spectrum

Specialising in Personality Disorder and Complex Trauma

To what extent do our genetics contribute to the development of BPD?

A/Prof Jillian Broadbear

Head of Research & Development

Eastern Health

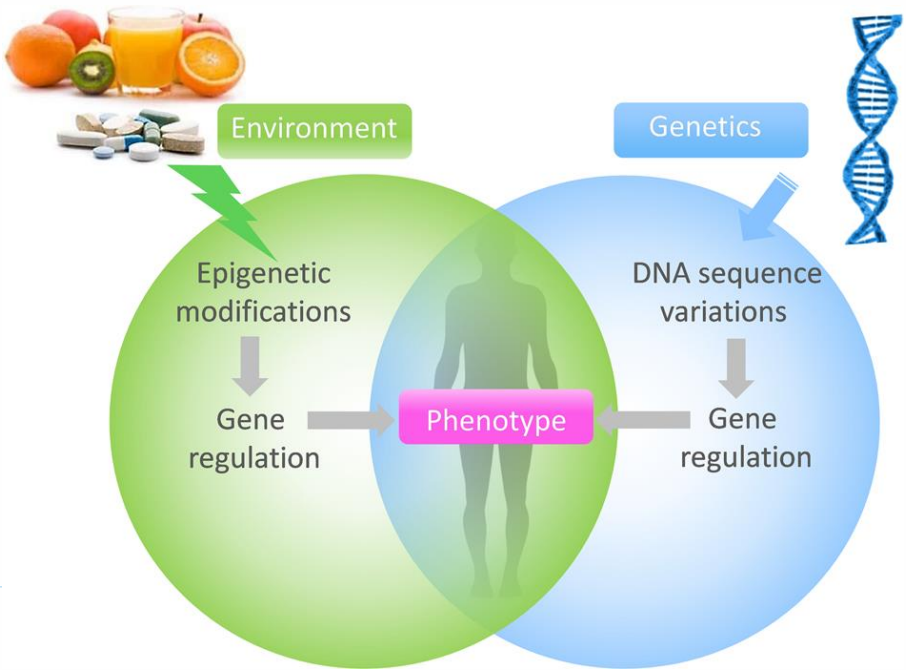
Brief Introduction to Genetics

Why should we be interested in the contributions that our genes make to our mental health?

- To understand processes underlying mental health difficulties
- To ascertain individual vulnerability
- To facilitate targeted treatment and preventative strategies
- An important step towards ‘personalised medicine’

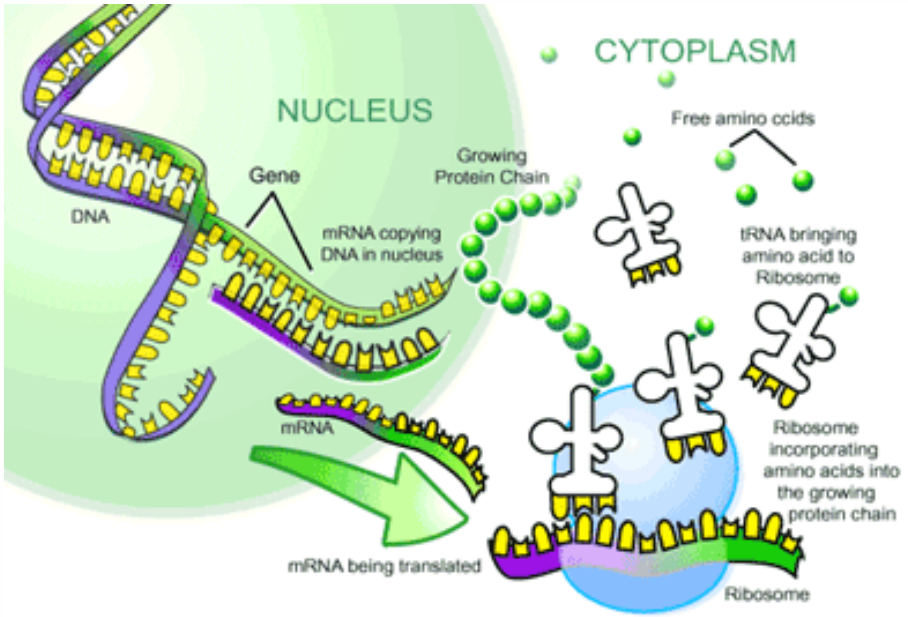
Epigenetics

- Genes contain our ‘programming’
- Gene expression is influenced by our behaviour and life experiences. These can cause changes that affect the way our genes work.
- Unlike genetic changes, epigenetic changes are reversible and do not change our DNA sequence. They can change how our body reads a DNA sequence.



