Feeling anxious: a twin study of panic/somatic ratings, anxiety sensitivity and heartbeat perception in children

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Background: Little is known about mechanisms of genetic influence on panic, particularly in childhood. Cognitive theories of panic disorder highlight threatening interpretations of physical sensations, and increased awareness of such sensations. Specifically, anxiety sensitivity (AS) and heartbeat perception (HBP) have been associated with panic in adults and children. We examined genetic and environmental influences on childhood AS, HBP, panic/somatic ratings, and their associations. Methods: Self-ratings of AS and DSM-based anxiety (including panic/somatic items) were obtained from 300 eight-year-old twin pairs (600 individuals), selected for mother-rated child anxiety at age 7. HBP was also assessed. Results: Panic/somatic ratings were significantly correlated with both AS (r = .55) and continuous HBP error scores (r = −.13). AS and HBP scores showed significantly greater correlations with panic/somatic ratings than with all other anxiety scales, except for HBP and school anxiety. Genetic influences on panic/somatic ratings were modest (15%), and moderate for both AS (37%), and HBP (30%). Non-shared environmental influences were substantial. The genetic correlations between panic/somatic ratings and both AS and HBP error scores were .98 (95% CI: .74–1.00) and −.46 (95% CI: −1.00–1.00) respectively. Conclusions: Self-ratings of panic and AS overlap genetically. Future research should consider whether AS mediates genetic risk for panic disorder. Keywords: Heartbeat perception (HBP), anxiety sensitivity, panic attacks, genetic, twins.
with some studies demonstrating this specificity (e.g., Taylor, Koch, & McNally, 1992) and others not (Rabian, Peterson, Richters, & Jensen, 1993). The second relates to whether AS is a predictive risk factor rather than a concurrent covariate. In support of this hypothesis, AS has been found to predict first onset of panic attacks in adults (Ehlers, 1995), and to predict panic attacks after controlling for previous trait anxiety in adults (Schmidt et al., 2006) and children (Calamari et al., 2001). However, other studies fail to find such associations (Plehn & Peterson, 2002). In sum, there are inconsistencies in the field as to the exact nature of the association between AS and panic versus anxiety more generally, and this paper aims to add to that debate by examining genetic influence on AS and its association with panic/somatic ratings.

Heritability for AS has been estimated at around 50% in adults (Stein, Jang, & Livesley, 1999), with the remaining variance due to non-shared environment. There are no twin studies of AS in children, or of the links between AS and panic (or any type of anxiety) at any age-range. Data from family studies are mixed with some finding elevated AS levels in the offspring of anxiety disordered adults (Pollock et al., 2002) and others not (Mannuzza et al., 2002).

Studies of the awareness of physical symptoms in PD have mainly focused on heartbeat perception (HBP), as palpitations (racing and/or pounding heart) are among the most prominent symptoms in PD patients. A commonly used task to measure HBP is the Mental Tracking Paradigm in which subjects are asked to count their heartbeats during a signaled period of time without taking their pulse (Schandry, 1981). Initial studies found that patients with PD showed significantly better HBP (lower error scores) than non-anxious, phobic and depressed controls (e.g., Ehlers & Breuer, 1992; Ehlers, 1995). However, only some subsequent studies were able to replicate these findings, resulting in the association being seen as controversial (Van der Does, Antony, Ehlers, & Barsky, 2000). To clarify the situation a meta-analysis was conducted which confirmed that accurate HBP, defined by a dichotomous cut-off score on the continuous error score, whilst being rare, distinguished between adult patients with panic disorder (prevalence in the region of 17%) and healthy and depressed controls (prevalence generally below 8%; Van der Does et al., 2000). In a prospective study, good HBP predicted poorer outcome (increased likelihood of relapse) in treated and remitted PD patients (Ehlers, 1995). In children, accurate HBP was found to be associated with AS and panic/somatic ratings, but not other types of anxiety (Eley, Stirling, Ehlers, Gregory, & Clark, 2004). There are no published twin or family studies of HBP.

