



Acta Genet Med Gemellol 38:49-56 (1989)  
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Received 3 February 1989  
Final 2 March 1989

## **Maternal Alcohol and Pentazocine Abuse: Neonatal Behavior and Morphology in an Opposite-Sex Twin Pair**

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**Abstract.** A pair of preterm, opposite-sex twins were examined during the lying-in period for behavioral and morphological effects of maternal alcohol and pentazocine abuse during pregnancy. A few morphological features typical of fetal alcohol syndrome were observed in each infant, and the male infant only was above the standardized mean in minor physical anomalies. The male's behavioral scores were more likely to be deviant from the standardized mean than the female's. Specifically, the male was more irritable, both spontaneously and in response to specific stimuli; highly active while awake and handled for the presentation of stimuli; more active than average during sleep; and low on ratings that reflect the attitude of the examiner toward the infant. These findings imply individual and gender differences in behavioral susceptibility to teratogens.

**Key words:** Twins, Alcohol abuse, Drug abuse, Neonatal behavior, Sex differences

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### **INTRODUCTION**

In recent years research in teratology has demonstrated the deleterious effects of maternal consumption of alcohol and various drugs on offspring. Whereas initial reports of children exposed to alcohol in utero included morphological changes and mental retardation [7], subsequent work has indicated the presence of functional deficits during the neonatal period which include irritability, tremulousness, hyperactivity, poor sucking ability, and poor habituation on day one [19,22]. The observed effects have not been consistent, and they may reflect genetic factors,

patterns and chronicity of alcohol use, and cessation of alcohol abuse during the pregnancy [13,14, 19].

Similarly, it has been demonstrated that other abused drugs have an effect on the newborn [16,20]. One such drug is pentazocine (Talwin) which, when used alone or in combination with other drugs such as tripeleennamine citrate or codeine, can result in a neonatal withdrawal syndrome consisting of tremors, irritability, feeding difficulties, and hyperactivity, in addition to low birth weight and a high pitched cry [3-6,9,15]. Again, individual differences are found, so that an infant may appear to be unaffected by daily prenatal exposure, or when the drugs have been discontinued at least two months prior to birth [3]. In one case study an exposed infant who had exhibited neonatal symptoms appeared to be normal at one month of age [15].

The issue of individual differences in fetal susceptibility to prenatal substance abuse can be addressed by use of the twin method. Morphological differences between DZ twins have been described for infants of alcoholic mothers, with MZ twins having more affected physical similarities than DZ twins [1,13,19,21]. Of further significance is the effect of prenatal exposure to teratogens on behavior, and the evaluation of twins can examine genetic differences in behavioral susceptibility to abused substances. Therefore, for this study, a pair of DZ twins exposed to several commonly abused substances, predominantly alcohol and pentazocine, received a standardized behavioral assessment during the lying-in period. A neonatal evaluation of fraternal twins exposed prenatally to several substances allows for a description of individual differences in both behavioral and morphological manifestations resulting from this combination of substances.

The behavioral assessment was part of a sequence of procedures designed to examine behavioral characteristics in full-term and preterm neonate twins [10-12]. Previous research [11] with this procedure demonstrated internal consistency within four areas of behavior: irritability, resistance to soothing, reactivity, and reinforcement value. In addition, two measures of activity were obtained: one during sleep and one while awake. Differences in behavior have been observed between full-term and preterm infants, with full-term infants receiving higher average ratings than preterm infants on irritability, resistance to soothing, and reactivity; and preterm infants being rated as more active during the active sleep period than the full-term infants[12].

## METHOD

### Subjects

The infants were opposite-sex twins born at 35 weeks gestation to a 32-year old black female with a history of substance abuse. The twins were delivered by Cesarean section after the onset of premature labor, with the second twin in the breech position.

Twin A was a 1,191 g small-for-gestational-age male with Apgars of 6 and 8.

Twin B was a 1,148 g small-for-gestational-age female with Apgars of 1, 6 and 9. Twin B was given a single dose of 0.01 mg Narcan in the delivery room.

