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ARTICLE AVAILABLE ONLINE
Twin Research and Human Genetics
Volume 14 ▮ Number 6 ▮ pp. 573–579

Twin-to-Twin Delivery Time: Neonatal Outcome of the Second Twin

Susanne Schneuber,[1] Eva Magnet,[1] Josef Haas,[1] Albrecht Giuliani,[1] Thomas Freidl,[2] Uwe Lang[1], and Vesna Bjelic-Radisic[1]

[1] *Department of Obstetrics and Gynecology, Medical University Graz, Graz, Austria*
[2] *Department of Pediatrics and Adolescent Medicine, Medical University Graz, Graz, Austria*

Objective: To examine the effect of twin-to-twin delivery time (TTDT) on neonatal outcome. *Methods:* We evaluated twin deliveries >34 weeks of gestation. Twin pregnancies with both twins delivered by cesarean section and pregnancies with antenatal complications were excluded. We analyzed TTDT and neonatal outcomes of the second twin (umbilical arterial pH value (pH_{art}), Apgar scores at 1, 5 and 10 minutes, need for intensive care). The study population was divided into two homogenous groups based on the mode of delivery: (A) vertex presentation and vaginal delivery of both twins, (B) vertex presentation and vaginal or vaginal operative delivery of twin I, breech or transverse presentation and vaginal breech delivery or cesarean section (CS) of twin II. *Results:* A total of 207 twin pairs were included in our study. In Group A (n = 151) there were no significant correlations between TTDT and pH_{art} or Apgar scores at 1,5 and 10 minutes of twin II (p = .156; 0.861; 0.151 and 0.384, respectively). In Group B (n = 56), the mean pH_{art} of twin II was inversely correlated to TTDT, but not significantly (p = .417). TTDT was inversely related to 1-min and 5-min Apgar scores, but not significantly (p = .330; p = .138, respectively). The 10-min Apgar score showed no correlation with TTDT (p = .638). *Conclusion:* Increasing TTDT was not associated with adverse fetal outcome. Expectant management of the second twin appears possible and elapsed time alone does not appear to be an indication for intervention.

Keywords: twins, twin-to-twin delivery time, umbilical arterial pH, neonatal outcome

The incidence of twin pregnancies has increased in past decades, mainly as a result of assisted reproduction techniques. Twin gestation is estimated to complicate 1–2% of all pregnancies (Carvalho et al., 2007; Suh et al., 2007) and twin pregnancies are associated with increased perinatal morbidity and mortality (Smith et al., 2007). Morbidity at second twins is higher than at first twins (Bjelic-Radisic et al., 2007; Oyelese et al., 2005; Yang et al., 2006), mainly due to intrapartum hypoxia (Smith et al., 2002; Suh et al., 2006).

Obstetric management of twin pregnancies is controversial. There is no consensus whether the TTDT has any effect on the morbidity or mortality of the second twin or whether there is a cut-off for optimal TTDT. After delivery of twin I there may be a risk that the significant reduction in uterine volume may lead to partial placental separation and reduced uterine perfusion, placental circulation and fetal supply. (Ferguson, 1964; Leung et al., 2004; Spurway, 1962; Ware, 1971) Therefore, TTDT theoretically should be kept brief. Some studies suggest that the second twin should be delivered within 15–30 minutes of the first twin (Edris et al., 2006; Erdemoglu et al., 2003; Hartley & Hitti, 2005; Leung et al., 2004; MacLennan, 1994; McGrail & Bryant, 2005; Stein et al., 2008; Suh et al., 2007); other studies concluded that the TTDT is of minor importance. (Bartnicki et al., 1992; Briese et al., 1994; Rayburn et al., 1984; Rydström & Ingemarsson, 1990)

The present study investigated the relationship between TTDT and neonatal outcome. Our hypothesis was that increasing TTDT was associated with a decline of arterial pH (pH_{art}) and adverse neonatal outcome of twin II.

RECEIVED 20 May, 2011; ACCEPTED 28 July, 2011.

