Small for Gestational Age as a Predictor of Behavioral and Learning Problems in Twins

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The study examines the effects of being born small for ges-The study examines the effects of behavioral problems in twins tational age (SGA) on rates of behavioral problems in twins and siblings, utilising data from the Australian Twin Study of disruptive behavior disorders in twins and their siblings. Participants were 3944 twins and their siblings who were assessed at two intervals three years apart. At the first assessment (1991), they ranged between 4 and 12 years of age. Items assessing Attention Deficit /Hyperactivity Disorder were based on DSM-III-R criteria (Time 1) and DSM-IV criteria (Time 2). Other measures included history of speech and reading therapy, demographic information and obstetric and neonatal history. Results indicated that both male and female twins, who were extremely growth restricted (small for gestational age up to the third percentile-WGA3) showed more inattention, and poorer speech and reading scores. The effects were greater for males. Male twins who were small for gestation age, up to the10th percentile, were more likely to have a DSM-IV diagnosis of Inattention. Implications of these results included WGA3 male twins being at a "triple disadvantage" for subsequent behavioral and learning problems, in that being male, being a twin and being small for gestational age are all significant factors. Recommendations are made for early intervention for low birthweight male twins. The study is consistent with recent follow-up studies of very-low-birthweight singletons, indicating male disadvantage in cognitive outcome. While there is some genetic component to SGA, it does constitute a potentially major contribution to common environmental effects that must be considered in twin-based genetic analyses.

Perinatal complications such as being born small for gestational age (SGA) are associated with mortality and significant morbidity, such as cerebral palsy (Palmer et al., 1995; Stanley & English, 1986). Indeed, there is evidence that being both pre-term and SGA may be exponentially associated with cerebral palsy (Palmer et al., 1995). In addition, there are less easily identifiable behavioral disorders such as attention deficit hyperactivity disorder (ADHD), which have been associated with being SGA (Dammann et al., 1996; Breslau et al., 1996).

Having a low weight for gestational age has been defined as being below the 10th percentile of average weights in the general population (WGA10), while babies that weigh less than the third percentile (WGA3) have been described as severely growth restricted (Henderson-Smart, 1995). A number of variables have been identified as contributing to mean birthweight for a particular gestational age. These include gender, being a twin versus a singleton,

pregravid weight, maternal height and birth order and gestational weight gain (e.g., Blair & Stanley, 1985). It has been recommended that criteria for growth restriction should include skin fold thickness and ratio of weight to length or head circumference as a more accurate measure of the infant's status, specifically, "reduced subcutaneous tissue or muscle mass" (Henderson-Smart, 1995). However, many studies have simply gathered data on weight for gestational age (Hawdon et al., 1990; Robertson et al., 1990; Watt, 1989).

Henderson-Smart (1995) reviewed the literature on neurological development during childhood and discussed reports of a high rate of hyperactivity, inattention and behavioral problems among children who were small for gestational age. Henderson-Smart also found that babies born SGA to mothers of a higher socioeconomic status tended to perform better at school, suggesting that social factors also influenced behavior. A further contributing factor may be the genetic relationships between socioeconomic factors and IQ (Fulker, 1979). It is important to note that babies born SGA as well as pre-term, are faced with additional risk factors to those present for babies born SGA at term (≥ 37 weeks gestation; Palmer et al., 1995). Particularly for those born extremely pre-term (< 32 weeks), the problems include cardiorespiratory failure and chronic lung disease. Pre-term birth is generally classified as less than 37 weeks gestation (Palmer et al., 1995). Wang et al. (2002) have reported an association between maternal smoking during pregnancy and low birthweight, which was modified by maternal metabolic genes CYP1A1 and GSTT.

While a number of researchers and reviews have reported mixed results in behavioral and cognitive outcome for SGA children in general (e.g., Low, 1992; Watt, 1989), findings restricted to males have been less equivocal, showing cognitive and intellectual disadvantage as well as hyperactivity (Botting et al., 1997; Breslau et al., 1996; Dammann et al., 1996; Hawdon et al., 1990; Laucht et al., 2000; Paz et al., 1995). Breslau et al. found an association

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between ADHD and low birthweight (≤ 2500g) in urban as opposed to suburban areas, using *Diagnostic and Statistical Manual of Mental Disorders* criteria (*DSM-III-R*; American Psychiatric Association [APA], 1987). However, this finding was confounded by differences in social class and ethnic background between the two samples.

Gender differences have been reported in a number of studies. A study of 323 premature children aged 4 to 13 years by Schothorst and van Engeland (1996) reported an increased risk of clinically significant mental health problems (measured by the Child Behavior Checklist), as well as social skill problems. The boys proved to have more attention and more externalising problems than the girls. Prematurity was defined as gestational age equal to or less than 37 weeks and small for gestational age as a birthweight at or below the 10th percentile.

