

DATA BASE OF STUDIES ON PRENATAL COCAINE EXPOSURE AND CHILD OUTCOME

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A computerized data base of characteristics and findings of the literature on prenatal exposure and child outcome was developed. The data base can be used to summarize and describe the literature resulting in a more objective understanding of the findings as well as to determine methodological problems that can shape the direction of future studies. Based on a literature search 99 studies were identified, 76 of which met methodological criteria and were included in the final data base. The data base shows that our knowledge base is limited, scattered, and compromised by methodological problems that mitigate any conclusions about whether or not or how prenatal cocaine exposure affects child outcome. Only a few studies have followed children beyond age 3. In addition, the cocaine problem is more complicated than first envisioned. It is a multifactorial problem including the use of other drugs and parenting and environmental lifestyle issues.

Introduction

Concerns about the published literature on prenatal cocaine exposure and child outcome led us to develop a computerized data base of characteristics and findings of the literature that enables us to provide an ongoing record of the literature. The data base can be used to summarize and describe the literature, resulting in a more objective understanding of the findings as well as to determine methodological problems that can shape the direction of future studies.

The first report from this data base was published in 1996 as part of a National Institute on Drug Abuse monograph and was based on 50 studies that met the inclusion criteria. In this article the data base has been expanded to 76 studies that met the inclusion criteria.

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Method

A literature search is conducted from *Medline* and *PsycLit*. Each article is reviewed to determine eligibility for inclusion in the data based on the inclusion criteria described below. Information from the articles are then abstracted, coded and entered into the data base. Variables are defined that represent either characteristics of the study such as sample size or the method of drug detection or that indicate behavioral outcomes, such as an intelligence quotient (IQ) score. Summary statistics are then generated across studies.

Criteria for Inclusion

Seven criteria are used to determine studies that are included in the final data base, although information is also coded for studies that are not included. The seven inclusion criteria are: (1) cocaine use during pregnancy, (2) human subjects, (3) neurobehavioral measures, (4) original research, (5) inclusion of control or comparison group, (6) statistical analysis of data, and (7) publication in a peer-reviewed or refereed journal.

Studies Reviewed

Based on the literature search, 99 studies were initially identified. Of these, 76 studies (77%) met the inclusion criteria and were included in the final data base. Of the 23 studies (23%) that were excluded, 13 (13%) had no control group, 4 (4%) had no statistical analysis, 3 (3%) were not original research, and 6 (6%) were not published in peer-reviewed journals. Some studies were excluded for more than one methodological limitation. A list of the 76 studies is provided in the Appendix.

Results

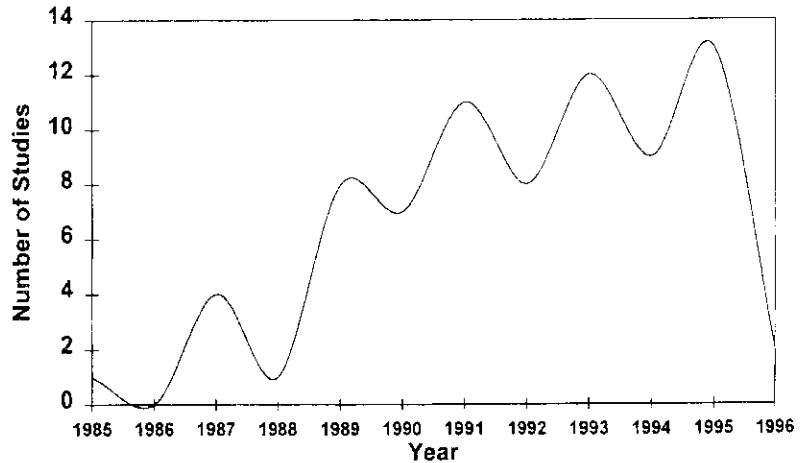
Figure 1 shows the year of publication of the 76 studies. The first studies were published in the mid-1980s followed by a sharp increase in 1989-90. Figure 2 shows the sample size of these studies. Most studies are based on relatively small sample sizes of less than 50 subjects per group, which is problematic given the multifactorial nature of the problem and the need to control for confounding and mediator variables. Arguably the most important question about drug-exposed infants is their long-term developmental outcome. Figure 3 shows the age of the subjects in these studies at their last follow-up visit. Most of what we know about drug-exposed infants is confined to early infancy, only one study has studied these children beyond age 4. Attrition is a common problem in all longitudinal studies and is especially problematic with high risk samples. High attrition not only limits the sample size but is also a threat to generalizability when the characteristics of the subjects remaining in the study differ from those that did not remain. Therefore, it is noteworthy that of the 76 studies only 15 (20%) reported compliance rates. In the three studies that followed children beyond 24 months of age, compliance rates were 68%, 28%, and 52% for the exposed groups and 49%, 62%, and 50% for the non-exposed groups.

