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Coordination difficulty and internalising symptoms in adults: A twin/sibling study

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Email: a.gregory@gold.ac.uk

Word count: 4,786

Abstract

Increased anxiety and depression symptoms have been reported in individuals with neurodevelopmental disorders, and have been found to be associated with motor coordination difficulties, but little is known about the aetiology of these associations. This study aimed to assess genetic, shared (making twins/siblings alike) and non-shared (individual-specific) environmental influences on the association between poor coordination and symptoms of anxiety and depressed mood using a sample of adult twin and sibling pairs. Participants were asked about their coordination skill and anxiety and depression symptoms. About half of the variance in coordination difficulty was explained by familial (combined genetic and shared environmental) influences, with the remaining variance explained by non-shared environmental influences. Phenotypic associations between coordination and anxiety ($r = .46$) and depression symptoms ($r = .44$) were largely underpinned by shared familial liability for the three traits. Non-shared environment accounted for about a third of the phenotypic association. Results suggest that both familial and non-shared environmental influences play a role in the aetiology of coordination difficulty and its association with internalizing symptoms. The current study highlights that both biological and environmental pathways shared between these symptoms should be examined in future research to inform prevention and treatment approaches in clinical settings.

Keywords: anxiety; coordination; depression; Developmental Coordination Disorder; twin study

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1. Introduction

Motor coordination difficulties are associated with a number of neurodevelopmental disorders, including autism spectrum disorder (ASD) (Bhat et al., 2011), attention deficit-hyperactivity disorder (ADHD) (Pitcher et al., 2003) and dyslexia (Fawcett and Nicolson, 1995), and are central to the diagnostic criteria for developmental coordination disorder (DCD) (American Psychiatric Association, 2013). Poor motor skills early in life predict later anxiety and depression symptoms, suggesting that coordination difficulties might be a developmental risk factor for internalizing problems (Piek et al., 2010; Sigurdsson et al., 2002). Indeed, symptoms of anxiety and depression are often reported in children and adults with DCD (Hill and Brown, 2013; Kirby et al., 2013; Pratt and Hill, 2011) and are associated with lower life satisfaction (Hill et al., 2011; Kirby et al., 2013). Furthermore, general coordination difficulties have been reported in children with anxiety and depression (Ekornas et al., 2010; Emck et al., 2011; Skirbekk et al., 2012). However, although there is evidence for an association between coordination difficulties and anxiety and depression symptoms across the lifespan, little is known about the role of genetic and environmental influences on these associations. Furthermore, while the links between coordination difficulty and anxiety and depression are becoming clearer in children and adolescents, there is sparse literature focusing on adults.

The current study aimed to assess a number of influences on self-reported coordination difficulty, and the association between coordination difficulties and symptoms of anxiety and depression, using a sample of adult twin and sibling pairs: genetic (A), shared environmental (those making individuals within a family more alike: C) and non-shared environmental (those making family members less similar: E) were considered. Understanding the role of genetic and environmental factors involved in poor coordination

might be important for the future identification of individuals 'at-risk' of developing motor difficulties. To date, genetically-informative studies have examined the aetiology of DCD/coordination in childhood and adolescence only. Specifically, one study compared the similarity of siblings on parent- and teacher-reported motor problems, and identified moderate familial influences (combined genetic and shared environmental influences: F=.22 and .47, for parent- and teacher-report respectively) on motor problems in children (Fliers et al., 2009). Furthermore, two previous twin studies (Martin et al., 2006; Moruzzi et al., 2010) found moderate to high genetic influences (A=.44-.69) on coordination difficulties in childhood and adolescence, with the remaining variance explained by non-shared environmental influences. To our knowledge, no study to date has estimated genetic and environmental influences on coordination difficulties in adults. Given that genetic influences on psychopathological traits tend to increase with age (Bergen et al., 2007), it is possible that the heritability of coordination problems might be even higher in adults.

Next, the current study aimed to add to the emerging literature concerning the association between emotional and coordination difficulties in adults, moving away from a focus on the prevalence of anxiety and depression symptoms in these individuals to an improved understanding of the aetiology of these psychological outcomes. Understanding the overlap between coordination difficulty and symptoms of anxiety and depression may provide opportunities for targeted interventions for these emotional problems in individuals with DCD or other motor disorders, which might otherwise be overlooked when focusing on the core diagnostic criteria for these disorders. This could improve the quality of life of individuals with coordination difficulties by providing them with strategies for dealing with increased symptoms of anxiety and depressed mood, which may otherwise interfere with their daily functioning and employment opportunities. It has been suggested that symptoms of depression may be associated with unemployment amongst those with DCD (Kirby et al.,

2013). As mental health issues are one of the biggest causes of absences from work across Europe (World Health Organization, 2010), understanding the underlying causes of such problems are important for society, as well as for those who experience these traits.