Recently, Hack et al. (2002) compared a cohort of 242 survivors among very-low-birthweight infants born between 1977 and 1979 (mean birthweight 1179g: mean gestational age at birth, 29.7 weeks), with 233 controls, who had normal birthweights. They assessed the level of education, cognitive and academic achievement, and rates of chronic illness and risk-taking behavior at 20 years of age, with outcomes adjusted for sex and sociodemographic status. Their results indicated that fewer very-low-birthweight young adults had graduated from high school. Very-low-birthweight men, but not women, were very significantly less likely than normal birthweight controls to be enrolled in post-secondary study. The very-low-birthweight participants had a lower mean IQ and higher rates of neurosensory impairment, but reported less alcohol and drug use.

An epidemiological study by Zubrick et al. (2000) commented that ideally studies of mental health outcome should compare children on the basis of the appropriateness of fetal growth and gestation at delivery, rather than absolute birthweight (McNeill, 1995). The authors reported that severely growth-restricted infants experienced widespread mental health problems, as assessed by the Child Behavior Checklist. Boys were at significantly increased risk and the risk of mental health morbidity increased also with earlier gestational age at delivery, lower birthweight and aboriginality. Children below the 2nd centile of percentage of expected birthweight were nearly three times more likely to have a mental health problem than infants above the 90th centile of expected birthweight. In terms of odds ratios and after adjusting for key demographic factors, the subscales of Withdrawn, Attention, Aggression and Social Problems were the ones most associated with growth retardation.

The measures employed in most of the above studies were not based on current standardised diagnostic criteria such as the *DSM-IV* (APA, 1994). While the *DSM-III-R* diagnosis of ADHD was a unitary concept requiring eight out of 14 possible symptoms of inattention or hyperactivity/ impulsivity, the more recent *DSM-IV* describes predominantly inattentive and predominantly hyperactive/impulsive subtypes. *DSM-IV* criteria for the inattentive subtype require six out of nine symptoms of inattention and distractibility, while the hyperactive-impulsive sub-type requires six out of nine questions relating to hyperactivity and impulsivity

symptoms (see Appendix). The symptoms must have persisted for at least 6 months to a degree that is maladaptive. A further diagnosis of combined type is obtained when at least six out of nine criteria are met on *both* inattentive and hyperactive criteria.

It is well documented that twins experience more preand perinatal complications than singletons, including growth restriction, particularly in the third trimester of pregnancy (Powers et al., 1995). In addition there is evidence of negative postnatal effects on behavior, such as reduced interaction with parents (Conway et al., 1980) and modeling from one's language disabled co-twin (Haden & Penn, 1985). Recent studies have shown that twins are more at risk for ADHD, language and learning problems than are singletons (Levy et al., 1996). McEvoy and Dodd (1992) found in their sample of 2- to 4-year-olds that multiple birth children (17 twin sets and 2 triplet sets) performed more poorly than matched control singletons on measures of phonology and syntax. Hay et al. (1987) found that in addition to language, symbolic representation and pro-social behavior were delayed in twins suggesting a more generalised delay. Mogford-Bevan (1999) reviews the evidence for different models of language development in multiples and potential aetiologies.

The concept that male twins might be at particular risk was first proposed by Hay et al. (1984). In an Australiawide survey of academic skills, twins of both genders were less likely to reach the criteria for adequate literacy and numeracy in the 10-year-old cohort. In the 13- to 14-yearold cohort, the twin girls were now doing as well as their singleton peers but the twin boys were not. There was some evidence (Hay et al., 1986) their problems were attentional, in that their worst performance was in areas that demanded sustained attention (e.g., arithmetic). Levy et al. (1996) provided clearer evidence that male twins might be particularly at risk for ADHD and that this was associated with speech and reading problems. Levy et al. (1996) carried out a longitudinal study involving over 5000 twins and siblings between the ages of 4 to 12, who were followed up three years later. At Time 1, they found that male twins had the highest rate of ADHD, as well as speech and reading problems, compared to female twins and singletons. Levy et al. (1996) found that speech and reading problems best predicted whether symptoms of inattention would persist at the follow-up, while oppositional defiant symptoms predicted persistence of hyperactivity-impulsivity symptoms.

There is a dearth of evidence to date regarding the relationship between SGA twins and later learning problems. The current study is a large investigation involving standardized criteria of inattention, hyperactivity-impulsivity, and twin growth standards. The aim was to investigate whether being small for gestational age influenced subsequent inattention and hyperactivity-impulsivity, as well as the need for speech or reading interventions.

Method

Participants

The Australian Twin ADHD Project (ATAP) has obtained three waves of data (1991, 1994 and 1998–99) from families with twins registered with the Australian National Health

and Medical Research Council Twin Registry. The registry is a voluntary registry with participants recruited from a number of sources such as media releases, maternity hospitals, and the Australian Multiple Birth Association.

A detailed description of the process by which families were identified for the twin project is provided by Levy et al. (1996) and Hay et al. (in press). From the 3049 identified families, 2350 families responded. Four hundred and twelve families were excluded from the study where one or more children in the family had a major disability. The number of eligible and contactable families who responded to the questionnaire at Time 1 was 1938 (5067 children) giving a response rate of 73.5%. Three years later at Time 2, questionnaires were received from 1601 families with 3944 children who had been included in 1991. Excluding anyone who had developed any further major disability, this represented a response rate of 78% of Time 1 respondents.

