What is known about interactions between genes and the environment in relation to early intervention?

Rachel M. Latham

University of Sussex and the Early Intervention Foundation

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Introduction

Scientific research over the last three decades has significantly advanced our understanding of the influences of – and interplay between – nature and nurture for human development. Notably, findings from behaviour genetic research using twin and adoption designs have highlighted the prevalent role of genes in explanations of individual differences and provided an impetus to identify the relevant genes involved. However, the topic of genetics and human behaviour has proven to be a contentious one. There has been a degree of hype and exaggeration, in both the academic literature (see Rutter, 2002) and mass media, that has typically stemmed from misunderstandings of this very complex area of research.

One such example, with headlines proclaiming "Genetics outweighs teaching" (The Guardian, 11 October 2013), was the widely reported story of Dominic Cummings, then special advisor to the Education Secretary, claiming that '70% of a child's academic achievement is genetically derived and, therefore, their genes are more important than the teaching they receive.' A polar-opposite view, that there is no scientific basis for the belief that there is a genetic element to any psychological trait, has been voiced by Oliver James. Headlines querying "Are you to blame for your child's mental health issues?' (The Telegraph, 24 February 2016) present his view that the environment in which you grow up is completely responsible for psychological traits, as well as for illnesses such as schizophrenia and depression. Such polarised opinions provide provocative headlines but both positions are inaccurate. The first instance illustrates the common mistake of applying 'heritability', which is a measure of population level differences, to explain a single individual's development. In the latter, Oliver James dismisses the very notion of heritability on the mistaken basis that its existence relies on having identified the specific genes involved. The publicity of such polarised views gives the impression of a field of research still fighting the war of nature '*versus'* nurture, yet this is certainly not the case. Neither of these two positions accurately reflect the current state of scientific knowledge, nor the balanced view adopted by the majority of scientists – one that acknowledges the contribution of both nature *and* nurture and instead concerns itself with understanding the complex interplay between them.

These examples – along with many others – do however indicate that the topic of behaviour genetics is not one limited to academic realms. Instead, it is apparent that such incorrect interpretations of the research findings feature in discussions that may impact policy, and convey the implicit message that heritability limits the attempts of practitioners (such as teachers, social workers and health visitors) to improve outcomes for children and families. The reality is that heritability in itself says

nothing about the possibility of successful intervention. Even though there may be substantial genetic influence on individual differences in characteristics such as aggression, intelligence and parenting, this does not imply that these are pre-determined, and certainly does not mean that nothing can be done to change or improve them. It is therefore important to clarify precisely what heritability is, and what it can and can't tell us.

Importantly, heritability is derived from 'traditional' behaviour genetic research utilising twin and adoption designs, and it is necessary to distinguish these from 'molecular genetic' studies. It is the purpose of the former to quantify the relative strength of genetic and non-genetic influences on observed differences between individuals, which is quite different to the latter, whose concern is identifying the specific genes involved at the DNA level. The focus of this paper will be on the traditional designs – detailing their approaches, clarifying their concepts and presenting key overarching findings that have emerged from decades of research employing such methods. However, since the history of behaviour genetics can be viewed as an attempt to move from findings of heritability towards the identification of the actual genes involved (Turkheimer, 2016b), some key findings from molecular genetic and epigenetic research will be touched on, in order to provide appropriate context to this discussion. A thorough review of these types of methods, and the literature relating to them, is however beyond the scope of this paper, though the interested reader is referred to more detailed information on both molecular genetics and epigenetics.

Whilst it will be demonstrated that the concept of heritability has no direct implication for intervention or policy, it is argued here that behaviour genetic research has much else to offer those interested in intervention. A greater understanding of the role of genes, in conjunction with the role of the environment, for example, offers the potential to understand who may be most at risk, and may also highlight aspects of the environment that may be best targeted by interventions. Furthermore, understanding that genetic differences mean that not all individuals will respond to the same intervention in the same way has the potential to facilitate approaches that are more tailored and therefore more effective. Much of this potential, however, has not yet been fully realised; this is still a relatively young area of science where much remains unknown, especially in terms of understanding gene-environment interactions. Thus, we do not yet have all the information needed to fully implement findings into intervention. It should also be noted that the potential for genetic research to help identify genes and environments that place individuals at particular risk raises important ethical issues, which will need to be carefully considered (see Nuffield Council on Bioethics, 2002).

The purpose of this paper is therefore to: 1) introduce the reader to the field of behaviour genetics and clarify its core concepts; 2) provide a narrative overview of key findings from the literature, with a particular focus on traits and characteristics that are important for children's outcomes; 3) highlight the relevance of behaviour genetic findings for those interested in early intervention; and 4) detail pertinent issues to be considered in the interpretation of these findings.

Section 1: Behaviour genetics – estimating heritability and environmental influence

Mid-nineteenth century observations by Gregor Mendel of physical trait inheritance in pea plants, and by Francis Galton of familial similarity in intelligence, laid the foundations on which contemporary genetic research has been built. Fundamental to this was the extension of Mendel's "laws of inheritance", from explaining simple, single gene inheritance to explaining much more complex, polygenic (determined by more than one gene) traits. Subsequent genetic research has explored a wide range of complex psychological traits – including, cognitive ability, aggression, personality and mental health – and has consistently demonstrated that genetic differences between individuals contribute not only to abnormal difference, but to normal variation too (Plomin, DeFries, Knopik, & Neiderhiser, 2013)

As many commentators have noted, the last 30 to 40 years have seen a significant paradigm shift in the behavioural sciences (e.g. Johnson, Penke, & Spinath, 2011; Plomin et al., 2013) with the dominance of behavioural explanations until behaviour genetic studies also highlighted the role of genes. This recognition that both genes and the environment are important and that they work together to influence behaviour brought the debate of 'nature *versus* nurture' to an end. Since then, it has been reframed into a more useful question – to what extent are observed individual differences influenced by genetic differences and influenced by differences in the environments people inhabit? It is this question that the field of behaviour genetics seeks to address.

Section 1 will introduce 'behaviour genetics' and the key concepts of heritability, shared and non-shared environmental influence. Given the prevalence of misunderstandings about the meaning of heritability, this section will also clarify some of the common misconceptions, to make clear what heritability is, and what it is not.

BEHAVIOUR GENETICS

Behaviour genetic research is concerned with the extent to which individual differences in genetics and experience within a given population relate to a phenotype of interest. A 'phenotype' is any observed physical or psychological characteristic of an individual. Within a given population, people will vary on such traits – e.g. people vary in physical characteristics such as height, weight, eye colour and skin colour; in personality characteristics such as extraversion; in behaviours such as aggression; and in abilities such as athleticism and intelligence – such individual differences are referred to as

'phenotypic variation.' Using quasi-experimental designs involving family members of varying genetic relatedness, behaviour genetic researchers are able to indirectly estimate the relative contribution of genetics and environment to explain this phenotypic variance (see Box 1).

BOX 1: METHODOLOGICAL DESIGNS

Behaviour geneticists commonly use two naturally occurring experimental situations to study the relative influence of genes and environment on human behaviour – twinning, as an experiment of nature, and adoption, as an experiment of nurture (Plomin et al., 2013).

Child-based twin studies: Monozygotic (MZ) or identical twins share 100% of their segregating genes, so that, for twins reared together, any observed differences for a particular phenotype are assumed to be the result of non-shared environment. By contrast, dizygotic (DZ) or non-identical/fraternal twins share around 50% of their genes, just like ordinary siblings. Comparisons of MZ and DZ twin pair correlations for a particular phenotype of interest enables inferences to be made about the relative contribution of genetics and environment.

Adoption studies: In a typical family study, parents provide children with both their genes and their environment and it is therefore not possible to disentangle the relative influence of each. Adoption studies provide an opportunity to do exactly that. If a child is adopted soon after birth, a situation is created in which there are genetically related parents who do not provide an environment for the child (at least, not a post-natal rearing environment) and non-genetic parents who do provide a rearing environment. Comparing similarity on a particular phenotype of interest between the child and their genetic and non-genetic parents allows inferences to be drawn regarding the relative contribution of genes and environment to that trait. As well as comparing resemblance between parents and offspring, adoption studies can also utilise comparisons of siblings, since adoption also creates sets of genetically related siblings who are reared apart and sets of genetically unrelated siblings who are reared in the same home.

Combination designs: Twin and adoption designs are each based on their own core assumptions (discussed in Section 3) and therefore each have their associated limitations. Designs that combine both approaches are the most powerful for separating the relative influence of genes and environment on human behaviour. However such studies of twins separated at birth and raised apart are, unsurprisingly, relatively rare.

The logic of these research designs is relatively straightforward – if genetic factors affect a phenotype, then resemblance for this trait should increase with increasing genetic relatedness. This means that monozygotic (MZ or identical) twins would be more similar to each other on a particular measured trait than dizygotic (DZ or non-identical/fraternal) twins, and adopted children would be more similar to their biological relatives than to their adopted relatives. Similarly, if environmental factors affect a trait, relatives who share an environment should be more similar than those who do not. This means that adopted children would be more similar to their adoptive family than to their biological family. These genetic designs can be depicted as path models (see Figure 1) and structural

equation modelling can be used to fit the best model of genetic and environmental relatedness to the observed data. This enables the effect size of environmental influence and heritability to be estimated (Plomin et al., 2013). Univariate analysis involves the estimation of genetic and environmental influences on one phenotype at a time, whereas multivariate analysis examines the influences on the covariance between traits, and thus allows the exploration of more complex questions – examples of which will be presented in Section 2.