The initial problem of prenatal cocaine exposure has been redefined as a problem of polydrug exposure. As shown in table 1, cocaine as the only drug was only reported in 10 studies (13%). Alcohol (68%), marijuana (63%), and tobacco (66%) are the drugs most commonly used along with cocaine. Opiate use was reported in 25% of the studies. Maternal use of cocaine during pregnancy can be determined by history (including self-report) and/or toxicology analysis of urine, meconium, or hair.

PRENATAL COCAINE EXPOSURE

As shown in table 2, the most common method has been the combination of urine and self report, which was used in 41% of the studies. The meconium assay provides a record of drug use from approximately 20 weeks gestational age in contrast to the urine assay, which only provides a 72-hour record of drug use. However, most of these studies were conducted before the meconium assay was in widespread use. The route of administration of cocaine was only reported in 8 (10%) of the studies and included intranasal, intravenous, and freebase. The amount of cocaine use was reported in 9 studies (12%), the frequency of use in 12 (16%), and the timing of use by trimester in 21 studies (28%). Attempts at computing a dose response effect were reported in eight studies (11%).

Figure 1
Distribution of Studies by Year of Publication



Cocaine use is often associated with three classes of potential confounding variables; other drugs, medical factors, and sociodemographic factors. These factors could provide alternative explanations for effects attributed to cocaine and, therefore, need to be controlled if cocaine effects are to be isolated. Table 3 shows the number and percentage of studies in which control for confounding variables was not reported. Most studies have not controlled for the use of other drugs even though, as we saw in table 1, other drugs are used in most cocaine studies. Table 3 also shows that obstetrical and perinatal factors are not often controlled including prenatal care, parity, and gravida. Factors such as birthweight, gestational age, and medical complications are mediator variables because they can be a consequence of prenatal drug exposure. Similarly, sociodemographic factors have not been well controlled and may provide yet another set of explanations for effects attributed to cocaine. Finally, given the high risk nature of this population, it would be reasonable to expect that many of the infants and mothers in these studies are receiving intervention services. Although intervention may affect the outcome of the child, information about intervention provided to the child or the mother was only mentioned in 28 (37%) of the studies.