There is an ongoing debate in the literature regarding the reasons for the co-occurrence of coordination difficulties and internalizing symptoms. The "environmental stress hypothesis" put forward by Cairney et al. (2010) suggests that DCD/poor coordination could lead directly to an increase in internalizing symptoms through the disruption of a child's typical social activities, including taking part in team sports and games, and by lowering self-worth and self-concept through repeated failures to complete seemingly simple motor tasks, and comparison with peers whose motor skills are superior (Cairney et al., 2013). In line with this view, a previous study with children and adolescents suggested that within monozygotic twin pairs, the twin who had a motor disorder had higher levels of parent-reported depression than their co-twin who did not have a motor disorder (Piek et al., 2007). This finding suggests an environmental contribution to the association between coordination difficulty and depression. Furthermore, another study from the same research group found that twins who were discordant for a motor disorder had higher levels of parent-reported anxiety than those in concordant twin pairs (Pearsall-Jones et al., 2011). The authors suggest that the association between motor and anxiety symptoms can in part be explained by non-shared environmental influences; affected individuals in discordant twin sets are able to directly compare their motor ability and performance with a twin who has no coordination difficulties, whereas concordant twin pairs do not have this immediate social comparison (Pearsall-Jones et al., 2011).

To our knowledge only one twin study (comparing monozygotic and dizygotic twin pairs) to date has examined the association between coordination difficulties and anxiety symptoms (Moruzzi et al., 2010). The study investigated a range of emotional and

behavioural problems, as well as physical 'clumsiness' (or motor difficulties), in children and adolescents, using the parent-report Child Behavior Checklist 6-18 (Achenbach et al., 2003). Of the different DSM-oriented scales completed, only anxiety and ADHD problems were independently correlated with clumsiness. Twin modelling analyses revealed that genetic factors explained more than half of the phenotypic association between clumsiness and anxiety, with the remaining variance explained by shared and non-shared environmental influences. Furthermore, using co-twin design, the study was able to show that the association between clumsiness and anxiety was due to genetic and environmental covariation rather than direct causal effects. Taken together, the studies using genetically-sensitive designs suggest that both genetic and environmental influences may play a role in the co-occurrence of coordination problems and internalizing symptoms in children and adolescents.

The current study aimed to elucidate the role of genetic, shared and non-shared environmental influences in self-reported coordination difficulty, anxiety and depression in a sample of adult monozygotic and dizygotic twins, as well as sibling pairs. These data will be highly valuable in the study of self-reported coordination difficulties, in which there are few studies of internalizing symptoms in adults, and could be relevant to understanding the shared aetiology of coordination difficulty, anxiety and depression in this population. In line with previous studies in young people, we hypothesised that adult coordination problems would be moderately heritable in adults. Furthermore, in line with previous epidemiological evidence we expected that self-reported coordination problems and anxiety and depression symptoms would co-occur in our sample, and that this association would be largely underpinned by genetic influences, as suggested by the one previous twin study with children and adolescents. Finally, given that the genetic influences on anxiety and depression significantly overlap in adults, including in our sample (Kendler et al., 1992; Waszczuk et al., 2014), we

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hypothesised that there might be a single set of genetic influences common to coordination problems, anxiety and depression.

2. Method

2.1 Participants

The analyses use data from wave 5 of a longitudinal twin and sibling study, the Genesis 12-19 (G1219) as this is the only wave at which coordination difficulties have been assessed. Full recruitment and sample characteristics details are provided elsewhere (Barclay et al., In Prep; McAdams et al., 2013). Ethical approval for wave 5 data collection was provided by Goldsmiths Research Ethics Committee, University of London. Written informed consent was obtained from all participants. The sample size and zygosity is presented in Table 1. The mean age was 25.30 years (SD = 1.81, range = 22-32 years) and 66% of the sample were female. Parental education level in the G1219 participants was slightly higher than the general population, with 39% educated to A-level or above compared to 32% in the nationally representative sample (Meltzer et al., 2000). Parents from the G1219 sample were also more likely to own their own homes (82% compared to 68% in the nationally representative sample).

---Insert Table 1 about here ---

2.2 Measures

Coordination difficulty was measured by asking participants to report how uncoordinated they felt: 'not at all', 'a little', 'somewhat' or 'very' uncoordinated. Score frequency is presented in Table 1. Anxiety was measured using the Revised Symptoms of

Anxiety Scale (Willis et al., Unpublished), an age-appropriate version of the Revised Child Anxiety and Depression Scale (RCADS) (Chorpita et al., 2000), consisting of 36 self-report items designed to assess (the then current) DSM-IV anxiety disorder symptoms (RCADS also contains depression items but these were not included). The internal consistency in the current sample was excellent (α=.94). Depression was measured using the Short Mood and Feelings Questionnaire (Angold et al., 1995), a 13-item self-report measure assessing how often depression symptoms occurred in the past two weeks. The measure demonstrated excellent internal consistency in the current sample (α=.90). Responses were summed to give total anxiety and depression scores, respectively. Both measures demonstrate sound psychometric properties (Angold et al., 1995; Chorpita et al., 2000; Gregory et al., 2011; Turner et al., 2014).

