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A Prospective Study of Prenatal Cocaine Exposure:
Language, Play, and Global Cognitive Abilities in 2-Year-Olds

by

Susan Toth-Sadjadi

A dissertation submitted in partial fulfillment
of the requirements for the degree of

Doctor of Philosophy

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Approved by

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Abstract

**A Prospective Study of Prenatal Cocaine Exposure:
Language, Play, and Global Cognitive Abilities in 2-Year-Olds**

by Susan Toth-Sadjadi

Chairperson of the Supervisory Committee: Professor Philip S. Dale
Department of Psychology

The relationship between prenatal cocaine exposure and 2-year developmental outcome was examined in a sample of 200, 2-year-old children followed prospectively from birth. Adverse cocaine effects were hypothesized to emerge in highly-exposed children, rather than the whole group, and in the specific developmental abilities of language and play, rather than global cognitive skills. Cocaine-exposed toddlers ($n = 100$) were successfully group-matched with non-cocaine-exposed toddlers ($n = 100$) on selected maternal demographics, child characteristics, and other prenatal drug exposures. Women in both groups completed 12 years of education, were in their mid-20's, primarily white, and similar on marijuana use and binge alcohol use during pregnancy (but greater parity and cigarette use for cocaine-using women). Prenatal cocaine use was gathered via self report on the day after delivery and later verified by maternal hair analysis. Productive child language was obtained from caregiver report and videotaped, caregiver-child interaction. Quality of play behaviors were coded from videotaped, child-alone play. Global cognitive skills were assessed with the Bayley. Total grams of cocaine used throughout pregnancy was the predictor in dose-response regression analyses, while group differences were compared with t-tests. Confounds not dealt with by study design (e.g., postnatal environment) were adjusted in statistical analyses.

Neither dose-response nor group difference analyses revealed independent, adverse effects of prenatal cocaine exposure. For both groups, productive language was within normal age limits, global cognitive skills were in the low-average range, and the quality of most play behaviors was age- and context-appropriate. However, subtle signs of immature play behaviors (e.g., unelaborated play) were exhibited by both groups and a subset of children in both groups exhibited general cognitive delay. Findings suggest that early language, play, and general cognitive abilities are not adversely affected by cocaine, even for the most highly-cocaine-exposed children, but may be more related to moderating postnatal environmental factors. Results confirm the need to examine developmental outcome in terms of the complex interrelationships between cocaine exposure and the risk and protective factors in the postnatal environment.

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Introduction

Since the mid-1980's, cocaine has become the primary illicit drug used by women of childbearing age (Hawley & Disney, 1992; Hutchings, 1993a). Cocaine use cuts across all socioeconomic and ethnic boundaries, although most research on cocaine effects has focused primarily on minority populations (Neuspiel, 1993; 1995). Estimates of the use of cocaine during pregnancy range from 8% to 10% (e.g. Gillogley, Evans, Hansen, Samuels, & Batra, 1990) to as high as 31% (e.g., Ostrea, Brady, Gause, Raymundo, & Stevens, 1992). Cocaine readily and rapidly crosses the placenta and the blood-brain barrier exposing the unborn child to the pharmacological and neurobiological effects of this stimulant drug, and thus potentially places the child at risk for developmental difficulties (Dixon, 1994; Mayes, 1994). Understandably, many sectors of society, including parents, educators, researchers, and policy makers, are concerned for the welfare of cocaine-exposed children. Consequently, there has been a surge of political, societal, and academic interest over the last decade in understanding the effects of cocaine on the developing child. Recent research has illuminated the possible mechanisms by which cocaine affects the developing fetus and speculated on how these neurotoxic effects may translate into postnatal developmental impairments. Unfortunately, methodological challenges continue to plague this field of research and hinder interpretation and generalization of results. Well-designed, longitudinal studies which evaluate the extent of the relationship between prenatal cocaine exposure and child development, independent of other risk factors known to compromise development, are sorely needed in the cocaine effects field.