- We share 99.9% of our genes
- Our external and internal differences are dictated by this 0.1%, making each of us unique
- Some differences are advantageous; others are not
- These differences may only become evident under particular environmental conditions

Consider the following example:



Contributions of genetic and environmental factors

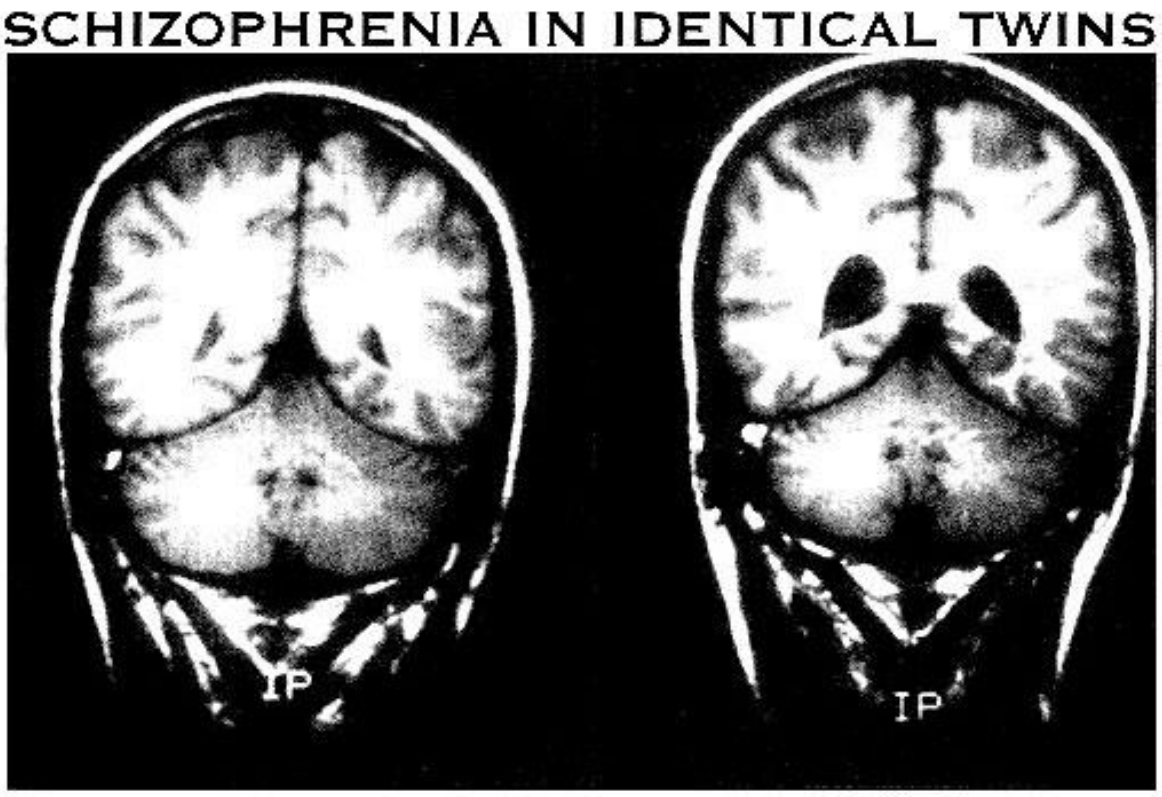
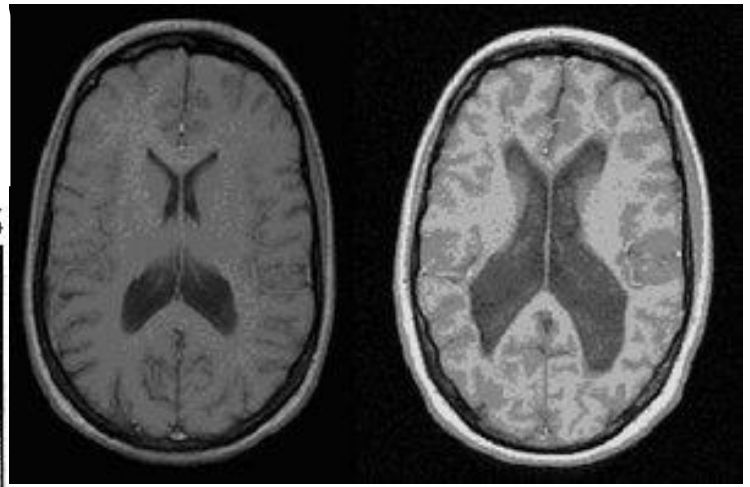


Photo courtesy of Drs. E. Fuller Torrey and Daniel Weinberger.