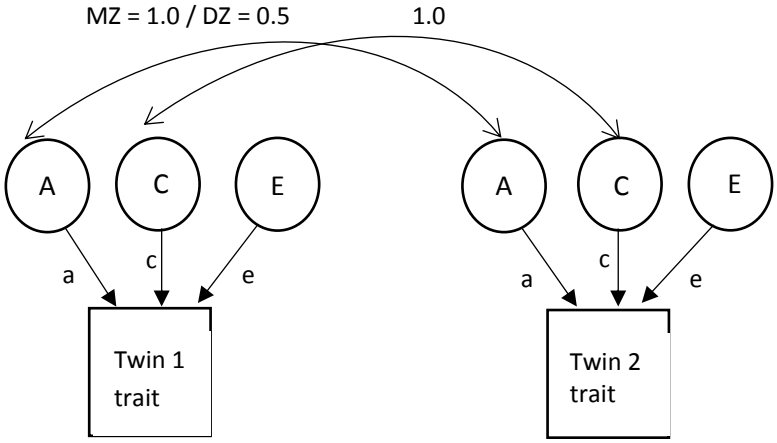

Figure 1. Univariate twin ACE path diagram. A = additive genetic variance; C = common/shared environment variance; E = non-shared environment variance & measurement error. Paths (drawn as arrows) reflect the statistical effect of one variable on another, independent of all other variables. Variables in boxes are observed measured variables (e.g. the phenotype of interest) and variables in circles are latent/unmeasured variance components. The covariance (drawn as curved arrows) between the two latent A variables for MZ twins is 1.0 and for DZ twins is 0.5 (i.e. reflecting the genetic relatedness of 100% and 50% respectively). By definition, the covariance between the latent C variable is set at 1 and there is no covariance between the E variables as this is non-shared. Path analysis involves the estimation of paths a, c and e. (For a detailed description of statistical methods in behaviour genetics see Purcell, 2013)

ENVIRONMENTAL INFLUENCE

Using twin and adoption designs, behaviour geneticists are able to estimate the extent to which individual differences in experience (relative to genetic effects) explain phenotypic variation within a population. This variation can be partitioned into shared (or common) and non-shared

environmental effects. So-called 'shared' environmental effects refer to those that result in family members being similar to each other, whereas 'non-shared' environmental effects refer to those that result in family members being different to one another (and this latter component also includes measurement error). Thus, it is the *effect* of the environment, rather than the environment event per se, that is of relevance when defining it as 'shared' or 'non-shared.' To illustrate this, two siblings in a family may both experience parental divorce, making it a shared event. However if it was found that the children experienced this event differently (thus making them different to one another), it would be considered a source of non-shared environmental variance.

Child-based twin designs provide a neat method for estimating the relative influence of the shared and non-shared environment. MZ twins raised together share the same genes and environment, therefore any differences within such pairs is assumed to be the result of non-shared environmental influences. Since DZ twins' genetic similarity is half that of MZ twins', if there was only genetic influence on a particular trait, then DZ twins would be half as similar as MZ twins. Therefore, if DZ twins are more than half as similar as MZ twins, this implicates environmental influences that are making siblings more similar – so-called shared environment. Using adoption designs, greater similarity on a measured trait between the child and their adoptive relative, compared to their genetic relative, is indicative of shared environmental influence.

HERITABILITY

Alongside estimates of environmental influence, behaviour geneticists also estimate 'heritability'. This is an effect size statistic that quantifies the proportion of phenotypic variance that is accounted for by genetic differences between individuals. Essentially, a finding of heritability indicates that genetic differences and phenotypic differences are correlated, but importantly, this correlation is not evidence of genetic cause. Genetic cause can be assumed by molecular genetic studies when a correlation between a DNA variant and a particular behaviour can only be interpreted in one direction – DNA sequence differences can cause behaviour differences, but not the other way around (note though that this does not necessarily imply a direct genetic cause). Thus, it is important in this discussion of behaviour genetics that the terms 'heritability' and 'genetic influence' are not taken to mean 'genetic cause'.

To illustrate with some examples, let's say that twin and adoption research has estimated the heritability of a particular trait to be approximately 40% - this means that 40% of the differences between individuals on this trait (the variation) within a population can be explained by differences

in their genotypes (their genetic makeup). So, let's say that the trait measured in this example is children's aggression; this would tell us that 40% of the difference between the most aggressive and the least aggressive children could be attributed to differences in their genes. It does not mean that any one child's aggression is influenced 40% by their genes and the remaining 60% by their environment. Recall the example of Dominic Cummings (from the introduction) and his reported claim that '70% of a child's academic achievement is genetically derived and, therefore, their genes are more important than the teaching they receive'. This is exactly the mistake that has been made here; heritability – an estimate that reflects population variance – has been applied to explain the development of an individual, leading to a highly erroneous conclusion.

Heritability estimates may either be 'broad sense' and include all sources of genetic variance, or 'narrow sense' and include only variance accounted for by additive genetic effects. It is not possible to simultaneously estimate both shared environment and non-additive heritability in a twin design since their inference relies on the same information. As such, research most commonly measures narrow sense heritability (and, unless otherwise specified, is the heritability referred to here). Narrow heritability is (as a very rough estimate) twice the difference between the MZ and DZ correlation on a trait. For example, if MZ twins correlate 0.8 for aggression and DZ twins correlate 0.6 (a difference of 0.2) then the heritability estimate would be approximately 0.4 or 40%. This is based on the assumption that MZ twins share 100% of their genes whereas DZ twins share only 50%. Thus, if a trait were 100% heritable the DZ correlation would be half that of the MZ.

It is important to note that estimates of heritability assume that environmental and genetic influences are independent, however this is problematic when applied to human behaviour. Gene-environment correlation (rGE) and gene-environment interaction (GxE) are two ways in which such an assumption may be violated – both of these are discussed in greater detail in Section 2. Briefly, gene-environment correlation refers to the notion that people create their own experiences which are, to an extent, influenced by their individual genes – therefore what may first appear to be an environmental effect may actually reflect genetic influence. For this reason genetic propensities often correlate with particular environments and experiences (rGE), a phenomenon that has also been referred to as the 'nature of nurture' (Plomin & Bergeman, 1991). Gene-environment interaction, on the other hand, refers to a genetic sensitivity or susceptibility to particular environments. In other words, the effect of genes on a particular behaviour may depend on a certain environment and, similarly, the effect of an environment on a particular behaviour may depend on the individuals' genes.

Gene-environment correlation and gene-environment interaction are hypothesised to contribute to the population variation of a phenotype in addition to the independent effects of genes and the environment. However, most studies cannot separately estimate these components, and therefore such effects are included within the estimate of heritability. This has important implications for how heritability is interpreted as it means that it is not a 'pure' measure of genetic influence – even when a trait has high heritability, environmental influence may still be a very important mediator. Furthermore, the presence of rGE and GxE can introduce bias to heritability estimates – the direction of which depends on the nature of the correlation and interaction (see Box 2).

BOX 2: GENE-ENVIRONMENT INTERPLAY AND HERITABILITY ESTIMATES

Genetic influence will be **underestimated** if:

- Genetic and shared environmental influences that make relatives more similar are correlated in ways that affect trait development
- Genetic and non-shared environmental influences interact

Genetic influence will be **overestimated** if:

- Genetic and non-shared environmental influences that make relatives different are correlated in ways that affect trait development
- Genetic and shared environmental influences interact

Given the different potential combinations of these correlations and interactions, there are numerous possibilities for the direction of bias introduced to heritability estimates (Johnson, Penke, & Spinath, 2011)

The scientific concept of heritability therefore has a very specific meaning; unlike to the common sense interpretation, heritability is not a measure of "how inherited" an individual's characteristics are. Rather, it is a measure of the total proportion of phenotypic variance that is attributable to genetic differences among individuals. Why is heritability important? It is assumed that heritability provides evidence that genes are, somehow, involved in a phenotype, but beyond that, heritability alone says very little about the kinds of genetic processes that take place, or the degree to which the trait may be responsive to environmental manipulation (Johnson et al., 2011). Misunderstanding about what heritability is has contributed to inaccurate interpretations, including explanations of racial differences in intelligence and concerns about eugenics, 'designer babies' and the implication for rehabilitation and intervention. As such, before proceeding to review what we have learnt about the heritability of traits that are important for child development (Section 2), it is important to first clarify some of the most common misconceptions about heritability.

1. **Heritability is specific to the population and doesn't tell us anything about a particular individual**

To reiterate an earlier distinction, behaviour genetics is concerned with explaining the variation of a phenotype in a population; it is *not* concerned with the development of a phenotype in any particular individual. For example, if height has a heritability estimate of 80%, this does not mean that a person's genes explain 80% of their height while the environment explains the remaining 20%. That is to say, a person does not grow to 80% of their full height for genetic reasons and then grow the remainder due to environment, because heritability tells us nothing about any one individual. Instead the estimate tells us that, among a particular population, 80% of the differences in people's height can be explained by them having different collections of genes, and 20% of the differences in height can be explained by differences in their environment (perhaps differences in their nutrition, prenatal and/or early years environments, or unique experiences such as disease that may have impacted growth). Furthermore, since heritability estimates reflect the influences on variation within a specific population, these estimates are specific to this population but may be different for populations of different ages, or genders, or those measured in a different historical period – to highlight just a few examples. To illustrate this point, imagine a scenario in which all environments that influence educational outcomes are equalised. Since all environmental variance has been removed, behaviour geneticists would hypothesise that any variation in the educational outcomes of individuals would have to be explained by genetic variation – therefore heritability would be high. As this example demonstrates, heritability estimates depend on variation in both genetic and environmental factors, so any reduction in the variation of environments will likely produce increased heritability of the characteristic being measured. Understanding of this is of primary importance when considering what heritability means for prevention and intervention; high heritability does not remove the possibility of environmental intervention.

2. **There is <u>not</u> a single heritability estimate for any given phenotype**

Given that heritability estimates may be different for different populations, it should be evident that a particular phenotype does not have one single figure of heritability that researchers can 'discover' (Turkheimer, 2016). Rather, the heritability they estimate will be different depending on factors such as the population being tested, and the definition and measurement of the phenotype of interest – for example, self-report and observation measures may yield different heritability estimates (see Rhee & Waldman, 2002, and Tuvblad & Baker, 2011, as applied to human aggression). Thus, behaviour genetic studies will likely vary in the exact heritability estimate they report, but together they indicate a possible range of estimated genetic influence.

