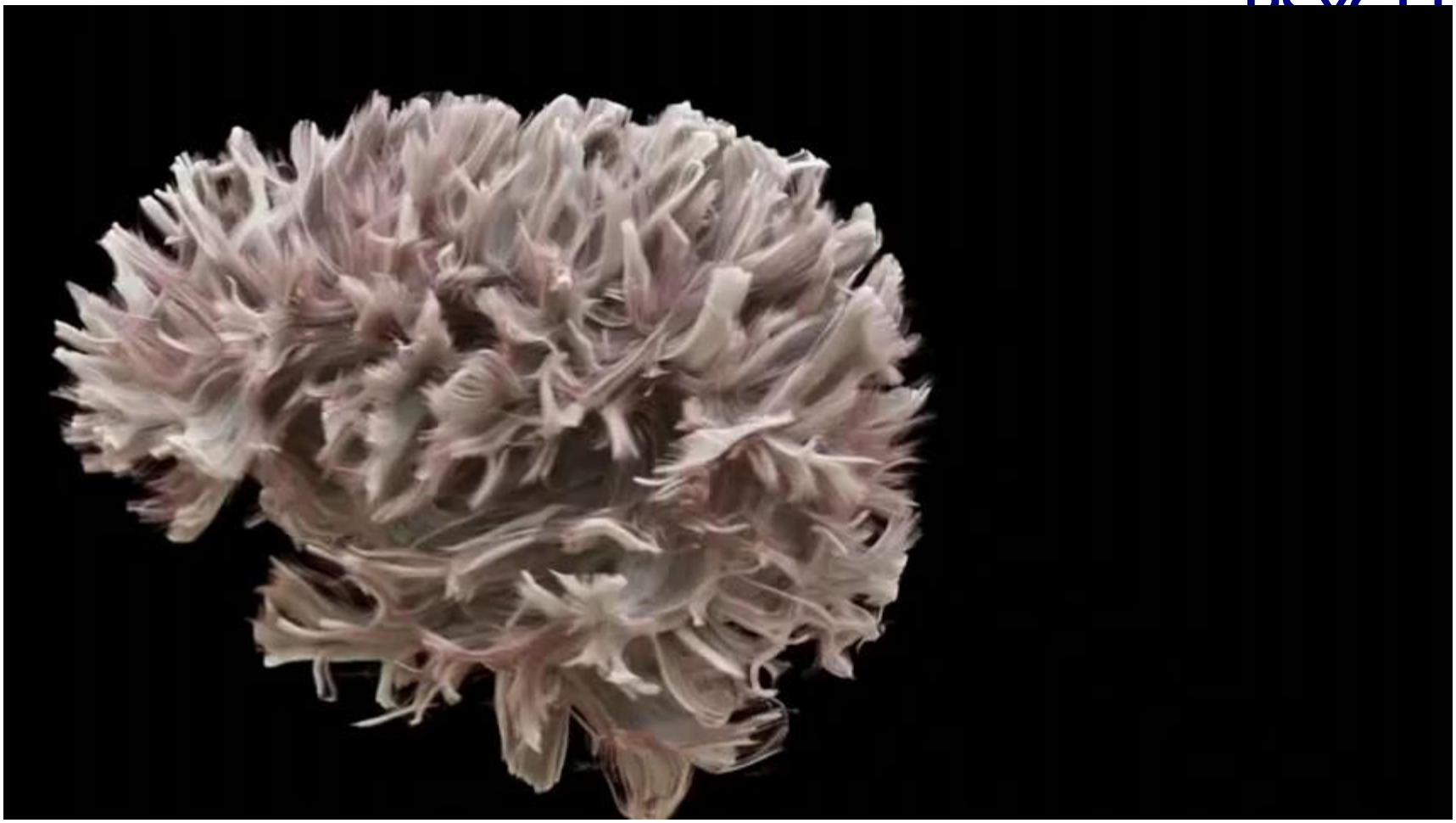
Neuroscience Board: Members

- **Professor Wendy Burn** *(co-Chair), President, RCPsych*
- **Dr Mike Travis** *(co-Chair), UPMC, Pittsburgh*

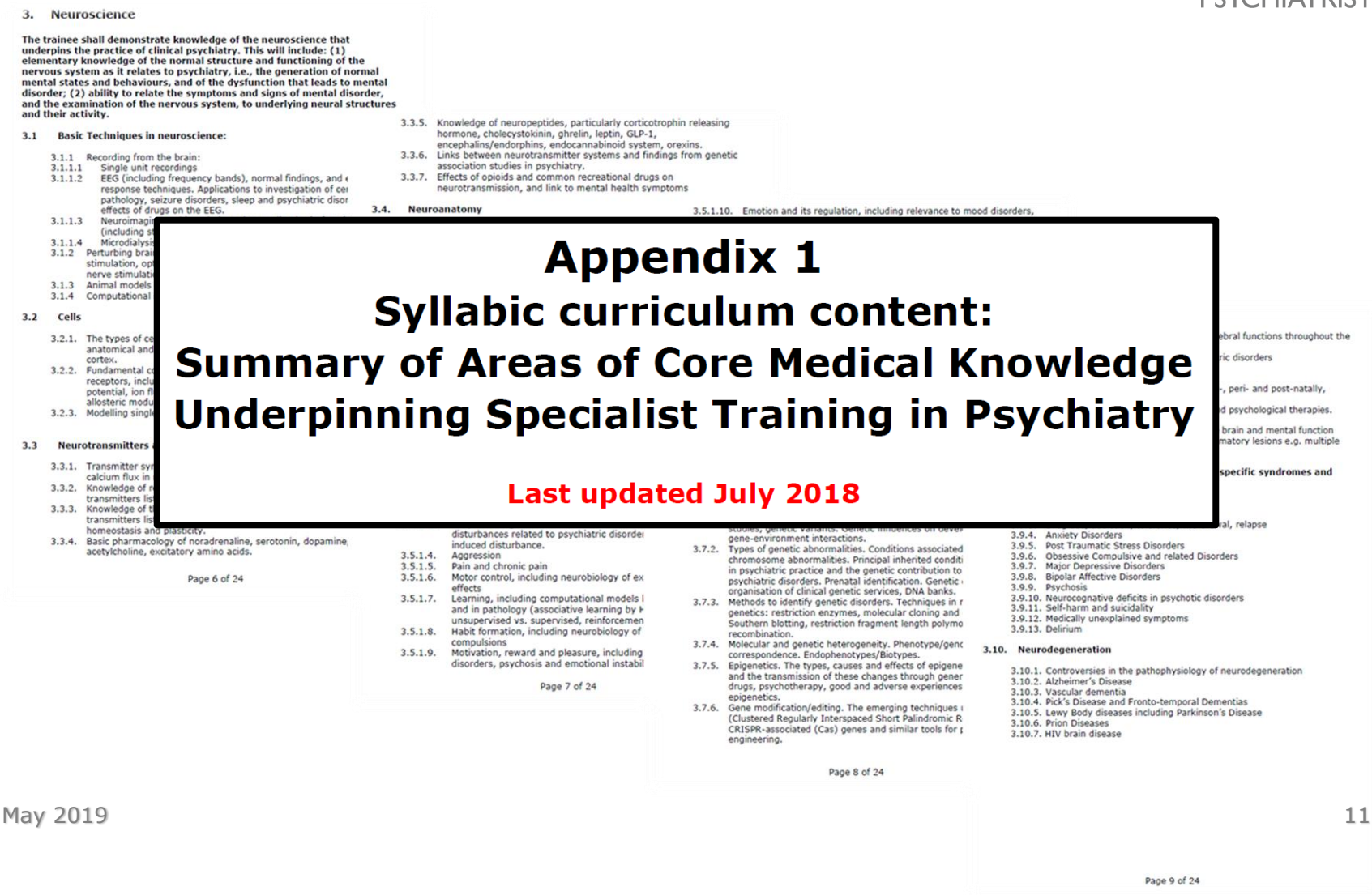
- **Dr Kate Lovett** *Dean, RCPsych*
- **Professor Ed Bullmore** *University of Cambridge*
- **Professor Sophia Frangou** *Mount Sinai, New York*
- **Professor Eileen Joyce** *UCL, London and Chair, Faculty of Neuropsychiatry, RCPsych*
- **Professor Anne Lingford-Hughes** *Imperial College, London and Chair, Academic Faculty, RCPsych*
- **Professor David Ross** *Yale University*
- **Dr Rick Adams** *UCL, London*
- **Dr Mary-Ellen Lynall** *Academic Clinical Fellow, Cambridge*
- **Dr Sarah Caddick** *Gatsby Charitable Foundation*
- **Dr Andrew Welchman** *The Wellcome Trust*

