Chapter 2
ADHD and Genetics: A Consensus Reconsidered

Jay Joseph


Attention deficit hyperactivity disorder (ADHD) illustrates psychiatry’s transformation of childhood misbehavior into medical diagnosis, as seen in a 2002 ‘Consensus Statement on ADHD’ by Russell Barkley and more than 80 other ADHD researchers (Barkley et al., 2002). For a response to the Statement, see Timimi et al., (2004). In their Statement, Barkley et al. claimed that there is ‘no disagreement’ among ‘scientists who have devoted years, if not entire careers’ to the study of ADHD, that it is a ‘real medical condition’. Twin studies were said to have provided evidence that ADHD is ‘primarily inherited’, and that the importance of genetic factors influencing deficits in attention and inhibition are ‘nearly approaching the genetic contribution to human height’. Barkley et al. went on to claim that one (unnamed) gene ‘has recently been reliably demonstrated to be associated with this disorder’, and that ‘the search for more is underway by more than 12 different scientific teams worldwide at this time’.

By 2008, however, concerted worldwide efforts have failed to discover the genes presumed to cause ADHD and other major psychiatric disorders. It was expected that such genes would have been found in the current ‘post-genomic era’. However, they have not been found. This has led to sobering assessments by psychiatric geneticists Kenneth Kendler and Peter Propping, who have based their careers on the argument that important genetic factors underlie psychiatric disorders. In 2005, Kendler concluded, ‘The strong, clear, and direct causal relationship implied by the concept of “a gene for…” does not exist for psychiatric disorders. Although we may wish it to be true, we do not have and are not likely to ever discover “genes for” psychiatric illness’ (Kendler, 2005, p. 245).

Whereas genetics may be promising in the near future (Barkley, 1998, p. 250), the current evidence of the genetic theories of ADHD disorder suggests that the prefrontal lobe genetic theories are not cross-validating each other.

Reviewers of the genetic theories of ADHD disorder suggest that ‘the search for more is underway by more than 12 different scientific teams worldwide at this time’ (Barkley et al., 2002, p. 58).

In this chapter, I will discuss the current status of the research on the genetics of ADHD disorder. The research suggests that the genetic theories of ADHD disorder are not cross-validating each other. The evidence of the genetic theories of ADHD disorder suggests that the prefrontal lobe genetic theories are not cross-validating each other.

ADHD family studies

Research suggests that ADHD is inherited. However, the evidence of the genetic theories of ADHD disorder is not cross-validating each other. The evidence of the genetic theories of ADHD disorder suggests that the prefrontal lobe genetic theories are not cross-validating each other.

ADHD family studies

Research suggests that ADHD is inherited. However, the evidence of the genetic theories of ADHD disorder is not cross-validating each other. The evidence of the genetic theories of ADHD disorder suggests that the prefrontal lobe genetic theories are not cross-validating each other.

ADHD family studies

Research suggests that ADHD is inherited. However, the evidence of the genetic theories of ADHD disorder is not cross-validating each other. The evidence of the genetic theories of ADHD disorder suggests that the prefrontal lobe genetic theories are not cross-validating each other.
tics: A sidered

Illustrates psychiatry’s medical diagnosis, as by Russell Barkley kley et al., 2002. For 2004). In their State disagreement among areers’ to the study of a studies were said to y inherited’, and that fiscts in attention and contribution to human (unnamed) gene ‘has iated with this disor 
dy by more than 12

Kendler, 2005, p. 1250). And in the same year, Propping wrote, ‘Whereas genetically complex traits are being successfully pinned down to the molecular level in other fields of medicine, psychiatric genetics still awaits a major breakthrough’ (Propping, 2005, p. 2). Thus, the field of psychiatric genetics may be approaching a period of crisis.

Barkley has written elsewhere that ADHD is a ‘developmental failure in the brain circuitry that underlies inhibition and self-control’ (Barkley, 1998, p. 67), which he linked to genetic factors. Comings et al. (2005, p. 13) also cited genetics in support of brain dysfunction theories of ADHD, writing, ‘the finding that ADHD is a genetic disorder suggests the defective genes involved cause a dysfunction of the prefrontal lobes’. Thus, like other areas in psychiatry, questionable genetic theories and brain dysfunction theories of ADHD continue to cross-validate each other.

Reviewers of ADHD research often discuss the perceived importance of genetic factors, which they cite in support of a ‘predisposition-stress’ (diathesis-stress) model of causation. This model holds that ADHD is caused by an inherited predisposition combined with exposure to environmental triggers. However, Breggin and others have stressed the primacy of environmental factors and have questioned the validity of the ADHD diagnosis itself, seeing it as a label justifying the use of drugs to control children’s behaviour (see Breggin, 1998, 2001a, 2001b; see also DeGrandpre, 1999; Leo, 2002).

In this chapter I will argue that genetic theories of ADHD, a diagnosis already of questionable validity, rest on very shaky foundations. In the process, I will show that the research cited in support of these theories is flawed on several critical dimensions rarely discussed in scientific papers, in the media, in textbooks, in scholarly reviews, or in popular works.

ADHD family studies

Research suggests that ADHD-type behaviours, like most human behaviours, tend to cluster in families (Biederman et al., 1986; Biederman et al., 1995; Biederman et al., 1990; Cantwell, 1972; Faraone et al., 1991; Morrison and Stewart, 1971; Nichols and Chen, 1981; Welner et al., 1977). However, although ADHD-type behaviour may be familial in the sense that it ‘runs’ or clusters in families, we cannot determine whether this clustering is caused by the greater genetic resemblance of family members, since families also experience
similar environmental factors. As schizophrenia genetic researchers Gottesman and Shields (1982, p. 69) have written, ‘that a disease is familial does not necessarily imply that it is genetic. Familial clustering can also be transmitted through culture, infectious sources, or learning.’ And more recently, ADHD genetic researchers Faraone and colleagues (2005, p. 1313) observed that ‘family studies cannot disentangle genetic from environmental sources of transmission’. I agree with these assessments.

Twin research

Researchers’ understanding that the familial clustering of ADHD can be explained on environmental grounds led them to seek other methods to determine whether genetic factors play a role. According to Faraone and colleagues (2005, p. 1313), ‘adoption and twin studies are needed to determine whether genes account for the familial transmission of a disorder’.

All ADHD twin studies have used the ‘classical twin method’ (more commonly known as ‘the twin method’). This research technique compares the resemblance of reared-together MZ twins (also known as monozygotic or identical twins; who share 100 per cent genetic similarity), versus the resemblance of reared-together same-sex DZ twins (also known as dizygotic or fraternal twins; who share an average 50 per cent genetic similarity). Based on the assumption that both types of twins experience the same kinds of environments, known as the ‘equal environment assumption’ or ‘EEA’, twin researchers argue that a statistically significant higher concordance rate (which means that both twins are affected) or correlation of MZ versus same-sex DZ twins is caused by the greater genetic resemblance of the former. There have been no studies of ‘reared-apart’ ADHD twins.

Although the twin method depends on additional assumptions, the equal environment assumption has been the main area of contention between twin researchers and their critics. From the development of the twin method in the mid 1920s, until the early 1960s, twin researchers defined the EEA – without qualification – as the assumption that MZ and DZ twins share the same types of behaviour-influencing, physical, and treatment environments. I have called this the ‘traditional EEA definition’ (Joseph, 2004a). However, as most twin researchers now concede, the evidence clearly shows that MZ twins spend more time together, more often have the same friends, are treated more similarly by parents and others, and so forth (Kendler, 1983; Joseph, 2004).

In the face of such evidence, twin researchers attempt to disentangle the genetic factors. Instead, the equal environment assumption (EEA) is renamed the EEA as (Carey and DiLalla, 2005). When researchers discuss twin studies, they refer to the traditional EEA as the ‘trait relevant’ sense EEA.