MRI scans of 28-year-old male identical twins showing the enlarged brain ventricles in the twin with schizophrenia (right) compared to his well brother (left).



Axial MR image of the brains of the unaffected (left) and affected (right) twins from a monozygotic twin pair discordant for schizophrenia, showing ventricular enlargement in the affected twin.

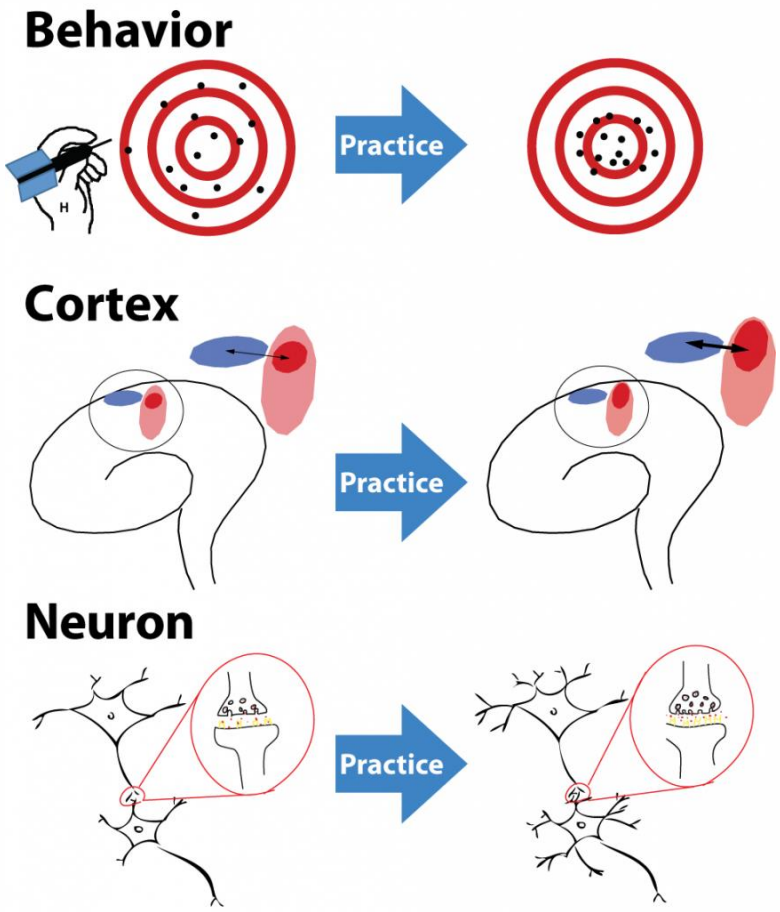
How might our genes influence our behaviour?

Our mood and behaviour are intrinsically linked to our brain chemistry.

This is a two-way ‘conversation’ wherein our genetic predisposition influences how we respond to our environment, which in turn influences our brain chemistry.

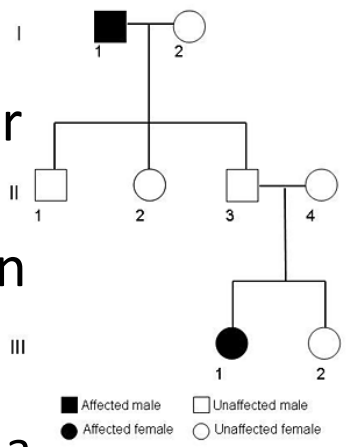
Dynamic interaction shapes brain development and subsequent neuroplasticity throughout life

What might this mean when considering BPD?



What we understand from family studies

- Family and twin studies suggest a 40% heritability of BPD (i.e. approximately 40% of the population variation associated with having BPD is attributable to genetic rather than environmental factors).
- BPD and the four domains of psychopathology measured in the DSM (*affective, interpersonal, behavioural, cognitive*) tend to aggregate in families
  - e.g. A person with a first degree relative diagnosed with BPD has a 3-4 fold increase in the risk of developing BPD
- *Symptoms/Traits:* Emotion dysregulation and impulsivity are strongly familial and may be inherited separately.