The present study selected twins and siblings who were born from 34 to 40 weeks gestation. There were insufficient numbers of subjects born prior to 34 weeks and after 40 weeks gestation to calculate accurate SGA percentile ranks at the extremes such as the 3rd percentile. Also, evidence suggests that those born earlier than 32 weeks may be particularly at risk for severe behavioral and cognitive problems (Henderson-Smart, 1995).

Characteristics of the Sample

The mean age and birthweight for male and female twins and siblings at Time 2 are shown in Table 1. (Only the siblings within the age-range 4–12 at Time 1 were included).

Measures

Weight for Gestational Age (WGA)

As can be seen in Table 1, the mean birthweight for twins was significantly lower than that for singletons, and differed significantly between the sexes. More specifically, for twins, the birthweights of 33% to 51% of male twins born between 34 and 40 weeks fell below the 10th percentile means for male singletons, with there being a trend to a greater proportion being SGA in the later weeks. Similarly, for female twins, 41%–55% fell below the 10th percentile for female singleton means. Cut-off weights for each of WGA categories were therefore calculated on the basis of twin means from the current ATAP (Australian Twin ADHD Project) sample, according to gestational age in weeks, and sex by the following procedure.

In order to maintain suitable subject numbers for comparison between groups, the extremely growth restricted category included those babies at or below the 3rd percentile in weight for their gestational age and gender rather than those below the 3rd percentile. Similarly, small for gestational age was taken as being at or below the 10th percentile, rather than simply below the tenth percentile. Participants were assigned to one of five categories of WGA:

- category 1 ≤ 3rd percentile (WGA3),
- category 2 > 3rd percentile and ≤ 10th percentile (WGA410),
- category 3 > 10th percentile and < 50th percentile (WGA1149),
- category 4 ≥ 50th percentile and < 90th percentile (WGA5089)
- category $5 \ge 90$ th percentile (WGA90100).

Table 1aThe Mean Age and Birthweight for Male and Female Twins and Siblings at the Second Time of Assessment

		Ag	ge	birthweight
	N	Years	(SD)	(Grams)
Male twins	1502	11.02	(2.61)	2629
Female twins	1541	11.03	(2.58)	2505
Male siblings	451	11.57	(2.27)	3566
Female siblings	450	11.68	(2.33)	3393

Table 1bMean Gestational Age in Weeks According to Weight for Gestational Age Category

	Weight for gestational age					
	3rd Percentile	4th-10th Percentile	>10th Percentile (n = 1012) 37.20 (1.76)			
Male Twins mean gestational age (SD)	(n = 41) 37.20 (1.75)	(<i>n</i> = 89) 37.28 (1.73)				
Female Twins mean gestational age (SD)	(<i>n</i> = 40) 37.42 (1.68)	(<i>n</i> = 90) 37.30 (1.71)	(<i>n</i> = 1014) 37.31 (1.69)			
Male Siblings mean gestational age (SD)	(n = 9) 39.33 (.87)	(<i>n</i> = 17) 38.94 (1.30)	(<i>n</i> = 245) 39.13 (1.20)			
Female Siblings mean gestational age (<i>SD</i>)	(<i>n</i> = 8) 38.75 (1.49)	(<i>n</i> = 14) 38.93 (1.33)	(<i>n</i> = 219) 39.20 (1.38)			

Those in the 90th to 100th percentile were excluded based on Powers et al. (1995) report of an increased mortality rate for twins weighing more than 4000g. Also, those twins who were in the heaviest category for each week of gestation are likely to be a special group with its own particular risk factors, distinct from SGA. The mean gestational age at the 3rd (WGA3), the 4th to 10th (WGA410) and the tenth (WGA10) percentile for males and females born from 34 to 40 weeks gestation inclusive, are shown in Table 1. The actual weights defining WGA3 and WGA10 for each week are given in Rooney et al. (1998).

Assessment of Zygosity

Zygosity was determined by Discriminant Function Analysis (DFA), using a zygosity questionnaire based on Cohen et al. (1975) with six questions on similarity and features and six on frequency of confusion by the mother, father and so forth. A more detailed description of this process of assessment of zygosity is described in Levy et al. (1997). In a cohort this size spread across a country as large as Australia, DNA assessment of zygosity is impractical.

Attention Deficit Hyperactivity Disorder

Items measuring ADHD were taken from the Australian Twin Behaviour Rating Scale (ATBRS) which was based on DSM-III-R and designed specifically for the ATAP (Hay et al., 2001). Of the 14 items assessing ADHD, eight involved hyperactivity-impulsivity, and six covered inattention (Appendix). Items at Time 2 also included items based on the (then) newly developed DSM-IV diagnoses of the predominantly inattentive subtype (nine items), and predominantly hyperactive-impulsive subtype (nine items), and the combined subtype (18 items) (APA, 1994). High rates of agreement have been shown for symptoms of ADHD assessed on the ATBRS questionnaire and a diagnosis of ADHD using a structured interview (The Diagnostic Interview for Children; DISC-P). The ATBRS was more conservative than the structured interview in that parents reported more symptoms at interview than in the questionnaire (Levy et al., 1997).

