

# Nuffield Council on Bioethics

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- 2002 Report

- *Genetics and Human Behaviour: the Ethical Context*

- 1998 Report

- *Mental Disorders and Genetics: the Ethical Context*

- 1993 Report

- *Genetic screening: ethical issues*

# Nuffield Council on Bioethics

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- Mental Disorders and Genetics

*“Methodology for genetic research is progressing rapidly and there seems little doubt that over the next ten years susceptibility genes will be identified and some of these will hold up to robust scientific scrutiny. These discoveries will certainly improve understanding of the causes of mental disorder though probably by small incremental steps rather than through major revolutions. The full potential of these discoveries will only be realised, however, if accompanied by a well-integrated and rigorous research programme covering all approaches to the understanding of mental health including the complex interactions of susceptibility genes, both with each other and with environmental influences.”*

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- Genetics and Human Behavior

- *“We conclude that research in behavioral genetics has the potential to contribute to the existing phenomenon of medicalisation”*
- *“... reducing social tolerance of previously normal behavioral traits; and the routine selection of genetic or medical interventions without adequate consideration given to environmental interventions and other options”*
- *“We recommend that health service providers, and in particular the Department of Health, specifically charge a named agency with monitoring and, if necessary, controlling, this means of the deliberate medicalising of normal populations”*

# Psychiatric Genetics – Behavioral Genetics

- Mental Disorders

- Rare Single Gene Disorders

- Mutations with a More Predictable Effect

- Common Mental Disorders

- Susceptibility Genes

- Behavioral

- ‘Normal behavior’;

- ‘Behavioral and personality traits’

# Clinical Correlates of MECP2 Mutations

## RETT SYNDROME

Fetal Encephalopathy

## MECP2 Mutations

MR	Mild Learning Disability	Normal Carrier
	Borderline MR	PDD
	Autism	

# Succinate Semialdehyde Dehydrogenase Deficiency

- Variable Phenotype
  - Severe Neurological Impairment
  - Mild Developmental Delay
- Maps to a region on chromosome 6 showing linkage to dyslexia
- Significant Association between a functional SNP in SSADH and general Intelligence (Plomin et al., 2004)

# Single Gene Disorders – Candidate Genes for Common Phenotype

## Hypertension

<b>Syndrome</b>	<b>Gene(s)</b>
<b>Apparent mineralocorticoid excess</b>	<b>11-beta - Ketoreductase</b>
<b>Glococorticoid -remediable aldosteronism</b>	<b>CYP11B2 and CYP11B1</b>
<b>17-alpha hydroxylase deficiency</b>	<b>17-alpha - hydroxylase</b>
<b>Pseudohypoaldosteronism. Type I, Liddle's Syndrome</b>	<b>SCNN1B and SCNN1G</b>
<b>Pseudohypoaldosteronism. Type II</b>	<b>WNK1 and WNK4</b>
<b>Early Onset, Autosomal Dominant Hypertension with Severe Exacerbation in Pregnancy</b>	<b>Mineralocorticoid receptor gene</b>
<b>Bardet -Biedl Syndrome Types 2 and 4</b>	<b>BBS2 and BBS4</b>

# Common Mental Disorder

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- Alzheimer Disorder
  - Rare mutations
  - Susceptibility Gene ApoE
- ApoE
  - Associated with cognitive decline in older adult men and women

# Psychiatric Genetics – Behavioral Genetics

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- Disease mutations cannot be studied in isolation
- Single Gene Disorders are Complex Disorders
- Mutations in Genes increasing the susceptibility to develop a disorder often affect “Normal” Behavior

**Psychiatric Genetics**



**Behavioral Genetics**

# Psychiatric Genetics

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- Search for Genes in the last two decades
  - Schizophrenia
  - Bipolar Disorder
  - Autism
  - ADHD
  - Dyslexia
  - Depression
  - Panic Disorder
  - Alcoholism

# The Emperor without Clothes

- Example - Autism

- Risk Increase

- Being Male 4-fold
    - Maternal Age >35 2-3 fold
    - Specific Genes ???<2 fold???

- No major genes have been found for either Psychiatric Diseases nor Behavioral Phenotypes

# What have we learned?

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**Genes are**

**Molecules**



**Interacting  
with**

**Molecules**

# Reality

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- “The very meaning of DNA sequence is relational” (Keller, 2005)
- Any phenotype is the result of interactions between a specific set of genes and specific environments
- Phenotype product of Development
- Prediction of the Future presence of a trait is not accomplished by identifying the trait with genes, but by understanding the developmental system
- A simplified Nature-Nurture Dualism is not tenable

# Conclusions

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- Researchers need to take Developmental Model seriously
  - Association of biology with uniformity and necessity is mistaken
- Psychiatric/Behavioral Genetics
  - Focus on interaction and dynamics of these interactions
  - Understand complexity instead of “oversimplification”
- Ethical issues are not specific to Psychiatric Genetics or Behavioral Genetics, but must be seen in context with other disciplines