Amadet al.. (2014). Genetics of borderline personality disorder: Systematic review and proposal of an integrative model. Neuroscience & Biobehavioral Reviews, 40,6-19. |

White et al. (2003). Family studies of borderline personality disorder: A review. Harvard Review of Psychiatry, 11(1), 8-19.

Gunderson JG, Zanarini MC, Choi-Kain LW, Mitchell KS, Jang KL, Hudson JI. Family Study of Borderline Personality Disorder and Its Sectors of Psychopathology. Arch Gen Psychiatry. 2011;68(7):753–762.

What about co-occurring mental health disorders?

Given the symptomatic overlap across diagnoses, it is reasonable to expect some genetic commonality.

- A German study analysed the genetic overlap of BPD with SCZ, BPAD, and MDD in 998 BPD patients and 1545 controls.
- The genetic overlap of BPD with BPAD is consistent with the observation that some of their diagnostic criteria overlap (affective instability, impulsivity).
- The overlap between BPD and SCZ and MDD is consistent with previous observations of genetic overlap among psychiatric disorders.
- BPD patients have specific clinical symptoms not observed in patients with other psychiatric disorders. Understanding shared and non-shared genetic and clinical features will be important for the development of personalized treatment approaches.

Witt, S. H., Streit, F., Jungkunz, M., Frank, J., Awasthi, S., Reinbold, C. S., ... & Lieb, K. (2017). Genome-wide association study of borderline personality disorder reveals genetic overlap with bipolar disorder, major depression and schizophrenia. Translational psychiatry, 7(6), e1155-e1155.

How might this work in real life?

- A review of the epigenetic BPD literature concluded that susceptibility genes to BPD or its underlying traits may be expressed under certain environmental conditions such as physical or childhood sexual abuse. Epigenetic modifications of neurodevelopment- and stress-related genes may underlie the relationship between early life adversity and BPD (Bulbena-Cabre et al., 2018).
- Methylation of particular genes (e.g. promotor region of the glucocorticoid receptor gene) may be positively associated with childhood trauma and clinical severity in people with BPD (Martin-Blanco, 2014).
- Epigenetic biomarkers may also predict the effectiveness of DBT in people with BPD (Knoblich et al., 2017)

How might this affect the future of treatment for BPD?

While promising, gene-environment and epigenetic studies on personality disorders are still in their initial phases.

Using whole genome epigenetic evaluations, we can now study the whole genome to detect epigenetic changes resulting from lifetime experiences, particularly childhood adversity, that shape personality traits.

The focus of treatment for personality disorder is primarily symptom management despite there being no robust evidence for specific pharmacological treatments for personality disorders. The discovery that epigenetic modifications are reversible with treatment suggests the possibility of innovative interventions – including new targets for medication development - which might address the core biological psychopathology of these disorders.

References

Amadet al.. (2014). Genetics of borderline personality disorder: Systematic review and proposal of an integrative model. Neuroscience & Biobehavioral Reviews, 40,6-19. |

Bulbena-Cabre, A., Bassir Nia, A., & Perez-Rodriguez, M. M. (2018). Current knowledge on gene-environment interactions in personality disorders: an update. Current psychiatry reports, 20(9), 1-14.

Gunderson JG, Zanarini MC, Choi-Kain LW, Mitchell KS, Jang KL, Hudson JI. Family Study of Borderline Personality Disorder and Its Sectors of Psychopathology. Arch Gen Psychiatry. 2011;68(7):753–762.

Nieratschker, V., Knoblich, N., Gundel, F., Brückmann, C., Becker-Sadzio, J., & Frischholz, C. (2019). DNA Methylation of APBA3 and MCF2 in Borderline Personality Disorder: Potential Biomarkers for Response to Psychotherapy. European Neuropsychopharmacology, 29, S986.

Witt, S. H., Streit, F., Jungkunz, M., Frank, J., Awasthi, S., Reinbold, C. S., ... & Lieb, K. (2017). Genome-wide association study of borderline personality disorder reveals genetic overlap with bipolar disorder, major depression and schizophrenia. Translational psychiatry, 7(6), e1155-e1155.

White et al. (2003). Family studies of borderline personality disorder: A review. Harvard Review of Psychiatry, 11(1), 8-19.