Mechanisms of action. The current animal and human literature does not support the notion that cocaine is a potent structural teratogen during fetal development (Church, 1993; Dow-Edwards, 1993, 1995, 1996; Fantel, 1993; Hutchings, 1993b; Koren, 1993). Instead, cocaine is viewed as a neurotoxin which potentially produces functional alterations

in the developing fetal brain, which in turn can compromise important developmental abilities mediated by those brain and/or neuronal processes that have been impaired (Anderson-Brown, Slotkin, & Seidler, 1990; Dow-Edwards, 1995; Dow-Edwards, Freed, & Fico, 1990; Dow-Edwards, Freed-Malen, & Hughes, 1993; Mayes, 1994). One mechanism by which functional alterations may occur is through cocaine's direct effects on the monoaminergic neurotransmitter systems (dopamine (DA), norepinephrine (NE), and serotonin) in the central nervous system (Gingras, Weese-Mayer, Hume, & O'Donnell, 1992; Mayes, 1994). In fetal development, the monoamines play a critical role in several phases of brain development, including cell proliferation, neuronal growth, neuronal differentiation, and synaptogenesis (Gingras et al., 1992; Mayes, 1994).

Another mechanism by which functional alterations in brain development may occur is through cocaine's NE-related vasoconstrictive effects on maternal and fetal vasculature, resulting in fetal hypoxia, tachycardia, hypertension, and/or malnutrition (Dow-Edwards, 1995; Gingras, et al., 1992; Woods, Plessinger, Scott, & Miller, 1989). Constriction of fetal vasculature (including the cerebral vessels), abrupt increases in fetal blood pressure, and compromised oxygen flow has been associated with alterations in the fetal brain (Dixon, 1994; Gingras et al., 1992; Webster, Brown-Woodman, Lipson, & Ritchie, 1991). One consistent finding in the human literature is microcephaly, or small head size, as a possible consequence of cocaine's vasoconstrictive effects (Dow-Edwards, 1996; Needleman, Frank, Augustyn, & Zuckerman, 1995). (See Appendix A for more detailed summary of models of cocaine effects and accompanying annotated bibliography.)

As a developmental neurotoxin, the biological risk for compromised functioning is evident, yet cocaine may only impact certain vulnerable and probably highly-exposed children (Church, 1993; Dow-Edwards, 1993; Hutchings, 1993b). Whether a specific fetus will be adversely affected by maternal substance use is likely determined by a combination of maternal and fetal factors (Koren, 1993; Gingras, et al., 1992; Mayes,

1994). For example, fetal susceptibility may be dependent on variability in maternal and fetal drug pharmacokinetics, such as the ability to metabolize cocaine, placental transfer of cocaine, placental response to cocaine, and cerebral vascular response to cocaine. Fetal vulnerability is also likely dependent on maternal substance use patterns such as frequency, dose, and gestational timing of drug exposures, and fetal characteristics such as genetic vulnerability and brain plasticity.

If cocaine impacts only certain vulnerable and highly-exposed children, group difference studies might not reveal adverse effects (Jacobson & Jacobson, 1996). A dose-response study, which adequately measures the pattern of cocaine use ("dose") during pregnancy, would be more appropriate to reveal subtle cocaine effects, particularly in certain highly-exposed children. Empirical examination of a dose-response effect of cocaine is scarce, but suggests that greater cocaine exposure is related to more compromised neurobehavioral and cognitive functioning in newborns (Martin, Barr, Martin, & Streissguth, in press; Tronick, Frank, Cabral, & Zuckerman, 1994) and infants (Jacobson & Chiodo, 1996).

Neurobehavioral and cognitive outcomes. Group differences in neurobehavioral outcomes in the newborn period, typically assessed by the standardized, Brazelton Neonatal Behavioral Assessment Scale (NBAS), have not been consistently related to prenatal cocaine exposure. Some studies show effects in various early skills such as state regulation and habituation (e.g., Chasnoff, Griffith, MacGregor, Dirkes, & Burns, 1989; Eisen, Field, Bandstra, Roberts, Morrow, Larson, & Steele, 1991; Mayes, Granger, Frank, Schottenfeld, & Bornstein, 1993). On the other hand, some studies find no neurobehavioral effects (e.g., Coles, Platzman, Smith, James, & Falek, 1992; Woods, Eyler, Behnke, & Conlon, 1993) and still more studies find effects at one time point but not another, suggesting that adverse neurobehavioral outcomes are nonexistent or transient (e.g., Black, Schuler, & Nair, 1993; Espy, Riese, & Francis, 1995; Gardner, Karmel, &

Freedland, 1996; Neuspiel, Hamel, Hochberg, Greene, & Campbell, 1991). However, recent dose-response studies have found a relationship between greater prenatal cocaine exposure and poorer neurobehavioral performance (Martin et al., in press; Tronick et al., 1994).