In summary, there is some evidence to support AS and HBP as possible risk factors for panic, but there is little genetically informative data on them or their associations with panic. We examined links between panic/somatic ratings and both AS and HBP in a sample of 8-year-old twins. We predicted that AS and HBP would be specifically associated with panic/somatic ratings as compared to other types of anxiety. We expected AS and HBP to show greater genetic influence than panic/somatic ratings, and to share genetic influence with the panic/somatic scale.

Method

Participants

The ECHO study consists of 300 twin pairs aged 8 years 2 months to 8 years 11 months, a sub-sample of the Twins’ Early Development Study, a study of twins born in England and Wales during 1994–96 (TEDS; Trouton, Spinath, & Plomin, 2002). Data were collected at the Institute of Psychiatry, apart from a few families visited at home. Ethical approval was granted by the Maudsley Hospital Ethics Committee, London, UK. Informed consent from parents was obtained through the post in advance.

In order to maximise power we used a selected extremes design, with the majority of our twins (‘case’ pairs) selected because one or both twins scored high (top 15%) on parent-reported child anxiety at age 7 (N = 247 pairs). We also selected a sample of ‘control’ pairs where neither twin scored high on anxiety at 7 years to make sure we covered the full range of scores in our measures (N = 53 pairs). Following testing, data from 11 pairs were considered unusable because at least one of the twins had neurological impairments, autistic spectrum disorders, severe receptive language impairments or persistent difficulties with attention. Zygosity was diagnosed by a combination of parent-reported physical similarity and DNA assessment in uncertain cases (see Price et al., 2000). One pair of unknown zygosity refused to give DNA and were excluded from all analyses. The present sample consisted of 96 MZ and 192 DZ pairs (576 individuals). Fifty-seven percent of the sample were girls, and the majority of the families were white (n = 256 pairs, 87%). Most mothers and fathers were employed (n = 215 pairs, 74% and n = 269 pairs, 93% respectively) and had remained in education until 18 years of age (n = 157 pairs, 54% and n = 175 pairs, 61% respectively; for more details of the sample and selection process see Gregory, Rijssijk, and Eley, 2006).

Measures

Anxiety selection variable. Parent-rated child anxiety was assessed using the Anxiety Related Behaviours Questionnaire (ARBQ; Eley et al., 2003), a 21-item scale reflecting anxiety-related behaviours including negative mood, separation anxiety, shyness, and fears. Items were rated on a 3-point scale (0 = never; 2 = often, over the past 6 months); the internal consistency (alpha) was .81. This measure screened for anxiety-related behaviours in TEDS, and children in the top 15% were considered ‘cases’ in ECHO. The entire sample was analysed as one group (rather than
distinguishing between cases and controls), taking this selection process into account (by conducting analyses with the 7-year screening variable in the entire TEDS sample, see below).

**Questionnaire measures.** One year later the children completed the Screen for Childhood Anxiety Related Emotional Disorders (SCARED; Birmaher et al., 1999) and the Children’s Anxiety Sensitivity Index (CASI; Silverman, Fleisig, Rabian, & Peterson, 1991). Both used 3-point Likert scales and were administered on a laptop computer by a member of the research team. Items were read aloud to any children having difficulty reading them. The SCARED (41-item version) was used to rate anxiety and includes 5 sub-scales: panic/somatic, general anxiety, separation anxiety, social anxiety and school phobia. Scales are created by summing items that loaded most highly onto these factors (e.g., ‘I get really frightened for no reason at all’ for panic/somatic); test–retest reliabilities range from .6 to .9, internal consistencies from .7 to .9 (Birmaher et al., 1999). In this sample internal consistency ranged from .50 (school anxiety) to .75 (panic/somatic scale).