In order to compare the number of symptoms at Time 1 versus Time 2, analysis was restricted to the *DSM-III-R* symptoms utilizing a distinction between inattentive and hyperactive-impulsive subtypes described by Hart et al. (1995) and listed in Appendix. This enabled direct comparisons of each set of symptoms between Time 1 and Time 2 data sets. For analysis of diagnostic categories with the *DSM-IV* subtypes, the Time 2 (*DSM-IV*) data set was used.

Speech and Reading

Speech and reading problems at Times 1 and 2 were based solely on parental report of speech and reading therapy, past and present. Parental recall of early language development has been found to correlate 0.93 with the Goldman-Fristoe Test of articulation (Johnston et al., 1984). The reliability of such self-report measures has been discussed by Levy et al. (1996).

Results

Birth Order

Previous research has reported that the second- born of a set of twins may experience greater problems (Golding, 1991). In the current study, a series of paired sample *t* tests were carried out to investigate differences between first and second born twins. No differences were found between the twins for inattention, hyperactivity-impulsivity, speech and reading scores. Thus analyses were pooled over first and second born.

SGA, Inattention, Hyperactivity-Impulsivity, and Learning problems

Two-way multivariate analysis of variance (MANOVA) examined the number of inattention and hyperactivity-impulsivity symptoms, and history of speech and reading therapy, at Time 2. Analyses were confined to Time 2 measures as previous results have suggested that lifetime speech and reading scores are more genuinely reflective of actual scores at Time 2 (Levy, Hay, McLaughlin, et al., 1996; Levy, Hay & Rooney, 1996). Younger children's scores (e.g., 4- and 5-year-olds) are not as likely to be indicative of speech and reading problems as there has not been sufficient time for problems to be detected and referred for therapy.

The means for inattention, hyperactivity-impulsivity, speech and reading problems at Time 2 for male and female twins and siblings are shown in Table 2.

Given that previous research has indicated that those who are extremely growth restricted are most seriously disadvantaged (Henderson-Smart, 1995), two WGA categories were compared in the analysis: those who were WGA3 (\leq 3rd percentile), and those greater than WGA3, but below the 90th percentile. A multivariate main effect was found for WGA categories, F(4, 2544) = 4.62, p < .01. Those who were WGA3 had higher inattention, speech and reading scores than those who were not WGA3.

Gender differences have been reported previously (Levy, Hay & Rooney, 1996) and there was an interaction between WGA category and gender, F(4, 2544) = 3.56, p < .01.

Table 2Means and Standard Deviations of Inattention, Hyperactivity-impulsivity, Speech and Reading at Time 2 for Male Twins, Female Twins, Male Siblings, and Female Siblings

	male twins (SD)	female twins (SD)	male siblings (<i>SD</i>)	female siblings (SD)
Inattention	1.59 (2.05)	.86 (1.57)	1.41 (1.73)	.78 (1.31)
Hyp-imp.	1.41 (2.06)	.79 (1.50)	1.18 (1.83)	.67 (1.29)
Speech	.24 (.49)	.12 (.37)	.15 (.40)	.05 (.23)
Reading	.28 (.61)	.18 (.49)	.24 (.56)	.08 (.35)

Table 3

Univariate F Tests from MANOVA of Inattention, Hyperactivity-impulsivity, Speech, and Reading at Time 2 by Weight for Gestational Age and Sex. The WGA Comparison is for those at the 3rd Percentile or Less, Compared with the Rest. Data are for Male and Female Twins only

Effect and Dependent measure	Univariate F statistics				
WGA main effect					
Inattention	F(1, 2547) = 6.098, p < .05				
Hyperactivity-impulsivity	F(1, 2547) = .226, p = .635				
Speech	F(1, 2547) = 9.343, p < .01				
Reading	F(1, 2547) = 8.552, p < .01				
Sex main effect					
Inattention	F(1, 2547) = 41.813, p < .001				
Hyperactivity-impulsivity	F(1, 2547) = 26.672, p < .001				
Speech	F(1, 2547) = 21.653, p < .001				
Reading	F(1, 2547) = 4.498, p = .034				
WGA x Sex interaction effect					
Inattention	F(1, 2547) = 9.581, p < .01				
Hyperactivity-impulsivity	F(1, 2547) = 4.380, p < .05				
Speech	F(1, 2547) = 4.941, p < .05				
Reading	F(1, 2547) = .197, p = .657				

The effects of being WGA3 were significantly greater for males on inattention, hyperactivity-impulsivity symptoms, and speech score. The univariate components for the MANOVA analyses are shown in Table 3.

As an alternative confirmation of the results, discriminant function analyses were carried out to investigate if being small for gestational age could be predicted from inattention and hyperactivity-implusivity scores at Times 1 and 2, and speech and reading scores. Analyses were conducted separately for male twins, female twins, male singletons and female singletons. The only group for which the measures significantly predicted SGA status was male twins. A stepwise discriminant function analysis revealed that 73% of male twins up to the 3rd percentile were significantly correctly classified, with inattention at Time 2, F(1, 1048) = 12.97 and speech scores at Time 2 F(1, 1048) = 9.21 being the only significant predictors.