Continued work: Stakeholder consultation and engagement

- Mentioned in every talk I give as President
- College Faculty and Division conferences/meetings
- Presentations to Trusts, trainees, Foundation Trainees and medical students
- Using neuroscience videos like this next one to engage.....



Achievement: MRCPsych Syllabus updated



Appendix 1

Syllabic curriculum content:

Summary of Areas of Core Medical Knowledge Underpinning Specialist Training in Psychiatry

Last updated July 2018

Regional networks: NeuroNets

- Brain researcher—psychiatrist collaboration
- Regional excellence in neuroscience and neuroscience teaching
- Support for trainers

In place:

- Scotland
- Southwest England

Planning:

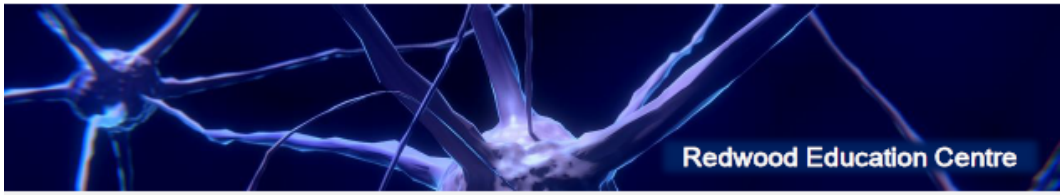
- Wales
- N. Ireland + NW England

Local course created by SWNeuroNet

RC PSYCH
ROYAL COLLEGE OF PSYCHIATRISTS

The Neuroscience in Psychiatry Course 2019

2gether
Making life better



To all Medical Colleagues:

We would like to invite you to NIP, a new and exciting course that has been designed to inspire collaborative learning of neuroscience concepts and shape our understanding of mental illness.

Explore The Role Of Neuroscience In Psychiatry
The course is inspired by the RCPsych Neuroscience Project, which aims to focus psychiatry tra advances in basic and clinical neuroscience" so that psychiatrists "are better equipped to provide the future".

An Interactive And Innovative Teaching Programme
This is a peer-led course packed with clinically relevant teaching resources, interactive learning upon expertise from leading figures in the field. The programme includes material from the high Neuroscience Curriculum Initiative but is highly tailored to 2gether doctors.

Not Just "Biological Psychiatry"
We'll be thinking about how neuroscience can complement our thinking about all aspects of psy and clinically focussed, with skills to take to the clinic.

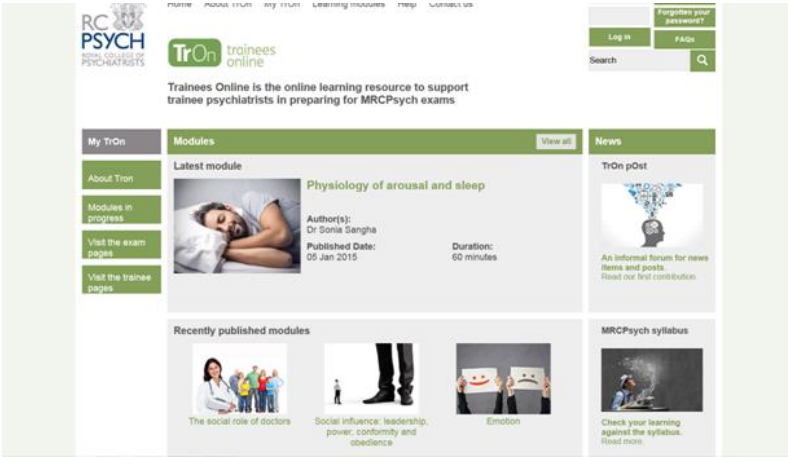
Monday 4th March, 2-5pm	Monday 11th March, 2-5pm	Monday 18h March, 2-5pm
Neuroscience Refresher	**Applications in Clinical Psychiatry**	**The Bio-Psychosocial Interface**
Exploring the Role of Neuroscience in Psychiatry	New Insights Into Schizophrenia And Depression	Visualising Psychotherapy Through Neuroimaging
Neuroanatomy Refresher	Integrating Neuroscience Into Conversations With Patients	Epigenetics: Trauma and the Brain
A Quick Guide To Research Techniques In Neuroscience	Developing New Treatments	A Neuroscience Model Of Personality Disorder

Course Facilitators:
Dr George Morris, Dr Lindsey Sinclair, Dr Nik Bhandari, Dr Emma Phillips, Dr Kim Humby, Dr Clara Martinez, Dr Adrian Yan

May 2019

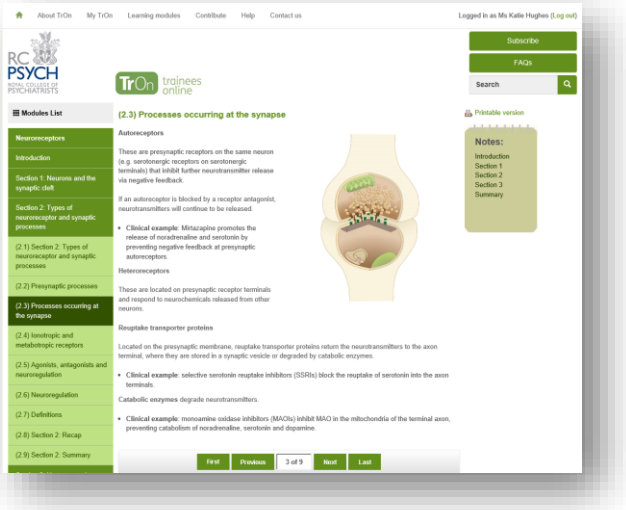
Developing resources: Trainees Online (TrOn)