3. Heritability is <u>not</u> informative about between-group differences

A further extension to point number 1 is that, because heritability estimates explain within population variance, these estimates do not allow conclusions to be drawn about between-group differences. Just because a measured trait shows high heritability *within* a particular group, this does not mean that any observable differences *between* groups are down to genetics. For example, if GCSE attainment was to show high heritability, it would not be correct to conclude from this that a mean difference between boys' and girls' GCSE grades was also due to genes.

4. Heritability does not mean there is a gene 'for' a particular behaviour

Estimates of heritability and environmental influence do not tell us anything about *how* genes and the environment have their influence. A common misconception is that genetic influence means there is a gene 'for' a particular trait – a gene *for* obesity, or a gene *for* antisocial behaviour – suggesting that a gene has a direct effect on a certain phenotype. Certainly, there are disorders for which a single gene, or mutation to a single gene, is directly responsible (Box 3) – so-called single gene disorders, such as Huntington's disease, sickle cell disease and fragile X syndrome. However, for complex social behaviours and personality traits that show quantitative variation, it is implausible and incorrect to believe that one single gene could be responsible in this manner. Relatedly, even if several genes are involved, heritability does not mean that these are necessarily having a direct influence on the phenotype. The ways in which genes come to influence human behaviour are rather more complex – as will be illustrated by research findings discussed in Section 2.

5. Heritability does <u>not</u> imply genetic determinism

Once it is understood that there is not a single heritability estimate for any given phenotype, or a single gene 'for' a behaviour, but rather that human behaviour is influenced by multiple genetic and environmental factors that work together in complex ways, this fifth misconception about heritability becomes much clearer – heritability does not imply genetic determinism. High heritability simply means that, in the population measured, the phenotype of an individual is a good predictor of the genotype, but not that the phenotype is determined once we know the genotype (Visscher, Hill, & Wray, 2008). The reason being that the environment can change or be manipulated in ways that alter the phenotype – the classic example to illustrate this is human height. Height is highly heritable (estimated around 80%) and yet there has been secular rise in height documented across numerous populations, most likely attributed to environmental changes including improved nutrition and health care. This illustrates nicely that environmental "intervention" is compatible with heritability.

BOX 3: SINGLE GENE DISORDERS OF COGNITIVE DISABILITY

General cognitive ability, as measured by IQ scores, is normally distributed around an average score of 100 with a standard deviation of 15. Findings from twin and adoption studies suggest that the genetic and environmental influences responsible for individual differences in this average range are the same influences evident in the lower range of the curve – for individuals considered to have mild cognitive disabilities (IQ in the region of 50-70). Moderate and severe cognitive disability, however, is an under-researched area in behaviour genetics, with no twin or adoption studies being reported (Plomin et al., 2013). Whilst cognitive disability can of course result from environmental trauma such as a head injury or birth complications, there are also many known instances of moderate and severe impairments that are caused by chromosomal abnormalities (such as Down's syndrome) and single gene mutations – one particularly interesting example is Phenylketonuria.

Phenylketonuria (PKU) is an inherited form of moderate cognitive disability affecting 1 in 10,000 people. Those affected typically have IQ scores below 50 although individual differences remain, and some people have near-normal scores. PKU is a single gene disorder where affected individuals inherit two recessive alleles. This causes problems in the metabolism of phenylalanine, an essential amino acid, thus causing an excess in the blood and brain which impacts on healthy brain development. Molecular genetic research successfully identified the gene responsible for PKU as residing on chromosome 12, enabling widespread genetic screening for the condition at birth. What is most interesting about PKU – and of particular relevance here – is that despite being a single gene disorder that shows a straight-forward pattern of inheritance, genetic research and screening has resulted in an intervention that is entirely environmental. PKU is treated by dietary adaptations – avoidance of high protein foods (which contain phenylalanine) such as red meat and dairy products throughout childhood and adolescence – an intervention that has been highly successful in preventing the associated cognitive disability. As this example neatly demonstrates, there is no straightforward relationship between genetic influence and the potential for environmental intervention. Here we can see that PKU, a disease whose presence is entirely determined by genetic inheritance, is malleable to the environment.

The behaviour genetic concept of heritability, therefore, has a very particular meaning, awareness of which is essential in order to avoid incorrect and overstated interpretations of the research evidence. With some of the most common misconceptions clarified (for a more extensive discussion see Visscher et al., 2008), we now turn to review some key findings from the behaviour genetic literature with regard to behaviours relevant to children's outcomes.

Section 2: What has behaviour genetic research revealed about the influence of genes and environment on traits and behaviour that are important for child development?

Behaviour genetics is a highly interdisciplinary field – encompassing social science, psychology, biology, molecular genetics and neuroscience – and the resultant literature is vast. Accordingly, this is not intended as a full systematic review of the evidence, rather the focus will be on three overarching findings that have emerged from behaviour genetic research using twin and adoption designs: 1) All human traits show significant heritability; 2) Genes and the environment interact; and 3) Measures of the 'environment' also show significant heritability (see Plomin, DeFries, Knopik & Neiderhiser, 2016, for a discussion of replicated findings in behaviour genetics). These will each be illustrated using example research that has explored traits and behaviour important for children's development and associated with long term outcomes – these include general intelligence, aggressive behaviours, depression and parenting. The relevance of this research for those seeking to provide effective prevention and intervention will also be highlighted.

ALL HUMAN TRAITS SHOW SOME DEGREE OF HERITABILITY

Behaviour genetic designs have explored numerous personality traits and behaviours, and studies using different samples and designs have repeatedly demonstrated significant heritability. This has led to recognition of the 'first law of behaviour genetics,' (Turkheimer & Gottesman, 1991) that all human traits (normal and abnormal) show significant heritability. As Table 1 (replicated from Bouchard, 2004) illustrates, evidence of moderate genetic influence has been found across domains of personality, psychiatric illness, intelligence, social attitudes and psychological interests. Contrary to initial expectations that some psychological traits would be much more heritable than others (Bouchard, 2004), in actuality heritability estimates between traits differ far less than had been expected.

Whilst the pervasiveness of genetic influence on human behaviour has been highlighted, it is important to note that these heritability estimates are significantly less than 100% therefore genetic factors alone do not fully account for the observed variation between individuals. In this way, behaviour genetic research has also provided the best available evidence for the importance of the environment (Plomin & Daniels, 1987). Indeed, twin and adoption design studies provide valuable insight into shared and non-shared environmental influences, along with how these change across

child development, by highlighting potential targets for intervention. If the shared environment is found to account for significant variance, then studies which measure family-wide factors can be used to identify environmental aspects that may be modifiable by intervention. If, on the other hand, the non-shared environment is found to account for significant variance, then aspects of each child's unique experience – such as their peer influence or classroom experience – may be a much better intervention target (Leve, Harold, Van Ryzin, Elam, & Chamberlain, 2012).

Table 1. Reproduced from Bouchard (2004). Representative estimates of broad heritability and shared environmental influence and indications of non-additive genetic effects in heritability for human psychological traits.

Trait	Broad heritability	Non-additive genetic effect	Shared environmental effect
Personality (adult samples)			
Big Five			
Extraversion	.54	Yes	No
Agreeableness (aggression)	.42	Yes	No
Conscientiousness	.49	Yes	No
Neuroticism	.48	Yes	No
Openness	.57	Yes	No
Big Three			
Positive emotionality	.50	Yes	No
Negative emotionality	.44	Yes	No
Constraint	.52	Yes	No
Intelligence			
By age in Dutch cross-sectional twin			
Age 5	.22	No	.54
Age 7	.40	No	.29
Age 10	.54	No	.26
Age 12	.85	No	No
Age 16	.62	No	No
Age 18	.82	No	No
Age 26	.88	No	No
Age 50	.85	No	No
In old age (>75 years old)	.54-.62	Not tested	No
Psychological interests			
Realistic	.36	Yes	.12
Investigative	.36	Yes	.10
Artistic	.39	Yes	.12
Social	.37	Yes	.08
Enterprising	.31	Yes	.11
Conventional	.38	Yes	.11

Psychiatric illness (liability estimates)			
Schizophrenia	.80	No	No
Major depression	.37	No	No
Panic disorder	.30-.40	No	No
Generalised anxiety disorder	.30	No	Small (female
Phobias	.20-.40	No	No
Alcoholism	.50-.60	No	Yes
Antisocial behaviour			
Children	.46	No	.20
Adolescents	.43	No	.16
Adults	.41	No	.09
Social attitudes			
Conservatism			
Under age 20 years	.00	Not relevant	Yes
Over age 20 years	.45-.65	Yes	Yes in females
Right wing authoritarianism	.50-.54	No	.00-.16
Religiousness			
16 year olds	.11-.22	No	.45-.60
Adults	.30-.45	No	.20-.40
Specific religion	Near zero	Not relevant	Not available

Two phenotypes frequently associated with child outcomes that have been the focus of a large body of behaviour genetic research are general cognitive ability (general intelligence) and aggressive behaviours. Key findings from these areas will illustrate the relative proportion of genetic and environmental influence, as well as the developmental patterns relating to their influence on behaviour continuity and change.

General cognitive ability: Individual differences in general cognitive ability (or general intelligence) are considered one of the most robust observations in psychology, showing rank stability throughout development (Moffitt, Caspi, Harkness, & Silva, 1993). Longitudinal studies have shown intelligence to be highly predictive of important outcomes, including educational achievement (Deary, Strand, Smith, & Fernandes, 2007), occupational success (Hunter, 1986), income and social mobility (Strenze, 2007), and health and mortality (Batty, Deary, & Gottfredson, 2007; Gottfredson & Deary, 2004). Such ability was one of the earliest traits to be the focus of genetic research, by Galton (1865) as well as early adoption studies (Leahy, 1935), and it has since received the most attention in the behaviour genetic literature. Twin and adoption studies have consistently converged on the finding that intelligence is highly heritable; a review of over 100 familial resemblance studies of general cognitive ability reported a correlation of 0.24 between adopted children and their biological parents, and also between genetically related but adopted apart siblings, producing a heritability estimate of 48% (2 x 0.24 = 0.48). Twin studies also support these conclusions, with average MZ

twin correlations of 0.86 and DZ correlations of 0.60 – producing a heredity estimate of 52% (2*[0.86-0.60] = 0.52) (Bouchard & McGue, 1981).