2.3 Statistical Analyses

Prior to twin modelling, one-way analyses of variance (ANOVA) with Bonferroni correction were conducted, using one randomly selected twin from each pair, to compare anxiety and depression scores in four coordination difficulty groups.

The twin design compares the degree of similarity between monozygotic (MZ, sharing 100% of their genes) and dizygotic (DZ) twin pairs and full siblings (both sharing on average 50% of their segregating genes). Relative differences in within-pair correlations allow estimation of the influences of additive genetics, shared environment and non-shared environment on a trait. Where correlations are higher for MZ twins than for DZ/sibling pairs, genetic influence is assumed to be playing a role. Within-pair similarity that is not due to genetic factors is accounted for by shared environmental influences, which contribute to the resemblance between family members. Shared environmental influences are evident when DZ/sibling correlations are more than half MZ correlations. Non-shared environment

accounts for individual-specific factors that create differences among siblings from the same family. These are estimated from within-pair differences between MZ twins. Any measurement error present is included in this term. Quantitative genetic designs and methods are described comprehensively elsewhere (Plomin et al., 2013; Rijsdijk and Sham, 2002).

All twin analyses were conducted using OpenMx (Boker et al., 2011) within R (www.R-project.org) (TeamRDC, 2010), a structural equation modelling package for the analysis of genetically informative data that recognises the non-independence of family members. As is standard in model fitting analysis, the continuous (anxiety and depression) variables were regressed for age and sex (McGue and Bouchard, 1984), and depression was transformed to correct for skew. Outliers of 3 or more standard deviations above or below the mean, and participants with unknown zygosity, were omitted. Ordinal (coordination difficulty) and continuous (anxiety and depression) measures were analysed jointly assuming a liability threshold model to reflect the risk for coordination difficulty. Three thresholds were fixed to z-values corresponding to the frequency of the coordination scores in the sample. The assumption of a joint multivariate normal distribution for anxiety, depression and the four coordination categories ('not at all', 'a little', 'somewhat' or 'very' uncoordinated) allowed the estimation of within and across MZ/DZ/Sibling correlations. The MZ/DZ/Sibling ratios of these correlations indicate the relative importance of genetic and environmental influences on variation within each measure and on the covariance between them (Rijsdijk and Sham, 2002). Polychoric correlations were used to calculate cross-twin within-trait correlations for coordination difficulty, polyserial correlations for cross-twin cross-trait correlations between coordination difficulty and anxiety and depression, and Pearson's correlations for cross-twin within/cross-trait correlations in anxiety and depression.

First, univariate analyses assessing the influences of A, C and E on each variable were conducted. The sample size was underpowered to investigate sex differences in the aetiology

of these traits. Second, two multivariate models explored how the etiological influences on coordination, anxiety and depression are related, both in terms of their individual correlations (correlated factors solution) and latent structure (independent pathways model). The Cholesky decomposition, represented as a multivariate correlated factors solution (Figure 1a), was used to examine the genetic and environmental relationship between coordination difficulty, anxiety and depression. The correlated factors solution assumes that each variable has A, C and E influences, and that these variable-specific influences can correlate with the aetiological influences on other traits (r_A=genetic correlation, r_C=shared environmental correlation and r_E=non-shared environmental correlation). The proportions of the phenotypic correlations accounted for by A, C and E influences were also calculated. Third, a one-factor independent pathway model was fitted to examine the structure of genetic and environmental influences on the three variables (Figure 1b). The model allows one set of common (A_C, C_C and E_C) and variable-specific (A_S, C_S and E_S) genetic and environmental influences on each variable. The model tests whether there is a single set of common etiological factors that influence coordination difficulty, anxiety and depression, accounting for their correlations, in addition to variable-specific factors.

---Insert Figure 1 about here---

All models were fitted using raw data maximum likelihood. The core fit statistic was minus twice the log likelihood (-2LL) of the observations. This is not an overall measure of fit, but provides a relative measure of fit, since differences in -2LL between models are distributed as χ^2. The fit of each sub-model was assessed by χ^2 difference tests, the Akaike's and the Bayesian's Information Criterion, with lower χ^2 values, and more negative AIC and BIC values suggesting a better fit (Wagenmakers and Farrell, 2004). Information about the precision of parameter estimates was obtained by likelihood-based 95% confidence intervals.

3. Results

3.1 Univariate results

Coordination difficulty. Over half of the participants did not report any coordination difficulties, about a third of the sample reported feeling a little uncoordinated, about 10% reported feeling somewhat uncoordinated and about 5% felt very uncoordinated (Table 1). The MZ correlations were about twice the size of the DZ and sibling correlations, suggesting that the trait is heritable (Table 2). The univariate analyses revealed comparable moderate genetic and non-shared environmental influences on coordination difficulty, with very small shared environmental influences. To test whether parameters can be dropped, the submodels (AE, CE and E) were compared to the full ACE model (eTable 1). Both the AE and CE models fitted the ACE model equally well, while dropping both A and C parameters together (E model) led to a significant deterioration of the fit. The results indicate that there is a significant familial influence, but A and C cannot be distinguished. Thus, the AE models are presented as best fitting models, where A should be interpreted broadly as a familial liability. After dropping C from the full model, coordination difficulty was 50% due to familial and 50% due to non-shared environmental influences (A=.50, CI: .29-.67 and E=.50, CI: .33-.71).