General cognitive functioning through the third year of life does not appear to be adversely impacted by prenatal cocaine exposure, at least when measured by a standardized developmental assessment such as the Bayley Scales of Infant Development or the Stanford-Binet Intelligence Scale. Group difference studies typically report that cocaine/polydrug-exposed infants fall within normal limits on standardized assessments (e.g., Behnke, Eyler, Conlon, Woods, & Wobie, 1996; Chasnoff, Griffith, Freier, & Murray, 1992; Coles, Raskind-Hood, & Platzman, 1995; Graham, Feigenbaum, Pastuszak, Nulman, Weksberg, Einarson, Goldberg, Ashby, & Koren, 1992; Griffith, Azuma, & Chasnoff, 1994; Jacobson & Chiodo, 1996; Mayes, Bornstein, Chawarska, & Granger, 1996; Richardson, Day, & Goldschmidt, 1995). Yet Chasnoff and colleagues (1992) found that a higher number of cocaine/polydrug-exposed children and non-cocaine/polydrug-exposed children scored greater than one standard deviation below the standardized mean on the Bayley Mental Scale than did drug-free comparison two-year-olds. These results were not replicated on the Stanford-Binet at 3 years of age (Griffith et al., 1994).

Thus, converging evidence suggests that cocaine does not adversely impact general neurobehavioral or cognitive skills, at least on a group level when assessed with standardized assessments. However, the full story of cocaine's effects on development may not yet be known given the design flaws of these studies. Reasons for inconsistent findings in both neurobehavioral and cognitive outcome are likely due to methodological differences and limitations among studies, including: 1) diverse sample characteristics among related studies (social drug users vs. addicts; treatment/intervention sample vs. non-

intervention; ethnic minority vs. white women); 2) high sample attrition in the few longitudinal studies; 3) incomplete or absent assessment of cocaine use patterns during pregnancy (most studies typically assess cocaine exposure as exposed versus not-exposed, offering no information about frequency, timing, or amount of exposure); 4) use of various, and sometimes ambiguous, comparison groups; and 5) minimal or no control for confounding factors that may impact development independent of cocaine exposure (such as other prenatal exposures and postnatal environment) in either study design or statistical analyses. Each of these methodological flaws limits the interpretation and generalizability of results to the larger population of cocaine/polydrug-exposed children.

Standardized assessment of global developmental functioning may not be specific or sensitive enough to uncover the possible subtle effects of prenatal cocaine exposure, and the predictive validity of global scores is typically poor (Bendersky, Alessandri, Sullivan & Lewis, 1995). Cocaine's neurotoxic effects may be better discerned in impairments in important, specific developmental skills that predict later competence, such as arousal and attention in early infancy or play and language in toddlerhood (Lester, Freier, & LaGasse, 1995; Mayes, 1996), rather than in deficits in global skills measured on structured developmental assessments. Recently, assessments of more specific infant behaviors have documented cocaine-related neurobehavioral, cognitive, and self-regulatory impairments in infancy. For example, group difference studies have demonstrated arousal, affective, and instrumental learning decrements in 3-month old cocaine/polydrug-exposed infants (Mayes, Bornstein, Chawarska, Haynes, & Granger, 1996) and impairments in arousal and affective regulation in 4 to 8 month old cocaine/polydrug-exposed infants (Alessandri, Sullivan, Imaizumi, & Lewis, 1993). Cocaine effects on specific developmental skills beyond the first year of life have been virtually unexplored, but this is a promising area of research for detecting cocaine-related impairments.

Representational abilities. In the second year of life, the representational abilities of play and language enable the child to translate experience into mental symbols or "representations," and then use this information for interaction and communication with others (Fiese, 1990; Sigman & Sena, 1993; Ungerer & Sigman, 1984). Play and language are positively related to one another (Tamis-LeMonda & Bornstein, 1993), and in the toddler years may be the cognitive/linguistic outcomes most significant for later intellectual and social-emotional functioning (McDonald, Sigman, & Ungerer, 1989). Play is a context in which children learn about the object and social world by actively engaging their environment, and is indicative of a child's current cognitive and social/emotional development (Fiese, 1990; Tamis-LeMonda & Bornstein, 1991). Assessing the ability to actively engage the environment through play may be a salient dimension of behavior not easily captured by standardized assessments (Beckwith, Rodning, Norris, Phillipsen, Khandabi, & Howard, 1994; Garwood, 1982).