Both twins exhibited some initial mild transient respiratory distress including nasal flaring, grunting, and moderate substernal retractions, but required no assistance or oxygen therapy. Jaundice was mild and short-term in both infants, with peak bilirubin levels on day 2 at 5.7 for the male and 7.0 for the female. The rest of the hospital course was unremarkable except for the detection of a heart murmur in Twin A on day 29 and in Twin B on day 27.

The mother's prenatal care was begun during the fourth month of pregnancy, with obstetrical visits made approximately every three weeks until delivery. Twin gestation was confirmed by ultrasound during the fifth month. Trichomoniasis was diagnosed in the fourth month of pregnancy and was treated with Flagyl tablets (metronidazole).

Substance abuse varied during pregnancy as the mother made an attempt to eliminate the effects of what she considered to be the more serious chemicals on the fetuses. During the first trimester she administered to herself daily injections of a combination of pentazocine (Talwin) and pyrobenzomine (a common combination of abused substances), and drank approximately one pint of bourbon daily. These substances were discontinued during the second trimester, and for the remainder of the pregnancy the mother occasionally took tylenol with codeine, and Bromanyl (a combination of codeine phosphate, some expectorants and some antihistamines), and drank beer on a daily basis. During the first trimester she smoked two packs of cigarettes a day, but by the third trimester smoking had been reduced to one pack a day.

## Procedures

Twin A was examined at 22 days of age, and Twin B at 29 days of age. Whereas the healthy, full-term infant is generally examined during the first few days of life, preterm infants are examined when they are medically stable and ready to be discharged. The detailed procedures have been described elsewhere [11,12]. In brief, the assessment was as follows: the infants were examined during an assessment period that went from one feeding to the next (ie, three hours for small infants).

At the scheduled feeding time the infants were fed by the examiner. Behavioral state and irritability were rated by the examiner before, during, and immediately after the feeding. Ratings also were made of the infant's feeding adequacy (ie, rooting, sucking, spitting, etc).

For a 10-minute period during the first active sleep state, 15-second time-sampling recordings were made of spontaneous activity, consisting of the number and vigor of limb movements, to obtain an index of activity during sleep.

Midway between feedings the infant was awakened so that maturational level, sensorimotor status, and orienting behaviors could be assessed. Measures included visual or auditory orienting responses toward a bulls-eye, rattle, bell, voice, face and voice combined; reflexive responses such as foot withdrawal, Moro, and sucking; summary measures of alertness, cuddliness, activity level, and reinforcement value

of the infant's behavior; and patterns of irritability and soothability in response to specific items.

Ratings were then made of the infant's response to a potentially stressful stimulus. For this procedure, a metal disc was chilled in ice water for three minutes, then placed against the infant's thigh and held there for five seconds. The procedure was repeated five times, and after each presentation behavioral responsiveness, irritability, and soothability were rated.

Finally, ratings were made of spontaneous irritability and consolability of the infant. A standard series of soothing procedures was applied, and responsiveness to the various types of soothing, as well as the level of intervention needed to soothe the infant after each episode of irritability was rated.

The behaviors were rated on five-point scales, with a higher score indicating a higher level of the measured attribute. The assessment items were then combined, and the scaled scores were averaged to form four composite scales: irritability, resistance to soothing, reactivity, and reinforcement value. In addition, two measures of activity were included: one during sleep, and one while awake. Interrater reliabilities, determined by intraclass correlations, were as follows: irritability,  $r = 0.94$ ; resistance to soothing,  $r = 0.99$ ; reactivity,  $r = 0.94$ ; reinforcement value,  $r = 0.90$ ; activity awake,  $r = 0.79$ ; and activity asleep,  $r = 0.92$ .

In addition, each infant was examined for the presence of any morphological features typical of fetal alcohol syndrome (FAS) as described by Streissguth et al [22].