---Inset Table 2 about here---

Anxiety and depression symptoms. The descriptive statistics for anxiety and depression symptoms are presented in Table 1. The MZ correlations were about twice the size of the DZ and sibling correlations, suggesting that both traits are heritable (Table 2). The univariate analyses revealed moderate genetic, very small shared environmental and large

non-shared environmental influences on anxiety and depression symptoms. Similarly to the univariate analyses of the coordination variable, the model comparisons revealed that A and C cannot be dropped simultaneously, suggesting that there were significant familial influences on the traits (eTable 1). Focusing on the AE models (which provided the best fit), where A should be interpreted broadly as familial liability, anxiety symptoms were 40% due to familial and 60% due to non-shared environmental influences (A=.40, CI: .26-.53 and E=.60, CI: .47-.74), while depression was 26% due to familial and 74% due to non-shared environmental influences (A=.26, CI: .11-.40 and E=.74, CI: .60-.89).

3.2 Multivariate results

Anxiety and depression symptoms were significantly higher in individuals with coordination problems than in those without (anxiety: $F(3,405)=35.11$, $p<.01$, $\eta^2=.21$, depression: $F(3,405)=26.70$, $p<.01$, $\eta^2=.17$). Specifically, the group without any coordination problems had significantly lower anxiety scores (mean=16.20) than three groups that reported feeling 'little', 'somewhat' or 'very' uncoordinated (mean=26.29, 32.26 and 36.17, all $p<.01$), with the same pattern of results for depression (mean=3.46 for group without any coordination problems was significantly higher than means=7.19, 8.54 and 9.05 for 'little', 'somewhat' or 'very' uncoordinated groups, all $p<.01$).

Cross-twin cross-trait correlations are presented in eTable 2. Multivariate model comparisons are presented in Table 3. The correlated factors solution and independent pathway models were comparable in terms of parsimony and model fit statistics, thus both are presented as they describe different aspects of the relationship between etiological influences on the variables. Similarly to the univariate analyses, the E models did not provide sufficient fit to the data, indicating significant familial influences. Although shared environmental influences were very small, the models were underpowered to reliably

distinguish them from genetic influences. Thus, the AE models are discussed in the results, where in the interest of accuracy the A influences in the AE models should be interpreted broadly as familial liability. For completeness, the results of the full ACE models are presented alongside AE models in Tables 4 and 5.

---Insert Table 3 about here---

Correlated factors solution. Coordination difficulty was moderately correlated with anxiety and depression symptoms (r_{ph}=.46, CI: .39-.52 and r_{ph}=.44, CI: .37-.51, respectively) (Table 4). When focusing on the AE model, coordination difficulty had high familial and small non-shared environmental correlations with both internalizing symptoms (correlations with anxiety: r_A=.64, CI: .43-.86 and r_E=.29, CI: .09-.47, correlations with depression: r_A=.83, CI: .55-1.00 and r_E=.16, CI: -.05-.37). Familial influences accounted for over half of the phenotypic correlations between coordination difficulty and internalizing symptoms.

Anxiety and depression symptoms were highly correlated (r_{ph}=.72, CI: .37-.51) and, when focusing on the AE model, this phenotypic association was underpinned comparably by familial (A=.44, CI: .23-.61) and non-shared environmental (E=.56, CI: .39-.77) influences. The familial and non-shared environmental correlations between the two internalizing symptoms were high.

---Insert Table 4 about here---

Independent pathways model. When focusing on the AE model, the independent pathways model results revealed that most of the familial influences on coordination difficulty, anxiety and depression were common to the three traits (A_C=.29-.34, CI: .16-.60),

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highlighting a substantial overlap of familial liability for these problems (Table 5). There were small but significant variable-specific familial influences on anxiety (A_S=.15, CI: .06-.22), but not on coordination difficulty and depression. The non-shared environmental influences on coordination difficulty were largely variable-specific (E_S=.45, CI: .29-.63). The non-shared environmental influences were common to anxiety and depression (E_C=.29-.55, CI: .17-.70), with additional moderate variable-specific non-shared environmental influences on depression (E_S=.36, CI: .13-.43).

---Insert Table 5 about here---

4. Discussion

This is the first study to investigate etiological underpinnings of coordination difficulty and its relationship with anxiety and depression symptoms in adults. Coordination difficulty was influenced by both familial influences and non-shared environmental factors. Combined genetic and shared environmental influences explained most of the moderate association between coordination difficulty and anxiety and depression symptoms. Most of the familial influences on these three symptoms overlapped, suggesting a common familial liability to coordination difficulty and internalizing symptoms. Conversely, the non-shared environmental correlations between coordination difficulty and internalizing symptoms were small, indicating largely separate non-shared environmental etiology of coordination difficulty and internalizing problems.