By ‘trait relevant’, t

<table>
<thead>
<tr>
<th>Table 2.1</th>
<th>Trait relevant EEA</th>
</tr>
</thead>
<tbody>
<tr>
<td>The ‘traditional EEA’ definition</td>
<td></td>
</tr>
<tr>
<td>MZ twins and environments</td>
<td></td>
</tr>
<tr>
<td>‘Trait relevant’ EEA</td>
<td></td>
</tr>
<tr>
<td>MZ twins and environments</td>
<td></td>
</tr>
</tbody>
</table>

The traditional trait relevant EEA assumes that MZ twins are equally influenced by environments that are relevant to the trait under study.
a genetic researchers ten, 'that a disease is
enetic. Familial clus-
infectious sources, or
earchers Farone and
ly studies cannot dis-
transmission'. I agree
stering of ADHD can
 to seek other meth-
a role. According to
ption and twin stud-
count for the familial
l twin method' (more
search technique com-
twins (also known as
 per cent genetic simi-
er same-sex DZ twins
 share an average 50
 that both types of
 s, known as the 'equal
chers argue that a sta-
ch means that both
same-sex DZ twins is
re former. There have
litional assumptions,' the
 main area of con-
icts. From the devel-
until the early 1960s,
qualification – as the
me types of behaviours.
I have called this
a). However, as most
early shows that MZ
 the same friends, are
and so forth (Kendler,
1983; Joseph, 2004a, 2006). Moreover, MZs share a closer emotional
bond than DZs, and more often view themselves as being two halves
of the same whole (that is, they experience what some psychologists
call 'identity confusion'; see Ainslie, 1985; Jackson, 1960).
In the face of such evidence, twin researchers should have recog-
nized that the twin method – just like a family study – is unable
to disentangle the potential influences of genetic and environmen-
tal factors. Instead, while belatedly recognizing that MZ twins do
indeed experience more similar environments than DZs, some twin
researchers attempted to rescue the twin method by redefining the
equal environment assumption. Behaviour geneticists and others have
renamed the EEA as the 'equal trait-relevant environment assumption'
(Carey and DiLalla, 1994), referred to here as the 'trait-relevant EEA'.
According to Kendler and his colleagues, who define the EEA in the
'trait relevant' sense:

The traditional twin method, as well as more recent biometrical
models for twin analysis, are predicated on the equal-environment
assumption (EEA) – that monozygotic (MZ) and dizygotic (DZ)
twins are equally correlated for their exposure to environmental
influences that are of etiologic relevance to the trait under study
[emphasis added]. (Kendler et al., 1993, p. 21)

By 'trait relevant', twin researchers mean aspects of the environment
that have been shown to contribute to the psychiatric disorder in ques-
tion. For example, exposure to trauma contributes to post-traumatic
stress disorder. Table 2.1 outlines the two current definitions of
the EEA.

<table>
<thead>
<tr>
<th>Table 2.1</th>
<th>The two definitions of the equal environment assumption (EEA) used by contemporary twin researchers</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>The 'traditional' EEA definition</strong></td>
<td>MZ twins and same-sex DZ twins experience equal environmental influences</td>
</tr>
<tr>
<td><strong>The 'trait relevant' EEA definition</strong></td>
<td>MZ twins and same-sex DZ twins experience equal environmental influences that are of etiologic relevance to the trait under study</td>
</tr>
</tbody>
</table>
Proponents of the trait-relevant EEA recognize that MZ twins experience more similar environments than DZs, but argue (e.g., Bouchard, 1993, 1997; Lyons et al., 1991) or imply (e.g., Kendler, 1983) that critics of the twin method bear the burden of proof for demonstrating that MZ and DZ twins experience dissimilar trait-relevant environments. However, it has been observed that ‘a basic tenet of science is that the burden of proof always falls squarely on the claimant, not the critic… Consequently, it is up to the proponents of these techniques to demonstrate that they work, not up to the critics of these techniques to demonstrate the converse’ (Lilienfeld et al., 2003, p. 3).

Thus, twin researchers bear the burden of proof for demonstrating that the greater environmental similarity of MZ versus same-sex DZ twins does not completely explain the common finding that MZs are more concordant for psychiatric disorders than are same-sex DZs. Several twin researchers (e.g., Hettema et al., 1995; Kendler, 1983) have argued that the twin method is supported by a body of empirical ‘EEA test’ research. However, it has been shown elsewhere (Joseph, 2006; Pam et al., 1996) that these studies do little to uphold the validity of the EEA and the twin method. Indeed, most twin researchers performing EEA test studies found that MZs experience much more similar environments than same-sex DZs (e.g., LaBuda et al., 1997; Loehlin and Nichols, 1976; Morris-Yates et al., 1990; Scarr and Carter-Saltzman, 1979).

It is noteworthy that Kendler and other twin researchers do not require critics to identify ‘environmental influences that are of etiologic relevance to the trait under study’ to invalidate genetic interpretations of family studies. In this case they recognize that, because family members share a common environment as well as common genes, family studies are unable to determine whether genetic factors are operating. Arbitrarily, contemporary twin researchers who define the EEA in the trait-relevant sense apply the trait-relevant requirement to the twin method, but not to family studies.

Therefore, despite previous attempts to redefine or test the EEA, the simple fact that MZ twins experience more similar environments and treatments than DZs invalidates genetic interpretations of MZ–DZ comparisons, for the same reason that genetic interpretations of family studies are invalid. There is no reason, therefore, to accept that the twin method measures anything other than the more similar environments of MZ versus DZ twins, and all conclusions in favour of genetic influences on psychiatric disorders (including ADHD) derived from the twin method must be disregarded (Joseph, 2004a, 2006).

ADHD twin studies

Nevertheless, twin studies in support of a gene (p. 68), twin studies can contribute that MZ twins are for ADHD-type bel than 20 ADHD twin 2002; Edelbrock et Heiser et al., 2006; 1965; Saudino et Willcutt et al., 2000

Although most A resemblance for AD (2002) defined the majority of studies researchers other th:ions supporting the all but one group o: on the traditional a: twins are equal, yet environments are ac:

An example of AI EEA are Thapar an

traditional sense:

The basic premis (MZ) twins are go share on average :cally influenced tr: DZ twins, assum: the same extent [e the MZ correlat order to be great p. 106)

Thapar et al. ask on ADHD on the and DZ twins share researchers in other
hat MZ twins experi-
argue (e.g. Bouchard,
ndler, 1983) that crit-
of for demonstrating
tent-relevant environ-
ics tenet of science is
in the claimant, not the
of these techniques to
p 3).
finding that MZs are
versus same-sex DZ
Kendler, 1983) have
of empirical ‘EEA
where (Joseph, 2006;
told the validity of the
researchers performing
more similar envi-
1997; Loehlin and
and Carter-Saltzman,
researchers do not
that are of etiologic
interpretations
factors are operate-
the EEA in
requirement to the twin

sh the EEA, similar environments
interpretations of MZ-
etic interpretations of
therefore, to accept that
more similar en-
ning ADHD) derived

ADHD twin studies

Nevertheless, twin studies constitute the most frequently cited evidence in support of a genetic basis for ADHD. According to Barkley (1998, p. 68), twin studies furnish ‘the most conclusive evidence that genetics can contribute to ADHD’. Twin research has found consistently that MZ twins are more concordant for ADHD, or correlate higher for ADHD-type behaviours, than same-sex DZ twins. To date, more than 20 ADHD twin studies have been published (e.g. Cronk et al., 2002; Edelbrock et al., 1995; Gilger et al., 1992; Gillis et al., 1992; Heise et al., 2006; Hudziak et al., 2003; Levy et al., 1997; Lopez, 1965; Saudino et al., 2005; Sherman et al., 1997; Thapar et al., 1995; Willcutt et al., 2000; Willerman, 1973).

Although most ADHD twin studies found greater MZ versus DZ resemblance for ADHD or ADHD-type behaviours, only Cronk et al. (2002) defined the EEA in the trait-relevant sense. Moreover, the majority of studies failed to mention the EEA, and no ADHD twin researchers other than Cronk et al. cited previous research or publications supporting the validity of the EEA. Thus, implicitly or explicitly, all but one group of ADHD twin researchers based their conclusions on the traditional assumption that the environments of MZ and DZ twins are equal, yet only Gillis and associates (1992) argued that these environments are actually equal.