- College online learning resource
- Free for trainees registered with the college
- Covers Paper A



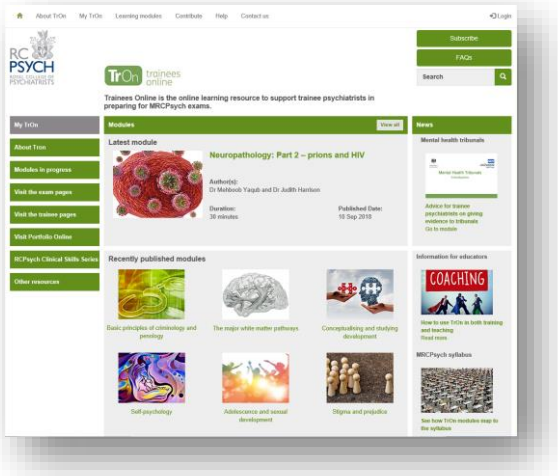
TrOn

- **Produced by higher specialist trainees and junior consultants who have recent knowledge of the examinations themselves**



TrOn modules

- Modules cover the whole of the basic sciences syllabus
- Each module includes three pieces of 'Key Reading'
- Extra neuroscience modules will be written



Training events

- Med Ed Conference, Belfast, Sept 2017
- Brain Camp, London, October 2017
- Brain Camp II, Birmingham, June 2018
- Brain Camp III, Manchester, January 2019

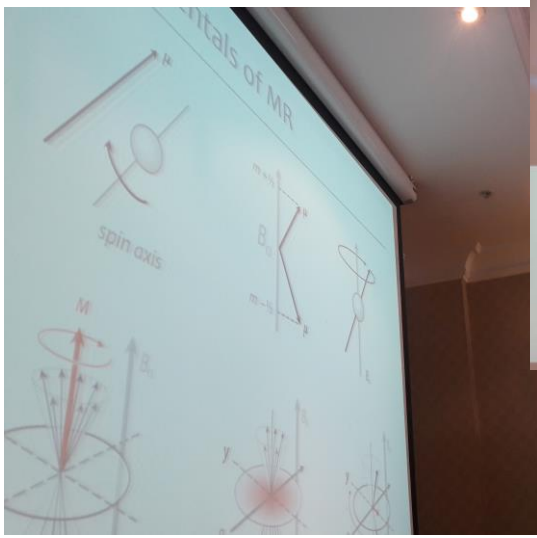
Collaboration:

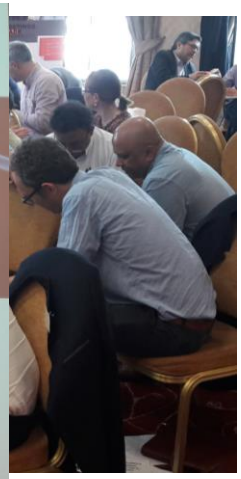
NNCI NATIONAL NEUROSCIENCE CURRICULUM INITIATIVE

BNA British Neuroscience Association

Brain Camps

- Over 200 psychiatric educators have taken part to date
- Each event heavily oversubscribed
- Participants from Tewkesbury to Toronto





Brain Camp format

- One-day event
- Refresher on selected cutting-edge, clinically-relevant brain research topics
- Workshops on teaching strategies
- Run by researchers & educationalists
- Training Programme Directors, Clinicians with no background in neuroscience

Programme

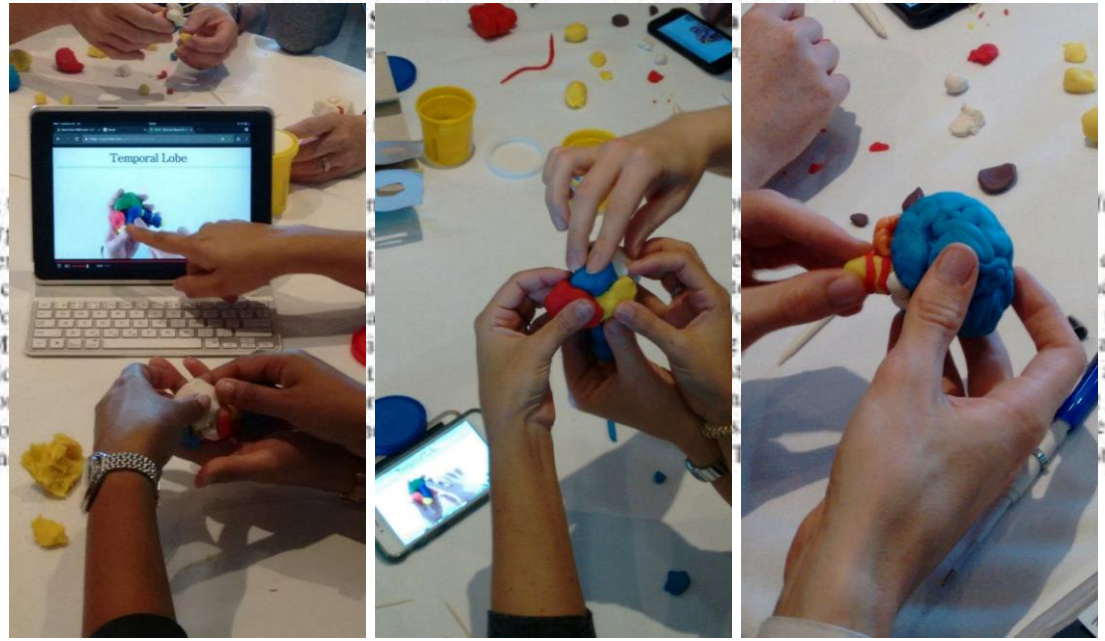
09:30-10:00	Registration and refreshments
10:00-10:15	Welcome and Introduction with Dr Kate Lovett, Dean, RCPsyc
	Advances in brain research
10:50	*Investigating neuropsychological mechanisms in depression using novel rodent models* Professor Emma Robinson (Bristol)
11:25	*Epigenetics and the challenge of chronic pain* Dr Sandrine Géranton (UCL)
12:00	*Experimental models of cortical rhythms: translational biomarkers for drug development for the treatment of schizophrenia* Professor Mark Cunningham (Newcastle)
12:45	Lunch and networking
	Teaching workshops
13:35	*Storytelling: the role of narrative in neuroscience* Dr Derek Tracy (IPPN, KCL)
14:25	*How to build a brain* Dr Gareth Cuttle (RCPsych)

Building Play-Doh brains

- **Scientifically proven to educate……**

Adv Physiol Educ 35: 241–243, 2011;
doi:10.1152/advan.00087.2010.