ADDRESS FOR CORRESPONDENCE: Susanne Schneuber, Department of Obstetrics and Gynecology, Medical University of Graz, Auenbruggerplatz 14, A-8036 Graz, Austria. E-mail: susanne.schneuber@medunigraz.at

Materials and Methods

We reviewed all twin deliveries > 34 weeks of gestation at our institution between 1993 and 2002. A total of 300 twin pairs were identified from computerized records. In order to eliminate factors that may influence neonatal outcome, we excluded twins with any maternal and following fetal complications:

1. discordant growth
2. intrauterine death of a fetus before the onset of labour
3. intrauterine growth restriction
4. fetal malformations
5. preeclampsia or HELLP syndrome
6. both twins delivered by elective or secondary cesarean section (CS)

These criteria were used in an attempt to eliminate cases where poor fetal outcome could be related to criteria other than the method and timing of delivery. Overall, 207 twin pairs met the inclusion criteria.

Obstetric data included the presentation and route of delivery of both twins, the interval between the delivery of both twins (TTDT) and neonatal outcome. Continuous electronic fetal heart rate monitoring of each twin was performed throughout labour. All deliveries were supervised by an experienced obstetrician. After delivery of the leading twin, the position of twin II was controlled by ultrasound. If in transverse position, twin II was stabilized into a longitudinal position by external version. Epidural anesthesia was offered to all women. Oxytocin was used liberally to induce or augment labour.

We separated the overall population into two groups based on presentation and mode of delivery:

(A) vertex presentation and vaginal delivery of twin I and twin II

(B) vertex presentation and vaginal or vaginal operative delivery of twin I, breech or transverse presentation and vaginal breech delivery or cesarean section (CS) of twin II.

This was done because in complicated deliveries, such as breech delivery, vaginal operative delivery or CS TTDT was interrupted and therefore not easily controllable.
We used three categories for the time delay between twin I and II in order to examine trends: ≤ 15, 16–30 and > 30 minutes. Relationship between TTDT and neonatal outcome was evaluated in 15-minute intervals.

Neonatal outcome was assessed on the basis of:

1. umbilical arterial pH (pH_{art})
2. Apgar scores at 1, 5 and 10 minutes
3. postpartum need for neonatal intermediate or intensive care (NICU)
4. perinatal or neonatal morbidity or mortality at 28 days of age.

We performed a subgroupanalysis on severe asphyxia, which was defined as umbilical pH_{art} < 7.00; Apgar score 0–3 beyond 5 minutes, encephalopathia or multiorgan complications (Nelson & Ellenberg, 1981, Leuthner & U. G., 2004). The second objective was to determine the correlation between severe asphyxia and TTDT.

Some data of our study population were used in the manuscript by Bjelic-Radisic et al. published in this journal in 2007. However, issue of this manuscript was different.

Statistical Methods

For clinical data descriptive statistics were used (mean ± standard deviation; *SD* for symmetric data, and median for skewed data). Categorical variables are presented as absolute frequency (percentage, %). TTDT was categorized into three subgroups: ≤ 15 min, 16–30 min and > 30 min. Hypothesis testing was done with t-tests and Wilcoxon-Mann-Whitney, after checking the normality assumption with Shapiro-Wilks test and QQ-plots. The comparison of the factors group A/B and TTDT was done with a two-way ANOVA and Bonferroni post-hoc tests; linearity of Apgar values within the TTDT categories was checked with the Jonckheere-Terpstra test. In the results, only *p* value of the primary analysis (usually ANOVA) are reported. Nonparametric tests and linearity tests yielded different *p* values, but no change in significances was observed. Crosstabs were analyzed with Pearson's chi-square test (using the exact option in SPSS) and Fisher's exact test, depending on the size of expectation values. Statistical analysis was done with SPSS 17 (SPSS Inc. Chicago, Il.) and StatXact 7.0 (Cytel Corp., Cambridge, Ma). *P* values < .05 were considered significant.

Results

A total of 207 cases met the inclusion criteria and were assigned to group A or B. The baseline characteristics of the two groups are shown in Table 1. Mean maternal age was 29.3 ± 5.0 years, mean gestational age was 37.5 weeks. Birthweight of twin I averaged by 2509 ± 446 grams, mean birthweight of twin II was 2462 ± 429 grams. Mean TTDT was 16 min (range 1–173). Mean pH_{art} of twin I was 7.29 ± 0.07, while it was was 7.22 ± 0.10 in twin II.