The current twin modelling results highlight the role of both familial factors and individual-specific environmental influences in adult coordination difficulty. The familial influences estimate for coordination difficulty in our adult sample was moderate (F=.50),

which is similar to the heritability estimates in child and adolescent sample investigated by

Moruzzi et al. (2010) (A= .44), but somewhat lower than the heritability reported by Martin

et al. (2006) (A=.69, although note that the confidence intervals overlapped between these

three estimates). In line with the evidence for moderate heritability of coordination difficulty

in previous studies conducted in young people, our ACE model indicated that genetic effects

largely underlay familial effects, with shared environmental effects estimated at close to 0.

Although our sample lacked sufficient power to rule out the possibility of definitively

identifying whether shared environmental or genetic factors explained the within-family

similarity, it suggests that genetic influences might play a role in the etiology of adult

coordination difficulty. Future molecular research should identify specific genes associated

with motor difficulty to inform prevention and treatment strategies, with some initial work in

ADHD children suggesting that genes involved in motor disease and muscle function might

be associated with coordination problems in this population (Fliers et al., 2012). The

remaining variance in coordination difficulty was largely due to non-shared environmental

influences, and future research focused on identifying these environmental factors may

inform targeted clinical and resilience interventions. These factors might include reduced

physical activity, as reported in both adults (Hill and Brown, 2013) and children with DCD

(Rivilis et al., 2011), unemployment in adults (Kirby et al., 2013) and pre- and perinatal

complications (Pearsall-Jones et al., 2008; Pearsall-Jones et al., 2009). The impact of

environmental influences on coordination may also happen via epigenetic mechanisms,

which involve changes in gene expression that play a role in a range of neurological disorders

(Jakovcevski and Akbarian, 2012; Urdinguio et al., 2009) and these processes should be

explored in future studies.

The multivariate analyses indicate strong familial influences on the association

between coordination difficulties and anxiety, in line with the evidence for moderate genetic

correlations between these traits in young people (Moruzzi et al., 2010). We also extend these findings to demonstrate similar high familial influence on the association between coordination difficulties and depression symptoms. The results suggest a combination of biological and shared environmental pathways linking coordination difficulty, anxiety and depression. One tentative suggestion for a potential biological mechanism which has been implicated in DCD (McLeod et al., 2014; Zwicker et al., 2010), and in both anxiety (Terasawa et al., 2012) and depression (Sprengelmeyer et al., 2011), is the atypical volume and functioning of the insular cortex (IC). The IC is central to processing information about the physiological state of the body, monitoring sensations and connecting to other systems, such as the anterior cingulate cortex, to allocate attention towards particular stimuli and to plan appropriate actions (Paulus and Stein, 2006). The connections between the IC and the limbic system also suggest a potential relationship between IC functioning and internalizing symptoms, with the processing of body state information being disrupted and affecting an individual's emotional interpretations of these sensations (Paulus and Stein, 2006). Future research should investigate this, as well as other potential mechanisms, which could contribute to the co-occurrence of coordination difficulties and internalizing symptoms, including the influence of genetic and epigenetic factors on the development of these mechanisms.

Small non-shared environmental correlations point to environment pathways shared between coordination difficulties and internalizing symptoms, in line with previous studies with concordant and discordant twin pairs suggesting that internalizing symptoms are related to motor difficulties due to non-shared environmental factors (Pearsall-Jones et al., 2011; Piek et al., 2007). However, in agreement with Moruzzi et al. (2010) the current data suggest that non-shared environmental influences were not sufficient to account for the total covariance between these traits. This suggests that the "environmental stress hypothesis"

(Cairney et al., 2010) may not fully explain the co-occurrence of coordination and internalizing problems. Cairney et al. (2013) suggested that the model used to assess the causal pathways between environmental stress and internalizing symptoms in DCD could incorporate biological vulnerability as a moderating factor. Specifically, the authors suggest that when 'stress' (i.e., having DCD) is present, an increased genetic risk of developing anxiety or depression would act as a moderating factor, significantly increasing the likelihood of the development of internalizing problems in DCD. The finding of non-shared environmental influences common to coordination difficulties and internalizing symptoms does not provide insight into the direction of this relationship. Future longitudinal twin studies should elucidate the causal pathways set out in the environmental stress model, allowing researchers to better understand the role of genetic and environmental factors, as well as their correlations and interactions, on the association between coordination difficulties and internalizing symptoms.