The CASI was used to assess AS and includes items such as ‘It scares me when I feel like I am going to faint’, has internal consistency around .8–.9 (.93 in this sample), and test–retest reliability around .7–.8 (Silverman et al., 1991). There were two items on the panic/somatic scale that either reflected AS as much as panic, ‘I am afraid of having anxiety (or panic) attacks’, or seemed to bear little relation to panic disorder itself, ‘People tell me I look nervous’. All analyses were repeated with a scale created excluding these two items (alpha = .72) but were so similar to those for the full scale that we present here analyses for the scale as published.

**Heartbeat perception.** HBP was assessed with the Mental Tracking Paradigm (Schandry, 1981). Subjects were asked to count silently the heartbeats that they felt in their body during three signalled intervals (counted numbers of heartbeats). During each trial, the electrocardiogram was recorded and a computer program scored the number of R-waves (actual number of heartbeats). Participants were told not to take their pulse or to use any other strategies such as holding their breath, which was visually checked by the researcher (trained psychology graduates). During each trial, subjects first heard a warning stimulus (800 Hz, 65 dB, 100 ms) to prepare them for the task (as in Ehlers & Breuer, 1992). The warning was given 500 ms after an R wave was recorded on the subjects ECG. The start signal (1000 Hz, 65 dB, 50 ms) was triggered immediately after the third R wave that followed the warning stimulus. The tone signalling the end of the counting period (1000 Hz, 65 dB, 50 ms) was given when the timed interval was up and 300 ms after the last R wave had elapsed. Each child undertook three trials (of 35, 25 and 45 seconds respectively), preceded by a practice trial of 10 seconds (data not used). After each trial, the child told the tester how many heartbeats they had counted. To prevent distraction and remove the possibility of cheating, children were seated so that they could not see the computer screen or ECG whilst doing the test. Internal consistency (alpha) for the error scores was .93. Test–retest reliability for this task in adults ranges from .73 to .83 (Ehlers & Breuer, 1992). At present there is very little data on this task in children, and no test–retest reliability.

**Data analysis**

Percentage error scores in heartbeat perception were defined as the absolute difference between the actual number of heartbeats (AB) and counted heartbeats (CB), as a percentage of the number of actual heartbeats (i.e., \( \frac{|(AB-CB)|}{AB} \times 100 \)) as in previous work (Ehlers & Breuer, 1992)). A score of zero means no errors (totally accurate), whereas a score of 100 means totally inaccurate performance (feeling no heartbeats at all). Accurate HBP has been defined a number of ways in the adult literature, and we chose a cut-off in line with Van der Does et al. (2000) who describe accurate HBP as accurately counting HBP in term of error rates in the 10–20% range. As our sample was of children, we considered error scores of less than 20% \((N = 31, 5.5\%)\) as accurate. Good HBP was scored as zero for inaccurate and +1 for accurate, thus positive correlations with other variables indicate greater scores in the accurate group. We analyse both the dichotomous variable and the continuous error scores and use the variable-names ‘good HBP’ and ‘continuous HBP error scores’ respectively.

**Correcting for the selection variable.** All model-fitting was conducted in Mx (Neale, Boker, Xie, & Maes, 2002). This was used to control for the selected nature of the sample, by conducting all analyses including descriptive statistics, correlations amongst the measures, and genetic analyses jointly with the 7-year anxiety screening variable from TEDS. This effectively links our data back to the distribution of scores from these individuals on the original selection variable, available on the entire sample, and uses the association between the test variables and the selection variable to estimate the distribution the test variables would have had if the entire sample had been assessed. This is somewhat similar to using a weight, but more accurate as it uses maximum-likelihood to estimate the corrected distributions, variances and covariances. Statistically, the technique treats TEDS participants not included in the ECHO sample as ‘missing’ in the testing phase (see Little & Rubin, 1987). The reasons for this approach were two-fold. First, practical considerations meant we could see only a small proportion of the TEDS sample. Selecting from the extremes increases not only the power, but the likelihood of including children with clinically significant anxiety. However, secondly, by including controls and grounding our analyses within the larger unselected TEDS sample we were able to generalise our conclusions to a population-based sample that was not selected on the basis of anxiety.