The analysis so far has been based on the number of ADHD symptoms rather than children who had reached DSM-IV criteria. The percentages of children with a diagnosis of the ADHD subtypes by DSM-IV criteria are shown in Table 4. A series of chi-square analyses were run to investigate differences between WGA categories for male and female twins and siblings according to the three ADHD diagnoses. There was a significant difference between WGA categories for male twins only. This was found for inattention between WGA10 (including WGA3) and WGA1189 (the "medium" WGA groups, ranging between the 10th percentile and the 90th percentile), chi square (1) = 7.81, p < .01. The percentages for each of these categories in male twins are also shown in Table 4b.

No significant differences were found between the measures for singletons according to WGA10 or WGA3. However these results are inconclusive as there were only 9 WGA3 male siblings and 8 WGA3 female singletons. The sibling sample was a relatively healthy one given the exclusion criteria, since from 34 to 40 weeks gestation, only 4% of female siblings and 3% of male siblings fell below the 10th percentile of the local standards for mean birthweights for singletons (Blair & Stanley, 1985).

Birthweight Resemblance

The percentage of MZ and DZ twin pairs born from 34 to 40 weeks of gestational age that were concordant for WGA3 was 13% (5/39) and 0% (0/34), respectively. Comparable percentages concordant for WGA10 (4th to 10th percentile) were 22% (24/107) and 9% (10/107), respectively. Chi square analysis revealed a significant difference in concordance rates between MZ and DZ twins (combining WGA3 and WGA410 categories because of very small numbers), chi-square (1) = 8.63, p < .005.

Birthweight differences on inattention and hyperactivity-implusivity symptoms at Time 1 and Time 2, and history of speech and reading therapy were assessed in MZ and DZ twins whose birthweight difference was ≥ 20%, or < 20% of the heavier twin. These twins were born at many different hospitals throughout Australia and there was no clear way to check chorionicity or even to determine if it

Table 4a(a) Percentage of *DSM-IV* Diagnoses Obtained by Twins and Siblings

DSM-IV diagnosis	Male Twins	Female Twins	Male Siblings	Female Siblings	Overall
Inattention	10.5%	4.8%	8.9%	3.1%	7.3%
Hyp-imp	3.4%	1.8%	1.6%	0.7%	2.3%
Combined	6.5%	2.0%	4.0%	1.1%	3.8%

Table 4bPercentage of Male Twins Meeting the Diagnostic Criteria According to Weight for Gestational Age Category

DSM-IV diagnosis	WGA3	WGA410	WGA10	WGA1189
Inattention	19.5%	15.9%	17.1%	9.2%
Hyp-imp	4.9%	2.3%	4.0%	4.0%
Combined	9.8%	4.5%	6.2%	6.1%

had been checked, far less to determine if there had been any more formal assessment of the twin-transfusion syndrome in MZ twins.

Within each of these groups, paired-samples t tests investigated whether the heavier twin had more symptoms/problems than the lighter twin. Any advantages were in the heavier twin and only for inattention symptoms. Those MZ twins who were more than 20% heavier than their twin had significantly lower Inattention scores than the lighter twins, both at Time 1: t(102) = 2.41, p < .05 and at Time 2: t(98) = 2.15, p < .05. There were no differences in DZ twins at either time. e.g. at Time 2, t(145) = 0.52. For the MZ and DZ twins where the difference in weight was less than 20%, the heavier twin also had fewer inattention problems, at Time 2, t(568) = 2.25, p < .01 and t(586) = 2.09, p < .05 respectively.

Demographic Factors

Previous research has shown that socioeconomic variables may affect behavioral outcomes (Zubrick et al., 2000). Regression analyses of inattention and hyperactivity-impulsivity, and discriminant function analyses of speech and reading were carried out on twins who were small for gestational age (up to, and including the 10th percentile, n = 258 with complete data). Only one variable reached statistical significance. Father's occupation was found to be related to reading score but the effect sizes were very small and of negligible influence.

Discussion

The major finding of this study was that both male and female twins who were extremely growth restricted (WGA3 — below the 4th percentile in weight for gestational age) were disadvantaged in terms of later inattention, speech and reading scores. This does represent a significant number of children, given the high proportion of twins who were so far below these singleton-based norms. There was a specific disadvantage for male twins compared with females in the areas of inattention, hyperactivity-impulsivity, and speech. The effects of SGA were confined to extremely growth-restricted twins, as those born between the 3rd and the 11th percentile (WGA10) showed few effects in terms of behavioral or learning problems. However, when the number of children reaching diagnostic criteria was considered, both WGA3 and WGA410 (i.e., from the 4th to the 11th percentile) male twins had a higher percentage of DSM-IV diagnoses of the inattention subtype of ADHD. It is likely that the problems detected in this sample were an underestimate of problems in the general population, and specifically of the relationship between SGA and ADHD in twins. Not only was this a volunteer sample, but also those with physical or intellectual disabilities had already been excluded.

For male and female twins, the fact that the ADHD effects of SGA were largely confined to inattention, tends to support the argument that there may be a different etiology for inattention and hyperactivity-impulsivity. SGA also influences speech and reading problems, adding weight to the argument these are more strongly associated

with inattention than with hyperactivity-impulsivity (Hay & Levy, 1996).