Limitations. The genetically-informative sample and a novel research question are strength of the study. However, a number of limitations are worth noting. First, our methodology is similar to that of Moruzzi et al. (2010), in that we have used a broad question relating to coordination difficulty, rather than a scale designed to measure DCD such as that used by Martin and colleagues. Although the latter method is preferable for understanding the aetiology of DCD, the current broad question allows the identification of more general coordination trait across our population. Furthermore, the prevalence of self-reported "very uncoordinated" participants in the current sample (5%) was similar to the estimated prevalence of DCD in the population (American Psychiatric Association, 2013), and falls between the rates of 2% and 8% reported by Martin et al. (2006) when using a more extensive range of questions in the Developmental Coordination Disorder Questionnaire (DCD-Q) (Wilson et al., 2000). We are therefore confident that the question used in the

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current study was sufficiently sensitive to identify those with real coordination difficulties, albeit we would not go so far as to say that these individuals would receive a diagnosis of DCD. Nevertheless, a more general problem with using self-report measures instead of clinical diagnoses and/or standardised assessments is evident across the studies discussed here. To inform understanding of comorbidity of coordination and internalizing disorders in clinical settings, the results should be replicated in clinical samples with comorbid diagnoses and using lifetime diagnostic interviews. However, common disorders are thought to be the more severe ends of quantitative traits (Plomin et al., 2009), thus we would expect these processes to be similar at symptom and disorder levels.

Second, it was beyond the scope of the current study to address the issue of comorbidity with other neurodevelopmental disorders, and the questionnaires used were not designed to identify these disorders in the population. However, previous twin studies investigating ADHD and coordination difficulties indicated shared genetic risk for these problems (Fliers et al., 2009; Martin et al., 2006). Although no concurrent reports of ADHD-related symptoms were available in the current study, earlier reports of ADHD symptoms (i.e., when participants were adolescents) could be taken into account. Importantly, once these symptoms from adolescence were controlled in the analyses, the phenotypic results did not change in a way that would alter interpretation, suggesting that earlier ADHD does not account for the association between coordination and internalizing problems. However, future research should investigate a larger range of neurodevelopmental disorders to identify disorder-specific and broad influences on the association of these disorders with coordination difficulty. Furthermore, the current study did not measure other medical diagnoses or physical symptoms that might be associated with coordination and internalizing problems and should also be explored in future studies.

Third, the current study was underpowered to distinguish between genetic and shared environmental effects, however submodel comparisons confirmed significant familial influences. Studies in adults do not generally find evidence for shared environmental influences on psychopathology (Bergen et al., 2007; Plomin et al., 2013), and the MZ, DZ and sibling correlations in the current study suggest that shared-environmental influences were unlikely to have a big contribution. For this reason we believe that familial influences consisted mainly of genetic influences, although future studies with larger sample sizes will be necessary to support this conclusion. Finally, there are a number of limitations inherent to the twin design, comprehensively discussed elsewhere (Plomin et al., 2013). These limitations have minimal and contrasting effects but suggest that parameter estimates should be taken as indicative rather than absolute values.

The current paper has added to the emerging literature regarding genetic and environmental influences on anxiety and depression in individuals with coordination difficulties, moving the focus away from children and adolescents to consider these associations in adulthood. The data presented suggests a strong familial liability underlying coordination difficulty and its association with internalizing symptoms. This will be important for future research into neurodevelopmental disorders that are associated with poor coordination, and will provide the basis for investigations of genetic overlap between these disorders. Given the impact that coordination difficulty has on activities of daily living, educational and occupational outcomes, physical and mental health for an individual, as well as the consequences of poor coordination and poor mental health on other outcomes (e.g., presenteeism/ absenteeism in the workplace), understanding these relationships is of great importance to individuals at-risk of these problems, and to society as a whole.

Acknowledgements

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Table 1 –Descriptive statistics

	N (MZ/DZ/Sib)	Score frequency (percentage of total scores)		
Coordination difficulty	858 (221/402/218)	not at all: 488 (57%) a little: 244 (28%) somewhat: 87 (10%) very: 39 (5%)		
	N (MZ/DZ/Sib)	Mean (SD), range	Skew	α
Anxiety	862 (221/398/216)	22.13 (14.81), 0-84	1.16	.94
Depression	861 (222/402/218)	5.31 (5.30), 0-26	1.42	.90

Notes

SD – standard deviation, α - internal consistency

N is presented in individuals. Maximum possible score for anxiety was 108, and for

depression was 26.

Twin pair zygosity was identified using a combination of parent-rated questionnaires (Cohen

et al., 1975) and DNA sequencing in uncertain cases.

Descriptive statistics are presented on full, untransformed and unregressed data for

comparison with other published samples. After the exclusion of outliers and individuals with

unknown zygosity the final Ns were 841 for coordination difficulty, 835 for anxiety and 842

for depression.