Active learning by play dough modeling in the medical profession



Building Play-Doh brains

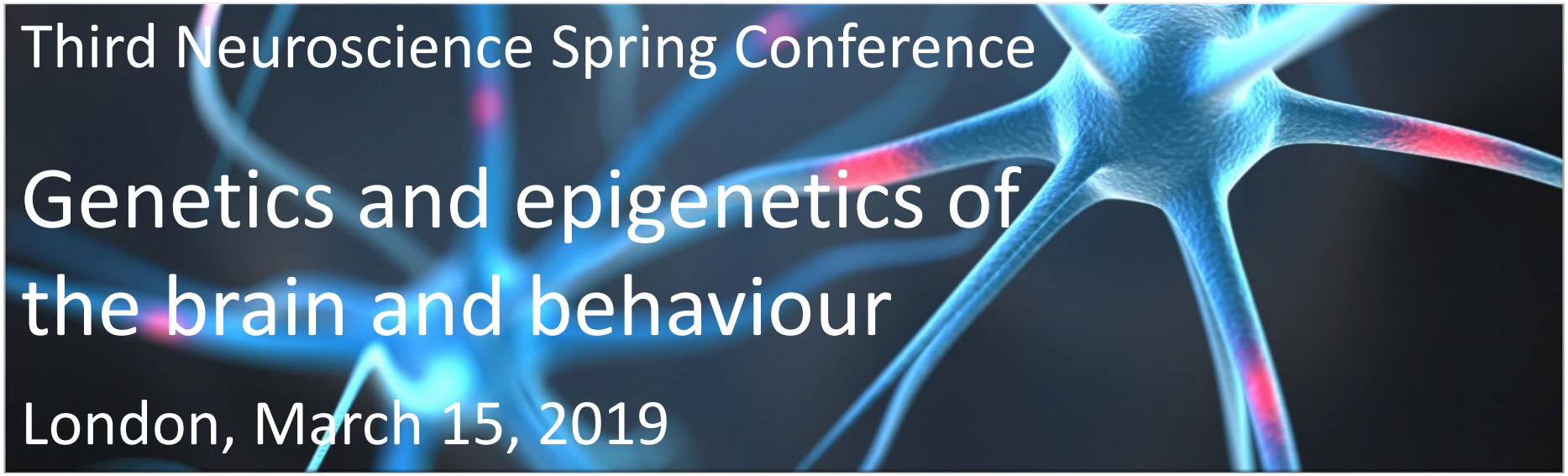
- Always included
- Enormous fun
- Teaches you how the parts of the brain relate to each other
- Team work

Psychiatric Trainee Neuroscience Champions

- One from each School
- Role:
  - Cascade news, information and opportunities to trainees; and
  - Feed back to Neuroscience Board on implementation of the new Syllabus for MRCPsych
- Benefits:
  - Extra educational opportunities - *Neuroscience Immersion Programme*
    One-day conferences with leading researcher speakers and visits to cutting-edge lab facilities

Neuroscience Champions: Launch

Neuroscience Spring Conference 2019



- **FREE to attend**
- **Travel and accommodation bursaries for Trainees and medical students**


HSBC
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Some highlights from the Programme

RC PSYCH
ROYAL COLLEGE OF PSYCHIATRISTS

8.45–9.30	Arrival and registration
9.30–9.45	Welcome and introduction *Professor Wendy Burn* *President, Royal College of Psychiatrists*
9.45–10.30	**KEYNOTE 1** The genetics of psychiatric disorders *Professor Sir Mike Owen* *Cardiff University*
10.30–11.00	Coffee and refreshments
11.00–11.40	**CUTTING EDGE 1** How life events change our behaviour at the molecular level *Professor John Quinn* *Institute of Translational Medicine, University of Liverpool*
11.40–12.20	**CUTTING EDGE 2** Understanding risk and resilience to psychiatric disorders *Professor Sophia Frangou* *Mount Sinai Hospital, New York*
12.20–13.30	Lunch
13.30–14.15	**KEYNOTE 2** Modelling human brain development and connectivity in "mini brain" organoids *...line Lancaster* *...y of Cambridge*
	...EDGE 3 ...of life experiences on mental and physical health across generations *...nen van Steenwyk* *...search Institute, University of Zurich*
	...n refreshments
	...EDGE 4 ...g genomic and imaging data in studies of depression *...Andrew McIntosh* *...y of Edinburgh*
	...y and closing remarks *...Wendy Burn* *..., Royal College of Psychiatrists*

The genetics of psychiatric disorders
Professor Sir Mike Owen
Cardiff University

How life events change our behaviour at the molecular level
Professor John Quinn
University of Liverpool

Modelling human brain development in 'mini brain' organoids
Dr Madeline Lancaster
University of Cambridge

Combining genomic and imaging data in studies of depression
Professor Andrew MacIntosh
University of Edinburgh


RC
PSYCH
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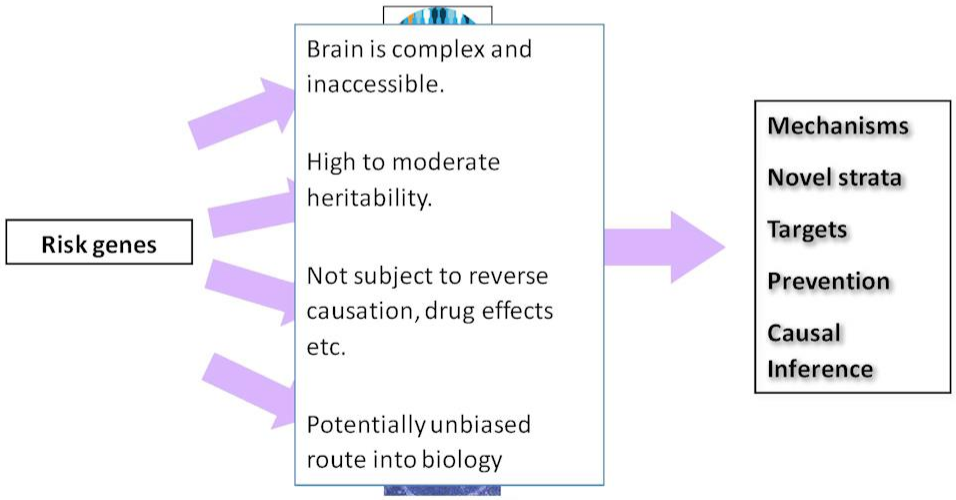
PSYCHIATRISTS

