## Genetics of Individual Differences

## Lecture 1 - Personality

## <u>Summary</u>

- 1. There is much behavioural evidence that personality can be inherited:
  - a. Selective breeding in animals.
    - Belyaev, in 40 generations, transformed a wild species of fox into a tame one. The Belyaev-Trut hypothesis is that the selection acts on the timing of ontogenetic processes. The adult animals retain juvenile traits (neoteny) not only of behaviour but also of anatomy.
    - ii. DeFries (1978) selected for open-field behaviour in mice.
- Twin studies in man. The heritability of personality is often estimated by comparison of monozygotic (MZ) and same-sex dizogotic (DZ) twins. Examples, extraversion-introversion, preference for fairness, neuroticism. A very recent meta-analysis (Vukasovic, 2015) concludes that twin studies give an average estimate of 0.47 for the heritability of personality. Problems with twin studies:
  - a. It is assumed that genes are additive. However, at one genetic locus, the alternative alleles may not be additive if the person is heterozygous. Similarly, the effect of a particular allele at one genetic locus may depend on the allele present at a different locus ('epistasis').
  - b. Epigenetics: Random X-chromosome inactivation inferior twins. Although female MZ twins are nominally identical in their sciences, this will not be true at the level of expression, owing to the random activation of X-chromosome inactivation.
  - c. It is assumed that the environment is equally similar for the two types of twin. However, the may not be true

d Civilarity of personality of vorsecondary to morphological similarity.

- e. The values of a tract may not be identically distributed in the population of MZ twins and the population of DZ twins. Neuroticism and smoking behaviour are two traits reported to be lower absolutely in MZ twins than in DZ twins.
  - f. Assortative mating. The DZ twins could average more or less than 50% shared genes if their parents are positively or negatively correlated in the relevant trait.

Behavioural evidence that personality can be inherited:

 Selective breeding in animals. Belyaev, in 40 generations, transformed a wild species of fox into a tame one by selectively breeding those that were most eager for human contact. Cross-fostering (or transplanting of embryos) showed that the changes were uninfluenced by the mother's behaviour. The behavioural changes were associated with morphological changes, such as piebald coat colour, rolled tails, floppy ears, broader skulls and shortened tails - although these were not actively selected for.

The Belyaev-Trut hypothesis is that the selection acts on the timing of ontogenetic processes. The adult animals retain juvenile traits (neoteny) not only of behaviour but also of anatomy, even though the selection has been only on the basis of behaviour. However, the age of sexual maturity has been reduced, and some females breed twice in the year. A

c. Daughters of normal transmitting males rarely express any symptom, whereas penetrance is high in sons and daughters of carrier women.

The disorder is caused by the **FMR1 gene** at Xq27. This gene encodes a protein that binds to RNA, so it regulates the expression of other genes, particularly those with a role in synaptic transmission. In most cases, the deleterious alteration is a trinucleotide repeat expansion (a string of repeated CGG) in the upstream, non-coding region of the gene: when the number of repeats exceeds 200, the gene is not transcribed (the mRNA of the extended repeat region binds to the promoter region of the gene, Colak, 2014). Commonly found in carriers are 'pre-mutations' - expansions between 50 and 200, which lead to a higher than normal rate of transcription. These pre-mutations may also expand when transmitted by a female carrier.

As is expected for an X-linked condition, fewer females than males exhibit mental retardation of the FXS type (but not as few as there ought to be). **Bennetto et al (2001)** studied women who were heterozygous for FXS and who were not actually mentally retarded. Their average IQ was 82.7 and they were particularly impaired on spatial tasks and on executive function. The carriers of pre-mutations (instead of full mutations) differed little from controls. Bennetto and colleagues measured, in the individual women, the bias in activation of one or other X chromosome, and this correlated with performance IQ and executive function.

- 2. Fragile X Tremor/Ataxia Syndrome (FXTAS). A distinct syndrome FXTAS is found in those who carry the premutation (55-200 repeats). The typical patient is a met (real grandfather of a fragile X boy. The patient may present with tremor, ataxia and cognitive impairment, and he may have recently become irritable and real gave 20% of patients exhibit an IQ <85. Females with FXTAS are rare. In FXTAS, the WMP protein is being made, but it tends to bind to itself and form pocketion polem (inclusion bodies in the nuclei of brain cells. So in this case, one of the and we genes for mental retariation is also contributing to the variance in usern the budy of the IQ distribution.
- 3. IQSEC2 and CTNS: IQ is a pressed in heterozygotes. IQSEC2 is a gene that encodes a guanine nucleotide exchange factor it is associated with X-linked mental retardation. Kalscheuer et al (2015) report that heterozygous females have learning difficulties. This is because IQSEC2 is one of the few genes that escapes X-inactivation in females and has a similar expression level in males and females. The authors hypothesise that in female carriers, the missense mutation is sufficient to produce symptoms but the mutant protein has residual function and in addition there is some compensation from the normal allele. If the gene suffers a more severe mutation, such as truncation, heterozygous females will often display with a very severe phenotype that may include epilepsy and autistic features.
- 4. Phenylketonuria (PKU): unlike FXS it is genuinely recessive and the crucial mutations are within the exons of the gene. Sufferers exhibit intellectual disability, a mousy odour, light pigmentation, eczema, and peculiarities of gait and stance. They are identified by high levels of the amino acid phenylalanine in their blood. The effected gene is usually PAH, the gene that encodes for the enzyme phenylalanine hydrolase, which converts phenylalanine to tyrosine. The gene is large, situated at 12q23, and the exons make up only 2.9% of the gene. Over 500 mutations of the gene are known, but most commonly they lie in exon 6 or 7. Globally, the R408W mutation accounts for 30% of cases.

There are interesting geographical variations in the incidence of PKU and in the distribution