**Univariate genetic analyses.** The twin design relies on the different levels of genetic relatedness between monozygotic (MZ) twins who are genetically identical, and dizygotic (DZ) twins who share 50% of additive genetic effects. This difference is used to estimate the
contribution of genetic (A), shared environmental (C), and non-shared environmental (E) influences to variation in the phenotype. Shared environment results in similarity within the twin pair, whilst non-shared environment is child specific and includes measurement error (for more detail see Plomin, DeFries, McClearn, & McGuffin, 2001). Only additive genetic models are reported, as there was insufficient power to differentiate additive from non-additive effects. As noted above all variables were analysed in conjunction with the selection variable (see Figure 1), so the parameter estimates presented here reflect only those in the box.

In order to maximise the sample, raw data were modelled, and saturated models were run for each set of variables in order to calculate model fit. Saturated models allow for all variables to covary, and thus produce a ‘perfect fit’; any difference in fit between this model and the genetic models reflects how well the genetic models fit the data. The fit of the raw models is given as twice the negative log likelihood (−2LL) and the difference in this statistic between two nested models is distributed as chi-square, with the degrees of freedom being the difference in degrees of freedom between the two models. There is a p-value associated with this calculated chi-square, which reveals whether the data is significantly different from that predicted by the model. For a good fit this is not the case, i.e., the data are not significantly different from the model predictions. We also calculated AIC, which assesses fit relative to the number of parameters and should be low, and ideally negative.

**Bivariate genetic analyses.** The second stage of the genetic analyses was bivariate modelling. We present a correlated factors solution of a Cholesky decomposition, which estimates the covariance between genetic and environmental influences on two or more variables (see Figure 2).

### Results

The means (standard deviation, range) for the entire sample, corrected for selection (see above), for all measures are given in Table 1. There were significant mean sex differences for general anxiety (mean [SD]: 5.78 [3.50] and 5.18 [3.44], for females and males \( p < .05 \)), separation anxiety (7.62 [3.38] and 6.49 [3.55], \( p < .0001 \)), and social anxiety (7.10 [2.91] and 6.02 [2.90], \( p < .0001 \)), which were incorporated into all further analyses by allowing the male and female means to be estimated separately in the model.

The mean heart rate across all three trials for the whole sample was 84.73 beats/minute (range = 54.78–123.37, SD = 11.14). There was no correlation between heart rate and HBP error scores \( (r = -0.02, \ p = .71) \). Children with higher body mass index (BMI) had higher mean heart rate \( (r = .09, \ p < .05) \) and lower mean HBP error scores \( (r = -0.09, \ p < .05) \). However, partial correlations between HBP and all other measures controlling for BMI differed by .01 or less from the full correlations and thus BMI was not considered further. Thirty-one children (5.4%) had error scores low enough to be classified as good HBP on the dichotomous score; they did not differ in mean heart rate or BMI from those classified as having poor HBP.

Table 1 also gives the correlations between AS, HBP continuous error scores and the anxiety scales, corrected for selection (i.e., estimated using the maximum-likelihood approach described above). Panic/somatic ratings correlated significantly with both AS and HBP error scores and the correlations were significantly greater than, for AS, those with general \( (p < .01) \), school \( (p < .0001) \), separation \( (p < .002) \) and social anxiety \( (p < .001) \); and for HBP than those with general \( (p < .014) \), separation \( (p < .004) \) and social anxiety \( (p < .05) \). As a result, all further analyses consider only the panic/somatic scale. The correlation between AS and HBP error scores was non-significant. AS and HBP error scores had additive effects in the prediction of panic ratings; the interaction between HBP and AS did not significantly add to the prediction \( (\text{Beta} = .12, \ p = \text{ns}) \) when AS and HBP were entered first.