An example of ADHD twin researchers who argue in support of the EEA are Thapar and colleagues, who defined the twin method in the traditional sense:

The basic premise underlying twin research is that monozygotic (MZ) twins are genetically identical, whereas dizygotic (DZ) twins share on average 50% of their segregating genes. Thus, for a genetically influenced trait or disorder, MZ twins will be more similar than DZ twins, assuming that MZ and DZ twins share environment to the same extent [emphasis added]. In simple terms, we would expect the MZ correlation...or concordance rate for a given trait or disorder to be greater than the DZ correlation. (Thapar et al., 1999, p. 106)

Thapar et al. ask us to conclude in favour of genetic influences on ADHD on the basis of the unsupported assumption that ‘MZ and DZ twins share environment to the same extent’, even as twin researchers in other areas of psychiatry have recognized that this is
not true (e.g. Kendler et al., 1993). Indeed, twin researchers Scarr and Carter-Saltzman (1979, p. 528) concluded more than 25 years ago that ‘the evidence of greater environmental similarity for MZ than DZ twins is overwhelming’.4

ADHD genetic researchers Hay, McStephen and Levy (2001) have written that, although identical twins ‘may well be treated more similarly than fraternal twins…this is far more a consequence of their genetic similarity in behaviour (and of ensuing responses by parents and others) than a cause of such similarity’. Like Kendler before them, who argued that ‘MZ twins might create for themselves more similar environments’ (Kendler, 1987, p. 706, emphasis in original), Hay and associates failed to understand that the reason MZ twins experience more similar environments than DZs is not relevant in assessing the validity of the twin method. For example, suppose that ADHD is caused solely by exposure to a toxic chemical. Because MZ twins spend much more time together than DZs, it is much more likely that both members of an MZ pair will be exposed to the chemical, and be subsequently diagnosed with ADHD, than it is that both members of a DZ pair will be exposed and diagnosed. However, even if MZs do indeed ‘create’ more similar environments than DZs because of their greater genetic similarity, it would be erroneous to conclude that higher MZ versus DZ concordance for ADHD is evidence that the condition has a genetic component. In this example – regardless of why MZs are together more often – higher MZ concordance is caused solely by MZs’ propensity to be together more often than DZs, which leads them to be more similarly exposed to the toxic chemical that causes ADHD.

Thus, in order to invalidate genetic interpretations of ADHD twin data – in the same way that we can invalidate genetic interpretations of ADHD family data (Hay et al., 2001, p. 12) – critics need only show that MZ and DZ environments are different.

Since the evidence overwhelmingly suggests that MZ twins are treated more alike, spend considerably more time together, and experience greater levels of identity confusion and closeness (Joseph, 2004a), we would expect MZ twins – on purely environmental grounds – to correlate higher than same-sex DZs on ADHD-related measures. Therefore, like ADHD family studies, ADHD twin studies are unable to disentangle the potential influences of genes and environment on ADHD-type behaviour.

As it turns out, MZ twins resemble each other more than same-sex DZs for most human behaviours, including many for which, intuitively, we would expect little if any genetic influence. For example,
researchers Scarr and Levine (1978) have be treated more sim-

ilar for MZ than DZ twins. And Levy (2001) have con-
sequence of their responses by parents Kendler before them, mselves more similar in original). Hay and MZ twins experience vant in assessing the the show that ADHD is more likely that both and, be subse-
cause of their greater member of a DZ en if MZs do indeed the condition has lude that higher MZ pate of why MZs are ause solely by MZs’ which leads them to h that causes ADHD. iions of ADHD twin genetic interpretations critics need only show that MZ twins are together, and experi-
ences (Joseph, 2004a, b), mental grounds – D-related measures. n studies are unable and environment on more than same-sex ny for which, intu-
tiveness. For example, twin method results have been used to claim important genetic influences on loneliness (Boomsma et al., 2005), the frequency of orgasm in women (Dawood et al., 2005), the results of the United States 2004 presidential election (Alford et al., 2005), perfectionism (Tozzi et al., 2004), and breakfast eating patterns (Keski-Rahkonen et al., 2004). Twin research in psychiatry, and in ADHD in particular, merely repeats the error of assuming that the greater resemblance of MZ versus same-sex DZ twins is the result of the former’s greater genetic relationship, when a plausible alternative explanation holds that MZ’s greater environmental similarity completely explains such results.

ADHD adoption research

Critics have argued for three generations that genetic theories in psychiatry are flawed because family and twin studies are confounded by environmental factors, and that we can draw no valid conclusions in support of genetics from the results of these studies. Psychiatric adoption studies were pioneered in the 1960s in order to eliminate these potential confounds. In theory, an adoption study is able to disentangle possible genetic and environmental influences on psychiatric disorders because adoptees receive their genes from one family, but are raised in the environment of another family.

Psychiatric geneticists Seymour Kety, David Rosenthal, Paul Wender, and their Danish associates published their first schizophrenia adoption studies in 1968 (Kety et al., 1968; Rosenthal et al., 1968). Their work was based on adoptions taking place in Denmark, and they had access to registers containing information on adoptions, and on people who had been admitted to a psychiatric facility. Kety and colleagues undertook this research on the basis of their astute observation that the evidence from schizophrenia family and twin studies was ‘inconclusive’, because ‘it fails to remove the influence of certain environmental factors… In the case of monozygotic twins it has been pointed out that such individuals usually share a disproportionate segment of environmental and interpersonal factors in addition to their genetic identity’ (Kety et al., 1968, p. 345). Thus, adoption studies would not be necessary if, as proponents of the twin method claim, MZ–DZ comparisons provided unequivocal evidence in support of genetics.

While the logic of adoption studies might appear straightforward, the most important psychiatric adoption studies contained important methodological problems and were subject to several biases (Heston,
1966; Kety et al., 1968, 1975, 1994; Rosenthal et al., 1968, 1971; Tienari et al., 1987, 2003, 2004; Wender et al., 1974. For critical reviews of schizophrenia adoption research, see Boyle, 2002; Cassou et al., 1980; Jackson, 2003; Joseph, 2004a, 2004b, 2006; Lewontin et al., 1984; Lidz, 1976; Lidz and Blatt, 1983; Lidz et al., 1981; Pam, 1995). Despite numerous flaws, however, schizophrenia adoption research possessed two qualities not found in ADHD adoption research: (1) the researchers made diagnoses blindly; and (2) the researchers studied or had psychiatric records for adoptees’ biological relatives.

The ‘adoptive parents’ method

As of this writing, ADHD adoption studies have been published by Alberts-Corush et al. (1986), Cantwell (1975), Morrison and Stewart (1973), Safer (1973), Sprich et al. (2000), and van den Oord et al. (1994). The results of these studies are frequently cited in textbooks, review articles, and scientific papers as supporting genetic theories of ADHD.

Because of the difficulty in obtaining the carefully guarded records of adoptees’ biological families, which the Danish and American researchers were able to obtain through their access to national registers, the authors of the most frequently cited ADHD adoption studies had to rely on the ‘Adoptive Parents’ method, which Wender and colleagues (1968) developed in the 1960s. The Adoptive Parents method compares the psychiatric status of three (and sometimes four) types of families as follows:

1. **BH (Biological Hyperactive)**. This group consists of non-adopted children diagnosed with ADHD who are reared in the homes of their biological parents.
2. **AH (Adoptive Hyperactive)**. This group consists of adopted children diagnosed with ADHD who are reared by adoptive parents, with whom they share no genetic relationship.
3. **BN (Biological Normal)**. This group typically consists of non-adopted normal (non-ADHD) children who are reared by their biological parents, and is designated as a control group.
4. **AN (Adoptive Normal)**. The AN control group consists of adoptees having no record of ADHD or related diagnoses, who are reared by their adoptive parents. (Only Alberts-Corush and colleagues utilized this group.)

The authors of the...
The authors of the four Adoptive Parents studies (Alberts-Corush et al., 1986; Cantwell, 1975; Morrison and Stewart, 1973; Sprich et al., 2000) assessed resemblance for ADHD among the relatives of groups 3 or 4 listed above. However, they had no information on their ADHD adoptees’ biological relatives.

In fact, no ADHD adoption study has investigated the biological relatives of adopted-away children, meaning that their authors were unable to make direct comparisons between the biological and adoptive relatives of the same child. Kety and colleagues’ schizophrenia adoption studies diagnosed the same adoptee’s adoptive and biological relatives, whereas the ADHD Adoptive Parents studies compared diagnoses in a group consisting of adopted-away ADHD children and their adoptive families (AH), versus a group consisting of the families of other ADHD children living with their biological parents (BH).

Unfortunately, ADHD genetic researchers usually fail to discuss the severe limitations of the Adoptive Parents design unless compelled to do so by critics (for example see Faraone and Biederman, 2000, 2002). Too often, they fail to state clearly that researchers were unable to study adoptees’ biological relatives, and sometimes write in potentially misleading ways about ADHD adoption research (Joseph, 2006). For example, Faraone and Biederman (2000, p. 57) wrote that a ‘testable psychosocial theory’ must be able to explain ‘the elevated rates of ADHD and associated traits among the biological relatives of adopted away ADHD children’, implying (incorrectly) that researchers obtained data on these biological relatives. And in a subsequent review article in which he discussed ADHD adoption research, Faraone (2004, pp. 305–6) wrote, ‘By examining both the adoptive and biological relatives of ill probands, one can disentangle genetic and environmental sources of familial transmission.’ This was the logic of Kety’s schizophrenia adoption studies. However, no ADHD adoption study has examined the ‘adoptive and biological relatives’ of the same ‘ill’ adoptees. Authoritative ADHD experts such as Barkley (2003, p. 117) then write for a larger audience in technically accurate, yet potentially misleading ways: ‘Cantwell . . . and Morrison and Stewart . . . both reported higher rates of hyperactivity in the biological parents of hyperactive children than in the adoptive parents of such children.’