Estimates of heritability for intelligence appear to be in the range of 30 to 80%, a range that is notably wide. This may be partially explained by the finding that such heritability increases with age – as seen in Table 1. The first longitudinal twin study of intelligence, the Louisville Twin Study, showed this pattern of increasing heritability; MZ twin correlations increased from 0.66 at 3 months of age, to 0.85 at 6 years of age, whereas DZ twin correlations remained relatively constant (at an average of 0.67). These values produce heritability estimates that increased from 0% at 3 months to 44% at 6 years (Wilson, 1983). Similarly, increasing genetic influence has also been reported by adoption design studies. For example, the Colorado Adoption Project (DeFries, Plomin, Vandenberg, & Kuse, 1981) noted that the correlation for general cognitive ability between parents and children in a control group (i.e. no adoption) increased from infancy (< 0.20) to middle childhood (0.20), and again to adolescence (0.30). Correlations between adoptees and their biological mothers showed this same pattern, as did adopted-apart siblings. Crucially, though, this pattern was *not* evident for adoptees and their adoptive parents – their correlations remained close to zero, thereby indicating the increasing salience of genes. This developmental trajectory of intelligence was formally tested and confirmed by Haworth et al., (2010) using data from six twin studies; model fitting estimated 41% heritability in childhood, which increased significantly to 55% in adolescence and again to 66% in adulthood. Additionally, an interesting finding of the environment was revealed – the magnitude of the variance accounted for by the shared environment decreased from childhood (33%) to adolescence (27%), and then even further into adulthood (19%). Given that environmental experiences accumulate over time, this appears to be a somewhat counter-intuitive pattern, though it is one that has been reliably evidenced across a range of phenotypes. It has been suggested that the explanation may lie in gene-environment correlation (rGE) – people do not experience environments completely at random and, as children develop, they are increasingly able to select and shape their own environments, which they will do so, in part because of their genetic propensities, which will reflect and accentuate their genetic differences (Haworth et al., 2010). The phenomenon of rGE is discussed more fully below.

Building on the finding that there are genetic influences on individual differences in intelligence, the field of neuroscience has contributed some interesting results in an attempt to further knowledge about the underlying biology. Brain imaging studies have not only demonstrated correlations between intelligence and larger brains, greater grey matter volume and thicker cortices (e.g. Luders, Narr, Thompson, & Toga, 2009; Shaw et al., 2006) but, when combined with genetic analyses, have

reported substantial (around 80%) genetic influence on individual differences in grey matter, white matter and whole brain volume (Baaré et al., 2001) . Genetic influence has also been reported for aspects of brain functioning such as brain oscillations, considered to be involved in executive functioning (Anokhin, Müller, Lindenberger, Heath, & Myers, 2006). Advances in molecular genetics, in particular the sequencing of the human genome, have led to much anticipation about the ability to identify the specific genes involved in general cognitive ability. However, despite numerous studies reporting gene-intelligence associations, there is yet to be any reliably replicable contributions from individual genes (Deary, Penke, & Johnson, 2010). Consequently, it has been suggested that there are likely to be a large number of genetic variants each having a very small effect, and each accounting for small percentages of the variance. (For detailed reviews of molecular genetic research of intelligence see Deary, Spinath, & Bates, 2006, and Plomin & Spinath, 2004).

Given the large amount of research and replicated findings within the quantitative genetic literature, it has been claimed that more is known about the genetics of individual differences in intelligence than any other behavioural trait (Plomin & Spinath, 2004). However, studies attempting to understand the underlying genes and biological mechanisms responsible are far from conclusive. Whilst the findings undoubtedly reflect positive steps forward, the exact relation between biology and intelligence, and ultimately how human intelligence develops, remains unknown.

Aggressive behaviours: Longitudinal research has linked aggression in childhood and adolescence with a range of adverse outcomes, including increased rates of antisocial personality disorder, oppositional behaviour and attention deficit/hyperactivity disorder (Reef, Diamantopoulou, van Meurs, Verhulst, & van der Ende, 2011). Findings from a large number of twin and adoption studies suggest that around 50% of the variance in human aggression can be explained by genetic factors and the remaining 50% by environmental factors – primarily of the non-shared variety (Craig & Halton, 2009; Tuvblad & Baker, 2011). The influence of the shared environment has been noted to wane across the lifespan, with most studies of adolescents and adults typically reporting none at all (Tuvblad & Baker, 2011). 'Aggression' does however encompass a variety of behaviours and, although genetic influences are found for all forms, it appears that different factors may be operating. Indeed, meta-analyses have demonstrated that heritability estimates are moderated by the way in which aggression is defined, and also at what age it is measured (Burt, 2009; Ferguson, 2010; Miles & Carey, 1997; Rhee & Waldman, 2002). One operational distinction is between 'aggression' and 'rule breaking', and genetic and environmental influence varies significantly across these two types. A meta-analysis of 34 studies demonstrated that although genetic influence was substantial for both aggression and rule breaking, this was significantly greater for aggression (65%

compared to 48%), whereas shared environmental influence was greater for rule breaking (18% compared to 5%). Another frequent distinction has been between 'reactive' and 'proactive' aggression – the former being a response to a perceived threat, and considered to be the result of an excess of emotional sensitivity; while the latter is a planned antisocial behaviour, perhaps in anticipation of reward or dominance over others, and is considered to result from a lack of emotional sensitivity (Craig & Halton, 2009). Individual differences in both reactive and proactive aggression appear to be mainly influenced by genetic and non-shared environmental factors, however comparison of the two indicates that these influences may have different developmental patterns. Tuvblad & Baker (2011) found that the stability in reactive aggression from childhood to adolescence could be explained by genetic (48%), shared environmental (11%) and non-shared environmental (41%) influences, whereas stability in proactive aggression was predominantly (85%) genetically influenced (Tuvblad, Raine, Zheng, & Baker, 2009). The genetic and environmental stability of these two types of aggressive behaviour therefore appear to differ.

As these few examples illustrate, the relative influence of genes, shared and non-shared environment in explaining population variation of different types of human aggression varies and does so across the developmental course also. The finding that environmental influences change across childhood, with shared environmental effects typically decreasing over time (Rhee & Waldman, 2002), broadly highlights that early childhood may be the developmental period in which to intervene by targeting shared family environmental factors associated with aggressive behaviours as it is at this time that these are most influential. The implication from the evidence that there may be aetiological differences in aggressive behaviours also has important consequences for designing effective interventions since it suggests one single approach may not be successful for all forms of aggression or antisocial behaviour. Indeed, this may help explain why an intervention can sometimes have mixed success with some children responding well and others not, as a sample may contain a range of aetiologically distinct behaviours but the intervention may only effectively target the underlying mechanisms important for a certain form of aggression (see Frick, 2001 for a detailed discussion as this relates to conduct disorder). This research emphasises that innovative interventions must consider specific pathways that are theorised to be important for the aggressive behaviour – or subtypes of behaviour – being targeted.

GENES AND ENVIRONMENT INTERACT (GXE)

Behaviour genetic research clearly indicates that genetic *and* environmental influences are important for explaining individual differences – as shown by the previous examples of intelligence and aggression. However, in addition to the independent influences of genes and the environment, evidence also suggests that genes and the environment interact (GxE) in complex ways to produce variations in phenotypes. This notion has been considered theoretically important for some while – particularly for evolutionary theories – but only relatively recently has research on human behaviour begun to explore it empirically.

Twin and adoption designs have been utilised in the investigation of GxE. Such studies measure a specific environmental factor of interest (e.g. harsh parenting, maltreatment, or socioeconomic status) and use the genetic relatedness of relatives as an index of overall inherited genetic risk. If we use depression as an example – an adopted child whose biological parent has a diagnosis, or an MZ twin whose co-twin has a diagnosis, would be considered to have high genetic risk for the condition.

Anti-social behaviour and depression are two phenotypes that have been the focus of considerable GxE research. Here, replicated findings from twin and adoption designs have largely converged on the notion that genetic risk interacts with early adverse environments (Thapar, Harold, Rice, Langley, & O'Donovan, 2007). For example, the risk of adopted children developing conduct disorder was found to be highest in those who were raised in an adverse adoptive environment (defined as those in which the existence of divorce, marital problems, legal problems, substance abuse or anxiety or depression were present), and whose biological parent also had antisocial personality disorder (Cadoret, Yates, Woodworth, & Stewart, 1995). Furthermore, a study of 5 year old twins found that the experience of maltreatment was associated with an increased probability of conduct disorder for children with high genetic risk (24%), compared to those with low genetic risk (2%; Jaffee et al., 2005). Similarly, a study of female twin pairs found that the effect of stressful life events on major depression was 2.6 times greater for those who were also at greater genetic risk for the disorder, compared to those with low genetic risk (Kendler et al., 1995).

Findings from studies like these, that use latent measures of genetic risk, have been used to inform molecular genetic studies in which a specific environment *and* a specific variation in the DNA sequence are explored (sometimes referred to as cGxE). Two of the most studied candidate genes in cGxE studies are monoamine oxidase A (MAOA) in relation to aggression and family adversity, and 5HTTLPR in relation to depression.

Interaction between MAOA and family adversity for aggressive behaviours: Caspi et al., (2002) explored the hypothesis that a polymorphism in the gene that encodes for the neurotransmitter MAOA moderates the effect of child maltreatment on aggression. They found that children who had been exposed to maltreatment and whose genotype conferred low levels of MAOA expression were more likely to develop conduct disorder, personality disorder and more likely to commit violent crime as adults than those children who were maltreated but who had a high activity MAOA genotype. A recent review identified 31 studies exploring links between the MAOA polymorphism, family adversity and externalising behaviour (Weeland Overbeek, de Castro, & Matthys, 2015). It noted that the findings of Caspi et al., (2002) have been replicated 16 times, whilst four studies have reported findings to the contrary (i.e. that effects were larger among individuals with high activity MAOA alleles), and ten studies have reported null findings.