For the analysis of the dichotomous good HBP score, panic/somatic and AS scores were dichotomised into three categories of roughly equal size (calculation of tetrachoric correlations required that all variables be ordinal). There was no association between good HBP and panic/somatic ratings (tetrachoric \( r = .02, \ p = \text{ns} \)), although children with good HBP were more than twice as likely to have a computer-administered mother-reported clinician-rated anxiety diagnosis (Goodman, Ford, Richards, Gatward, & Meltzer, 2000) as those with poor HBP (11.6% versus 4.8%, chi-square = 3.57, \( p < .06 \)), though low numbers preclude genetic analysis of this data.

### Univariate genetic analyses

The first stage of the genetic analyses was to estimate the within-pair correlations for each variable (Table 2, first two columns). Within-pair correlations for MZ twins were at least twice the size of those for DZ pairs, indicating moderate genetic and minimal shared environmental influence.

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**Figure 1** Behavioural genetic model for analysis of individual study variables, showing the inclusion of the selection variable. The model illustrates just one member of a twin pair, and only data within the box (i.e., those for the study variable) are presented.
The second stage of model-fitting supports this interpretation (Table 2, columns 3–5 for parameter estimates, columns 6–13 for fit statistics). Genetic effects were modest for the panic/somatic scale, and moderate for AS and HBP (accounting for around one-third of the variance), reaching significance for AS. Shared environment was minimal and non-significant whereas non-shared environment was substantial and significant for all measures. The fit statistics were excellent, as indicated

Table 1

Descriptive statistics and phenotypic correlations for the entire sample corrected for selection

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean</th>
<th>SD</th>
<th>Range</th>
<th>Correlation with AS</th>
<th>Correlation with HBP error scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety Sensitivity (AS)</td>
<td>30.75</td>
<td>6.35</td>
<td>18.00–52.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HBP error scores (HBP)</td>
<td>70.10</td>
<td>28.20</td>
<td>2.96–100.00</td>
<td>−.07</td>
<td>−</td>
</tr>
<tr>
<td>Panic</td>
<td>6.87</td>
<td>4.61</td>
<td>.00–16.00</td>
<td>.55***</td>
<td>−.13***</td>
</tr>
<tr>
<td>General anxiety</td>
<td>5.51</td>
<td>3.46</td>
<td>.00–22.00</td>
<td>.46***</td>
<td>−.03</td>
</tr>
<tr>
<td>School anxiety</td>
<td>2.28</td>
<td>1.76</td>
<td>.00–8.00</td>
<td>.31***</td>
<td>−.09*</td>
</tr>
<tr>
<td>Separation anxiety</td>
<td>7.17</td>
<td>3.59</td>
<td>.00–16.00</td>
<td>.43***</td>
<td>−.01</td>
</tr>
<tr>
<td>Social anxiety</td>
<td>6.63</td>
<td>2.95</td>
<td>.00–14.00</td>
<td>.35***</td>
<td>−.04</td>
</tr>
</tbody>
</table>

Note. *p < .05, **p < .01, ***p < .001.

Table 2

Within-pair correlations, and univariate genetic analyses

<table>
<thead>
<tr>
<th>Variable</th>
<th>Within-pair correlations</th>
<th>Parameter estimates for study variable</th>
<th>Saturated Model fit</th>
<th>Genetic model fit</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>rMZ</td>
<td>rDZ</td>
<td>A</td>
<td>C</td>
</tr>
<tr>
<td>Panic symptoms</td>
<td>.24</td>
<td>.15</td>
<td>.04</td>
<td>.81***</td>
</tr>
<tr>
<td>Anxiety Sensitivity</td>
<td>.48</td>
<td>.37**</td>
<td>.00</td>
<td>.63***</td>
</tr>
<tr>
<td>HBP continuous error scores</td>
<td>.38</td>
<td>.30</td>
<td>.06</td>
<td>.64***</td>
</tr>
<tr>
<td>Good HBP (dichotomous)</td>
<td>.39</td>
<td>.36</td>
<td>.01</td>
<td>.63***</td>
</tr>
</tbody>
</table>