Most reviewers and textbook authors have overlooked another important limitation of the Adoptive Parents model, which is that adoptive parents constitute a population screened for mental health as part of the adoption process. They are – by definition – a group
in which we would expect to find fewer psychiatric disorders than in the general population. Thus, as behaviour geneticist Michael Rutter and his colleagues (Rutter et al., 1990, p. 15) pointed out, low rates of psychological disturbance among adoptive parents in ADHD adoption studies ‘could be no more than an artifactual consequence of the tendency to select mentally healthy individuals as suitable adopting parents’. Elsewhere, Rutter and colleagues (2001, p. 298) noted, ‘Although claims are often made that adopting parents are typical of the general population . . . manifestly they are not’, and that adoption studies in psychiatry ‘are markedly constrained by the fact that adopting families are not representative of the general population and, in particular, involve a markedly restricted range of adverse rearing environments’ (p. 301).

Therefore, the Adoptive Parents method’s comparison of diagnoses among two groups of relatives— one in which parents are screened for psychopathology (AH), and another in which parents are not screened for psychopathology (BH)—provides no support for genetic theories of ADHD.

Yet another issue in ADHD adoption research is evidence that adoptees as a population are more likely than non-adoptees to receive an ADHD diagnosis (Deutsch, 1989; Deutsch et al., 1982). If true, this casts further doubt on ADHD adoption researchers’ already extremely shaky conclusions. If adoptees and non-adoptees constitute different populations with respect to ADHD, it would be difficult to generalize findings of an ADHD adoption study to the non-adoptive population. Although adoption researchers usually do not address this, many adopted children are psychologically scarred on the basis of having been abandoned by their primary caregivers. Thus, as Cassou and colleagues (1980) pointed out, a more evocative designation for adoption studies would be ‘the study of abandoned children’ (Les Études D’Enfants Abandonnés).

Having reviewed the individual ADHD adoption studies in detail elsewhere (Joseph, 2000a, 2002, 2006), I will merely list their main problems here. These include: (1) the researchers’ failure to study adoptees’ biological relatives; (2) researchers’ use of non-blinded diagnoses, which they sometimes make on the basis of relatives’ recollections; (3) inadequate definitions of ADHD; (4) researchers’ inability to control for environmental confounds; (5) researchers’ inability to control for the status of adoptive parents as a population screened for psychiatric disorders; (6) potential researcher bias; and (7) the use of late-separated adoptees.

Conclusions regard
The Adoptive Parer studies, provides n other reasons, it do atives. In addition, van den Oord et al. (Joseph, 2000a, 20 (2001, p. 228) re have few and Biederman (2000, j ies ‘relatively min of any inferences - methodological pro are actually massi

Heritability
The authors of textbook heritability of ADH heritable of psychia researchers arrive a difference. For exa at 0.50, twin resea. However, in additi validity of the twir, heritability est misleading (Joseph, The heritability s results of a selective 1949). However, as tability estimate (c relative contribution single-gene disorder by a dietary interven cannot determine ‘l attributable to gene environmental int heritability as high .

If we are to belie also believe the sa
Conclusions regarding ADHD adoption research

The Adoptive Parents method, used in four of the six ADHD adoption studies, provides no evidence in favour of genetics because, among other reasons, it does not assess the status of adoptees’ biological relatives. In addition, the two studies using other designs (Safer, 1973; van den Oord et al., 1994) are flawed on other important dimensions (Joseph, 2000a, 2006). Behaviour geneticists Plomin and colleagues (2001, p. 228) recognized that ADHD ‘adoption studies to date have been few and quite limited methodologically’. And Faraone and Biederman (2000, p. 570) acknowledged that ADHD adoption studies’ ‘relatively minor methodological problems... limit the strength of any inferences we can draw from these studies’. However, the methodological problems Faraone and Biederman dismissed as ‘minor’ are actually massive.

Heritability

The authors of textbooks and review articles frequently report that the heritability of ADHD is about 76 per cent, making it ‘among the most heritable of psychiatric disorders’ (Faraone et al., 2005, p. 1313). Twin researchers arrive at this figure by doubling the MZ–DZ correlation difference. For example, if MZs correlate at 0.90, and DZs correlate at 0.50, twin researchers would estimate heritability at 0.80 (80%). However, in addition to the fact that these estimates are based on the validity of the twin method’s untenable equal environment assumption, heritability estimates in psychiatry and psychology are potentially misleading (Joseph, 2004a, ch. 5; Moore, 2001).

The heritability statistic was developed in agriculture to predict the results of a selective breeding programme (Joseph, 2004a; Lush, 1945, 1949). However, as Hirsch (1997, 2004) has argued, a numerical heritability estimate (coefficient) is not a ‘nature–nurture ratio’ of the relative contributions of genes and environment, and ‘highly heritable’ single-gene disorders such as phenylketonuria (PKU) can be prevented by a dietary intervention. Thus, even if genes play a role in ADHD, we cannot determine ‘how much’ of the ‘ADHD phenotype’ variation is attributable to genes because, like PKU, a timely (and possibly simple) environmental intervention could prevent a condition with a stated heritability as high as 1.0 (100%).

If we are to believe that ADHD is ‘significantly heritable’, we must also believe the same about loneliness (48% heritability; Boomsma
et al., 2005), the frequency of female orgasms when masturbating (51% heritability; Dawood et al., 2005), breakfast eating patterns (approximately 60% heritability; Keski-Rahkonen et al., 2004), perfectionism (moderately heritable; Tozzi et al., 2004, p. 490), and political beliefs (32% heritability; Alford et al., 2005). These examples again point to the faulty conclusions one can reach about genetics on the basis of twin research and accompanying heritability estimates.

The presumed genetic basis of ADHD rests on the results of family, twin, and adoption studies. However, although research seems to indicate that ADHD is familial, the fact that families share a common environment as well as common genes permits no valid conclusions in support of genetics. In addition, we have seen that twin and adoption studies also fail to provide scientifically acceptable evidence in support of a genetic basis for ADHD.

ADHD molecular genetic research

Genetic interpretations of the family, twin, and adoption studies I have just outlined have laid the basis for molecular genetic investigations in ADHD. In the early stages of this research, investigators such Thapar and colleagues justified the search for ADHD genes as follows:

Overall, genetic factors have been shown to be important across a variety of studies. There is thus a compelling argument for now searching for susceptibility genes at a molecular level. (Thapar et al., 1999, p. 108)

More recently, Faraone and colleagues (2005, p. 1313) argued that ‘Family, twin, and adoption studies provide compelling evidence that genes play a strong role in mediating susceptibility to ADHD.’ Thus, the ongoing search for ‘ADHD genes’ is based on the assumption that the condition’s genetic basis has already been established. Interestingly, we will see that mathematical calculations used in some recent claims of gene findings are based on the very same questionable assumption.

As I have outlined previously (Joseph, 2006), the search for genes is based on mainstream psychiatry’s assumptions and beliefs about ADHD. These include: (1) that ADHD is a valid diagnostic category that can be reliably diagnosed; (2) that ADHD is a familial disorder; (3) that ADHD involves a malfunction of the brain; (4) that the greater resemblance of MZ versus same-sex DZ twins on ADHD-related measures is the result of the former’s greater genetic similarity; (5) that the results of ADHD factors; (6) that re: (7) that gene disco ADHD. However, s, and point 7 is de

Research methods

Molecular genetic association studies markers associate guineous family m rhythm of odds (LO linkage occurred t 3 (1000:1 odds in statistically signific chromosomal regic are unable to ident ies. A genome sca against a set of it known. A genome between these mar linkage regions on ses, which freque genome scans mal genes. Association ers among unrel are performed wit samples. A genetic able physical locat followed.