Dividing the TTDT into subgroups, no statistical signifance was observed for pH_{art} (ANOVA, p = .417) and Apgar scores at 1 and 10 minutes in twin II (ANOVA p = ,431, p = .151). The Apgar score at 5 minutes was different (ANOVA, p = .042; see Table 2, Figure 1). Seventy-one (34.3%) first-born twins and 92 (44.4%) second-born twins were admitted to the neonatal intensive care unit (NICU), but these differences were not statistically significant (chi-square test, p=0.044). There were four second twins with severe acidosis, but none of those had severe asphyxia (umbilical pH_{art} < 7.00; Apgar-Score 0–3 beyond 5 min, encephalopathia or multiorgan complications).

https://doi.org/10.1375/twin.14.6.573 Published online by Cambridge University Press

TABLE 1

Study Population

	Group A (n = 151)	Group B (n = 56)	p	Total (n = 207)
Maternal age	29.2 ± 5.3 (29)	29.6 ± 4.0 (29)	0.572	29.3 ± 5.0 (29)
Gestational age	37.5 ± 1.6 (37)	37.5 ± 1.7 (37.5)	0.820	37.5 ± 1.7 (37)
Primigravidae	46 (30.5%)	13 (23.2%)	0.387	59 (28.5%)
Twin I				
pHart	7.29 ± 0.06	7.30 ± 0.07	0.451	7.29 ± 0.07
Apgar score 1	8.65 ± 0.92	8.71 ± 1.04	0.683	8.67 ± 0.95
Apgar score 5	9.74 ± 0.56	9.89 ± 0.37	0.060	9.78 ± 0.52
Apgar score 10	9.94 ± 0.26	9.98 ± 0.14	0.330	9.95 ± 0.23
Need for intensive care	55 (36.4%)	16 (28.6%)	0.326	71 (34.3%)
Weight (gram)	2465 ± 440	2625 ± 446	0.022	2509 ± 446
Twin II				
pHart	7.24 ± 0.09	7.17 ± 0.12	< 0.001	7.22 ± 0.10
Apgar Score 1	8.2 ± 1.6	6.6 ± 2.3	< 0.001	7.78 ± 1.9
Apgar score 5	9.7 ± 0.7	9.2 ± 0.9	< 0.001	9.59 ± 0.8
Apgar score 10	9.9 ± 0.4	9.8 ± 0.4	0.097	9.87 ± 0.4
Need for intensive care	63 (41.7%)	29 (51.8%)	0.218	92 (44.4%)
Weight (gram)	2477 ± 430	2421 ± 426	0.403	2462 ± 429
TTDT (minutes)	13 ± 12 (median 10)	22± 26 (median 13)	0.003	16 ± 17

There was no morbidity or mortality within 28 days in either group. Increasing TTDT was not associated with admission to NICU.

Group A

Group A consisted of 151 twin pregnancies, in which both twins were in vertex presentation and were delivered spontaneously (Table 1). The mean TTDT was 13 minutes (range 1–76). The mean pH_{art} of twin I was significantly higher than that of twin II (7.29 ± 0.06 vs. 7.24 ± 0.09; t-test, $p < .001$) (Table 1).

Table 2 and Figure 1 describe umbilical arterial blood gas parameters grouped by TTDT. Increasing TTDT was not significantly associated with the pH_{art} of twin II ($p = .156$).

In Group A no significant relationship was seen between TTDT and 1-, 5- and 10 min-Apgar scores (ANOVA, $p = .861$; 0.151; 0.384, respectively). A total of 63 (41.7%) second twins in Group A needed intensive care but there was no asphyxia-related morbidity or mortality within 28 days. No case with severe asphyxia was reported.

Group B

Group B included 56 twin pairs with twin I in vertex presentation and delivered vaginally, twin II either in breech or transverse presentation and vaginal breech delivery, or CS for the twin II. In 48 cases twin II was in breech presentation and delivered vaginally, in the remaining 8 cases twin II was delivered by CS. Indication for CS was transverse presentation in 6 cases and breech presentation and suspicious cardiotocogram in 2 cases.

TTDT averaged 22 min. (range, 1–173). Mean pH_{art} was 7.30 ± 0.07 in twin I and 7.17 ± 0.12 in twin II (t test $p < .001$; Table 1).