Note. HBP: Heartbeat perception; A: Additive genetic; C: shared environmental; E: non-shared environmental estimates. ** signifies p < .01, ***, p < .001. −2LL is the likelihood statistic for each model. The difference in −2LL between two nested models (e.g., the saturated and genetic model for each variable) is distributed as a chi-square with the difference in degrees of freedom between the two models allowing the estimation of the p-value for the fit.
were largely specific to each variable. indicating that nonshared environmental influences somatic ratings were.38 for AS and non-shared environmental correlations with panic/somatic ratings were.98 and highly significant (95%CI ¼ .74–1.00) describing the correlations clearly indicated this term to be more important than the shared environment. The fit of the final models was excellent (chi-square ¼ 39.27, 50.06, df ¼ 38, 38, p ¼ .41, .09, AIC ¼ −36.73, −25.94, for models with AS and HBP respectively). Parameter estimates in Figure 2 are unsquared, and thus need to be squared to become variance components. For example, heritability of AS is 37% (.61 * .61). Genetic influences on panic/somatic ratings were significant in both bivariate models, owing to the increased power gained by the inclusion of more data (in twin models each covariance counts as a new data point, and in this multivariate model the cross-twin cross-measure covariances, such as panic in twin 1 with HBP scores in twin 2, are used here in addition to the univariate twin covariances). The genetic correlations between panic/somatic ratings and AS were.98 and highly significant (95%CI ¼ .74–1.00), indicating substantial genetic overlap for these measures. The genetic correlations between panic/somatic ratings and HBP continuous error scores were −.47 (95%CI ¼ −1.00–1.00), a large but nonetheless non-significant correlation. In contrast, the non-shared environmental correlations with panic/somatic ratings were.38 for AS and −.001 for HBP, indicating that nonshared environmental influences were largely specific to each variable.

Discussion

We examined the associations between, and genetic and environmental influences on, panic/somatic ratings, anxiety sensitivity (AS) and heartbeat perception (HBP) in 8-year-old twins. There were significant correlations between panic/somatic ratings and both AS and continuous HBP error scores. Heritability estimates were modest for the panic/somatic scale, and moderate for both for AS and HBP. Thus, in line with our conceptualization of these cognitive biases as potential endophenotypes, both were more heritable than panic/somatic ratings. Shared environment was small and non-significant, non-shared environment large and significant for all variables. Bivariate analyses revealed substantial genetic correlations between panic/somatic ratings and both AS and HBP, though only the former reached statistical significance.

There were a number of limitations. First, whilst our panic/somatic scale has been shown to discriminate between children aged 9–16 years with panic disorder versus other anxiety disorders (Birmaher et al., 1999), it was just self-rated items, rather than a diagnosis of panic disorder. Furthermore, there was some overlap in items with AS, and at least one item did not reflect PD symptomatology. However, replicating the analyses removing these items had no effect on the results. Second, both the panic/somatic scale and AS were child-rated, allowing for the influence of informant bias which may have increased their association. Third, the scales rated varied in the number of items. The AS and panic/somatic scales both had a greater number of items than any of the other scales, which would contribute to lower error for both of these scales. This could account in part for the associations found. Lower error would also lead to greater heritability estimates, which may partially account for the lower heritability estimate for the panic/somatic ratings (which were less reliable) than AS. Thus, it is possible that panic/somatic ratings are more heritable than found here. Fourth, the SCARED means were higher than expected, particularly for separation anxiety–probably due to the correlation between this scale and our mother-rated anxiety selection variable. Replication in non-selected samples would be useful. Finally, whilst there are clear advantages to experimental tasks over questionnaire measures, tasks such as the HBP paradigm have their own methodological limitations. People may make errors in the Mental Tracking task for reasons other than poor heartbeat perception, for example, temporary distraction or miscounting. This would increase error variance and decrease estimates of genetic influences on HBP and its association with panic. Young children may be particularly prone to such errors, which could have led to an underestimation of the proportion of children with good HBP in this sample. Indeed in both this study and our previous pilot work we found rather higher mean error rates for the HBP (around 70%) than generally found in adults (~30% region for normal controls), reflecting the difficulties the children had with this task. Furthermore, the proportion of children who were classified as accurate perceivers in this study (5.4%) was rather lower than in our previous study of 8- to 11-year-old children (9%, Eley et al., 2004). This led to low power in detecting associations with this measure, and the only significant association found was with anxiety disorders reported by the children’s mothers. On the other
hand, some people may also be able to accurately guess the number of beats in the Mental Tracking task without feeling their heartbeats. The chances of guessing correctly repeatedly is small, but it is conceivable that people arrive at correct answers by estimating the time interval that has elapsed and calculating their heartbeats from general knowledge of their heart rate. This explanation for good performance has been ruled out in adult studies (e.g., Ehlers & Breuer, 1992), and it is very unlikely that it would apply to children to a larger extent than to adults.