Play. A few recent studies of polydrug-exposed samples (including cocaine) support the notion that cocaine effects may emerge in specific, important developmental skills such as representational abilities in toddlerhood. Beckwith et al. (1994) examined the frequency of play acts (manipulative, relational, functional, and symbolic), the number and type of play sequences, and ratings of 8 qualitative play behaviors (e.g., elaborating themes, purposeful selection of toys, transitional strategies, etc.) of 31 polydrug-exposed (mainly PCP and cocaine) toddlers and 19 demographically-similar drug-free comparison children in a 16-minute child-alone spontaneous play situation. Group difference analyses revealed that drug-exposed toddlers exhibited more immature play (e.g., manipulative acts, functional acts, and lowest level of sequenced play) than non-drug-exposed toddlers. Differences in play behavior (except for manipulative acts) persisted when birthweight and developmental level were statistically controlled. On qualitative play ratings, the drug-exposed children were judged to combine objects less often, to randomly select toys, to

make abrupt transitions, to be less absorbed in play, and to show more deviant play behavior. Differences in qualitative play behaviors persisted even after birthweight and developmental level were statistically controlled. Group by gender effects were also observed: 1) control girls exhibited higher-level sequences characterized by decentered functional acts more than did all other groups, 2) drug-exposed boys were less likely than all other groups to expand themes, and 3) control boys were more positive with their caregivers than drug-exposed boys. In contrast, both groups of toddlers performed within normal limits on standardized developmental assessments (Rodning, Beckwith, & Howard, 1989). The authors suggest that the presence of immature and deviant play behaviors among age-appropriate play in the drug-exposed group indicates incoherence within developmental domains, a pattern of behavior consistent with non-normative patterns of development.

Beeghly and colleagues (Beeghly, Tronick, Brilliant, High, Flaherty, Cabral, & Frank, 1995) coded object play maturity (relational, functional, and symbolic), socio-affective behavior (positive and negative emotion, responsivity to caregiver), and play disengagement (object and social) of 49 cocaine/polydrug-exposed 12-month-olds and 41 demographically-matched comparison infants in a 16-minute free play sequence consisting of both child-alone and caregiver-child play episodes. Although there were no differences between groups on object play maturity or time disengaged from play, cocaine/polydrug-exposed infants smiled less often and appeared to benefit less from dyadic play than the comparison group. These findings suggest a subtle, yet potentially compromising effect of polydrug exposure on affect regulation and caregiver-child interaction during play. Hagan (1995) rated the play behaviors of 13 cocaine/polydrug-exposed toddlers and 13 demographically-matched drug-free comparison toddlers in a 16-minute caregiver-child spontaneous play situation using a modified version of Beckwith et al.'s (1994) qualitative rating system. In contrast to the studies of Beckwith et al. and Beeghly et al., this small

sample study found no group differences in 10 of 11 child play behaviors, nor differences between the two groups of caregivers in the amount, quality, or appropriateness of involvement with the child during play.

Methodological differences among these studies of play, including sample size, sample attrition, control for confounds, and age at evaluation, are possible reasons for the discrepant findings. In particular, differences in the context in which play was assessed may explain why Beckwith et al. found immature play during a child-alone play context and Hagan found no impairments in the mother-child interaction context, even though both studies coded quality of play similarly. The developmental level of child play has been shown to increase when interacting with a play partner for both normal (Fiese, 1990; Slade, 1987) and drug-exposed samples (Beeghly et al., 1995).