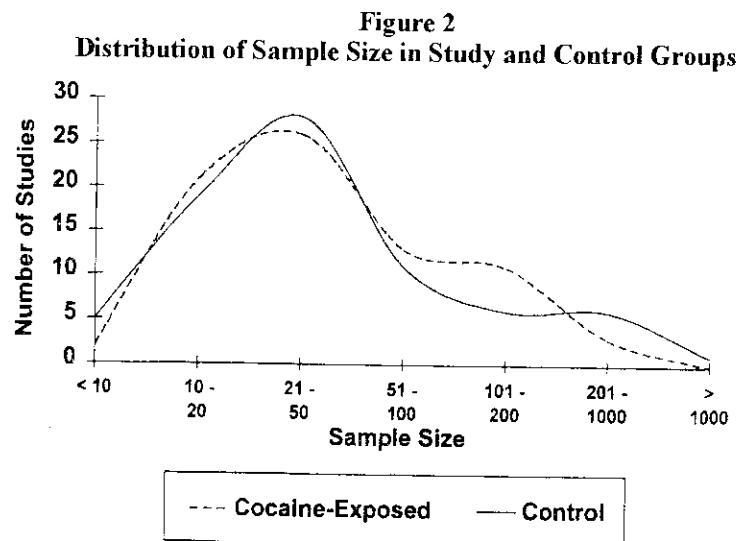


Figure 3
Age at Last Follow Up

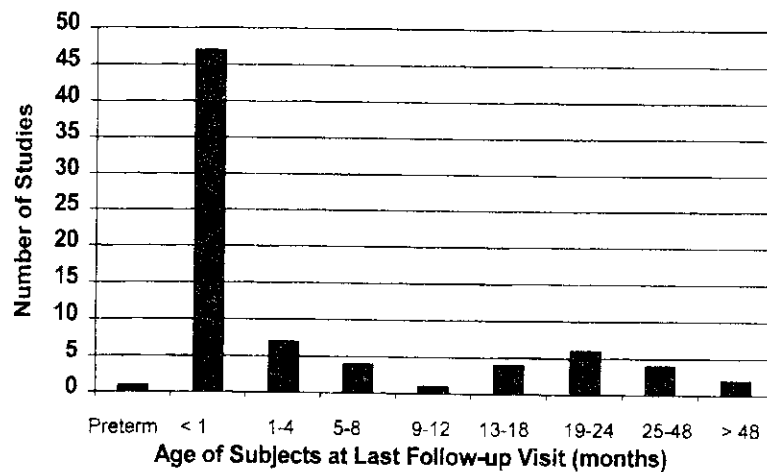


Table 4 shows the neurobehavioral measures used in the studies, including the number of times each measure was used and if statistically significant cocaine effects were found. An interesting corollary to these findings is that examiner blindness to the exposure status of the child was only reported in 51% of the studies. It is apparent from table 4 that a wide range of measures has been used with few measures used across studies. Only two measures (Neonatal Behavioral Assessment Scale and stress abstinence measures) were used in more than 10 studies and these are both measures applied during the neonatal period, again showing that most of what we know pertains to young infants. The Neonatal Behavioral Assessment Scale does show cocaine effects in 10 of 12 studies, although the effects that are reported

PRENATAL COCAINE EXPOSURE

are not consistent scores across studies. Abstinence or withdrawal effects were reported in 10 of 18 studies and may be related to the additional effects of opiates as a confounding variable. It is also interesting that five of eight studies using the Bayley Scales did not find cocaine effects and that seven of nine studies did find cocaine effects related to infant temperament.

Table 1
Polydrug Use Within Cocaine Groups

	Number of Studies (N=76)	Percentage (N=76)
None (cocaine only)	10	13
Marijuana	48	63
Alcohol	52	68
Heroin	16	21
Methodone	12	16
Amphetamine or methamphetamine	11	15
Opiates	19	25
PCP	11	15
Tobacco (nicotine)	50	66
Methaqualone	1	1
Unspecified narcotics	2	3
Unspecified polydrug use	11	15
No information reported	3	4

Table 2
Means of Identification of Maternal Cocaine Use in Included Studies

	Number of Studies (N=76)	Percentage (N=76)
Single index		
Urine only	10	13
Self-report only	4	5
Meconium only	0	0
Multiple indices		
Urine and self-report	31	41
Urine and hair	2	3
Urine, self-report, and hair	1	1
Urine and maternal history	3	4
Self-report and maternal history	1	1
Urine, self-report, and meconium	2	3
Urine, self-report, and maternal history	1	1
Alternative indices		
Urine and/or self-report	15	20
Urine and/or maternal history	3	4
Urine, self-report, or maternal history	2	3
Urine, self-report, or meconium	10	1
Not reported	0	0

Table 3
No Mention of Control for Confounding Variables

	Number of Studies (N=76)	Percentage (N=76)
Drug		
Alcohol	45	59
Barbiturates	45	59
Heroin	52	68
Marijuana	47	62
Methadone	47	62
Opiates	44	58
PCP	49	64
Tobacco/nicotine	37	49
Obstetrical and perinatal factors		
Prenatal care	57	75
Parity	53	70
Gravidity	63	83
Medical complications	32	42
Prematurity	31	41
Birth weight	49	65
Gestational age	24	32
Demographics		
Socioeconomic status	45	59
Race	26	34
Gender-child	39	51
Maternal age	33	43
Education	54	71
Work status	70	92
Welfare status	67	88
Marital status	62	82

Our knowledge base is virtually confined to early infancy with a striking absence of long-term follow-up studies and follow-up studies have attrition rates that limit the generalizability of the findings. The reliance on history and urine assay to determine prenatal drug use increases the likelihood of drug exposed infants being included in comparison or control groups. Reliance on history may also be related to the lack of reporting frequency and timing of cocaine use as the validity of this kind of recall data has been questioned. Reliable frequency and timing of use data would enable computation of dose-response relationships. The results of meconium toxicology analysis does generate values of the concentration of drug metabolites and could be useful for dose-response analysis. However, these concentrations only represent the presence or absence of the drug as the value depends on factors such as when and how often the drug was used, transport mechanisms in the mother, and uptake mechanisms in the fetus. For example, two infants could have the same

PRENATAL COCAINE EXPOSURE

nanagram per gram level of a cocaine metabolite with one fetus having a recent single exposure and the other fetus having continuous but earlier exposure.