Little is known about the causal relationship between perinatal events such as being SGA with disorders of attention and language processing (Emory et al., 1992), but there is some evidence that subclinical perinatal insults such as hypoxia have been associated with impairment involving secondary and tertiary neuropsychological processes. Secondary and tertiary neuropsychological processes involve more sophisticated cortical processes and functioning as opposed to primary or more "gross" functions (Luria, 1973, 1981, cited in Emory et al., 1992). For example, damage may affect "cognitive processes involving elaboration, amplification, and interrelated perception of incoming sensory information (secondary) and cross-modal integration of information (tertiary) across different sensory modalities and cortical zones" (Beaumont, 1983; Luria, 1973, cited in Emory et al., 1992, p. 32). In children who have been born full-term in the absence of evidence of intellectual disability, damage to these areas is shown in disinhibition syndromes such as hyperactivity and attention, as well as more generally in learning disorders (Emory et al., 1992). It is possible that being born SGA involves a degree of hypoxia and other subclinical perinatal insults and provides an explanation of impairment in secondary and tertiary functioning shown in this study. The present data showing the effects of SGA on inattention symptoms may imply that the area of cortical functions most severely affected involves attentional processes. This effect was most obvious in male twins who have more severe symptoms and appear to be more vulnerable (Gilberto & Santos, 1997).

No evidence was found to suggest that the WGA3 or WGA10 sibling sub-sample experienced any disadvantages in terms of ADHD or learning problems. However, these results remain inconclusive, as the number of siblings who were SGA was small. Relatively low subject numbers in previous research on SGA effects in singletons may contribute to the ambiguous results obtained to date and emphasise the need to distinguish multiples and singletons in perinatal research.

Comparison of MZ and DZ concordance rates suggests a genetic link in being SGA (consistent with Wang et al., 2002). The number of MZ twins who were concordant at WGA3 and WGA10 was much higher than for the DZ twins. The genetic effects of foetal growth may be due to one of three possibilities: the genetic effect of the mother, the foetus, or an interaction between the foetus and the mother (Harrison et al., 1997). Analysis of the relative likelihood of each, is beyond the scope of the current paper, but is a direction that should be pursued in the future.

The role of the twin transfusion syndrome was impossible to demonstrate, given the impossibility of obtaining data nationwide on chorionicity. While both MZ and DZ heavier twins generally had fewer inattention symptoms at Time 2, when the birthweight difference was less than 20%, the pattern was different in those with a birthweight difference more than 20%. Here it was only the MZ twins where the heavier twin had fewer symptoms and this was common to both times of measurement. Future investigations need to include formal pathological assessment of

placentas to determine if this is associated with SGA in general or specifically with the transfusion syndrome.

In conclusion, it appears that male twins born small for gestational age are at a triple disadvantage and extends previous findings of male twins being "doubly" disadvantaged in terms of learning and ADHD (Hay et al., 1987; Levy, Hay, McLaughlin, et al., 1996). That is, being male, twin and small for gestational age puts them at even greater risk of developing later problems. For SGA singletons, no major behavioral consequences were demonstrated, though it should be pointed out that the low birthweight sibling numbers were very small, and the gender differences in the Hack et al. (2002) study are consistent with the present findings. Implications for speech and reading warrant further investigation.

It was also clear that there are differences in mean birthweight between twins and singletons as well as between sexes. Roberts and Lancaster (1999) have reported Australian national birthweight percentiles by gestational age and Min et al. (2000) have reported foetal and birthweight percentiles for twins, from a cohort study, based on 1831 pregnancies of twins born alive at 28 or more weeks of gestation. While the overall pattern of foetal growth was slower for twins versus singletons from about 30 weeks gestation, there still remained a cohort of twins who had no growth problems and do not differ as much as previously believed.

Future clinical efforts should target interventions towards male twins. Male twins who are small for gestational age in particular should be identified as at risk and carefully assessed. Twins are already at a higher risk for behavioral and learning problems and if they are SGA as well, they are at further risk. Parents and professionals should be alerted to these additional risks, so that SGA male twins may be appropriately monitored and early intervention introduced where appropriate. The fact that if anything problems were more obvious at the second assessment when the children were 8- to 12 years old does give more reason to ignore the old adage that "they are twins and will grow out of it".

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References

- American Psychiatric Association. (1987). *Diagnostic and statistical manual of mental disorders* (3rd ed. rev.). Washington, DC: Author.
- American Psychiatric Association. (1994). *Diagnostic and statistical manual of mental disorders* (4th ed.). Washington, DC: Author.