Mean pH_{art} of twin II tended to be inversely related to TTDT, but did not show any significance (ANOVA, $p = .417$). TTDT also tended to be inversely related to Apgar 1- (ANOVA, $p = .330$) and Apgar 5- ($p = .138$) scores without statistical significance, while 10-min was not associated with TTDT ($p = .638$). In Group B 29 (51.8%) second twins were admitted to NICU (Table 2 and Figure 1). There were 4 cases of severe acidosis in Group B: 1 case ≤ 15 minutes TTDT, 1 case between 16 and 30 minutes and 2 cases > 30 minutes (Table 3), but no severe asphyxia. There was no 28-day morbidity or mortality.

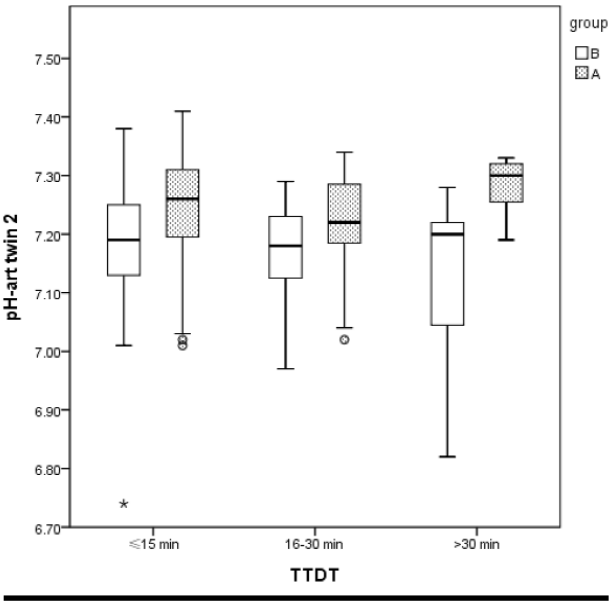

FIGURE 1

pH_{art} of twin II according to TTDT.

https://doi.org/10.1375/twin.14.6.573 Published online by Cambridge University Press

TABLE 2

pH_{art}, 1-, 5- and 10 min Apgar Score in Twin II According to TTDT

Interval (min)	*n*	arterial pH	Apgar 1	Apgar 5	Apgar 10	Intensive care
Group A						
≤ 15	111	7.24 ± 0.09	8.2 ± 1.7	9.7 ± 0.7	9.9 ± 0.3	45 (41%)
16–30	33	7.22 ± 0.79	8.4 ± 1.5	9.7 ± 0.7	9.8 ± 0.7	16 (48%)
> 30	7	7.28 ± 0.06	8.6 ± 0.5	9.6 ± 0.5	9.8 ± 0.4	2 (29%)
Total	151	7.24 ± 0.09	8.2 ± 1.6	9.7 ± 0.7	9.9 ± 0.4	63 (42%)
		$p = .156$	$p = .861$	$p = .151$	$p = .384$	$p = .531$
Group B						
≤ 15	34	7.18 ± 0.12	6.9 ± 2.0	9.5 ± 0.7	9.9 ± 0.4	17 (50%)
16–30	11	7.17 ± 0.09	6.6 ± 2.5	8.9 ± 1.1	9.6 ± 0.5	5 (45%)
> 30	11	7.13 ± 0.14	5.8 ± 2.8	8.8 ± 1.2	9.7 ± 0.5	7 (64%)
Total	56	7.17 ± 0.12	6.6 ± 2.3	9.2 ± 0.9	9.8 ± 0.4	29 (52%)
		$p = .417$	$p = .330$	$p = .138$	$p = .638$	$p = .752$

TABLE 3

Outcome of Newborns With Severe Asphyxia ($pH_{art} < 7.00$)

	pHart	TTDT	Short-term outcome	Long-term outcome
Patient 1	6.82	67	HIE I*, IVH II**	Normal findings
Patient 2	6.99	1	Fract.humeri dext.	Normal findings
Patient 3	6.97	21	IRDS I***, pulmonal hemorrhage	Normal findings
Patient 4	6.74	39	Early onset Sepsis, IRDS II, pulmonal hemorrhage	Normal findings

Note: *hypoxic ischemic encephalopathia; **intraventricular hemorrhage; ***infant respiratory distress syndrome

Comparison Group A – Group B

There were no significant differences in terms of maternal age, gestational age or birthweight of twin I and II and between Group A and B [Table 1]. In Group B TTDT was significantly longer than in Group A (*t* test, $p = .03$). Defined by pH_{art} we found statistical significant worse neonatal outcome for twin II in Group B compared to twin II in Group A ($p < .001$). In addition significant lower 1-min and 5-min Apgar scores for twin II were found in Group B compared to twin II in Group A ($p < 0.001$). No significant differences were noticed in Apgar-Score 10 ($p = .097$).