Interaction between 5HTTLPR and life stress for depression: Candidate GxE studies of depression and environmental adversity have focused on the promoter region of the serotonin transmitter gene 5HTTLPR – here the variant in this gene affects the amount of serotonin transporter that is produced. Data from the Dunedin Longitudinal Study (Caspi et al., 2003) indicated that individuals who had one or two copies of the short allele form exhibited more depressive symptoms and suicidality following the experience of stressful life events than those individuals who had two copies of the long allele. Interestingly, there was no evidence of a main effect – the link between the genetic polymorphism and an increased risk of depression was *only* evident in the presence of adverse life events. In their review of GxE and psychopathology, Thapar et al., (2007) note that findings for 5HTT variants and life events have been reported across development (from childhood to adolescence and into adulthood), and conclude that, despite some published non-replication, the weight of the evidence appears to be in favour of GxE for depression.

These GxE findings suggest that some individuals may have a genetic predisposition to be more vulnerable to the negative effects of an environmental risk, knowledge of which raises the possibility of successfully targeting intervention. Relatedly, certain experiences may exacerbate or reduce individuals' genetic risk, which highlights the potential of the environment to serve as a protective factor. In this way, interventions that modify an environmental factor to successfully moderate a genetic risk may be thought of as a positive form of GxE.

It is important to note that the GxE studies described thus far are correlational in nature, and limitations of these have been identified (including problems associated with skewed distributions, measurement error and the correlation between genes and environment – see Bakermans-Kranenburg & Van IJzendoorn, 2015, for a detailed discussion). One method proposed to address

the problems of correlational GxE studies is genetically informed randomised control trials (RCTs). As with standard RCTs, participants are randomised to an experimental group in which the environment is manipulated – a key advantage here is that this randomisation breaks any correlation between their genes and the environment. To illustrate, an RCT design was used to explore the role of the DRD4 gene (which has been linked with externalising behaviour) in explaining differential responses to a parenting intervention designed to reduce child externalising behaviour problems (Bakermans-Kranenburg, Van IJzendoorn, Mesman, Alink, & Juffer, 2008). The findings indicated that the parenting intervention did indeed reduce externalising symptoms, however, this was only the case for children who were carriers of the DRD4 7-repeat allele. Furthermore, for parents who showed a greater than average increase in their use of positive parenting, the decline in child behaviour problems was strongest in those with the DRD4 7-repeat. Thus, in a design where the environment was experimentally manipulated, GxE was demonstrated; the children were found to be differentially susceptible to experimentally induced changes in the environment depending on their genetic factors (Bakermans-Kranenburg et al., 2008).

This finding that children who had a genotype associated with a risk for externalising behaviour benefitted most from the positive parenting environment promoted by the intervention, lends support to a perspective of GxE called 'differential susceptibility' (Ellis, Boyce, Belsky, Bakermans-Kranenburg, & Van IJzendoorn, 2011). This theory builds on the notion (referred to as 'diathesis stress' or 'dual risk') that the developmental outcomes of children with a genetic risk, who also experience a particular poor environment, will likely be worse than those children without such risk (as in the MAOA and 5HTTLPR examples above) and proposes that these same "vulnerable" children will also be the ones most susceptible to the positive effects of supportive environments. Bakermans-Kranenburg & Van IJzendoorn (2015) provide a review and meta-analysis of GxE RCT experiments and conclude that the evidence supports the hypothesis of the differential susceptibility model. If correct, this perspective has clear applicability to intervention – it shows us a possible reason why interventions might not be successful for all, by highlighting that those most at risk may be the ones who benefit most from support.

As these illustrative examples show, the findings of GxE research are especially interesting and have potential to inform intervention – the utilisation of GxE experiments, in particular, may facilitate better understanding of 'what works for whom' (Belsky & van Ijzendoorn, 2015). Despite the large amount of research in this area, however, there remains much that is uncertain and unknown about GxE. Fundamentally, whilst we may be able to detect the presence of a specific GxE, at present we are yet to fully understand the underlying mechanisms that explain exactly *how* this interaction

works. Even for phenotypes that have been the subject of extensive study – such as those detailed above – the findings do not yet form a conclusive picture. The presence of contradictory findings, and some failures to replicate (which are likely underestimated due to the publication bias towards significant findings), reflects the youth of this area of science. As Weeland et al., (2015) suggest, this apparent mixture of results may also reflect the large variation in methodologies used by these existing studies and make cross-study comparison of findings difficult (particularly if it is the case that cGxE in one population does not in fact replicate in another, or at a different age or developmental stage). Indeed, an interesting question which requires more research is whether there are sensitive periods in development for specific cGxE (e.g. Choe, Shaw, Hyde, & Forbes, 2014). This insight would be of substantial clinical importance since knowing who is likely to be most at risk, under what environmental conditions, and at what developmental stage, will enable much greater specificity for early intervention and the potential to better tailor intervention to individuals.

Epigenetic research: Until very recently, molecular genetic research into GxE focused on polymorphisms in DNA sequence and their associations with psychopathology – as in the MAOA and 5HTTLPR examples illustrated above. However, there is accumulating evidence supporting the view that the environment can effect genes at the epigenetic level – that is, the environment can induce molecular change that does not change the DNA sequence, but does change the DNA structure such that gene expression is altered. It has been proposed that such alterations underlie the long term impact of early life experience (Roth & David Sweatt, 2011). One epigenetic mechanism in particular that has been the focus of much of this research is DNA methylation, a biological mechanism by which genes can be silenced or 'switched off.' Laboratory studies using rodent models have found that during the pre-natal and post-natal period, DNA methylation is particularly sensitive to environmental regulation (for a review see Champagne, 2010, and Roth & Sweatt, 2011). Although more difficult to conduct, there have also been some human studies. Some of these have made use of MZ twin comparisons and have, for example, found differential methylation in the promoter region of the dopamine D2 receptor gene in their lymphocytes for twins who are discordant for schizophrenia (Petronis et al., 2003). Other approaches have used post mortem analysis which have, for example, revealed altered levels of DNA methylation in the hippocampal tissue of individuals exposed to abuse in infancy (McGowan et al 2007), and in hypermethylation of ribosomal ribonucleic acid among suicide victims with a history of abuse and neglect (McGowan et al., 2008). These results suggest that experiences of human caregiving may also effect genes through epigenetic changes.

Moreover, there is evidence that epigenetic changes can occur not only in early development, but that this plasticity persists in adulthood too. Rodent studies involving fear conditioning have been found to induce rapid changes in DNA methylation of reelin and brain-derived neurotrophic factor (BDNF) promoter regions with consequent alterations to gene expression (Lubin, Roth & Sweatt, 2008; Miller & Sweat, 2007). Furthermore, pharmacological manipulation of the epigenome has been shown to successfully reverse the negative effects of post-natal care in rodents (Weaver et al., 2004). In this way, such studies have highlighted the potential importance of the epigenome for understanding how experiences may be incorporated at a biological level and the possible implications that this plasticity has for intervention (Champagne, 2010). Interestingly, there has been some demonstration using animal models of the ability to improve developmental trajectories, not only by means of pharmacology but also by manipulation of the social and physical environment. Animal studies of environmental enrichment, for example, have been able to reverse the heightened neuroendocrine and emotional reactivity effects of maternal deprivation on offspring (Francis, Diorio, Plotsky & Meany, 2002), and also reverse cognitive deficits among offspring who received low levels of postnatal maternal licking and grooming (Bredy et al., 2003).

Results such as these from well-designed animal models are particularly compelling. However, insight into epigenetics remains very much in its infancy, particularly with regard to how well these findings apply to humans. We still do not know which particular experiences drive epigenetic variation or exactly what epigenetic responses are to the social environment. Nonetheless, this body of research makes clear once again that nature and nurture should not be considered separately. Rather, studies exploring the interplay between nature and nurture should consider these epigenetic effects since they could be implicated in the GxE discussed previously (Rutter, 2006).

MEASURES OF THE ENVIRONMENT SHOW HERITABILITY

An interesting – and at the time unexpected – finding from behaviour genetic studies that has subsequently been widely replicated, is that measures of the environment also show heritability. That is to say, when environmental measures such as parenting, the home environment or the peer group are used as the dependent variable, a significant proportion of the variance in these can be explained by genetic influence. Since environments do not possess genes, this heritability reflects the phenomenon of gene-environment correlation (rGE) – the process by which an individual's genotype correlates with, or influences, their environment. Fundamentally, this means an association between an environmental measure and a child outcome may not reflect a direction of

causation that is exclusively environmental (Plomin et al., 2013). Rather, an individual's own genetically influenced behaviour impacts on the environment. There are three ways by which genetic factors have been hypothesised to correspond to individual differences in experience; passive, active and evocative rGE (Box 4). These are hypothesised to be causal influences, however it should be remembered that correlation does not necessarily imply causation.

BOX 4: TYPES OF GENE-ENVIRONMENT CORRELATION

Passive: Children passively inherit genes from their parents and the effects co-vary with their family environment. E.g. if conduct problems are heritable, a child with conduct problems is likely to have parents who provide them with both the genes and the environment conducive to the development of conduct problems.

Evocative: Individuals evoke reactions from others on the basis of their genetic propensities. E.g. A child with conduct problems may behave in ways that evoke harsh parenting.

Active: Individuals select or construct experiences based on their genetic propensities. E.g. A child with conduct problems may seek out conflict with their parents and other individuals.

(See Scarr & McCartney, 1983)

Evidence suggests that genetic influences are pervasive and modest to moderate in impact across a range of environmental measures including significant life events, marital quality, peer interactions, social support and parenting behaviour (Kendler & Baker, 2007). Such estimates tend to fall within the range of 7% to 39% (with most lying between 15% and 35%). The prevalence of rGE poses the possibility of an alternative explanation for apparent 'environment-outcome' associations; rather than there being a true environmental link, this may be accounted for by common genes. For example, research exploring the impact of maternal depression on child psychological development, which has focused on mothers' parenting and the mother-child relationship as a mediator of this association, has consistently been carried out using biologically related mothers and offspring. Given that such individuals share around 50% of their genes, the observed association may be explained by the genes shared by mother and offspring. This hypothesis can be tested using genetically sensitive research designs, such as adoption studies, because these control for the genetic overlap between parent and child. In the instance of maternal depression, utilising this design has shown that common genes do not explain the association with child psychopathology and thus the link is in fact due to environmental reasons (Tully, Iacono, & McGue, 2008). Similarly, Harold et al (2012) used a genetically sensitive design to explore the role of harsh parenting in explaining the link between inter-parental conflict and child antisocial behaviour. They concluded that common genes could not explain this association, since harsh parenting explained the link for

both genetically related and unrelated parent-child pairings. On the contrary, research utilising an adoption design to investigate the association between parental alcoholism and impulsive adolescent behaviour revealed that this association existed only for biological offspring, suggesting that genes common to the parent and child did explain the link (King et al., 2009).