Although methodological limitations hinder firm conclusions about drug effects on the developmental level or quality of play, assessment of the way in which young children engage their environment, particularly when playing alone in an unstructured and unsupported situation, appears to be a promising measure for revealing drug effects. What remains unclear is the specific role of prenatal cocaine exposure on possible play behavior impairments. Does prenatal cocaine exposure adversely affect the quality of engaging the environment through play, independent of other risk factors? Are impairments in play behaviors only evident in the most highly cocaine-exposed toddlers? An evaluation of cocaine's independent, dose-response relationship with toddler play behaviors is needed to answer these questions. In addition, assessment of cocaine-exposed children's play behaviors in a child-alone play context is needed to replicate or refute Beckwith et al.'s findings of atypical play behaviors in a group initially labeled as cocaine-exposed (but were in fact polydrug-exposed).

Language. Several initial studies show interesting links between prenatal polydrug exposure (including cocaine) and language development in the toddler and preschool

periods. Using retrospective techniques, Angelilli and colleagues (Angelilli, Fischer, Delaney-Black, Rubinstein, Ager, & Sokol, 1994) found that language-delayed 2 to 4 year-old clinic patients were more likely to have been prenatally exposed to cocaine than were children with normal language development. A prospective study of drug-exposed children (not specifically focused on cocaine) indirectly assessed language via the Dutch version of the Bayley Scales of Infant Development and found that lower scores on the MDI were attributable to problems in understanding and executing language items from the test (van Baar, 1990). Griffith et al. (1994) found that 3-year old cocaine/polydrug exposed children scored lower on the Stanford-Binet verbal reasoning subtest than did the drug-free comparison children, with cocaine exposure accounting for 9% of the variance. Malakoff and colleagues (Malakoff, Mayes, & Schottenfeld, 1994) found that 60% of children living with a cocaine-dependent mother showed evidence of serious language delay, with particular impairment in receptive rather than expressive language skills. Lastly, Mentis & Lundgren (1995) examined the language development profiles (discourse-pragmatics, semantic, syntax and form components) from a 30 minute language sample of 5 cocaine/polydrug-exposed toddlers and 5 matched non-exposed control toddlers. The two groups did not differ on measures of syntax (i.e., mean length of utterance) or semantics (i.e., number of different words), but did differ in the discourse-pragmatic area.

Given the methodological limitations of these preliminary studies, it is premature to attribute observed language impairment specifically to cocaine. However, these studies do suggest that language is at risk for disruption in prenatally drug-exposed children, and perhaps cocaine-exposed children in particular. A well-designed study of prenatal cocaine exposure is needed to determine whether cocaine specifically impacts language development independent of other known risk factors (e.g., poor postnatal environment), whether cocaine affects language globally or only impacts specific language skills, and

whether adverse effects on language are only evident in the most highly cocaine-exposed children.

The Seattle Cocaine and Pregnancy Study. A prospective, longitudinal study of prenatal cocaine exposure was specifically designed to address many of the methodological challenges that plague the cocaine effects field to provide solid data on the independent, dose-response effects of cocaine through the first 2 years of life. The study design is described in detail by Carmichael Olson, Grant, Martin, & Streissguth (1995). Briefly, the Seattle Cocaine and Pregnancy Study (Seattle Study) involves a large cohort of over 500 children, about half of whom were born to women who used cocaine during pregnancy (COC), and half born to women who did not use cocaine (NON-COC). Many of the common confounding factors were either carefully stratified between groups (e.g., other prenatal exposures such as marijuana, alcohol, and tobacco (MAT)), limited or eliminated from the sample (e.g., no opiate users were included), or balanced between groups (e.g., maternal demographics). Many aspects of the postnatal environment were carefully measured, allowing for statistical adjustment of these important developmental influences. Unlike any other developmental study of prenatal cocaine effects, the Seattle Study confirmed maternal self-report of drug use during pregnancy with a biological assay of cocaine use called radioimmunoassay of maternal hair. This procedure improves the accuracy of the measure of cocaine "dose" in this unique longitudinal cohort study. Sample maintenance has been very high, remaining at or above 90% in the four follow-up visits made to the laboratory at ages 4, 6 1/2, 12, and 24 months of age. This high level of follow-up success is rare in research on fetal drug effects.