- Blair, E., & Stanley, F. (1985). *Intra-uterine growth charts*. Fyshwick, ACT: Canberra Publishing and Printing Co.
- Botting, N., Powls, A., & Cook, R. W. I. (1997). Attention deficit hyperactivity disorders and other psychiatric outcomes in very low birthweight children at 12 years. *Journal of Child Psychology and Psychiatry*, 38, 931–941.
- Brito, G. N., & Santos, T., R. (1997). Behavioural and neuropsychological correlates of inattention and hyperactivity in school children. Paper presented at the *International Society* for Research in Child and Adolescent Psychopathology, Paris.
- Breslau, N., Brown, G. G., DelDotto, J. E., Kumar, S., Ezhuthachan, S., Andreski, P., et al. (1996). Psychiatric sequelae of low birth weight at 6 years of age. *Journal of Abnormal Child Psychology*, 24, 385–400.
- Bryan, E. (1992). The twin fetus. In E. Bryan (Ed.), *Twins and higher multiple births pregnancies: A guide to their nature and their nurture* (pp. 46–72). London: Edward Arnold.
- Conway, D., Lytton, H., & Pysh, F. (1980). Twin-singleton language differences. Canadian Journal of Behavioral Science, 12, 264–271.
- Dammann, O., Wlather, H., Allers, B., Schroeder, M., Drescher, J., Lutz, D., et al. (1996). Development of a regional cohort of very-low-birthweight children at six years: Cognitive abilities are associated with neurological disability and social background. *Developmental Medicine and Child Neurology*, 38, 97–108.
- Dudley, D. K. L., & D'Alton, M. E. (1966). Single fetal death in twin gestation. *Seminars in Perinatology, 10,* 65–72.
- Emory, E. K., Savoie, T. M., Ballard, J., Eppler, M., & O'Dell, C. (1992). Perinatal. In A. E. Puente, & R. J. McCaffrey (Eds.), Handbook of neuropsychological assessment (pp. 15–49). London: Plenum Press.
- Fulker, D.W. (1997). Nature and nurture: Heredity. In H. J. Eysenck (Ed.), *The structure and measurement of intelligence* (pp. 102–132). New York: Springer.
- Golding, J. (1991). The epidemiology of perinatal death. In M. Kiely (Ed.), *Reproductive and perinatal epidemiology* (pp. 401–444). Washington, DC: CRC Press.
- Hack, M., Flannery, D. J., Schluchter, M., Cartar, L., Borawski, E., & Klein, N. (2002). Outcomes in young adulthood for very-low-birth-weight infants. *The New England Journal* of Medicine, 346, 149–157.
- Haden, R., & Penn, C. (1985). The twin situation and its effects on syntax and interactional language over time. *British Journal* of Disorders of Communication, 20, 19–29.
- Harrison, G. A., Humphrey, K. E., Jones, N., Badenhop, R., Guo, G. G., Elakis, G., et al. (1997). A genome-wide linkage study of preeclampsia/eclampsia reveals evidence for a candidate region on 4Q. American Journal of Human Genetics, 60, 158–167
- Hart, E. L., Lahey, B. B., Loeber., R., Applegate, B., & Frick, P. J. (1995). Developmental change in attention-deficit hyperactivity disorder in boys: A four-year longitudinal study. *Journal of Abnormal and Child Psychology*, 23, 729–749.
- Hawdon, J. M., Hey, E., Kolvin, I., & Fundudis, T. (1990). Born too small — Is outcome still affected? *Developmental Medicine* and Child Neurology, 32, 943–953.
- Hay, D. A., Collett, S. M., Johnston, C. J., O'Brien, P. J., & Prior, M. (1986) Do twins and singletons have the same language

- and reading problems? In C. Pratt, A. F. Garton, W. E. Turner, & A. R. Nesdale (Eds.), *Research Issues in Child Development* (pp. 125–134). Sydney: Allen and Unwin.
- Hay, D., & Levy, F. (1996). The differential diagnosis of ADHD. The Australian Educational and Developmental Psychologist, 13, 69–78.
- Hay, D. A., McStephen, M., & Levy, F. (2001) The genetic analysis of attentional disorders. In F. Levy, & D. Hay, Attention, genes and ADHD (pp. 7–34). Philadelphia, PA: Brunner-Routledge, Hove, Taylor and Francis.
- Hay, D. A., McStephen, M., Levy, F., & Pearsall-Jones, J. (2002). Recruitment and attrition in twin register studies of childhood behavior: The example of the Australian Twin ADHD Project. Twin Research, 5, 324–328..
- Hay, D. A., O'Brien, P. J., Johnston, C. J., & Prior, M. (1984). The high incidence of reading disability in twin boys and its implications for genetic analysis. Acta Geneticae Medicae et Gemellologiae, 33, 223–236.
- Hay, D. A., Prior, M., Collett, S., & Williams, M. (1987). Speech and language development in preschool twins. *Acta Geneticae Medicae et Gemellologiae*, 36, 213–223.
- Henderson-Smart, D. J. (1995). Postnatal consequences of chronic intrauterine compromise. Reproductive Fertility Development, 7, 559–65.
- Laucht, M., Esser, G., Baving, L., Gerhold, M., Hoesch, I., Ihle, W., et al. (2000). Behavioral sequelae of perinatal insults and early family adversity at 8 years of age. *Journal of the American Academy of Child and Adolescent Psychiatry*, 39, 1229–1237.
- Levy, F., Hay, D., McLaughlin, M., Wood, C., & Waldman, I. (1996). Twin-sibling differences in parental reports of ADHD, speech, reading, and behavioural problems. *Journal of Child Psychology and Psychiatry, 37*, 569–578.
- Levy, F., Hay, D., McStephen, M., Wood, C., & Waldman, I. (1997). Attention Deficit Hyperactivity Disorder (ADHD): A category or a continuum? Genetic analysis of a large-scale twin study. Journal of the American Academy of Child and Adolescent Psychiatry, 36, 737–744.
- Levy, F., Hay, D. A., & Rooney, R. (1996). Predictors of persistence of ADHD symptoms in a large-scale twin study: Preliminary report. *The ADHD Report, 6.*
- Low, J. A., Handley-Derry, M. H., Burke, S. O., Peters, R. D., Pate, E. A., Killen, H. L., et al. (1992). Association of intrauterine fetal growth retardation and learning deficits at age 9 to 11 years. American Journal of Obstetrics and Gynecology, 167, 1499–1505.
- McNeill, T. F. (1995). Perinatal risk factors and schizophrenia: Selective review and methodological concerns. *Epidemiological Reviews*, 17, 107–112.
- Machin, G. A., & Still, K. (1995). The twin-to-twin transfusion syndrome: Vascular anatomy of monochorionic placentas and their clinical outcomes. In K. L. Keith, E. Papiernik-Berkhauer, & D. E. Keith (Eds.), *Multiple pregnancy* (pp. 367–394). New York: Parthenon Publishing.
- Min, S-J., Luke, B., Gillespie, B., Min, L., Newman, R. B., Mauldin, J. G., et al. (2000). Birth weight references for