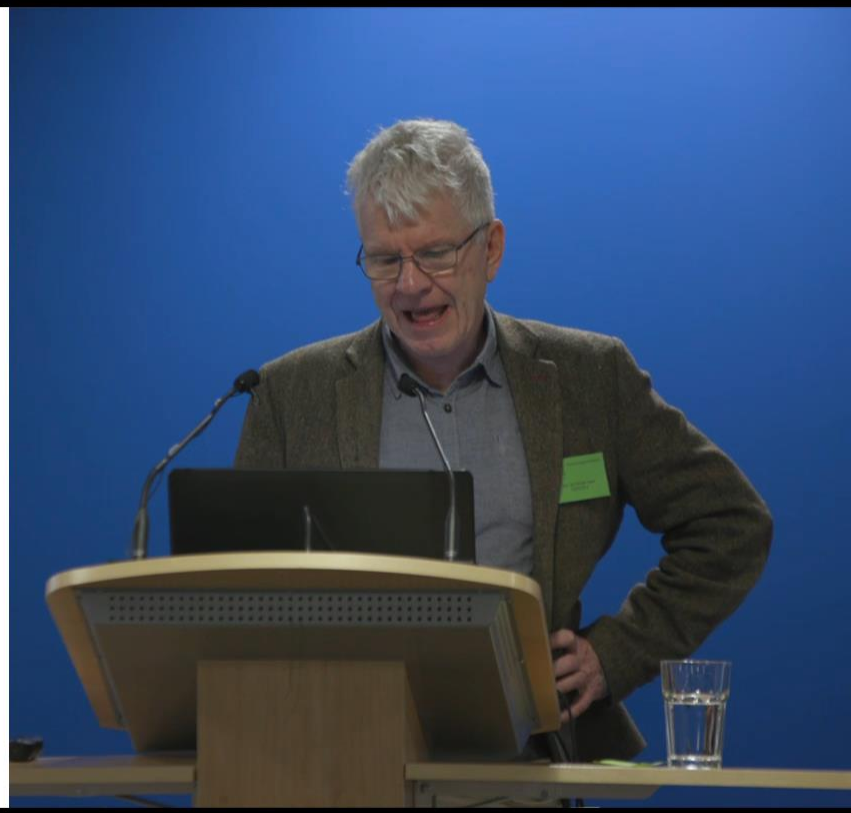
KEYNOTE 1

- **The genetics of psychiatric disorders**

- **Professor Sir Mike Owen**
  Cardiff University

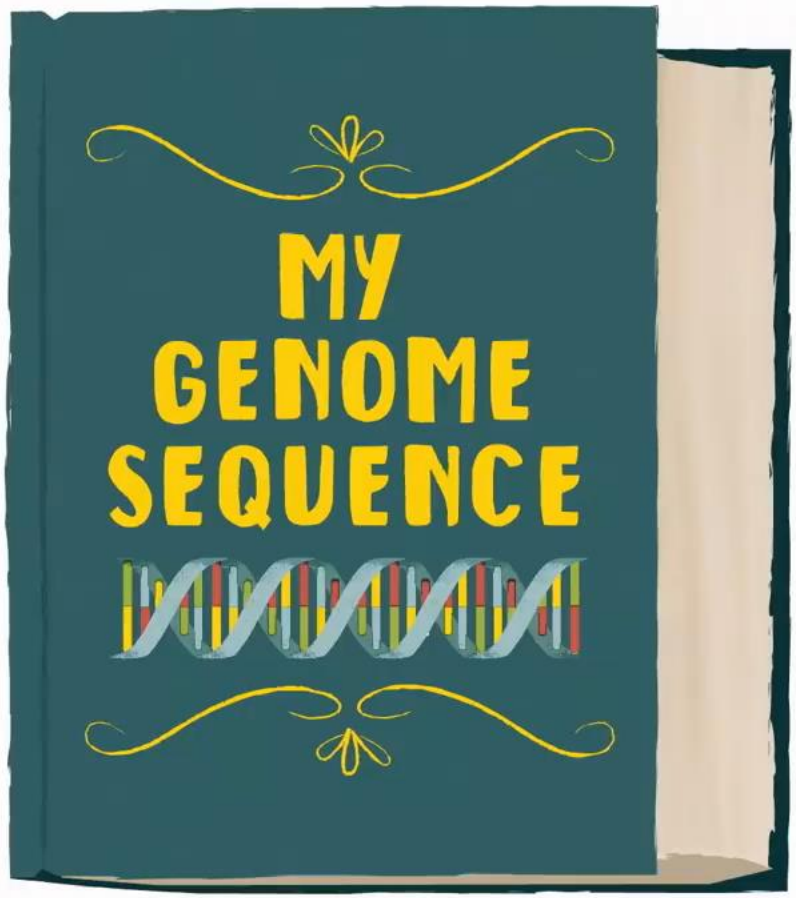
Genomics offers a route to new treatments and strata





Genetics

- A complex area
- A bit of revision for you……


MY
GENOME
SEQUENCE

Content

- Review of the recent advances in psychiatric genetics and genomics

- Outline likely impact on psychiatric research and practice over the next 10-15 years

Genomics

- Offers a new way to understand psychiatric illnesses
- Brain is complex and inaccessible
- Genes are generally not subject to drug effects
- Potentially unbiased route into biology
- Identifying genes involved could give greater understanding of the illness

The Psychiatric Genomics Consortium (PGC)

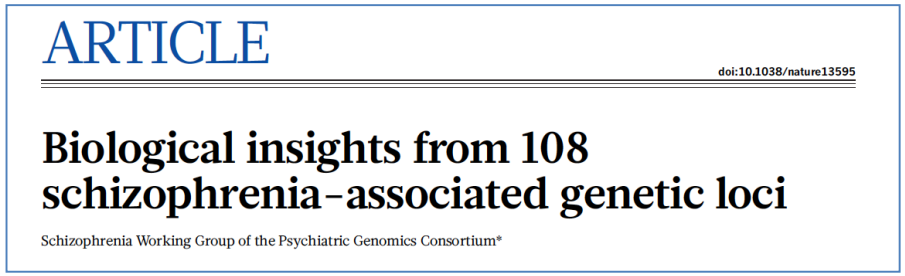
- Largest global consortium in the history of psychiatry
- Aims to deliver "actionable" findings – genomic results that:
  - reveal the fundamental biology
  - inform clinical practice
  - deliver new therapeutic targets

Schizophrenia Working Group *of the* Psychiatric Genomics Consortium

- Schizophrenia is a highly heritable disorder
- Genetic risk is conferred by a large number of alleles including common alleles of small effect that might be detected by genome-wide association studies

Multi-stage schizophrenia genome-wide association study

- Schizophrenia Working Group *of the* Psychiatric Genomics Consortium
- 36,989 cases and 113,075 controls
- 108 specific loci found
- 33% of genetic risk from common SNPs (single nucleotide polymorphisms)