Second twins in Group B were admitted to NICU more often than those in Group A, but this was not statistically significant (51.8% vs. 41.7%; p = ,22). Regarding to the difference in transfer to the NICU within the groups, our results showed that in Group B twin II was admitted significantly more often to NICU than twin I (chi-square test, 51.8% vs. 28.6%; p = .020), in Group A these indices did not differ significantly (41.7% vs. 36.4%; p = .401).

Discussion

In our study increasing TTDT was not associated with a significant decline of the umbilical cord pH_{art}. In both groups we could not find a significant increase in the incidence of metabolic acidosis of second twins according to increasing TTDT. The data do not suggest a clear cut-off level of TTDT to identify a higher probability of fetal acidosis.

Our findings are consistent with several studies in which TTDT was not considered to have any significant effect on the acid-base status or perinatal mortality of second twins (Rydström & Ingemarsson, 1990). Similarly, Briese et al. found no correlation between morbidity of the second twin and the time interval between the two deliveries (Briese et al., 1994). In contrast to our study, McGrail and Bryant (2005) found that longer TTDT is associated with a continuous slow decline in umbilical cord pH, though these small differences were not large enough to influence clinical management.

Bartnicki et al. (1992) used more precise criteria to evaluate the influence of the time interval on the second twin. These authors concluded that it is impossible to assess the influence of the time factor on the status of the second twin because in cases with suspicious cardiotocogram there was an obvious necessity for delivery by intervention. These results are consistent with our conclusion. In cases of uncomplicated twin delivery with a normal cardiotocogram there is no necessity for the second twin to be born as soon as possible after the birth of the first twin (Rayburn et al., 1984). This was borne out by our Group A, in which both twins were in vertex presentation and delivered vaginally. In this group there was no significant influence of TTDT on pH_{art}. Group A was compared with another group in which twin I was in vertex presentation and vaginal or vaginal oper-

https://doi.org/10.1375/twin.14.6.573 Published online by Cambridge University Press

ative delivery was performed, while twin II was in breech or transverse presentation and delivered vaginally or by CS. This group represented complex deliveries (vaginal delivery in breech position) and deliveries, in which suspicious fetal heart rate tracings (FHR) or imminent fetal asphyxia required immediate delivery by CS (8 cases). In the latter subgroup cases with suspicious FHR were included and fetal distress was an obvious indication for immediate delivery of the second twin. Still even in this group we could not find a significant decline of pH_{art} with increasing TTDT.

The outcome of twin II should not be assessed only on arterial blood gas levels or Apgar scores. Requirement for resuscitation, need for intensive care or multisystem organ dysfunction should be included when defining a hypoxic-ischemic event. The Apgar score itself has limitations, and should not be used alone to establish the diagnosis of asphyxia. An Apgar score of 0–3 at 5 minutes may correlate with neonatal mortality but taken alone does not predict later neurological dysfunction (Committee on Obstetric Practice, ACOG, 2006). Nelson & Ellenberg concluded that a score of 0–3 at 5 minutes was associated with a slightly increased risk of cerebral palsy compared with higher scores. However, 75% of children with cerebral palsy had normal scores at 5 minutes (Nelson & Ellenberg, 1981).

The correlation of fetal acidosis ($pH_{art} < 7.00$) on neonatal outcome has been discussed controversially. A recent metaanalysis, in which cord pH was compared with neonatal long-term outcome demonstrated that low arterial cord pH was significantly associated with neonatal mortality, hypoxic ischemic encephalopathy, intraventricular hemorrhage, periventricular leucomalacia or cerebral palsy (Malin et al., 2010). Nonetheless, earlier publications showed that most neonates with a $pH_{art} < 7.00$ had no significant long- or short-term morbidity (Goldaber et al., 1991, Low et al., 1997). Some authors suggest that other variables, such as base deficit (BD) or lactate, should be included in the analysis (Low et al., 1997). Andres et al. (1999) concluded that the metabolic component of fetal acidemia (i.e., base deficit and bicarbonate) is the most important variable in subsequent neonatal morbidity (Andres et al.). Unfortunately we did not have BD data available for our study.