- twins. American Journal of Obstetrics & Gynecology, 182, 1250–1257.
- Mogford-Bevan, K. (1999). Twins and their language development. In A. Sandbank (Ed.), *Twin and triplet psychology* (pp. 36–60). London: Routledge.
- Palmer, L., Blair, E., Petterson, B., & Burton, P. (1995). Antenatal antecedents of moderate and severe cerebral palsy. *Pediatric* and Perinatal Epidemiology, 9, 171–184.
- Paz, I., Gale, R., Laor, A., Danon, Y. L., Stephenson, D. K., & Seidman, D. S. (1995). The cognitive outcome of full-term small for gestational age infants at late adolescence. *Obstetrics* and Gynecology, 85, 452–456.
- Powers, W. F., Kiely, J. L., & Fowler, M. G. (1995). The role of birth weight, gestational age, race and other infant characteristics in twin intrauterine growth and infant mortality. In L. G. Keith, E. Papiernik-Berkhauer, & D. M. Keith (Eds.), *Multiple pregnancy* (pp. 163–174). New York: Parthenon Publishing.
- Roberts, C. L., & Lancaster, P. A. L. (1999). Australian national birthweight percentiles by gestational age. *Medical Journal* of Australia, 170, 114–118.
- Rooney, R., Hay, D. A., & Levy, F. (1998). Weights defining small-for-gestational-age in twins. In S. J. Ulijaszek, F. E. Johnston, & M. A. Preece (Eds.), *The Cambridge encyclopedia of human growth and development* (p. 79). Cambridge: Cambridge University Press.
- Schothurst, P. F., & van Engeland, H. (1996). Long-term behavioral sequalae of prematurity. *Journal of the American Academy of Child and Adolescent Psychiatry*, 35, 175–183.
- Sokol, D. K., Moore, C. A., Rose, R. J., Williams, C. J., Reed, T., & Christian, J. C. (1995). Intra-pair differences in personality and cognitive ability among young monozygotic twins distinguished by chorion type. *Behavior Genetics*, 25, 457–466.
- Spitz, E., Carlier, M., Vacher-Lavenu, M., Reed, T., Moutier, R., & Busnel, M. (1996). Long-term effect of prenatal heterogeneity among monozygotes. *European Bulletin of Cognitive Psychology*, 15, 283–308.
- Stanley, F. J., & English, D. R. (1986). Prevalence of risk and risk factors for cerebral palsy in a total population cohort of low birthweight (<2000g) infants. *Developmental Medicine and Child Neurology*, 28, 559–568.
- Wang, X., Zuckerman, B., Pearson, C., Kaufman, G., Chen, C., Wang, G., et al. (2002). Maternal cigarette smoking, metabolic gene polymorphism, and infant birth weight. *JAMA*, 287, 195–202.
- Watt, J. (1989). The consequences of intrauterine growth retardation: What do we know? *Australian and New Zealand Journal of Obstetrics & Gynecology*, 29, 279–287.
- Zubrick, S. R., Kurinczuk, J. J., McDermott, B. M. C., McKelvey, R. S., Silburn, S. R., & Davies, L. C. (2000). Fetal growth and subsequent mental health problems in children aged 4 to 13 years. *Developmental Medicine & Child Neurology*, 42, 14–20.

APPENDIX

Inattention and Hyperactivity-Impulsivity Items based on DSM-III-R (indicated by *) and suggested by Hart et al. (1995), and DSM-IV criteria

Inattention	Hyperactivity-Impulsivity			
Inattentive*	Difficulty awaiting turn*			
Distractible*	Interrupts or intrudes*			
Does not follow instructions*	Blurts out answers*			
Does not seem to listen*	Dangerous acts*			
Loses things*	Fidgety and restless*			
Shifts activities*	Does not stay seated*			
Difficulty organising tasks	Does not play quietly*			
Avoids tasks	Talks excessively*			
Forgetful	Often "on the go" as if driven by a motor			