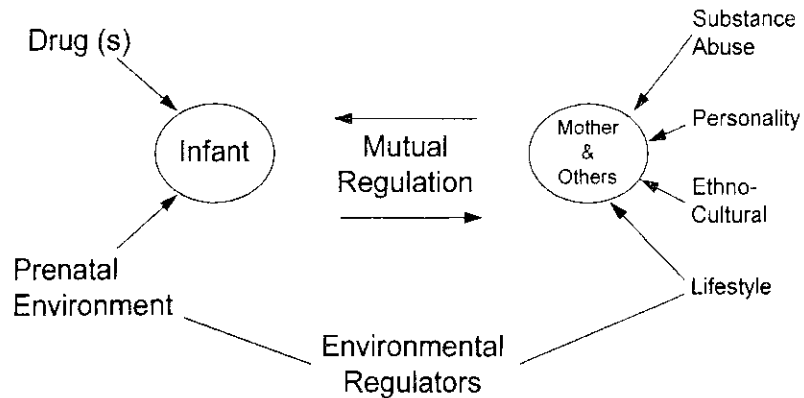
Table 4
Neurobehavioral Measures

Behavior	Number of Studies (N=76)			Percentage
	Significant	Not Significant	Total	
Neonatal behavioral assessment scale	10	2	12	16
Neonatal abstinence score	5	2	7	9
Stress, abstinence, withdrawal	5	6	11	15
Bayley scales	3	5	8	11
Fagan test of infant intelligence	2	0	2	3
Developmental quotient	2	0	2	3
Attachment	2	0	2	3
Play	3	0	3	4
Temperament	7	2	9	12
Stanford Binet	1	1	2	3
Mother-child interaction	1	1	2	3
Sleep	3	0	3	4
Caregiving environment	2	1	3	4
McCarthy	1	1	2	3
Habituation	1	1	2	3
Denver development screen	0	1	1	1
Feeding	1	1	2	3
Movement assessment inventory	1	0	1	1
Cry	2	0	2	3
Glabella	1	0	1	1
Sucking	1	0	1	1

We do know from the data base that the cocaine problem itself has been redefined in at least two ways as shown in figure 4. First, cocaine is a marker variable for a lifestyle that includes polydrug use. Second, cocaine is a marker variable for a lifestyle that includes environmental factors that have been shown to affect child development without drug exposure. In general, studies have not been able to

determine if cocaine affects the development of the child when confounding drug and environmental factors are explained. These kinds of analyses require larger sample sizes than are reported in the literature. In addition, mediator variables such as low birthweight can be a direct consequence of cocaine and affect behavior. Thus, relationships between cocaine and behavior may be due, at least partially, to factors such as low birthweight.

Figure 4
Systems Approach to the Effects of Prenatal Cocaine Exposure



The neurobehavioral findings are scattered across a wide array of measures, most of which have been used in few studies. There is a clear need for measures to be used across studies to determine if there is a consistent pattern of findings. There is also a question as to how measures are selected, few appear to have been theoretically or hypothesis driven and some measures may be too gross to detect the more subtle effects that have been attributed to cocaine. Factors such as failure to control for examiner blindness and intervention effects further cloud interpretation of the findings.

Although it seems as if the cocaine problem has been with us for a long time, most of the literature has been published in the last 10 years. In that time we have become acutely aware of the magnitude of this problem that affects a substantial number of children in our society, mostly children in poverty, and concern for the welfare of these children has led to increased research. We may not have definitive findings about the effects of cocaine exposure on child development but our knowledge has advanced considerably. We have learned that the cocaine problem is more complicated than first envisioned. It is a multifactorial problem including the use of other drugs and parenting and environmental lifestyle issues. We have also learned the effects of prenatal cocaine exposure are probably more subtle than first anticipated. Understanding these issues will enable us to design better, more theoretically driven studies and gain a clearer understanding of the processes by which prenatal cocaine exposure affects child outcome.

**Appendix
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