Table 2 –Cross twin/sibling correlations and univariate parameter estimates

	Cross Twin/Sibling Correlations			Univariate influences, ACE model			Univariate influences, AE model	
	r_{MZ}	r_{DZ}	r_{Sib}	A	C	E	A	E
Coordination difficulty	.48 (.21-.67)	.23 (.02-.42)	.32 (-.03-.61)	.49 (.00-.67)	.01 (.00-.22)	.50 (.33-.60)	.50 (.29-.67)	.50 (.33-.71)
Anxiety	.42 (.23-.57)	.21 (.05-.35)	.24 (-.04-.46)	.34 (.00-.33)	.05 (.00-.33)	.61 (.48-.78)	.40 (.26-.53)	.60 (.47-.74)
Depression	.26 (.06-.44)	.18 (.02-.33)	.02 (-.21-.24)	.22 (.00-.40)	.03 (.00-.27)	.75 (.60-.91)	.26 (.11-.40)	.74 (.60-.89)

Notes

MZ – monozygotic, DZ – dizygotic, Sib – sibling, A-additive genetic parameters, C –shared environmental parameters, E – non-shared environmental parameters.

95% Confidence Intervals (CIs) are presented in brackets. CIs not including 0 indicate significant estimates. Non-overlapping CIs mean significant difference between the values.

Correlations were performed on transformed and age and sex regressed variables, and after outliers and individuals with unknown zygosity were excluded.

Polychoric correlations were used for coordination difficulty; Pearson's correlations were used for anxiety and depression. The correlations control for the non-independence of data.

The somewhat lower sibling correlation for depression reflects the relatively small number of sibling pairs in the sample, leading to less precise estimates with wide confidence intervals.

The univariate parameter estimates were obtained from the univariate twin models. Although comparable and not significantly different, the univariate estimates are not expected to be identical to the estimates obtained in the multivariate models presented in Table 4 and Table 5.

Submodel comparisons for the univariate models are presented in eTable 1. Fit indices suggest that A and C cannot be distinguished, but also cannot be dropped from the model

simultaneously. For this reason A in the AE model should be interpreted broadly as a familial

liability for a trait.

Table 3 - Submodel comparisons: (a) Correlated Factors Solution, (b) Independent Pathways

Model

	-2LL	df	χ²	Δdf	p	AIC	Size-adjusted BIC
(a) Correlated Factors Solution							
ACE	9947.74	2499				4949.74	10031.57
AE	**9950.81**	**2505**	**3.07**	**6**	**.80**	**4940.81**	**10009.49**
CE	9952.27	2505	4.53	6	.61	4942.27	10010.95
E	10003.48	2511	55.74	12	.00	4981.48	10037.01
(b) Independent Pathways Model							
ACE	9948.05	2499				4950.05	10031.88
AE	**9951.31**	**2505**	**3.26**	**6**	**.78**	**4941.31**	**10009.99**
CE	9952.60	2505	4.56	6	.60	4942.60	10011.28
E	10003.54	2511	55.49	12	.00	4981.54	10037.07

Notes

-2LL – minus twice the log likelihood; df- degrees of freedom; Δ df – degrees of freedom

difference; p – probability; AIC – Akaike's information criterion; BIC – Bayesian's

information criterion.

Fit indices suggest that A and C cannot be dropped from the model simultaneously,

indicating significant familial liability. The C estimates are negligible (Table 2) and the AIC

and BIC indices support the AE model. For these reasons the AE models are presented,

where A should be interpreted as familial influences.

Table 4 - Results of the Correlated Factors Solution (a) Full ACE model, (b) AE model

	Phenotypic, genetic and environmental correlations				Proportion of the phenotypic correlation explained by A, C and E		
	r_{ph}	r_A	r_C	r_E	A	C	E
(a) ACE Model							
Coordination difficulty-Anxiety	.46 (.39-.52)	.65 (-1.00-1.00)	.69 (-1.00-1.00)	.30 (.08-.50)	.50 (.00-1.00)	.14 (.00-.65)	.36 (.09-.70)
Coordination difficulty-Depression	.44 (.37-.51)	.71 (-1.00-1.00)	.99 (-1.00-1.00)	.21 (.00-.41)	.39 (.00-.1.00)	.32 (.00-.74)	.29 (.00-.62)
Anxiety-Depression	.72 (.69-.75)	1.00 (-1.00-1.00)	.58 (-1.00-1.00)	.66 (.55-.75)	.36 (.00-1.00)	.08 (.00-.39)	.57 (.39-.79)
(b) AE Model							
Coordination difficulty-Anxiety	.46 (.39-.52)	.64 (.43-.86)		.29 (.09-.47)	.67 (.40-.91)		.33 (.09-.60)
Coordination difficulty-Depression	.44 (.37-.51)	.83 (.55-1.00)		.16 (-.05-.37)	.79 (.49-.1.00)		.21 (.00-.51)
Anxiety-Depression	.72 (.69-.75)	.82 (.65-.95)		.67 (.56-.75)	.44 (.23-.61)		.56 (.39-.77)

Notes

r_{ph} – phenotypic correlation, r_A – genetic correlation, r_C – shared environmental correlation, r_E – non-shared environmental correlation, A-additive genetic parameters, C –shared environmental parameters, E – non-shared environmental parameters.

95% Confidence Intervals (CIs) are presented in brackets. CIs not including 0 indicate significant estimates. Non-overlapping CIs mean significant difference between the values. Submodel comparisons for the multivariate models are presented in Table 3. Fit indices suggest that A and C cannot be distinguished, but also cannot be dropped from the model simultaneously. For this reason A in the AE model should be interpreted broadly as a familial liability for a trait.