There are two: ADHD and other p tance, in which a t by a single domin: researchers now be a single gene (Comi Gizer, 2006). The s genes of varying el addition to unspec for several genes,
when masturbating
fast eating patterns
et al., 2004), pers-
2004, p. 490), and
2005). These exam-
reach about genetics
reliability estimates.
the results of fam-
research seems to
ies share a common
valid conclusions in
and adoption
vidence in support

option studies I have
eic investigations in
icators such Thapa-
es as follows:
be important across
argument for now
level. (Thapar et al.,

1313) argued that
elling evidence that
t ADHD.’ Thus,
the assumption that
lished. Interestingly,
some recent claims
nable assumption.
s search for genes
 and beliefs about
dagnostic category
familial disorder;
(4) that the greater
ADHD-related me-
nilarity; (5) that the
results of ADHD adoption studies suggest the importance of genetic
factors; (6) that researchers possess the technology to find genes; and
(7) that gene discoveries would aid in the treatment or prevention of
ADHD. However, there is little evidence supporting points 1, 3, 4, and
5, and point 7 is debatable.

Research methods

Molecular genetic researchers use linkage studies, genome scans, and
association studies. In a linkage study, researchers search for genetic
markers associated with a presumed disease gene among consan-
guineous family members. Findings are often represented as a loga-
ithm of odds (LOD) score, which expresses the probability that the
linkage occurred by chance. In general, an LOD score higher than
3 (1000:1 odds in favour of linkage) is necessary in order to claim
statistically significant linkage. Linkage studies attempt to identify
chromosomal regions where relevant genes might be located, but they
are unable to identify actual genes. This is the task of follow-up stud-
ies. A genome scan analyses the complete genome of an individual
against a set of markers whose positions on the chromosomes are
known. A genome scan looks for common patterns of inheritance
between these markers and the disease characteristics, and identifies
linkage regions on the chromosomes. Unlike typical linkage analy-
ses, which frequently are based on hypothesized ‘candidate genes’,
genome scans make no assumptions about the possible location of
genes. Association studies compare the frequency of genetic mark-
ers among unrelated affected individuals and a control group, and
are performed with population-based case-control, or family-based
samples. A genetic marker is a segment of DNA with an identifiable
physical location on a chromosome, whose inheritance can be
followed.

There are two main types of theorized genetic transmission for
ADHD and other psychiatric disorders. The first is Mendelian in-
heritance, in which a trait or disorder is passed from parents to off-
spring by a single dominant, recessive, or sex-linked gene. However, most
researchers now believe that it is very unlikely that ADHD is caused by
a single gene (Comings et al., 2005; Faraone et al., 2005; Waldman and
Gizer, 2006). The second is polygenic inheritance, meaning that many
genes of varying effect sizes are believed to contribute to ADHD, in
addition to unspecified environmental factors. Investigators then look
for several genes, or individual genes thought to have a large-sized
effect. According to one group of genetic researchers, ‘The evidence suggests that ADHD is primarily a polygenic disorder involving at least 50 genes’ (Comings et al., 2005, p. 3). As a critic pointed out, however, ‘The argument that ADHD is “mediated by many genes acting in concert” is rather circular in that it is based primarily on the complete failure of molecular genetic studies to find such genes and replicate those findings’ (Pittelli, 2002, p. 496).

Cause and effect

ADHD is frequently put forward as a ‘multifactorial complex disorder’, meaning that there is a complex interacting admixture of multiple genes and multiple environmental risk factors’ (Rutter, 2001, p. 227). This is consistent with the previously discussed ‘predisposition-stress’ model of ADHD. However, the idea that ADHD is a complex disorder is merely a theory, not a fact. Psychiatric conditions such as ADHD remain ‘complex disorders’ even after initial gene-finding efforts come up empty, while subsequent gene-finding failures are explained on the basis of the ‘complex’ nature of the ‘disorder’. Circular reasoning of this type is seen in a 2003 review of autism research, where the authors wrote that the ‘current lack of success in finding genes for autism is similar to that of complex diseases’ (Volkmar and Pauls, 2003, p. 1136). In fact, the ‘lack of success’ in finding genes is currently a defining feature of ‘complex disorders’ in psychiatry.

However, even if a gene is associated (correlated) with ADHD, it still doesn’t mean that the gene contributes to its causation. For example, there is a strong correlation between having a Y chromosome and being the chief executive officer (CEO) of a Fortune 500 corporation. Yet, this does not mean that having a Y chromosome causes or predisposes someone to become a CEO. Most likely, the correlation is the result of social privileges granted to people with Y chromosomes (men) rather than the action of the chromosome itself. Furthermore, even if a gene is necessary for ADHD to appear, it still doesn’t necessarily mean that the gene is a causative factor. As Ratner (2004, p. 30) pointed out, ‘The fact that something is a necessary foundation for something does not mean that it causes it.’

Yet another problem is that, like twin and adoption studies, molecular genetic research depends on the acceptance of questionable assumptions. This is manifest not only in the investigators’ decision to perform this research, but also because they factor assumptions about genetics into mathem to McGuffin (2004, requires several assur than just multiple sn assuring genetic hon the disorder is know have written, ‘The n we must specify the ADHD molecular gc computer analyses of genetic transmissi on is occurring? Tl in psychiatry in gen example of question mature conclusion t (subsequently non-r false assumptions a calculations.

The fruitless search

Like other areas of gene-finding claims cation attempts hav 1998 Plomin and F associated with beh to be identified.’ Ar genetics textbook, I that ‘ADHD is ont genes have been id 2005 Plomin recog psychiatry and psyc When are we goin psychiatry?] Bein would be forgive before… A sma ment about the QTLs [genes of decided that we behav gen
hers, ‘The evidence involving at least pointed out, how-
many genes acting in
torial complex dis-
k factors’ (Rutter, ed) with ADHD, it
es even after initial sion studies, molecu-
questionable assump-
assumptions about
genetics into mathematical models of familial transmission. According to McGuffin (2004, p. 179), ‘Unfortunately, conventional linkage requires several assumptions. These are that major gene effects (rather than just multiple small gene effects) exist, that there is some way of assuring genetic homogeneity, and that the mode of transmission of the disorder is known.’ And Faraone and colleagues (1999, p. 131) have written, ‘The main drawback of the LOD score method is that we must specify the mode of genetic transmission.’ Thus, although ADHD molecular genetic researchers test multiple genetic models in computer analyses of their findings, all models assume that some type of genetic transmission is occurring. But what if no genetic transmission is occurring? The large number of false positive linkage findings in psychiatry in general, and ADHD in particular, may be another example of questionable assumptions leading researchers to the premature conclusion that genetic factors (or actual genes) exist. Their (subsequently non-replicated) results may be influenced by factoring false assumptions about genetic transmission into their LOD score calculations.

The fruitless search for ADHD genes

Like other areas of psychiatry, there have been a plethora of ADHD gene-finding claims in the past ten years. However, subsequent replication attempts have failed to confirm these claims. For example, in 1998 Plomin and Rutter (p. 1223) wrote optimistically that ‘Genes associated with behavioural dimensions and disorders are beginning to be identified.’ And in the fourth edition of their 2001 behavioural genetics textbook, Plomin, DeFries, McClearn, and McGuffin claimed that ‘ADHD is one of the first behavioural areas in which specific genes have been identified’ (Plomin et al., 2001, p. 1). However, by 2005 Plomin recognized the ongoing failure of gene-finding efforts in psychiatry and psychology:

When are we going to be there [finding genes in child psychology and psychiatry]? Being an optimist, my response is ‘soon’. But readers would be forgiven for being skeptical because they have heard this before… A small personal example of impatience and embarrassment about the slower-than-expected progress towards identifying QTLs [genes of varying effect sizes] is that my co-authors and I decided that we would not write the next edition of our [2001] behavioural genetics textbook… until we had some solid DNA
results to present. The reason for this decision was that our 2001 edition had enthused about the field being on the cusp of a new post-genomic era in which DNA risk indicators would add great value to behavioural research. We are still on that cusp [emphasis added]. (Plomin, 2005, p. 1030)

This quotation shows, along with the statements by Kendler and Propping I quoted earlier, that at least three leading genetic researchers recognized in 2005 that no genes have been found that cause major psychiatric disorders such as ADHD.