Parenting behaviour: Of all the environmental influences on children's outcomes, parenting – including both parental feelings and parental discipline strategies (also known as parental control) – has been a particular focus and behaviour genetic research has demonstrated that measures of parenting show significant heritability (rGE). This heritability may reflect genetically informed characteristics of the parent (passive rGE) but may also reflect genetically informed characteristics of the child who is being parented (evocative and active rGE). Indeed, the notion of parenting being an interactive, bidirectional process is well established (e.g. Bell, 1968) but, typically, the influence parents have on their child's development has been emphasised most by developmental psychology. Behaviour genetic designs can provide insight into the contribution of both parent and child characteristics to parenting behaviour. Child-based twin designs, such as the classic twin design described in Section 1, measure the extent to which child twin pairs are parented the same. The extent to which MZ twins are parented more similarly than DZ twins is indicative of genetically influenced characteristics of the child (such as their temperament) having an influence on the parenting they receive – that is, evocative and active rGE. Parent-based twin designs, on the other hand, compare the parenting behaviour of adult twin pairs. The extent to which the parenting behaviour of MZ twins is more similar than that of DZ twins is indicative of genetically influenced parental characteristics influencing their parenting (see Box 5 for further details of parent-based twin designs).

Child-based twin studies have been most commonly utilised and have yielded interesting findings. For example, reviews of the literature have consistently highlighted that measures of parental feelings (e.g. negativity, hostility and warmth) tend to yield moderate heritability estimates compared to parental control, where heritability is much lower (e.g. Kendler & Baker, 2007; Klahr & Burt, 2014; Plomin 1994; Rowe, 1981, 1983). This suggests that children's genetically influenced characteristics may be more important for eliciting parental feelings, than for parental control.

A recent meta-analysis that separately explored mothers' and fathers' parenting found that children's genetic influences on maternal control and negativity were significantly larger than on paternal control and negativity. Conversely, fathering was influenced to a greater extent by shared environmental factors than was mothering. This finding lends support to a differentiated view of mothering and fathering, and suggests that their foundations of parenting may be distinct; mothers

may be more sensitive and responsive to the individual characteristics of their children, whereas fathers may be more influenced by family-wide factors such as the couple relationship (Klahr & Burt, 2014).

BOX 5: THE CHILDREN OF TWINS DESIGN

This 'parent-based' twin design involves pairs of adult twins and their children. As it is the parents who are twins, this method focuses on influences that stem from the parent (passive rGE), whereas the traditional child-based twin design (as described in Box 1) focuses on influences that stem from the child (evocative and active rGE).

As with the methodologies previously described, the children of twins design is based on the varying genetic relatedness between the family members involved. The quirk of this design is that the offspring of MZ twins are as genetically related to their parents' co-twin (their aunt or uncle) as they are to that parent (genetic correlation being 0.5 compared to 0.25 for DZ offspring. It is this that enables the distinction between genetic and environmental transmission.

Comparing the intra-familial correlations for the parent and child phenotypes of interest enables inferences to be drawn about genetic influence:

- The difference between MZ and DZ avuncular correlations (those between aunt/uncle and niece/nephew) indicate possible mechanisms of intergenerational transmission.
    - If correlations are significantly higher in MZ than DZ families, then genetic influence is inferred (since there is greater genetic relatedness between the offspring of MZ twins and their parent's co-twin compared to DZ twins).
    - If there are no significant differences between MZ and DZ families, then this suggests there is no genetic transmission.

- If the parent-child correlations are larger than the respective avuncular correlations, this implies there is an effect of the parent phenotype on the offspring phenotype that is over and above familial confounding.

The children of twins design can be extended to include a sample of children who are twins, which then allows the effects of children on parents, as well as parents on children, to be explored. This extended design provides a useful means for disentangling passive rGE from evocative and active rGE.

For a comprehensive discussion of the children of twins design and a systematic review of studies, see McAdams et al., (2014).

The distinction between parental feelings and parental control is well established, however, an interesting finding has been reported when a further distinction is made – that between positive and negative parental feelings (e.g. warmth compared to hostility) and between positive and

negative parental control (e.g. remaining firm compared to physical discipline). Heritability has been found to be greater for the negative aspects of parenting (mean estimate = 44%) than for the positive aspects (mean estimate = 12%) (Oliver, Trzaskowski, & Plomin, 2014) regardless of whether parental feelings or control strategies were considered. This pattern of findings, which was evident at child age 9, 12 and 14, suggests that children's genetically influenced characteristics are more important for eliciting negativity than positivity from their parents. When considering child effects on parenting, it is important to distinguish between harsh parenting and maltreatment. Jaffee et al., (2004), sought to test the limits of child effects on parental behaviour, ranging from corporal punishment to abusive physical maltreatment. These authors found that while harsh discipline was moderately genetically influenced (25%), physical maltreatment was not (7%). This suggests that children's genetic influences are largely irrelevant for their vulnerability to maltreatment – rather, it is characteristics of the adult that are important here.

These results therefore indicate the influence of children's genetically informed characteristics – to a greater or lesser extent – on the parenting they receive. Child-based twin studies, such as those described above, provide evidence of rGE but do not enable researchers to disentangle passive from evocative and active types. This can be done by incorporating a parent-based design as well. This is because (as Table 2 summarises) finding significant heritability and/or environmental influence infers a different conclusion regarding the type of rGE at play, depending on whether a child- or parent-based design has been used.

To be clear, in a child-based design, the children are the twins and so finding significant heritability reflects genetic influences of the child on parenting (evocative & active rGE). Whereas, in a parent-based design, the adults are the twins and therefore finding significant heritability reflects the genetic influence of the parents on parenting (passive rGE). For environmental influences, in a child-based design, finding significant shared environmental influence is indicative of passive rGE (i.e. parents provide genes to both twins, which correlates with the environment they provide). Whereas, in a parent-based design, shared or non-shared environmental influence is indicative of evocative & active rGE (i.e. genetic influences from the child).

Table 2 Reproduced from Neiderhiser et al., (2004); Expectations for genetic and environmental influences on parenting given different types of rGE and child-based and parent-based designs

GE Correlation	Child-based design	Parent-based design
Passive rGE	shared environmental	genetic
Evocative & active rGE	genetic	shared and/or nonshared environmental
None	shared and/or non-shared environmental	shared and/or nonshared environmental

A recent meta-analysis combined 27 child-based and six parent-based designs to explore the types of rGE in three domains of parenting - warmth/acceptance, control and negativity (Klahr & Burt, 2014) . They found that child-based designs yielded moderate heritability across the three parenting domains (ranging from 23-40%) thereby offering confirmation of the importance of evocative and active rGE in parenting (the child is selecting or evoking their parenting based on their genetically influenced characteristics). Child-based designs also indicated the significance of the shared environment, which in this design indicates a role for passive rGE (children passively inherit genes from their parents which correlate with the parenting environment) thereby suggesting an influence of parent's genetic characteristics too (to the extent that they create similarities in parenting across children). Results from parent-based designs were less consistent across the three parenting domains but do augment these conclusions; heritability estimates were moderate for parental warmth and negativity (28-37%) which indicates a role of passive rGE but did not make any significant contribution to parental control. Furthermore, non-shared environment accounted for the largest proportion of variance for each of the three parenting domains which, in a parent based design, indicates evocative and active rGE – that is, genetically influenced effects of the child on the parenting they receive.

Together, child- and parent-based designs provide evidence of the existence of gene-environment correlation in parenting behaviours. This does not mean however that parenting is any less susceptible to intervention. Instead, the finding of evocative rGE provides insight in to a possible target for intervention – parenting interventions may benefit from having a specific element that supports the parents (and especially the mother) to understand the effect that the child's behaviour is having on their parenting and help teach them more adaptive parenting responses. In this way

recognising the bidirectional nature of parenting and focusing not only on the parent but recognising evocative characteristics in the child too. Furthermore, as Klahr & Burt (2014) note, the presence of evocative rGE raises the possibility that the observed consistency of negative parenting across generations may be partially due to the intergenerational consistency in child characteristics and not exclusively due to learning processes. That is, genetically related parents and offspring often exhibit similar behaviours which may evoke similar parental responses, which is repeated over generations. The task for research is now to identify the particular genes and the particular child behaviour that evokes particular parenting behaviour to help elucidate the mechanisms through which genetic effects influence parenting behaviour, this will also facilitate more specific interventions.

This section has thus illustrated some key overarching findings from the behaviour genetic literature, which together suggest that individual differences in a wide variety of traits and behaviours – including those that are important for children's future outcomes – are influenced by environmental (non-genetic) factors, genetic factors as well as complex interplay between the two. Such research has, however, moved far beyond simply partitioning the variance into that which is environmental and genetic, to include exploration of these patterns of influences across development, their contribution to stability and change in behaviours and increasingly towards attempts to identify the specific biological processes, genes and specific environments involved. In doing so, a greater understanding of the interaction between genes and environment has been achieved providing potentially valuable insights into ways that intervention may be most effective. Nonetheless, as recognised there are substantial limits to our existing knowledge about these complex processes which present a continuing challenge for scientists in this field.

Section 3: Considerations for the interpretation of behaviour genetic research findings

Having presented three key overarching findings that have emerged from the behaviour genetic literature using some examples from twin, adoption and molecular genetic studies, it is necessary to highlight some important issues that have arisen in their interpretation. Section 3 will firstly consider in more detail the core assumptions of the twin and adoption designs, with the purpose of highlighting ways in which these may be violated and the impact of such violations on estimations of genetic and environmental influence. Secondly, the matter of 'missing heritability' will be discussed, recognising the challenge this presented to the field and exploring its explanations.

