Multifactorial Inheritance, Heritability

What is Polygenic Inheritance?

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Checked version of the article can be found here (https://www.wikilectures.eu/index.php?title=Multifactorial_Inheritance,_Heritability&oldid=15119).

See also comparation of actual and checked version (https://www.wikilectures.eu/index.php?title=Multifactorial_Inheritance,_Heritability&diff=-&oldid=15119).

Polygenic inheritance involves the expression of a phenotype that is being determined by many genes at different loci. Each gene exerts an additive effect. The effect of the genes is cumulative and there is no dominance and recessivity. There are many human characteristics that follow a continuous distribution in the general population, that closely resembles a normal distribution (that is a symmetrical bell-shaped curve distributed evenly around the mean).

Multifactorial Inheritance

=== Definition===

Multifacorial inheritance is the type of inheritance followed by traits that are determined by multiple factors both environmental and genetic. Environmental factors interact with many genes to generate a normally distributed susceptibiity.

Concept

- According to this theory, individuals are "affected" if they lie in the wrong end of the distribution curve. A mutation resulting in disease is often recessive, and this follows that both alleles must be mutated for the disease to be expressed phenotypically. However, a disease may also be the result of the expression of mutant alleles at more then one locus. When more than one gene is involved (with or without the presence of environmental factors, or better, triggers), we conclude that the diseases is the outcome of multifactorial inheritance.
- Some diseases for example myocardial infarction, congenital birth defects, cancer, diabetes, mental illnesses and Alzheimer diseases cause along with morbidity, premature mortality in two out of three individuals during their lifetime. Many show clustering among families. However their inheritance pattern does not follow that of single gene disorders (Mendelian pattern of inheritance). These kind of diseases are thought to result from complex interactions between genetic and environmental factors, i.e. multifactorial inheritance pattern.
- The reason reason why these diseases show this kind of clustering among families is that family members share a significant portion of their genetic information and further more, they are exposed to the same environmental triggers (most of the times).

We can therefore conclude that family members experience the same gene-gene interactions and gene-environment interactions that may trigger, accelerate or exacerbate or even protect against the disease process.

Characteristics

1. There is no notable pattern of inheritance within family.
2. The lower the incidence of the disease within a population the greater the relative increase in risk for 1st degree relatives.
3. The risk is much lower for 2nd degree relatives, but it decreases less sharply for more remote relatives. This characteristic distinguishes MI from AD I, in which the risk drops by ½.
4. The recurrence risk is higher when more than one family member is affected. As opposed to single gene trait that the risk to the next child remains unchanged.
5. The more severe the malformation the greater the recurrence risk.
6. If an MI trait is more frequent in one sex than in the other, the risk is higher for relatives of patients of the less susceptible sex.
7. An increased recurrence risk when the parents are consanguineous suggests that multiple factors with additive effects may be involved, as oppposed to AR I (25%).
8. If the concordance rate in DZ twins is less than ½ the rate in MZ twins, the trait cannot be AD and if it is less

than ¼ of the MZ twins rate, it cannot be AR .

Heritability

Definition

It can be defined as the proportion phenotypic variation that belongs only tot he genetic variation between individuals. Another definition of heritability , if it makes it any easier, is the following: It is the fraction of phenotypic variability within a population for a quantitative trait that is caused by genes.

Concept

It is important to know that the phenotypic variation among individuals it is due to the genetic factor but as well as the environmental factor and random chance. Heritability, is an analysis of the respective contribution of the genetic factor and the non-genetic factor to the total phenotypic variance in a population. The higher the heritability the higher the is the “donation” of genes to the phenotypic variation, as opposed to other factors.

What is Variance?

Statistically is a measure of how much an individual is likely to vary from the mean of the group. In statistical terms variance = (standard deviation)^2.

Use of Heritability

Estimates of Heritability (h^2) of a condition or trait provide an indication of the relative importance of the genetic factors in its causation, so that the greater the value for h^2 the greater the role of genetic factor.

What is Concordance?

When two individuals in the same family share the same disease are said to be concordant. On the other hand when only one of a pair of relatives has the disease the wo individuals are said to be discordant for the disease. Discordance for relatives that share the same genotype at loci that predispose the disease but not the phenotype can be explained by the fact that the disease free individual has not experienced the other factors (environmental or chance occurrence) that are also required to expresse the disease phenotype.

Estimating the heritability of a trait

1. It is estimated from the degree of resemblance between relatives expressed in the form of a correlation coefficient which is calculated using statistics of a normal distribution. The correlation indicates the strength and direction of a linear relationship between two random variables.
2. Using data from the concordance rates in MZ (who share 100% of their genes) and DZ (who share 50% of their genes) twins.

h^2 = (variance in DZ pairs – variance in MZ pairs)/variance in DZ pairs.

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*  If the trait is determined mostly by the environment, the ratio approaches 0.
*  If determination is primarily genetic, MZ pairs show very little variance (almost 0) and ratio approaches 1.
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In practise it is desirable to try to derive heritability estimates using different types of relatives and to measure the disease incidence in relatives brought up together but living apart, so as to try to remove possible effects of common environmental factors.

For better understanding

Studies of heritability of identical twins (MZ) that have been separated early in life i.e. that have been raised in different environment, often contrast. Such individuals have identical genotypes and can be used to separate the effects of genotype and environment. Heritability estimates reflect the amount of variation in genotypic effects compared to variation in environmental effects.

Analysis of Variance

- Total phenotypic variance Vp = Vg + Ve where, Vp is total phenotypic variance; Vg is genetic variance contribution; and Ve is environmental variance contribution .
- Broad sense heritability: H^2=Vg/Vp.
- Narrow sense heritability: h^2=Va/Vp and quantifies only the portion of the phenotypic variation that is additive (allelic, Va) by nature (note upper case H2 for broad sense, lower case h2 for narrow sense).
- Variance in F1 only due to Ve, Variance in F2 due to Vg and Ve → h2 = (F2-F1)/F2 → Vg/(Vg+Ve) → Vg/Vp

Estimates of heritability for various disorders

Disorder	Frequency (%)	Heritability
Schizophrenia	1	85

Cleft lip +/- cleft palate	0,1	76
Hypertension	5	62
Congenital heart disease	0,5	35

Important practical implications:

1. High heritability → search for susceptibility genes.
2. Low heritability → search for favored environmental factors (Ve).

Links

Related articles

Bibliography

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