Researchers currently focus on genes involved with the brain's dopamine receptors, which they view as candidate genes on the basis of an a priori hypothesis derived from neurochemical and neuropharmacological research (Asherson and Curran, 2001; Barr, 2001). The major areas of interest have been the DRD4 dopamine receptor gene, and the DAT1 dopamine transporter gene. In their 2000 response to my article on the genetics of ADHD (Joseph, 2000a), Faraone and Biederman (2000, p. 573) claimed that 'molecular genetic studies have implicated these two genes...in the etiology of ADHD'. However, although the original claims have found some support, several subsequent studies have failed to replicate an association between ADHD and the DRD4 or DAT1 genes (e.g. Bakker et al., 2005; Langley et al., 2005; Mill et al., 2005; Ogdie et al., 2003; van der Meulen et al., 2005). In a detailed 2006 survey of the evidence in support of DRD4, DAT1, and other candidate genes, Waldman and Gizer (2006, p. 421) concluded, 'It should be clear...that for each [ADHD] candidate gene studied, there is a mixed picture of positive and negative findings'.

Several complete genome scans have also failed to find consistently replicated evidence in support of regions harbouring suspected ADHD genes (Arcos-Burgos et al., 2004; Bakker et al., 2003; Fisher et al., 2002; Hebebrand et al., 2006; Ogdie et al., 2003). According to Faraone and colleagues, 'The handful of genome-wide scans that have been conducted thus far show divergent findings and are, therefore, not conclusive' (Faraone et al., 2005, p. 1319). It is generous to state that these results are 'not conclusive'. It would be better to conclude that these genome scans found no replicated evidence that genes have anything to do with ADHD.

ADHD genetic researchers have resorted to citing meta-analyses (combining previous research) in support of associations between ADHD and chromosomal regions (e.g. Faraone et al., 2001; Langley et al., 2004; Li et al.). I find this trend of genetic linkage study a manipulation of appear to be such: catecuted in genetic rest another 'ADHD gene discovered.

We have seen pro argue that, although been found, we 'ar and other genetic possibility that ADI their supporters in they have made, an wripe as if they wee the virus causing a socially disapproves questionable wheth behaviours.

Generally speaking gene findings. Thus genes, they often w are making 'enorm be identified', or th Plomin wrote in 2 and psychology ha for child psycholo as we move from cators in our reses; researchere wrote t pinnings of ADHD psychiatric genetics optimistic stateme genes.

In other cases, i have already been Barkley, 2003; Far: Kuntsi et al., 2006; psychiatric genetics although they cert
n was that our 2001
in the cusp of a new
ors would add great
that cusp [emphasis
ments by Kendler and
ug genetic researchers
and that cause major
red with the brain's
e genes on the basis
ical and neurophar-
1; Barr, 2001). The
amine receptor gene,
eir 2000 response to
000a), Faraone and
et genetic studies have
f ADHD'. However,
support, several subse-
between ADHD
; Langley
; van der Meulen
idence in support of
an and Gizer (2006,
ach [ADHD] can-
positive and negative
al to find consistently
spected ADHD
; Fisher et al.,
003). According to
ide scans that have
and are, therefore,
is generous to state
be better to conclude
ence that genes have
oting meta-analyses
associations between
et al., 2001; Langley
et al., 2004; Li et al., 2006). As Pittelli (2004, p. 1134) wrote, however,
I find this trend of using meta-analysis to resurrect largely negative
genetic linkage studies disturbing. It appears to be nothing more than
a manipulation of data to obtain a desired result.' It does indeed
appear to be such a manipulation, yet readers relatively unsophisti-
cated in genetic research and terminology may well conclude that yet
another 'ADHD gene' has been discovered. In fact, not one has been
discovered.

We have seen prominent genetic researchers such as Robert Plomin
argue that, although genes for ADHD and other disorders have not
been found, we ‘are on the cusp’ of gene discoveries. What Plomin
and other genetic researchers rarely consider in print, however, is the
possibility that ADHD genes do not exist. Psychiatric geneticists and
their supporters instead write optimistically about the great strides
they have made, and how ADHD genes will soon be identified. They
write as if they were searching for the cure of a deadly disease, or
the virus causing an epidemic. But ADHD is simply a grouping of
socially disapproved behaviours falsely passed off as a disease, and it is
questionable whether finding genes would do anything to ‘cure’ these
behaviours.

Generally speaking, these investigators substitute language for real
gene findings. Thus, when they scan the genome and find no ADHD
genesis, they often write that genes are ‘implicated’, or that researchers
are making ‘enormous advances’, or that genes are ‘just beginning to
be identified’, or that studies ‘suggest’ the finding of genes, and so on.
Plomin wrote in 2005 (p. 1030) that, although genes in psychiatry
and psychology have not been discovered, this is ‘an exciting time
for child psychology and psychiatry. The field will be transformed
as we move from finding genes to using them as genetic risk indica-
tors in our research and eventually in our clinics.’ And another
researcher wrote in the same year, ‘Uncovering the genomic under-
pinnings of ADHD is proving to be one of the most exciting stories in
psychiatric genetics’ (McGough, 2005, p. 1371). Ultimately, however,
optimistic statements cannot eliminate the necessity of finding actual
genesis.

In other cases, it is mistakenly implied that several ADHD genes
have already been identified (for example, see Asherson et al., 2005;
Barkley, 2003; Faraone, 2004, 2005; Goldstein and Schwebach, 2005;
Kuntsi et al., 2006; Pauls, 2005). The fields of behaviour genetics and
psychiatric genetics have a long history of gene discovery claims which,
although they certainly do produce headlines in the popular media,
invariably fail to be replicated (Joseph, 2006). As science writer John Horgan (2004) observed:

Over the past 15 years or so, researchers have announced the discovery of ‘genes for’ attention-deficit disorder, obsessive-compulsive disorder, manic depression, schizophrenia, autism, dyslexia, alcoholism, heroin addiction, high IQ, male homosexuality, sadness, extroversion, introversion, novelty seeking, impulsivity, violent aggression, anxiety, anorexia, seasonal affective disorder, and pathological gambling. So far, not one of those claims has been confirmed.

We can add to this list a 2006 study in which the investigators claimed to have identified a chromosomal region harbouring genes for ‘loneliness’ (Boomsma et al., 2006).

**Biological markers (endophenotypes)**

Biological markers in psychiatry (also known as ‘endophenotypes’), have been defined as ‘any neurobiological measure related to the underlying molecular genetics of the illness, including biochemical, endocrinological, neurophysiological, neuroanatomical, or neuropsychological markers’ (Egan et al., 2003, p. 277). For example, the results of a glucose tolerance test are a biological marker for diabetes. Gottesman and Shields introduced this concept into psychiatry in 1972, hoping that one day researchers would discover biological or behavioural markers for schizophrenia ‘which would not only discriminate schizophrenics from other psychotics, but will also be found in all the identical co-twins of schizophrenics whether concordant or discordant’ (Gottesman and Shields, 1972, p. 336). Three decades later, Gottesman wrote that because ‘multiple genetic linkage and association studies using current classification systems [such as the DSM] ... have all fallen short of success, the [endophenotype] term and its usefulness have reemerged ... Endophenotypes are being seen as a viable and perhaps necessary mechanism for overcoming the barriers to progress’ (Gottesman and Gould, 2003, p. 637).

Given the ongoing failure to find the genes presumed to underlie ADHD, researchers seek to identify biological markers in order to improve their ability to identify people who have the condition. A group of researchers investigating biological markers for ADHD believe that ‘traditional nosological categories described in the DSM-IV ... and ICD-10 ... are suboptimal when it comes to describing who is affected and call to “unravel the genetic landscape” on the description of ADHD (pp. 1242–3). In o have led some recent searches to search for possible markers for and colleagues (2006) in schizophrenia and other related phenotypes [e.g., between first-degree relatives of which is the more recent search for biologic gas and Risch (2007) based solely on cllers, still lack con and the reliability and the usefulness and calls into question studies.

Breggin has ob that require extra In fact, most DSM and ‘having diffic mal’ children (AP, and ‘ADHD’ child of these behaviou often forgetful in ‘ADHD endophen ‘ADHD’ children can a gene or biol and ‘often’ in a giv Researchers will beca use is caused by faulty ‘I am not convinced finding QTLs for v as autism, hyperac
is a science writer John

 announced the dis-

 obsessive-compulsive

 tism, dyslexia, alco-

 nosexuality, sadness,

 impulsivity, violent

 disorder, and patho-

 s has been confirmed.

 which the investigators

 harbouring genes for

 s ‘endophenotypes’),

 sure related to the

 cluding biochemical,

 omical, or neuropsy-

 277). For example,

 gical marker for dia-

 into psychiatr

 d discover biologi-

 hich would not only

 ecies whether con-

 1972, p. 336). Three

 ltiple genetic linkage

 ns [such as the

 phenotype] term and

 s are being seen as a

 ccoming the barriers

 presumed to under-

 markers in order to

 have the condition.

 markers for ADHD

scribed in the DSM-

es to describing who

 is affected and carrying susceptibility genes and who is not’, and that to ‘unravel the genetic constellation of ADHD, emphasis should be on the description of endophenotypes’ (Sluts-Willems et al., 2003, pp. 1242–3). In other words, years of fruitless gene-finding attempts have led some researchers to conclude that they must find better ways than the DSM to define ADHD. Several traits have been proposed as possible markers to be studied (Doyle et al., 2005; Waldman, 2005).