ASSUMPTIONS AND BIAS OF TWIN AND ADOPTION DESIGNS

The twin and adoption designs used by behaviour geneticists each have their own assumptions and biases which should be carefully considered when interpreting the findings. The core assumptions of each are outlined below (for a more detailed discussion see Plomin et al., 2013 and Rutter, 2006).

Twin design

Equal Environments Assumption (EEA): As section 1 described, the premise of the twin design is that greater similarity of MZ twins compared to DZ twins is indicative of genetic influence on that trait. However, in order to make this inference it is assumed that any contrast between MZ and DZ twins is genetically, rather than environmentally, mediated and therefore it assumes that the environmental influences on the trait are no more and no less similar for both twin types. This is what is known as the equal environments assumption.

The assumption may therefore be violated if (a) MZ twin environments are *more* similar than that of DZ twin environments which influences a greater phenotypic similarity between them and also (b) if MZ twin environments are *less* similar than DZ twin environments such that this influences reduced phenotypic similarity between them. In circumstances of the former, the twin design will overestimate genetic influence whereas in circumstances of the latter, the twin design will underestimate genetic influence.

It is commonly assumed that is that EEA must surely be untenable – after all, it seems fairly obvious that MZ twins are more likely to be treated the same and may seek more similar experiences.

However, there are two important points to note about this. Firstly, this in itself does not necessarily violate EEA if this is genetically driven. For instance, if MZ twins are treated more similarly because they are genetically identical and therefore look and behave more similarly than DZ twins for genetic reasons, this does not violate the EEA as the similarity is genetically rather than environmentally mediated – in fact, this this is the very basis of the twin design. Secondly, for the assumption to be violated, any greater similarity in environments must be associated with the phenotype of interest. That MZ twins are dressed identically more than often than DZ twins, for example, does not in itself violate the EEA unless it results in greater similarity in the phenotype under study – let's say for example, IQ. In this instance it seems unlikely, though it demonstrates the point that EEA should be assessed with regard to the specific phenotype.

Instances in which MZ twin environments may be *less* similar than DZ environments such that phenotypic similarity is decreased may be less apparent. An example would be the larger difference in birth weight that is more common in MZ twins than DZ twins. This is often the result of MZ twins sharing a placenta (not all MZ twins do, in some cases the placenta divides) which can cause one twin to receive a greater blood supply than the other. Once again, however, only when this has an impact on the phenotype being studied would there be a risk to the EEA and it is noted by Rutter (2006) that these instances are indeed very minor.

In addition to these two scenarios described, there is an important point regarding gene-environment correlation (rGE) that is also relevant here. Because twin designs assume that any contrast between MZ and DZ twins is genetically rather than environmentally mediated, in circumstances where there is a strong genetic effect on an environmental variable (rGE) that in turn has effects on a phenotype, it is argued that EEA will to some degree be violated. To illustrate, it has been shown that there are genetic effects on children's exposure to negative parenting, an environmental factor that is associated with antisocial behaviour. However, within an MZ twin pair – despite being genetically identical – the twin who receives most negative parenting typically shows most antisocial behaviour therefore some of the difference in similarity between MZ and DZ twin pairs will be environmentally explained (Rutter, 2006). Accordingly, twin studies may overestimate heritability. Although it is very difficult to quantify by how much, Rutter (2006) has argued that it is unlikely to drastically change the overall conclusions of twin studies.

Rather than coming to one single overall conclusion regarding whether or not the equal environments assumption of the twin design is plausible, it is necessary for it to be considered on a trait by trait basis. Tests of EEA in respect of in psychiatric illness (Kendler, Neale, Kessler, Heath, & Eaves, 1993), children's aggression (Derks, Dolan, & Boomsma, 2006) as well as personality and

intelligence ((Matheny, Wilson, & Dolan, 1976; Plomin, Willerman, & Loehlin, 1976) have concluded that the environmental influence on these traits are not more or less similar for MZ or DZ twins, thus the assumption is not violated.

Adoption design

Assume non-selection of placement: The ability of adoption designs to untangle nature and nurture as causes of familial resemblance is based on the assumption that there is no selective placement of adoptive children. Of course, the process of adoption means that some element of selection is undertaken – typically families are screened to ensure, as far as possible, that they are able to provide good quality parenting for example – however a violation of this assumption would only be introduced if children were placed with adoptive families that are systematically matched with their biological families. For example, if children from biological parents with high intelligence were matched with adoptive parents of high intelligence; or children of biological parents with antisocial behaviour problems were matched to adoptive parents with antisocial behaviour problems. Whilst especially unlikely in this latter example, these examples illustrate how selective placement would inflate the similarity between adopted child and adoptive parent which would cause an overestimation of shared environment and underestimation of genetic effects. It is possible to statistically control for the effects of selective placement in the analysis of adoption data, by including in the model the correlation between the adoptive family and biological family on the trait of interest to partial out its effects.

Gene-environment interplay: By separating genetic influence from rearing environmental influence, adoption designs remove passive gene-environment correlation (e.g. parents providing both genetic and environmental risk). Whilst this has its advantages in terms of separating our nature and nurture, it also means that the proportion of the population who have genetic and environmental risk will be much smaller and therefore to the extent that genetic effects operate through gene-environment interaction, adoptee designs will underestimate genetic effects (Rutter, 2006).

Both designs

Assumption of random mating: Both twin and adoption studies assume random mating. Non-random mating (known as 'assortative mating') is indicated by a significant correlation of phenotypes between partners – for example, a significant correlation between couples' IQ scores. Assortative mating presents a problem for twin and adoption designs as it affects heritability

estimates by increasing correlations between first-degree relatives (Plomin et al., 2013). Specifically, in twin designs, positive assortative mating increases the genetic resemblance between DZ twins and therefore results in an upward bias of shared environment and a downward bias of heritability. In adoption designs it can cause two difference outcomes. Firstly, assortative mating in the biological parents would increase the genetic similarity between parents and offspring to more than 50% (assuming that genes influence the behaviour) which would inflate the genetic estimate. And/or secondly, assortative mating in the adoptive parents can cause adoptive parents to provide an environment more supportive of the trait than if only one parent had it (assuming that environment influences the behaviour) which would yield an overestimate of environmental influence (DiLalla, 2002). Although there is some positive correlation between spouses for physical characteristics, these are fairly low (around 0.2 for height) and even lower for personality (0.1 – 0.2 range) but notably higher for intelligence and education level (0.4 and 0.6 respectively) (Plomin & Spinath, 2004). For these reasons, it is important that behaviour genetic studies control for the effects of assortative mating in order to reduce the bias that this may otherwise introduce.

Generalisability: Traditional behaviour genetic research relies on particular samples – twins and adoptive families – and, as with any research, it is important to consider the extent to which their results can be generalised to the wider population. For twin designs, specific concerns relate to differences between twins and singletons, including the higher rate of pre- and peri-natal complications for twins – for example, shorter gestation, lower birth weight, delayed language. If the range of environmental influences in the twin sample is restricted in any way then genetic influences may be overestimated. Similarly, samples used by adoption designs may differ to the general population; adoptive parents are often better educated, of higher SES and have lower rates of psychopathology (at least at the time of the adoption). Furthermore, biological parents of adopted children likely contain a disproportionately large proportion of individuals with genetic risk characteristics and the adopted children themselves may differ from non-adoptive children – for example, receiving less-optimal pre-natal care. Once again, if the range of environments in adoption designs is restricted then environmental effects will be underestimated.

Like any scientific method, both twin and adoption designs therefore have their limitations which are important to the interpretation of their results. When considering how robust their findings are, comparing those of twin and adoption designs can help determine whether the findings may have been influenced by these assumptions and biases. To the extent that adoption and twin study results are similar, it is more likely that they reflect true influences of genes and environment.

However to the extent that they share similar biases, their findings may still be biased in the same direction and so does not rule out this possibility (Rhee & Waldman, 2002). Behaviour genetic researchers have been careful to consider and take the necessary steps to meet the methodological criticisms levied on it and these studies largely produce the same message as earlier, more problematic ones (Rutter, 2006). Furthermore, the relative plausibility of other explanations should be considered; none of the findings are compatible with there being zero genetic effect, nor with an explanation that genetic influence entirely explains individual differences and nor that the environment accounts for everything either. For these reasons it would seem a mistake to conclude that the limitations of the twin and adoption designs prevent any firm inferences about the strength of genetic and environmental influences being possible.

MISSING HERITABILITY

As has been detailed in section 2, traditional studies using twins and adoptees have repeatedly yielded heritability estimates indicating that a substantial proportion of the variance in complex traits (like intelligence and aggression) can be explained by differences in individuals' genetic make-up. This, together with scientific advances making it possible to estimate genetic influence using DNA of unrelated individuals (thus no longer needing to reply on traditional samples) provided an optimistic impetus for molecular studies (see Box 6) to identify the relevant genes involved.

These attempts to identify genetic influence on complex traits at the molecular level have, despite the initial optimism, turned out to be far more difficult than anticipated as the effects found have been extremely small. This disparity with the larger heritability estimates of twin/adoption designs has been termed the 'missing heritability problem' (Maher, 2008). Since it seems likely that that many genes are having small effect, it has been suggested that aggregating the effect of many genes into 'polygenic scores' (Box 6) will be of most use to developmental researchers (Plomin & Simpson, 2013). GWA Studies have identified over 1,200 genetic variants that are associated with over 165 common traits and diseases (Zuk, Hechter, Sunyaev, & Lander, 2012) however even when numerous genetic variants have been associated with a trait, individually and combined these have still typically only explained a very small amount of heritability – sometimes only around 1% (Plomin, 2013). More recently, research utilising the technique of GCTA (Box 6) has yielded much higher estimates that come much closer to the heritability estimated by traditional designs. For example, an aggregate effect of SNPs was found to explain 22% to 46% of the differences in childhood IQ (Benyamin et al., 2014) though, interestingly, a study exploring children's behaviour problems did not produce higher estimates (Trzaskowski, Dale, & Plomin, 2013). Thus, for some phenotypes the

'missing heritability' has been notably reduced, though not completely closed. (For critiques of the GCTA method, the interested reader is referred to Kumar, Feldman, Rehkopf, & Tuljapurkar, 2016; Turkheimer, 2016b).