Minor physical anomalies (MPAs) [23] were also assessed since the presence of such anomalies is presumably related to congenital insult(s) occurring within the first four months of fetal life [18]. There are 17 anomalies considered, including variables such as head circumference outside normal range, hypertelorism, adherent ear lobes, etc. Each infant was examined for both the morphological features of FAS and the MPAs by two examiners who reached 100% agreement.

## RESULTS

Table 1 lists the principal morphological features assessed and their presence or absence as noted in each infant. Both infants had several signs which the Fetal Alcohol Study Group of the Research Society on Alcoholism recommends for a diagnosis of FAS [13]. It is noteworthy that, although these are opposite-sex twins, the same morphological features of FAS were present in each infant. The full syndrome was not observed in either twin, however.

The minor physical anomalies observed are presented in Table 2. The number of MPAs noted were compared to those of a standardization sample of 76 twins born between 35 and 37 weeks gestational age. This standardization sample was found to have a mean number of 3.12 anomalies, with a standard deviation of 1.62. The male subject infant was found to have 5 MPAs, and the female subject infant had 4 MPAs. Thus, the male's score was more than one standard deviation above the mean, and the female's score was one half standard deviation from the mean. These findings suggested the possibility of congenital insult during the first

four months of fetal life for the male only, but the number of anomalies was not sufficiently high for a definitive conclusion based only on these variables. And, similar to the observation made regarding the morphological features of FAS, the four MPAs observed for the female twin also were observed for the male twin.

**Table 1 - Principal features of Fetal Alcohol Syndrome as assessed in a pair of opposite-sex twins**

Feature	Twin A (male)	Twin B (female)
Eyes: Short palpebral fissures	No	No
Epicanthal folds	Partial-Bilateral	Partial-Left only
Ptosis	No	No
Strabismus	No	No
Nose: Short, upturned	No	No
Hypoplastic philtrum	No	No
Mouth: Thinned upper vermillion	Yes	Yes
Maxilla: Hypoplastic	No	No
Low nasal bridge	No	No
Small head circumference	Yes	Yes
Cardiac murmur	Yes	Yes

**Table 2 - Minor physical anomalies observed in a pair of opposite-sex twins**

Anomaly <sup>a</sup>	Twin A (male)	Twin B (female)
Head circumference more than 1.5 standard deviations outside normal range	+	+
Epicanthus: partly covered	+	+
Adherent ear lobes	+	+
Ears soft and pliable	+	+
Bridge palmar crease	+	-

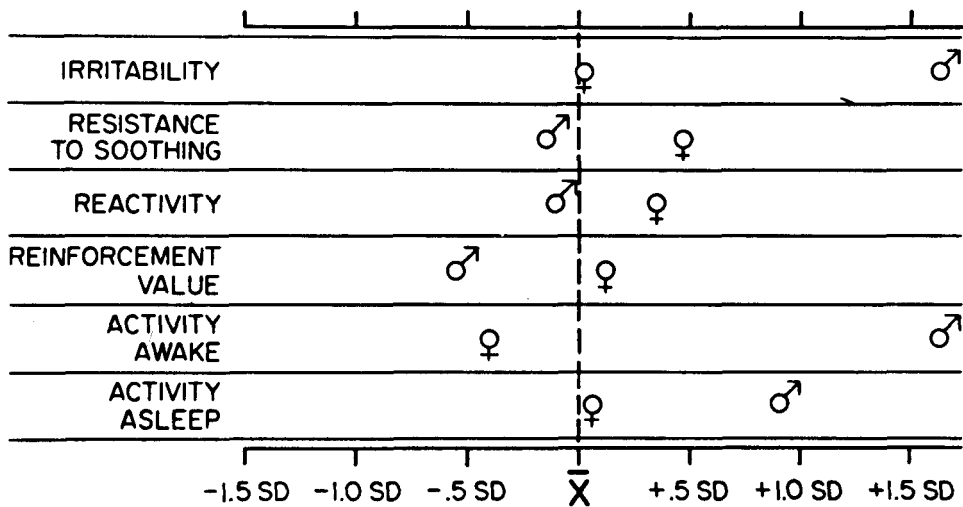
<sup>a</sup> 17 Anomalies are considered [cf. 23]

The behavioral data were combined so that each infant received a score for each behavioral category as described above. Since a difference between full-term and preterm infants in the average scores on these behavioral categories has been described [12], the scores for these infants were compared to the scores of the standardization sample born between 35 and 37 weeks gestational age [12]. These scores are presented in Table 3.