 However, if the DSM definition of a disorder is inadequate for gene searches, it is also inadequate for biological marker searches (Joseph, 2006). In schizophrenia research, molecular geneticists M. F. Egan and colleagues (2003, p. 280) wrote, ‘Most studies of intermediate phenotypes [endophenotypes] begin by looking for a difference between first-degree relatives and controls.’ But these are the first-degree relatives of people diagnosed with DSM-defined schizophrenia, which is the same faulty diagnostic scheme that necessitated the search for biological markers in the first place. According to Merikangas and Risch (2003, pp. 627–8), ‘Psychiatric disorder phenotypes, based solely on clinical manifestations without pathognomonic markers, still lack conclusive evidence for the validity of classification and the reliability of measurement.’ But if ADHD and other psychiatric diagnoses are of questionable validity and reliability, this alone calls into question the results of previous family, twin, and adoption studies.

 Breggin has observed that ADHD is ‘simply a list of behaviours that require extra attention from teachers’ (Breggin, 2001a, p. 203). In fact, most DSM diagnostic criteria, such as ‘fidgeting’, ‘forgetting’, and ‘having difficulty awaiting turn’ are found among most ‘normal’ children (APA, 2000, p. 92). The difference between ‘normal’ and ‘ADHD’ children, according to the DSM-IV-TR, is the frequency of these behaviours, denoted by the word ‘often’ (for example, ‘is often forgetful in daily activities’). Given these criteria, what type of ‘ADHD endophenotypes’ could we expect to find? If both ‘normal’ and ‘ADHD’ children exhibit symptoms, albeit in differing degrees, how can a gene or biological marker know the difference between ‘normal’ and ‘often’ in a given culture?

 Researchers will not be able to identify ‘ADHD biological markers’ because, unlike real diseases, there is little evidence that ADHD is caused by faulty biology. Even Plomin (2005, p. 1036) has written, ‘I am not convinced that endophenotypes will prove to be useful for finding QTLs for what are quintessentially behavioural disorders such as autism, hyperactivity, and reading disability.’ Thus, it is likely that
ADHD endophenotype research will soon arrive at the same impasse as ADHD molecular genetic research itself.

Is it necessary to find genes in order to study environmental factors?

Theoretically, the knowledge that children carry a genetic predisposition is useful to the extent that they can be helped to avoid environmental factors that might trigger ADHD. Thus, behaviour geneticists Hay and Levy (2001, p. 221) argued that if ‘early behaviour genetic markers’ or ‘molecular markers’ are discovered, ‘they will only be of real use if acceptable interventions are available’ while Cook (1999, p. 196) wrote that ‘as the genetic risks are determined, it may become more feasible to determine specific environmental risk factors in the context of identified genetic risk’. However, ‘early intervention’ strategies are complicated by the potential impact of knowing that a child carries genes for ADHD. This knowledge could, in itself, be a life-altering event, affecting how parents, classmates, teachers, and others treat a child. And even in the unlikely event that presumed ADHD genes are found in the future, society might still decide to concentrate on eliminating environmental factors contributing to ADHD-type behaviour. These interventions would be aimed at all children in the same way that an anti-smoking campaign, which does not target its intended audience by genotype, can help reduce tobacco use.

The future of ADHD molecular genetic research

Propping (2005, p. 6) put forward some explanations for the embarrassing number of false positive results in psychiatric molecular genetic research. Among these he mentioned ‘Premature publication because of competition pressure’, ‘Premature publication because of commercial interests’, ‘Selective publication of positive findings’, and the ‘Lower standard of investigators than in other fields’. Propping saw ‘selective publication of positive findings to be the most threatening one for our field’, and discussed the ‘danger that journals preferentially publish positive findings, because a silent coalition exists between author and editor: both are interested in publishing positive findings’.

For Plomin (2005, pp. 1032–3), a major factor in failed gene-finding attempts has been that the genes he believes underlie conditions such as ADHD are of much smaller sized-effect than previously believed, and that the ‘biggest effect’ of any particular gene is ‘not very big’. In his view, ‘Underpowered studies are likely to be responsible for the widespread failure to disorders, such as... called for the creation of tremendous samples of major QTLs of very small effect, and the discovery of genes, we be there? A major good reason to be there’.

In 2000 I predicted discovered, because... years later, I see little

Conclusions

The presumed genetic twin, and adoption models in that families share a permits no valid conclusion. The twin method than are family studies. MZ twins experience are the greater resemblance to ADHD-related fields.

ADHD adoption schizophrenia adoption no scientifically acce... no ADHD. Finally, des been unable to find it is unlikely that such... schizophrenia, bipol... towards environment... p. 60) point out, ‘Res... behaviours has... cause them.’ A major overlooked is the... in causing ADHD.
widespread failure to replicate linkages and associations for common disorders, such as... hyperactivity and the DRD4 and DAT genes'. He called for the creation of 'more powerful vehicles with bigger engines: Huge samples of many thousands of individuals are needed to detect QTLs of very small effect size'. Regarding the predicted future discovery of genes, we have seen Plomin ask, 'When are we going to be there?' A major goal of this chapter has been to show that there is good reason to believe, as the saying goes, that there is no there, there'.

In 2000 I predicted that ‘A gene (or genes) for ADHD will not be discovered, because it does not exist’ (Joseph, 2000b, p. 587). Several years later, I see little reason to modify this prediction.

Conclusions

The presumed genetic basis of ADHD rests on the results of family, twin, and adoption studies. Although ADHD may be familial, the fact that families share a common environment as well as common genes permits no valid conclusions in support of genetics.

The twin method is no less confounded by environmental factors than are family studies because, as most people clearly understand, MZ twins experience more similar environments than DZs. Therefore, the greater resemblance of MZ versus same-sex DZ twins for ADHD, or ADHD-related tests, is completely explainable on non-genetic grounds.

ADHD adoption studies are greatly inferior to the flawed schizophrenia adoption studies that preceded them, and therefore offer no scientifically acceptable evidence in favour of genetic influences on ADHD. Finally, despite concerted worldwide efforts, researchers have been unable to find presumed ADHD genes. As I have argued here, it is unlikely that such genes exist. Similarly, investigators searching for the genes presumed to cause other major psychiatric disorders such as schizophrenia, bipolar disorder, and autism, have also come up empty-handed (Joseph, 2006). Clearly, future research should be directed towards environmental factors. Unfortunately, as Timimi et al. (2004, p. 60) point out, 'Research on possible environmental causes of ADHD type behaviours has largely been ignored, despite mounting evidence that psychosocial factors such as exposure to trauma and abuse can cause them.' A major reason that environmental factors have been overlooked is the widespread belief that faulty genes play a role in causing ADHD. In this chapter, I have attempted to show that
there is little if any scientifically acceptable evidence supporting this belief.

Notes

1. However, in 2006 Kendler wrote, with more optimism, that ‘we are beginning to identify and replicate susceptibility genes for psychiatric disorders’ (Kendler, 2006, p. 1138).
2. Although most contemporary ADHD researchers understand that the results of family studies are explainable on environmental grounds, an author as influential as Russell Barkley (2003, p. 116) has written that ‘ADHD clusters significantly among the biological relatives of children or adults with the disorder, strongly implying a hereditary basis to this condition.’
3. Additional assumptions of the twin method include: (1) that there are only two types of twins, MZ and DZ; (2) that investigators are able to reliably distinguish between MZ and DZ twins; (3) that the risk of receiving the diagnosis is the same among twins and non-twins (generalizability); and (4) that the risk of receiving the diagnosis is the same among individual MZ twins as a population, versus individual DZ twins as a population.
4. Another example of contemporary researchers defining the EFA in the traditional sense include Kuntsi and colleagues (2006, p. 14), who wrote, ‘For shared environmental influences MZ and DZ twins are expected to correlate to the same extent.’
5. In ADHD adoption research, only Sprich et al. (2000) made blind diagnoses.
6. In their 1988 Annual Review of Psychology contribution, behaviour geneticists Loehlin, Willerman, and Horn (1988, p. 124) wrote, ‘We are witnessing major breakthroughs in identifying genes coding for some mental disorders.’ And 11 years before that, genetic investigators Julien Mendlewicz and John Rainer (1977, p. 327) claimed that ‘A genetic vulnerability to manic-depressive disorder has been demonstrated by family, twin, and linkage studies.’ Like ADHD, schizophrenia, and autism, however, manic-depression (bipolar disorder) genes remain undiscovered (Joseph, 2006).