BOX 6: MOLECULAR GENETIC STUDIES OF COMPLEX TRAITS

Candidate gene studies: These look for associations between pre-specified genes and the phenotype of interest. The candidate gene(s) are usually selected on the basis of existing knowledge of the gene's biological function and hypotheses about its involvement in the phenotype.

Genome-wide association studies (GWA): These take a 'hypothesis-free' approach and examine hundreds of thousands of DNA variants across the genome to see if any are associated with the phenotype of interest. Studies typically focus on a particular type of DNA marker – common frequency single-nucleotide polymorphisms (SNPs).

There have been several approaches to GWA studies:

- Identify single SNPs that are significantly associated with a trait.
- Aggregate SNP risk scores (including those that individually may fall below statistical significance). This approach is known as polygenic scores.
- Use all SNPs (not just those above or just below statistical significance) and assess the degree of similarity between pairs of unrelated individuals and use this to predict their phenotypic similarity. This approach is known as genomic-relationship-matrix restricted maximum likelihood (or GREML) and sometimes referred to as genome-wide complex trait analysis (GCTA).

(See Marian, 2012 and Wray et al., 2014 for a more detailed discussion)

This issue of missing heritability prompted some thought-provoking questions; on the one hand regarding the accuracy of the original estimates – did twin and adoption studies generate misleadingly high heritability estimates? And on the other hand, about the methodology of GWA studies – were sample sizes hugely underpowered to detect small effects? Or is a greater scrutiny of the genes required than the use of SNPs allows? However, these miss a fundamentally important point – the heritability estimates arising from twin and adoption studies and those arising from GWA studies using SNPs are not the same (Thapar & Harold, 2014). So, crucially, it is not a straight forward comparison of 'like with like'. To be specific, these GWA studies are limited to capturing the additive effects of causal genetic variants targeted by common SNPs, they do not for example capture genetic effects that may arise through such processes including epistasis, copy number variants and interaction. As such, their estimates of genetic influence reflect the very lower limit of the 'narrow-sense' heritability of traditional designs and, because of this, are expected to be comparatively somewhat lower. There is some optimism that advances enabling low-cost whole genome wide sequencing presents the opportunity to 'find' more of this 'missing' heritability as it

enables the identification of DNA sequence variation of every kind throughout the genome, rather than just the common SNPs that have largely been relied on to date. Thus, identifying many more genes with small effect has the potential for the creation of 'bigger and better' polygenic scores that can be used by developmental researchers make predictions of children's genetic propensities (Plomin 2013).

Conclusion

Behaviour genetic research using twin and adoption designs seeks to understand population-level individual differences in behaviour and traits by partitioning the variance into that explained by genetic and environmental factors. Over the course of the last three decades findings from such studies have consistently highlighted the importance of genes (heritability) *and* the environment, as well as the interplay between them. The pervasiveness of heritability has been particularly notable and has been the source of much misunderstanding, not least the misconception that it precludes the possibility of environmental intervention. It has been demonstrated herein that highly heritable traits and behaviours are no less amenable to intervention than those that show lower heritability and, therefore heritability in itself has no direct implication for the possibility of successful intervention.

However, to conclude from this that behaviour genetic research has nothing to offer the field of intervention would be a mistake, its findings are certainly very relevant to its theory and practice. Heritability has, for example, highlighted that correlations between biologically-related individuals can not necessarily be taken as evidence of sociocultural causal mechanisms (Turkheimer 2016). This has shed light on possible alternative explanations for the development of traits and behaviour important for children's outcomes as also being influenced by genes common to both parent and offspring. Furthermore, the relevance of gene-environment interaction for those interested in intervention has been highlighted. The notion of 'differential susceptibility' is particularly pertinent since it indicates the potential for the environment to not only exacerbate, but also reduce an individual's genetic risk. It posits that not all individuals will respond to intervention in the same way – some may have more success for certain individuals than others, and indeed this is supported by experimental study designs. Increased knowledge therefore of *which* genes and *which* environments interact to produce variations in phenotypic outcomes, as well as the mechanisms underlying *how* this interaction occurs will facilitate an improved understanding of what works for whom. In this lies the potential to better tailor interventions to individuals.

The translation of behaviour genetic findings to its practical application of informing intervention thus requires moving from the use of twin and adoption studies (that indicate genetic influence at a population level) to molecular genetic research that implicates specific genes and specific neuro-biological systems. Despite initial optimism, the latter has been neither quick nor straightforward. However, the field of molecular genetics has experienced enormous technological and methodological advances; it is anticipated that continued advances enabling low-cost whole genome

sequencing will drive this search for ‘many genes of small effect’ in to a new and exciting phase. Those interested in intervention are certainly advised to ‘watch this space.’

Glossary

Active gene-environment correlation Individuals select or construct their experiences that are correlated with their genetic propensities.

Additive genetic effects Genetic effects that add up across the loci.

Aetiology The cause or origin of a behaviour, disease or disorder.

Alleles Forms of the same gene with small differences in the sequence of their DNA bases

Candidate gene studies A molecular genetic approach that looks for associations between pre-specified genes and the phenotype of interest. The candidate gene(s) are usually selected on the basis of existing knowledge of the gene's biological function and hypotheses about its involvement in the phenotype.

Children of twins design A twin design study which utilises adult pairs of twins and their children.

Dependent variable The measured outcome of interest.

Dizygotic (DZ) twins Twins that develop from two different eggs that are each fertilised by separate sperm cells. These twins share on average 50% of their segregating genes – the same as ordinary full siblings. Also known as non-identical and fraternal twins.

Dominance A relationship between the alleles of a gene in which the effect of one allele on a phenotype dominates over (and therefore masks) the contribution of another. A dominant allele produces the same phenotype regardless of whether one or two copies are present.

DNA methylation A chemical process in which genes can be silenced or 'switched off.'

DNA sequence The order of base pairs that specifies what is inherited.

Effect size The size of the estimate or effect in the population.

Evocative gene-environment correlation Individuals evoke reactions from others on the basis of their genetic propensities.

Epistasis Interaction between alleles in different loci that contributes to non-additive genetic effect.

Epigenetic Changes that are heritable but do not change the DNA sequence.

First degree relative An individual's parent, sibling or child.

Gene The basic unit of heredity. Genes are made up of DNA and act as instructions to make proteins. Individuals have two copies of each gene, one inherited from each parent.

Gene-environment correlation (rGE) Individual's genetic propensities often correlate with particular environments and experiences.

Gene-environment interaction (GxE) A genetic sensitivity or susceptibility to a particular environments such that the effect of genes on a particular behaviour may depend on an environment and the effect of an environment on a particular behaviour may depend on the individuals' genes.

General cognitive ability (g) (also known as general intelligence) A construct originally proposed by Charles Spearman, derived from psychometrics that summarises the positive correlations between individuals' performance on different cognitive tasks. IQ scores are frequently regarded as estimates of g.

Genetic determinism The belief that genes determine behavioural phenotypes to the exclusion of environmental influence.

Genome-wide association studies (GWA) A molecular genetic approach that examines hundreds of thousands of DNA variants across the genome to see if any are associated with the phenotype of interest.

Genotype An individual's collection of genes. It may also refer to an individual's combination of alleles at a particular locus.

Heritability An effect size statistic that quantifies the proportion of phenotypic variance that is accounted for by genetic differences (relative to environmental differenced) between individuals. Heritability can be 'narrow' which includes only additive genetic factors, or 'broad' sense which also includes non-additive genetic effects.

Intervention An educational programme or practice aimed at improving outcomes.

Laws of inheritance (described by Mendel) Gregor Mendel described in terms of discrete 'factors' (which become known as 'genes') that are passed from one generation to the next according to certain laws; 1) The law of segregation: There are two forms of a genes, known as alleles, and during gamete production these alleles separate. A sperm or egg will only carry one allele for each inherited trait, and at fertilisation these unite to form pairs in the offspring. 2) The law of independent assortment: Each allele segregates independently during the formation of gametes. 3) The law of dominance: some alleles are dominant and others are recessive, recessive alleles will be masked by dominant alleles.

Latent measures (of risk) A measure which is used to infer risk rather than a direct measure of it.

Longitudinal study A research design that involves repeated observations or measures of the same group of people over an extended period of time. Often used to track developmental trends or delayed outcomes.

Mediator A measured variable that explains (statistically accounts for) the relationship between two other variables.

Meta-analysis Quantitative method of systematically combining effect sizes from multiple studies investigating similar outcomes in order to derive the most meaningful answer to a specific question. Effect sizes are statistically combined to calculate a meta-effect size.

Molecular genetics The field of biology and genetics that investigates the effects of specific genes at the DNA level.

Monozygotic (MZ) twins (Identical twins) Twins that develop from the fertilization of one zygote that splits to form two embryos. These twins share 100% of their segregating genes.

Non-additive genetic effects Genetic effects that occur through epistasis and dominance.

Non-shared environment Environmental influences that result in differences between family members.

Passive gene-environment correlation Offspring passively inherit genes from their parents and the effects covary with their family environment.

Phenotype An observed behaviour or trait that is measured separately for each individual.

Polygenic trait A trait that is influenced by many (as opposed to single) genes.

Polymorphism The occurrence of two or more alleles at the same locus.

Quantitative genetics The partitioning of population phenotypic variance and covariance into genetic and environmental components using twin and adoption designs.

Randomised Control Trial (RCT) A study design in which participants are randomly assigned to either one or more treatment groups and a control group to determine the efficacy of a treatment. The use of randomisation ensures that known or unknown confounding factors are evenly distributed across intervention groups.

Shared environment Environmental influence that result in similarities between family members.

Single gene disorders Inheritance of a single gene is necessary and sufficient to cause the disorder in offspring.

Systematic review Use of consistent and transparent methods to systematically search for, appraise and summarize all of the published information surrounding a specific topic.

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