At the present time, the relationship between prenatal cocaine exposure and behavioral child outcome in the Seattle Study has been analyzed at the neonatal and 4-month time points. At approximately 2 days of life, a subsample of 191 newborns (71 COC/MAT, 88 MAT, and 32 non-drug or light users of MAT) were assessed with a

neurobehavioral battery by examiners blind to exposure status (Martin et al., in press). Sample size was reduced because newborns were either not tested (e.g., mother left hospital before testing accomplished, baby in NICU, equipment malfunction) or did not meet analytic criteria (e.g., invalid tests, age outliers, non-White ethnicity), resulting in a sample of infants at lower risk than the remainder of the cohort. The cocaine-exposed newborns were found to be developmentally at risk compared to non-cocaine-exposed newborns. Importantly, a dose-response relationship was found, such that higher amounts of cocaine were associated with higher neonatal neurobehavioral risk scores.

At 4 months, a subsample of 306 infants (120 COC/MAT and 186 MAT) were assessed on a standardized neuromotor battery for risk of motor dysfunction (Swanson, 1992). Sample size was reduced because infants were lost to follow-up, infant exposure information was inconsistent, and infants did not meet analytic criteria (e.g., invalid tests, age outliers, prematurity). Infants in the COC group had less optimal full-scale neuromotor scores, particularly in primitive reflexes and volitional movements, than did the NON-COC group. However, effects became non-significant when amount of prenatal care was statistically adjusted. Further analysis suggested that longer duration of cocaine exposure (lasting through the third trimester of pregnancy) significantly accounted for the infants' poor volitional movement, even after statistical adjustment for potential confounds.

Objectives of the current study. The main goal of the current study was to assess the relationship between prenatal cocaine exposure and representational abilities and developmental status in the second year of life, independent of other risk factors known to compromise development. It was hypothesized that prenatal cocaine exposure was more likely to adversely impact a subgroup of highly-exposed children, rather than all exposed children. Thus, cocaine effects would more likely emerge in dose-response analyses instead of group difference analyses. In addition, it was hypothesized that cocaine effects were more likely to emerge in specific developmental skills salient to the toddler period,

such as the representational abilities of language and play, rather than as deficits in global developmental skills assessed by standardized tests. The current study was able to disentangle the effects of prenatal cocaine exposure from other risk factors typically associated with cocaine use by capitalizing on the methodological strengths of the Seattle Study design. In addition, complex covariate selection processes and data analytic strategies were employed to statistically control for important confounds not dealt with by study design.

Methods

Subjects

A subsample of 200 two-year-old children were the subjects for this study. The children participated in a prospective, longitudinal study on the effects of prenatal cocaine exposure on child development through the first two years of life. The sample was drawn from the larger Seattle Cocaine and Pregnancy Study (Seattle Study) which involved a cohort of over 500 children, about half of whom were born to women who used cocaine during pregnancy (COC group) and half born to women who did not use cocaine, but may have used other toxic substances (NON-COC group). The study design of the Seattle Cocaine and Pregnancy Study is discussed in detail by Carmichael Olson et al. (1995).

Several factors went into the decision to select from the Seattle Study cohort a subset of 200 subjects (100 children in each group) on which the labor-intensive qualitative play coding system and language-sample transcription was performed. First, a power calculation revealed that a sample of 200 subjects would be sufficient (at the .05 significance level) to detect a 1/2 standard deviation (7.5 point) group difference on the Bayley Scales of Infant Development-Second Edition (BSID2, 1993), Mental Developmental Index. Second, the subsample was chosen from the latter 2/3 of the Seattle Study cohort (350 subjects) for whom the BSID2 was available.¹ In addition to these factors, the subsample for this study was drawn from the Seattle Study cohort according to the following criteria: 1) complete data from both the 21-month and 24-month assessments²; 2) the COC group to include children with the full range of prenatal cocaine exposure, but weighted towards more highly-exposed children to allow detection of a dose-response effect of prenatal cocaine exposure on child outcome; 3) exclusion of infants with

¹ The standardization version of the BSID2 (1991) was used in this study, but was not available from the Psychological Corporation until approximately 1/3 of the way into 2-year data collection, as the assessment tool was still under development.

² There were less than 10% missing data on each outcome measure for each group.

gestational ages less than 30 weeks to eliminate the most premature (very low birthweight) infants; and 4) an attempt to group-match the NON-COC group to the COC group on theoretically important and potentially confounding risk factors such as maternal demographics (i.e., maternal age, education, race, and parity), other prenatal exposures (i.e., marijuana, alcohol and tobacco), and child characteristics (i.e., gender and age at 2-year assessment).