ARTICLE

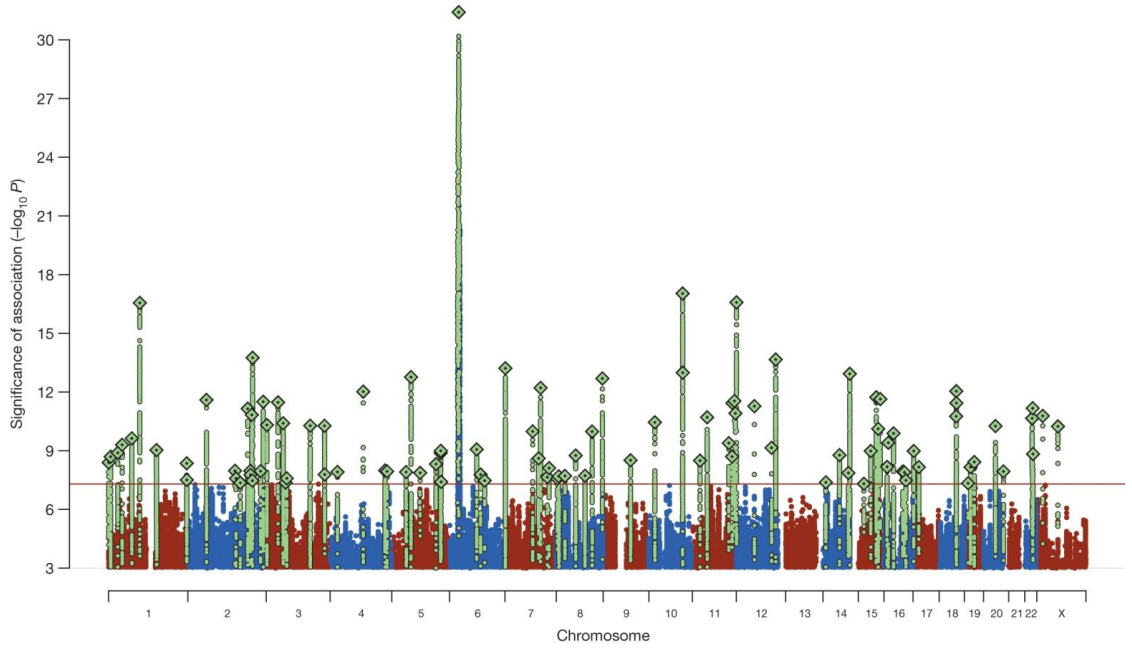
doi:10.1038/nature13595

Biological insights from 108 schizophrenia-associated genetic loci

Schizophrenia Working Group of the Psychiatric Genomics Consortium*

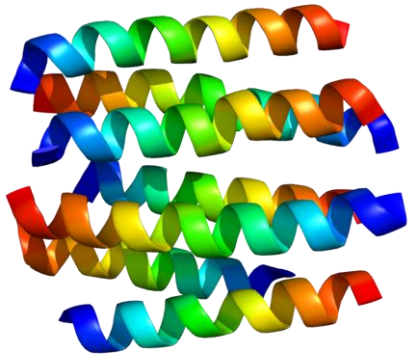
Manhattan plot showing schizophrenia associations

- X axis shows chromosomes, Y shows association significance in schizophrenia



What do the significant genes do?

- Multiple genes involved in glutamatergic neurotransmission
- Also in D2 subtype of the dopamine receptor
- This suggests schizophrenia is fundamentally a disturbance of synaptic transmission

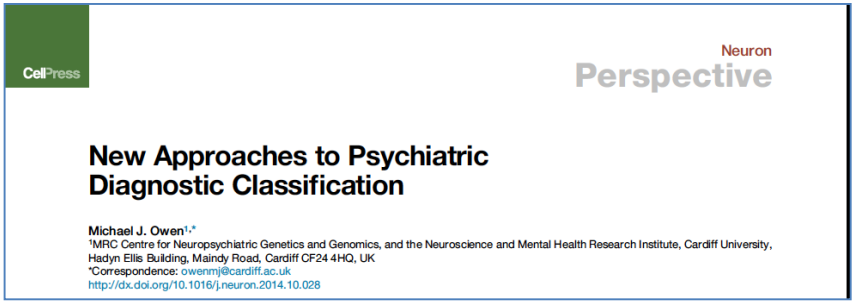


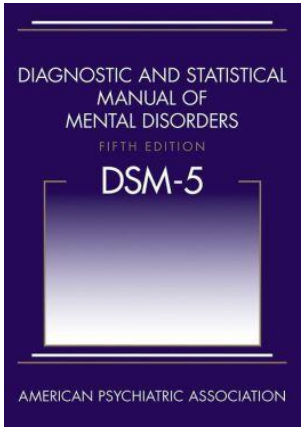
Genome wide association studies on depression

- Major Depressive Disorder has overlap of genetic risk with schizophrenia
- BiPolar type 1 strongly genetically correlated with schizophrenia
- BiPolar type 2 is more strongly correlated with Major Depressive Disorder

What do genetic studies tell us about our classification systems?

- Classifications based on symptoms likely to be incorrect
- Genomics has the potential to provide a robust, scientific way of classifying mental disorders

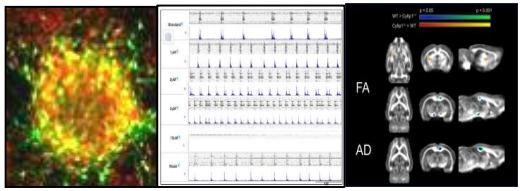




Conclusions

Identifying risk genes will lead to:

- **Newer and more scientifically valid diagnostic approaches**
- **Better understanding of disease mechanisms**
- **Discovery of new drug treatments**



Cutting Edge 1

- 'How Life Events Change Our Behaviour At The Molecular Level'

- Professor John Quinn
  Institute of Translational Medicine, University of Liverpool

Mother's touch could change effects of prenatal stress

OPEN

Citation: Transl Psychiatry (2015) 5, e560; doi:10.1038/tp.2014.140
www.nature.com/tp

ORIGINAL ARTICLE

Effects of prenatal and postnatal depression, and maternal stroking, at the glucocorticoid receptor gene

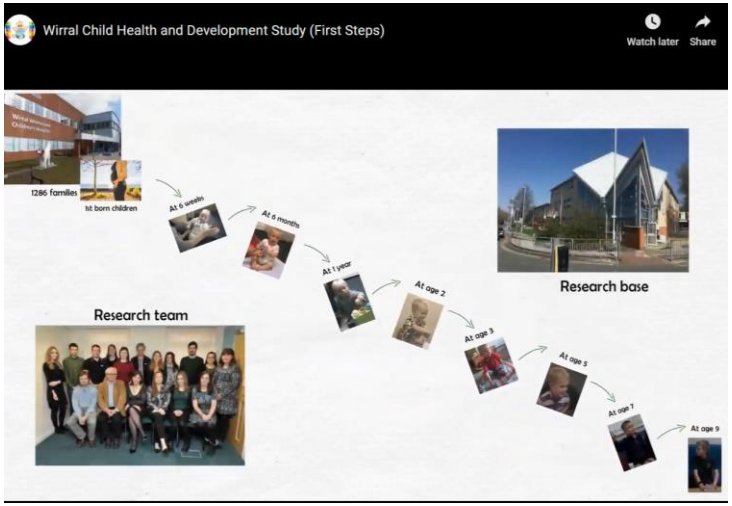
C Murgatroyd[1], JP Quinn[2], HM Sharp[3], A Pickles[4] and J Hill[5]

In animal models, prenatal and postnatal stress is associated with elevated hypothalamic–pituitary axis (HPA) reactivity mediated via altered glucocorticoid receptor (GR) gene expression. Postnatal tactile stimulation is associated with reduced HPA reactivity mediated via increased GR gene expression. In this first study in humans to examine the joint effects of prenatal and postnatal environmental exposures, we report that GR gene (*NR3C1*) 1-F promoter methylation in infants is elevated in the presence of increased maternal postnatal depression following low prenatal depression, and that this effect is reversed by self-reported stroking of the infants by their mothers over the first weeks of life.