In the present study the rate of intensive care for twin II — representing neonatal short-term-outcome — was not correlated with TTDT in either groups. Breech presentation of twin II was associated with longer TTDT and with worse short-term outcome of the second twin — defined by lower pH_{art} and Apgar scores and higher rate of admission to NICU. However, these indices did not have an effect on neonatal outcome at 28 days.

Recent publications contradicted earlier findings and suggested that the occurrence of intrapartum complications was more likely with increasing TTDT. It has been proposed that the TTDT should be less than 15 minutes and certainly not more than 30 minutes (MacLennan AH, 1994). Similarly, other authors suggest that fetal acidemia may develop when the TTDT exceeds 20 minutes (Suh et al., 2007). These observations have been supported by another cohort study that found a higher risk of metabolic acidosis of the second twin after a TTDT of more than 60 minutes (Edris et al., 2006).

These data are in line with those of a study of 118 patients showing a significant correlation between all umbilical cord blood gas parameters of the second twin and TTDT (Leung et al., 2002). Like us, Leung also focused on those twin pairs at or beyond 34 weeks of gestation and vaginal delivery of twin I. In contrast to our findings the risk of fetal distress and acidosis in the second twin were high when TTDT exceeded 30 minutes. Overall, Leung detected seven cases of severe acidosis (6.6%) and concluded that the pH_{art} of twin II was not less than 7.0 in any case delivered within 15 min after delivery of twin I, in 5.9% if within 16–30 minutes and in 27% if more than 30 minutes. In our study there were only 4 cases (1.9%) with a $pH_{art} < 7.00$: 1 case ≤ 15 minutes TTDT, 1 case between 16 and 30 minutes and 2 cases >30 minutes (Table 4). However, these numbers were not statistically significant and there was no influence on clinical management.

Erdemoglu included twin deliveries beyond 25 weeks of gestation and found the gestational age to be the most important factor influencing Apgar scores (Erdemoglu et al., 2003). A delivery interval time of > 15 minutes was the most important factor affecting the Apgar scores in the breech-presenting second twin or in a second twin of > 1900g. These results were not confirmed by our study, in which breech presentation was associated with lower Apgar-Scores and lower pH_{art} values, though this decline was not high enough to impact clinical procedure. Most recently, Stein et al. concluded that the TTDT itself seems to be a risk factor for adverse short-term outcome and therefore TTDT should be kept short.

Collectively these studies detected an association between TTDT and neonatal outcome and support a TTDT less than 30 min or 60 min, respectively. However, all these studies were retrospective and possible bias cannot be excluded.

The strength of our study was that considerations were not based only on short-term outcome but extended follow-up up to 28 days. Limitations of the present study include its retrospective nature and that BD was not included. Also we have no information on chorionicity, a factor that might have influence on neonatal outcomes. Although we have a large number of twin deliveries (207), we had no second-born twins meeting the criteria of birth asphyxia. The major strength of our study was that all patients were treated in the same institution with consistent guidelines and that neonatal outcome was extended to 28 days.

In conclusion, our data suggest that increasing TTDT by itself has no influence on neonatal morbidity. Expectant management of the second twin is reasonable and no inter-

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vention is necessary on the basis of time only. However, we believe that a continuous FHR monitoring of the second twin is important to ensure good perinatal outcome.

Based on our data the following recommendations are justified: In twin pregnancies > 34 weeks of gestation with both fetuses in vertex presentation TTDT is of minor importance and twin II need not be delivered promptly after twin I, if constant fetal monitoring is guaranted and immediate operative delivery is possible. Even in those cases, in which twin I is in vertex presentation and twin II is in breech presentation, expectative management is justified, as long as fetal monitoring is guaranted and the option of immediate operative delivery readily available.

Acknowledgment

We thank K. Tamussino, MD for the native speaker review of our manuscript.

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https://doi.org/10.1375/twin.14.6.573 Published online by Cambridge University Press