Table 1 presents the outcome of group matching. Group matching was successful for many confounding risk factors including maternal education and race (important variables in the study of child outcome), child gestational age, gender, and age at the 2-year visit, frequency of marijuana use during pregnancy (log score), and the percentage of women who reported “any alcohol binge during pregnancy.” Any binge drinking during pregnancy was considered the most important alcohol matching variable because among various measures of alcohol consumption it is the strongest predictor of poor developmental outcome among alcohol-exposed individuals (Streissguth, Bookstein, Sampson, & Barr, 1993). The effort to match groups on maternal demographics and drug use was not completely successful. The cocaine-using women were older, had more children, used more total ounces of absolute alcohol during pregnancy, and smoked more packs of cigarettes during pregnancy. A similar pattern of group matching was observed in this sample and the Seattle Study cohort (see Carmichael Olson et al., 1995 for demographic characteristics). Through study design, the COC and NON-COC groups were equated on some very important co-occurring risk factors for poor developmental outcome. Confounds not dealt with in the study design, and which were related to outcome, were statistically adjusted in data analysis.

Procedure

Women were recruited from 4 study hospitals in the metropolitan Seattle, WA area on the day following birth. This recruitment process provided a community-based sample that was fairly representative of Seattle's geographical region and included the full continuum of cocaine users. In the hospital on the day after delivery (whenever possible), women were given a brief, one-page questionnaire (the Hospital Screening Questionnaire (HSQ)) assessing their substance use during pregnancy and general demographic information. Women admitting to any cocaine use during pregnancy were invited to participate in the study and signed consent was obtained from 90% of those who appeared to be eligible. Women for the NON-COC group were similarly recruited from the 4 hospitals, but enrolled into the study on an as-needed basis in order to construct an appropriate control group stratified for other prenatal exposures and balanced on maternal demographics. A priori exclusionary criteria for the Seattle Study included: 1) report of street drugs other than cocaine and marijuana, 2) no mother under 17 years of age, 3) residence outside the Seattle metropolitan area, and 4) multiple births. In addition, medically fragile infants housed in the Neonatal Intensive Care Unit were unlikely to be included in the study.

Once consent was obtained, women were interviewed in detail in a private setting within the hospital by research staff (non-hospital personnel) to elicit the timing, dose, and pattern of licit and illicit substance use during the month prior to recognition of pregnancy and during each trimester of pregnancy. Hair samples were obtained from 90% of the women prior to discharge in order to verify and modify the cocaine exposure scores obtained from the self-report interview (see Grant, Brown, Callahan, Barr, & Streissguth, 1994 for details of the hair analysis and Carmichael Olson et al., 1995 for details on sample enrollment and stratification for the Seattle Study cohort). Data collection staff (i.e.,

examiners and coders/transcribers), except outreach workers, were blind to the child's drug exposure history or earlier developmental assessment findings.

When the children were 21 months old (age corrected for prematurity, if necessary) their primary caregivers were interviewed over the phone to obtain information about the quality of the child's current home environment and the child's current productive language skills using a questionnaire developed for the Seattle Study. At 24 months corrected age, the children and their caregivers were assessed in a laboratory setting by a trained examiner. The children were first administered a standardized developmental assessment, and then videotaped in two unstructured situations. First, the child played alone for 10 minutes with a set of age-appropriate, thematic toys (e.g., tea set including cups, plates, spoons, teapot and pan, dolls, crib, and blanket, dump trucks, cars, and a gas station) arranged in a preset order in the center of the room. During this child-alone play period the caregiver was seated at a table in a corner of the room filling out a questionnaire, and when finished with the questionnaire, reading magazines or sitting quietly. The caregiver was asked not to initiate interaction with the child during the 10 minutes of play, but to respond naturally to the child's initiations and attempt to redirect the child to play alone when the child initiated interaction with the caregiver. After the child-alone play, the caregiver was asked to play with the child and the toys for approximately 5 minutes and then clean up the toys as the caregiver would normally do at home. After the videotaped play sequences the examiner returned to the room and interviewed the caregiver about the child's health, development, current living situation, and exposure to substances of abuse after birth. Growth measurements including length, weight, and head circumference were obtained on the children. Following the 24-month laboratory session, the examiner rated items on the child's behavior, the caregiver's behavior, and the caregiver-child interaction.