Cross twin/sibling cross trait correlations are presented in eTable 2.

Table 5 - Results of the Independent Pathways Model (a) Full ACE model, (b) AE model

	Common Influences			Variable-specific Influences		
	A_C	C_C	E_C	A_S	C_S	E_S
(a) ACE Model						
Coordination Difficulty	.18 (.00-.59)	.14 (.00-.43)	.05 (.00-.16)	.17 (.00-.28)	.00 (.00-.19)	.47 (.30-.67)
Anxiety	.36 (.00-.57)	.02 (.00-.27)	.51 (.25-.74)	.00 (.00-.00)	.06 (.00-.17)	.05 (.00-.28)
Depression	.20 (.00-.46)	.13 (.00-.34)	.32 (.17-.64)	.00 (.00-.12)	.00 (.00-.10)	.35 (.09-.45)
(b) AE Model						
Coordination Difficulty	.33 (.16-.60)		.04 (.00-.12)	.18 (.00-.37)		.45 (.29-.63)
Anxiety	.29 (.20-.44)		.55 (.28-.70)	.15 (.06-.22)		.00 (.00-.00)
Depression	.34 (.17-.49)		.29 (.17-.58)	.00 (.00-.00)		.36 (.13-.43)

Notes

A-additive genetic parameters, C –shared environmental parameters, E – non-shared environmental parameters. The subscript indicates whether the influences are common all three variables (C) or variable-specific (S).

95% Confidence Intervals (CIs) are presented in brackets. CIs not including 0 indicate significant estimates. Non-overlapping CIs mean significant difference between the values.

Submodel comparisons for the multivariate models are presented in Table 3. Fit indices suggest that A and C cannot be distinguished, but also cannot be dropped from the model simultaneously. For this reason A in the AE model should be interpreted broadly as a familial liability for a trait.

Cross twin/sibling cross trait correlations are presented in eTable 2.
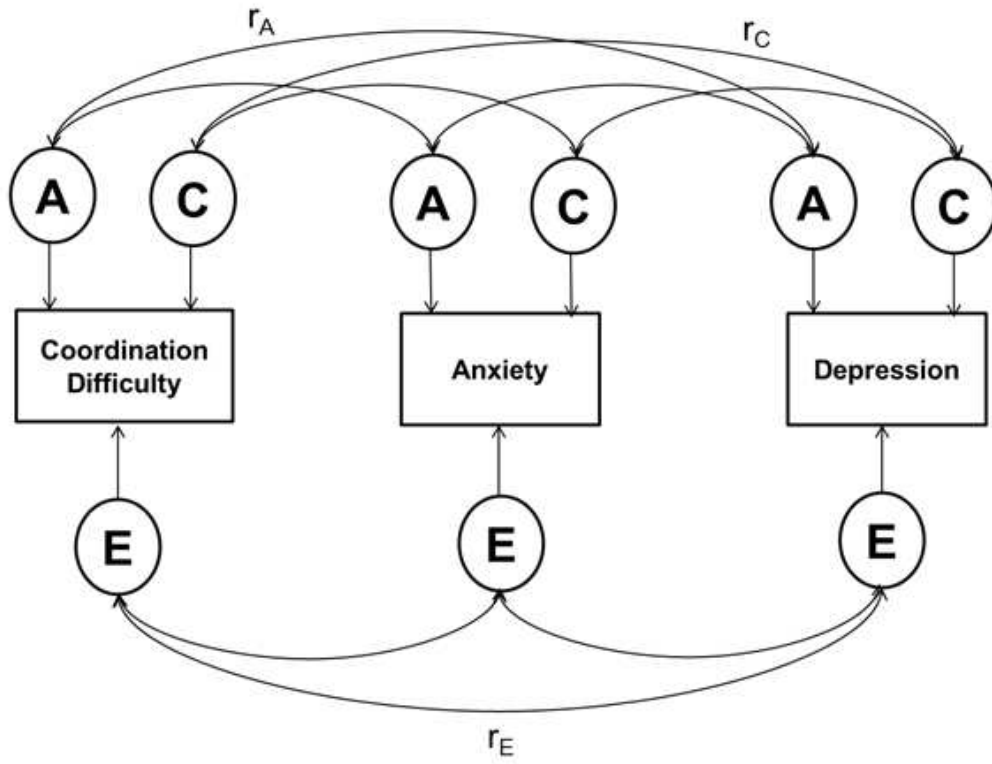
Figure Captions

Figure 1 – (a) Correlated Factors Solution, (b) Independent Pathways Model

Notes

A-additive genetic parameters, C - shared environmental parameters, E – non- shared environmental parameters, rA – genetic correlation, rC –shared environmental correlation, rE – non-shared environmental correlation. In independent pathways model the subscript indicates whether the influences are common (C) or variable-specific (S).

(a)

(b)