**Table 3 - Mean scores on behavioral variables: comparison of twins with standardized sample (35-37 weeks)**

	Standard (N=83) [12]		Twin A (male)	Twin B (female)
	Mean	SD		
Irritability	2.18	0.754	3.40	2.20
Resistance to soothing	2.94	0.959	2.80	3.40
Reactivity	2.91	0.744	2.83	3.17
Reinforcement value	2.87	0.984	2.33	3.00
Activity (awake)	3.39	0.986	5.00	3.00
Activity (asleep)	2.93	1.177	4.00	3.00

To examine the degree of similarity to, or deviation from, the standardization sample, the standard deviation from the group mean was plotted for each infant for each behavioral category. The results are presented in the Figure. It is evident from the Figure that the male's scores were more likely to be deviant from the group mean than the female's. The male was found to be more irritable, both spontaneously and in response to specific stimuli, than the standardization group. He was also highly active while awake and handled for presentation of stimuli (receiving the highest score possible), and moderately more active than average



**Figure.** Degree of similarity to, or deviation from, the standardized mean for each infant in each behavioral category.

during the active sleep period. And, he had a moderately low average rating for reinforcement value, the measure which reflects behaviors affecting the attitude of the caregiver (or examiner) toward the infant.

## DISCUSSION

For this pair of twins, the morphological features frequently associated with the fetal alcohol syndrome did not suggest differences in fetal susceptibility to in utero exposure to alcohol. Both infants were found to have the same features when measured in the lying-in period. An assessment of minor physical anomalies indicated a higher deviation from the mean for the male twin than for the female twin, although the total number of anomalies by itself would not be conclusive of possible congenital insult.

Individual differences in susceptibility to the effects of teratogens were most markedly observed from the assessment of behavior. The male twin was found to have more deviant behavioral patterns when compared with a standardized sample than the female twin, suggesting that the expectation of risk should be adjusted depending on the sex of the infant. Since higher risk has long been ascribed to males in several areas [17], the twin method suggests that it may be necessary to differentially evaluate the postnatal and early childhood effects of exposure to teratogens according to gender.

These infants did not demonstrate the functional deficits noted by Kopelman [8] in an infant born to a mother who had taken pentazocine throughout her pregnancy (ie, marked hypertonicity in all extremities, opisthotonic posturing, and inability to feed because her jaws were clenched shut). It is possible that elimination of this particular substance after the first trimester of pregnancy may have alleviated, if not totally eliminated, some adverse behavioral consequences in the infant.

Although these twins were exposed to several substances prenatally, multiple drug use is not uncommon, so that a "pure" study of the differential effects of teratogens on offspring twins may be difficult to perform. It is clear, however, that prolonged exposure to a combination of alcohol and pentazocine (the primary drugs abused) and codeine and antihistamines may be related to differences in fetal susceptibility to teratogens on behavior, mediated by genetic or constitutional factors including, in DZ twins, discordance of fetal vascular mechanisms [2]. Differential effects of exposure to teratogens on behavior can be assessed by studying twin pairs when such cases occur, and longitudinal studies can evaluate the potential implications of the differences observed early in development.

**Acknowledgments.** This work was supported by Grant 14352 from the National Institute of Child Health and Human Development (R.S. Wilson, principal investigator). The author wishes to thank Dr. Shirley Wilkerson for a critical review of the manuscript; and E. Harpring, S. Nuss, D. Sanders, and A. Weiss for assistance in testing, scoring, chart work, and manuscript preparation.

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