Mothers who stroke their baby's body in the first few weeks after birth may change the effects that stress during pregnancy can have on an infant's early-life development, researchers have found.

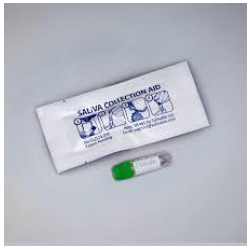
Wirral Child Health and Development Study

- UK prospective epidemiological longitudinal study of prenatal and infancy origins of conduct disorders
- Sample now in their teens



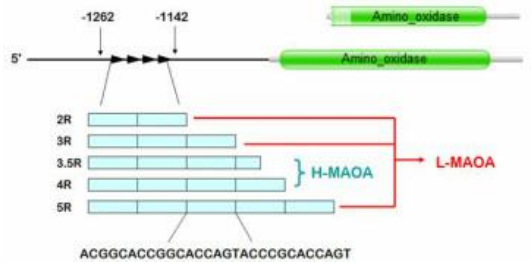
Subsample of 282 mothers and babies

- Life events in pregnancy identified
- Monoamine oxidase A gene (MAOA-LPR) measured in saliva of babies at 5 weeks
- Babies assessed for "negative emotionality"; this is linked to behavioural disorders in later life



Monoamine oxidase A gene (MAOA-LPR)

- Encodes mitochondrial enzymes which catalyse the oxidative deamination of amines eg dopamine, norepinephrine, and serotonin
- Low activity is associated with a variety of psychiatric disorders, including antisocial behaviour



Results

- Found an interaction between MAOA status and life events during pregnancy (P = 0.017)
- Those with low MAOA-LPR activity were more likely to be adversely affected by the negative life events

Conclusions

- **Strongly suggests that adverse life events during pregnancy affect babies' behaviour through modification of genes**

Genes, Brain and Behavior

Official publication of the International Behavioural and Neural Genetics Society

Genes, Brain and Behavior (2013) doi: 10.1111/gbb.12033

Evidence for interplay between genes and maternal stress *in utero*: monoamine oxidase A polymorphism moderates effects of life events during pregnancy on infant negative emotionality at 5 weeks

J. Hill[†,*], G. Breen[‡], J. Quinn[§], F. Tibu[†], H. Sharp[¶] and A. Pickles[**]

[†]Centre for Developmental Science and Disorders, University of Manchester, Manchester, UK, [‡]National Institute for Health Research (NIHR) Biomedical Research Centre for Mental Health, South London and Maudsley NHS Foundation Trust and Institute of Psychiatry, King's College London, London, UK

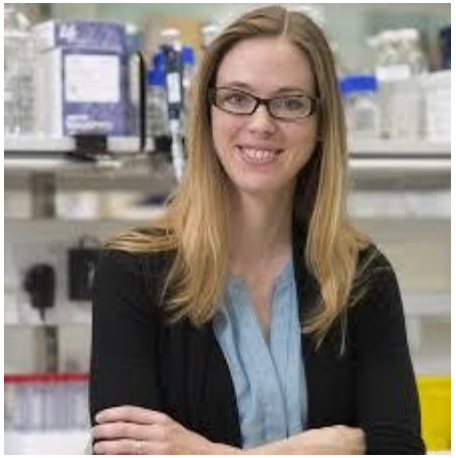
Received 7 January 2013; revised 22 February 2013; accepted for publication 25 February 2013

A genotype by environment interaction (G × E) occurs when a person's genotype moderates the effect of environmental experience on physical or mental health outcomes or

Keynote 2

- **Modelling human brain development and connectivity in "mini brain" organoids**

- **Dr Madeline Lancaster**
  University of Cambridge

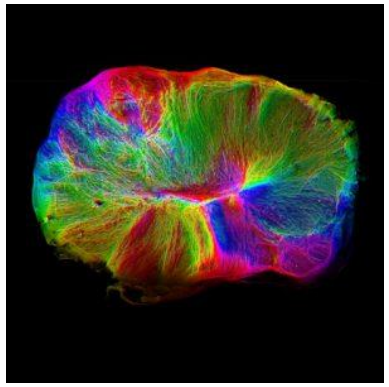


Engagement

- Have used her research on brain organoids as an example of neuroscience developing
- Lab-grown groups of cells that self-organise to resemble an organ
- She made this video about her work
- Everyone finds it fascinating

Latest work

- Neurons in the cerebral organoid seen to be maturing, showed neural activity
- Able to see patterns of connectivity between different regions of the mini-brain



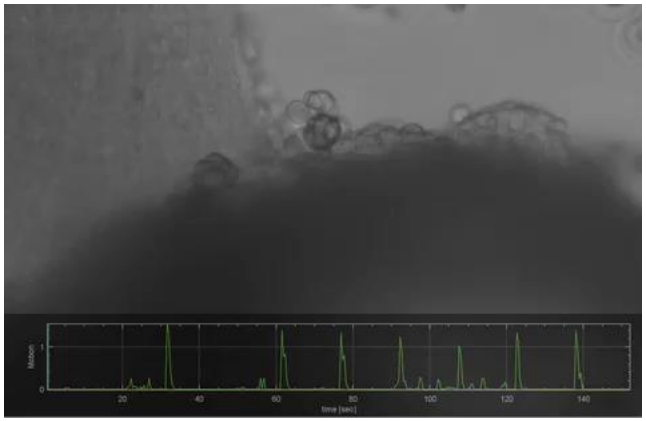
Growing neurons

- Piece of mouse spinal cord and adjacent back muscle was placed near to the organoid
- Neurons from the organoid grew out to connect with the spinal cord
- The mini-brain projecting neurons could stimulate muscle contractions
- First demonstration of a functional output from cerebral organoid tissues in a dish

Evoked Muscle Contractions

- Demonstration of evoked muscle contractions
- The brain organoid is stimulated at regular intervals
- Signal sent to the spinal cord, which relays the information to the muscle to make it contract
- NEXT SLIDE: see the muscle contracting

Brain organoid-stimulated muscle contraction



Future implications of this model

- Could be used to investigate how neurons connect up within the brain and with the spinal cord
- Defects in neuronal connectivity may underlie psychiatric illnesses such as schizophrenia, autism, and depression
- Improve understanding of conditions in which connectivity is disrupted, such as stroke and dementia