References


Alford, J. R., Funk, T., Parental perceptions genetically
American Deficit Disorders
American Journal of Mental Disorders
American Psychiatric Association
Arcos-Burgos, M., Caskey, T., and D. Rapo
Barkley, J. A. (2004) Attention Linkage to loci at 4q
Asherson, P., and Cuen
Asherson, P., and Cuen
Asherson, P., and Cuen
Asherson, P., and Cuen
Asherson, P., and Cuen
Bakker, S. C., van der D. L., Monsuur, A.
Pearson, P. L., and Sib-sib pairs with atten
Genetics 72, 1251–6
Bakker, S. C., van der P. L., Buitelaar, J. K
polymorphisms are t
Journal of Medical 50–2.
The Guilford Press.
Barkley, R. A., Cook, I
ADHD, European C
Barr, C. L. (2001) Gen
adoamine D4 receptor
Adolescent Psychiat
Biederman, J., Faraone
Family-genetic and
order, Journal of the 29, 526–33.
Biederman, J., Faraone, Guite, J., Ablon, J.
evidence supporting this

mism, that ‘we are begin-
for psychiatric disorders’
ners understand that the
vironmental grounds, an
 p. 116) has written that
al relatives of children
editary basis to this
le: (1) that there are only
ators are able to reliably
the risk of receiving the
is (generalizability); and
same among individual
ins as a population.
in the EEA in the tra-
06, p. 14), who wrote,
ins are expected to
2000) made blind diag-
ontribution, behaviour
 p. 124) wrote, ‘We are
genes coding for some
etic investigators Julien
id that ‘A genetic vulner-
srusted by family, twin,
and autism, however,
undiscovered (Joseph,

Lincoln: University of
(1986) Attention and
itive parents of hyper-
al of Orthopsychiatry

Alford, J. R., Funk, C. L., and Hibbing, J. R. (2005) Are political ori-
etinations genetically transmitted? American Political Science Review 99,

of Mental Disorders, 4th edn, text revision. Washington, DC: American
Psychiatric Association.

Arcos-Burgos, M., Castellanos, F. X., Pineda, D., Lopera, F., Palacio, J. D.,
Palacio, J. D., Rapoport, J. L., Berg, K., Bailey-Wilson, J. E., and Muenke,
M. (2004) Attention-deficit/hyperactivity disorder in a population isolate:
Linkage to loci at 4q13.2, 5q33.3, 11q22, and 17p11, American Journal of
Human Genetics 75, 998–1014.

disorders and their application in child psychiatry and psychology, British

of attention-deficit hyperactivity disorder: A behavioral genomic approach,

Bakker, S. C., van der Meulen, E. M., Buitelaar, J. K., Sandkuijl, L. A., Pauls,
D. L., Monsuur, A. J., van ’t Slot, R., Minderaa, R. B., Gunning, W. B.,
sib pairs with attention-deficit/hyperactivity disorder: Suggestive evidence
for linkage on chromosomes 7p and 15q, American Journal of Human
Genetics 72, 1251–60.

Bakker, S. C., van der Meulen, E. M., Oteeman, N., Schelleman, H., Pearson,
polymorphisms are not associated with ADHD in Dutch families, American
Journal of Medical Genetics, Series B (Neuropsychiatric Genetics) 132B,
50–2.

 Barkley, R. A. (1998) Attention-deficit hyperactivity disorder, Scientific Amer-
ican (September), 66–71.

 Barkley, R. A. (2003) Attention-deficit/hyperactivity disorder, in E. Mash and
 R. Barkley (eds), Child Psychopathology, 2nd edn (pp. 75–143). New York:
The Guilford Press.

ADHD, European Child and Adolescent Psychiatry 11, 96–8.

dopamine D4 receptor gene, Journal of the American Academy of Child and
Adolescent Psychiatry 40, 118–21.

Family-genetic and psychosocial risk factors in DSM-III attention deficit
order, Journal of the American Academy of Child and Adolescent Psychiatry
29, 526–33.

 Biederman, J., Faraone, S. V., Mick, E., Spencer, T., Wilens, T., Kiely, K.,
for attention deficit hyperactivity disorder among children of parents


Edelbrock, C., Rende and competence and \textit{Journal of Child Ps}

Egan, M. F., Leboyer, \textit{types in genetic stt}


Faraone, S. V. (2005) \textit{deficit/hyperactivity disorder and Adolescent Psych}

Faraone, S. V., and Big and \textit{B hyperactivity disorder}

Faraone, S. V., and B. \textit{[Letter to the editors] Adolescent Psychiatry}

Faraone, S. V., Biedert \textit{gene study of gi}

Faraone, S. V., Doyle \textit{analysis of the assoc}
udy, American Journal of..., Autor, S., Hoge, S. K.,
one in Dutch twin... Behavior... & Cacioppo, J.
ns to loneliness in adults:... 745–52.
al influences on adult per-
and I. Deary (eds), B... Kluwer
ared apart: Findings and
enko (eds), Intelligence,
k: Cambridge University
ion? 2nd edn. Hove, UK:
e, ME: Common Courage
 in the era of biological
out the drug treatment of
ds), This is Madness Too:
p. 47–58). PCCS Books:
 families of hyperactive
 e children: Psychiatric ill-
D. Rosenthal, and H. Brill
0). Baltimore: The Johns
psychopathology: Genetic
que et schizophrénie: Réé-
renia: Reevaluation of a
i, J. F., Blum, S. H., and
 aberrant behavioral co-
der (ADHD): Dispelling
myths, Theoretical Biology and Medical Modelling 2 (Published online 12/23/2005).
Faraone, S. V., Doyle, A. E., Mick, E., and Biederman, J. (2001) Meta-analysis of the association between the 7-repeat allele of the dopamine D4


Hetrenma, J. M., Neale, the equal-environme Behavior Genetics 2:


ity, in C. Coll, E. B.

Complex Interplay in Behavior and Develo


Higher Education <http://www.johndi

Hudziak, J. J., Copela

C., and Todd, R. D.

A twin study, *Journ

Psychiatry 42, 357-6

Jackson, D. D. (1960) A

nia, in D. Jackson (e York: Basic Books.


nia: A challenge to *Counselling and Psy

Joseph, J. (2000a) No at

attention-deficit hype


and Biederman, Deve


Journal of the American 1389-91.


ology Under the M Edition by PCS Boo

Joseph, J. (2004b) Schiz

in J. Read, L. Moshe

logical, Social and B

Andover, UK: Taylor


Search for Genes. New


schizophrenia. *Amer


Lyons, M. J., Kendler, of schizophrenia, in Issues in Psychosoci. Rutgers University Pr.


Li, D., Sham, P. S., Owen, M. J., and He, L. (2006) Meta-analysis shows significant association between dopamine system genes and attention deficit hyperactivity disorder (ADHD), *Human Molecular Genetics* 15, 2276–84.


Safier, D. J. (1973) Attention deficit hyperactivity disorder, Psychological Medicine 3, 175–86.


Safer, D. J. (1973) A familial factor in minimal brain dysfunction, Behavior Genetics 3, 175–86.


Wender, P. H., Rosen Crossfostering: A experiential factor, *Psychiatry* 30, 121

Childhood hyperactivity tition effects: Twin study

, R. (1999) Genetic basis journal of Psychiatry 174,

, K., Moring, J., Pohjola, ial factors in schizophre- nia Bulletin 13, 477–84.ienen, P., Sorri, A., Lahti, of the schizophrenia spec-

Study, American Journal

K., Moring, J., Naarala, otype-environment inter-

the international consen-

Psychology Review 7,

Mazzeo, S. E., Neale, M. ectionism: A twin study,


, D. L., Oteman, N., J., and Buitelaar, J. K. response but no associ-

curs with ADHD, Journal

362, 1133–41.
cplex phenotypes: Evalua-
tion-deficit/hyperactivity tics of attention deficit 26, 396–432.

Wish, E. (1977) A con-

journal of Nervous and

A psychiatric assessment enthal and S. Kety (eds), . New York: Pergamon


Willcutt, E. G., Pennington, B. F., and DeFries, J. C. (2000) Etiology of inat-