Despite these limitations, the results indicated a small association between continuous HBP error scores and panic ratings. It is plausible that HBP would be more strongly related to panic ratings in children who also have high AS, but we found no evidence of such an interaction, in line with Ehlers (1995). Interactions with environmental stress may also be relevant for AS (e.g., Schmidt, Lerew, & Jackson, 1997), but we did not have power to examine them.

A related and significant limitation of twin studies is that they do not traditionally address gene–environment interactions. Others include failure to incorporate gene–environment correlations, heritability, assortative mating, and the equal environments assumption. These have been discussed elsewhere (Plomin et al., 2001), and whilst some would inflate genetic and deflate environmental estimates, others would have the reverse effect. So long as only the general pattern of results is interpreted rather than values being taken as absolute these limitations can be accepted. Ideally, results from twin studies should be replicated using data from adoption studies.

Finally, the sample was not population based, and neither was it representative of the unselected British population. The families lived near London, and were of higher than average SES. Furthermore, some particularly anxious families did not wish to travel to London at a time of heightened terrorist threat (2001–03) and did not take part. However, it should be noted that our analytical approach weighted our data back to the full TEDS sample regardless of whether data for our measures were missing because we had not invited them or because they had decided not to take part.

Heartbeat perception and anxiety sensitivity: endophenotypes for panic?

We chose to explore potential endophenotypes during middle childhood primarily due to the lifelong continuity of anxiety disorders. If one can identify developmental precursors to subsequent disorders, these may be more heritable than vulnerability factors identified later in life when experiences are likely to have interacted with and possibly diluted the effects of genes. Thus it may be easier to find markers of genetic risk in young children than in adults.

The primary requirement of an endophenotype is an association (ideally predictive) with the disorder of interest. There was some evidence for associations (some predictive) with panic-related phenotypes for both HBP and AS prior to this study (e.g., Ehlers, 1995; Eley et al., 2004; Van der Does et al., 2000). We replicated concurrent associations here, and showed that they were significantly stronger than the associations with all other anxiety scales with the exception of HBP and school anxiety. The latter exception is interesting given the possible role for school phobia in the development of panic with agoraphobia (Perugi, Deltito, Soriani, & Musetti, 1988). Second, it is important that the marker has sound psychometric properties. In this study both AS and HBP error scores had internal consistencies of .93, and for AS this is representative of excellent psychometric properties found in other studies (Silverman et al., 1991). Third, such a marker should show genetic influence, for which there was previous evidence only for AS in adults (Stein et al., 1999). Fourth, any potential endophenotype should share genetic influence with the disorder of interest. There were no previous published data on the genetic influences on links between AS or HBP and panic. The size of genetic effects we found on HBP and their overlap with panic/somatic ratings suggest that whilst non-significant here, they might be worth exploring in a larger sample. We demonstrated not only significant genetic influence on AS in children, but a very high and highly significant genetic correlation between AS and panic/somatic ratings. Further research should examine whether AS mediates genetic risk on panic disorder in children.

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References

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