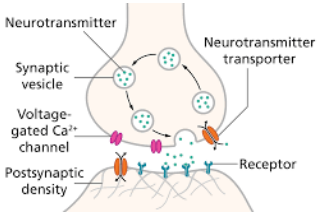
Cutting Edge 4

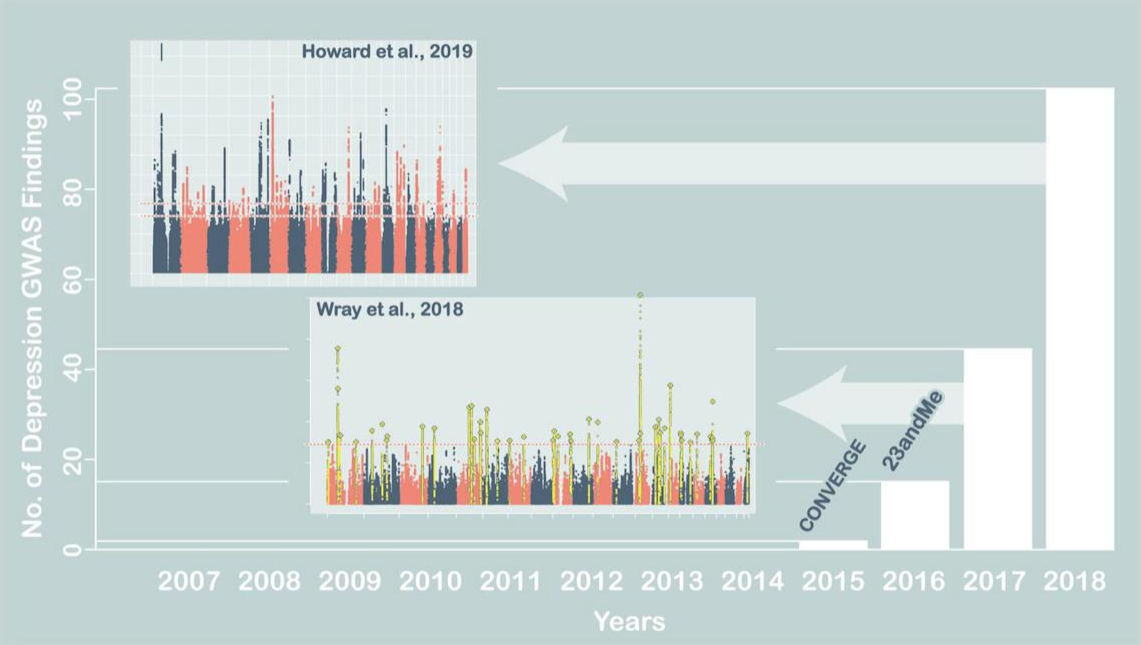
- 'Genomic and imaging studies of depression'

- Professor Andrew McIntosh
  University of Edinburgh

Genetics of Depression

- First studies to identify a genetic contribution to depression were twin studies (identical *versus* non-identical)
- These provided an estimate of the total genetic contribution to depression of around 37%
- Candidate gene studies inconsistent



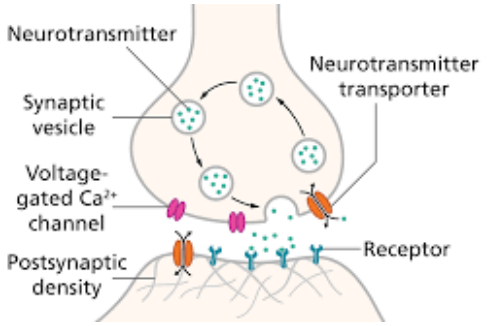

Howard et al., 2019
Wray et al., 2018
CONVERGE
23andMe
No. of Depression GWAS Findings
0
20
40
60
80
100
2007
2008
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018
Years

Psychiatric Genomics Consortium

- Genome-Wide Association Studies (GWAS) looked at depression, 9000 cases & 9000 controls
- No variants identified

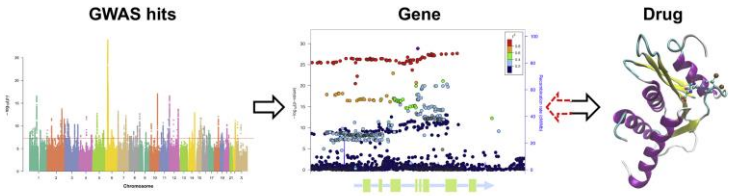
Larger study

- 800,000 people with depression
- 102 independent variants associated with depression
- 269 associated genes
- Genes encoding synaptic proteins are particularly relevant to the aetiology of depression



Genome wide association study

- Schizophrenia associated with variation in the Dopamine D2 receptor, site of action for antipsychotic medications



Trait	Gene with GWAS hits	Known or candidate drug
Type 2 Diabetes	*SLC30A8/KCNJ11*	ZnT-8 antagonists/Glyburide
Rheumatoid Arthritis	*PADI4/IL6R*	BB-Cl-amidine/Tocilizumab
Ankylosing Spondylitis(AS)	*TNFR1/PTGER4/TYK2*	TNF-inhibitors/NSAIDs/fostamatinib
Psoriasis(Ps)	*IL23A*	Risankizumab
Osteoporosis	*RANKL/ESR1*	Denosumab/Raloxifene and HRT
Schizophrenia	*DRD2*	Anti-psychotics
LDL cholesterol	*HMGCR*	Pravastatin
AS, Ps, Psoriatic Arthritis	*IL12B*	Ustekinumab

Save the date!

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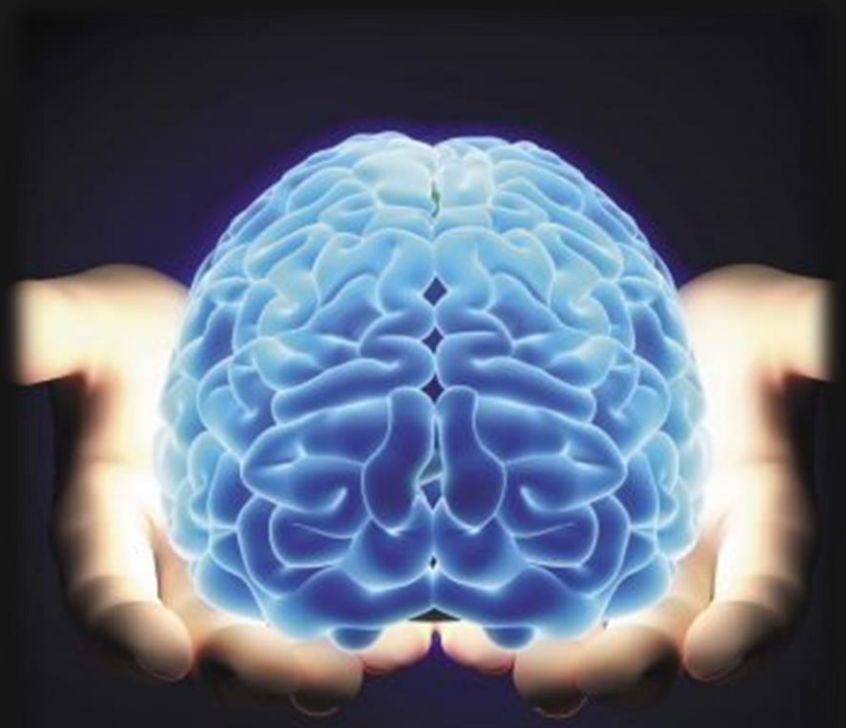

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