Measures

Tables 2 and 3 present the study measures which include prenatal cocaine use variables, measures from 4 outcome domains, and covariates.

Cocaine Use Variables. Self-report of illicit and licit substance use during pregnancy was obtained from a confidential, structured interview, the Postpartum Maternal Interview (PPMI), developed for the Seattle Study. The PPMI assessed the use of cocaine during the month prior to knowledge of conception and during each trimester of pregnancy for the following "dose" measures: frequency (number of times) of cocaine use, total amount (number of grams) of cocaine use, maximum amount of cocaine at any one time, average amount of cocaine per day, and any binge (≥ 1 gram at one time) cocaine use.

Radioimmunoassay of maternal hair (RIAH) was obtained on 85% ($n=405$) of the women who complied with a request for a hair sample ($n=478$) and provided a hair sample of sufficient length for analysis of all three trimesters of pregnancy. RIAH measures cocaine use during pregnancy in nanograms (ng) of cocaine-benzoyllecgonine per 10 mg of hair.³ The RIAH data validated self-reported cocaine use for the Seattle Study cohort (Grant, et al., 1994). For the present subsample of cocaine users ($n=100$), 20 women self-reported no cocaine use, but had positive hair assays (these cases are termed "false-negatives"). The percentage of false-negative cases in the Seattle Study cohort (36/257, 14%) is somewhat lower than the percentage in the subsample (20%). For the false-negative cases in the subsample as well as the Seattle Study cohort, self-report cocaine use values were imputed via regression equations based on raw score hair analysis data. Based on RIAH findings, there were no false-positive cases in the NON-COC sample ($n=100$).

RIAH yielded an average of 219 ng of cocaine/10 mg of hair ($SD = 517.3$) across three trimesters of pregnancy for the group of women who had valid hair data ($n = 87$,

³ Hair analysis of maternal substance use has several limitations, such as the chronological record of substance use depends on the length of hair and the rate of hair growth, women who report small amounts of drug use early in pregnancy might not be identified, and the drug use of women with damaged hair might be underestimated (Grant et al., 1994).

including false-negative cases). The 20 "false-negative" cases tended to use less cocaine throughout pregnancy ($M = 2.81$, $SD = 1.28$ ng/10 mg of hair, log score) than the rest of the sample ($M = 3.80$, $SD = 2.14$) ($F(1, 85) = 3.79$, $p < .10$). Log average ng of cocaine/10 mg of hair (the level of cocaine-benzoyllecgonine exposure over three trimesters) was moderately correlated with self-reported log frequency of cocaine used throughout pregnancy ($r = .55$, $p < .001$) and log total grams of cocaine used throughout pregnancy ($r = .51$, $p < .001$) for the 67 cases for which both hair and self-report data were positive (13 of the 80 women who were positive self-reporters did not have hair data).⁴ This finding suggests that self-reported cocaine use measures are also valid for the subsample of women in the current study. Imputed self-report cocaine values for the 20 false-negative cases were used in data analysis, except where noted.

Table 4 presents cocaine use during each trimester of pregnancy (raw data scores, not log-transformed values) for the full COC group ($n = 100$) and for women in the COC group with positive self-reports only ($n = 80$), excluding false-negative cases. The values for the full COC sample and the women who had positive self-reports were quite similar. On average, the full COC sample used approximately 1 gram of cocaine per cocaine-using day, for a total of 57 grams of cocaine throughout pregnancy. The average maximum amount used at any one time was 2 grams of cocaine throughout pregnancy. The COC group used cocaine approximately 45 times throughout pregnancy and 59% binged on cocaine at least once during pregnancy. Self-reported cocaine use decreased from prior through first trimester to second and third trimester of pregnancy. The intercorrelations among the log-transformed self-reported cocaine use variables for the COC group ($n = 100$) were significantly correlated (r s range from .27 to .93, p s $< .01$ to .0001), indicating

⁴ Hair and self-report raw-score data were log-transformed because of highly skewed distributions.

a high degree of redundancy among the self-reported cocaine use variables.⁵ (See Appendix B for correlation matrix.)

Toddler Outcomes: Productive Language . Child language measures were generated from three sources: (1) caregiver report of language production gathered from the phone interview around 21 months of age, (2) a verbal score computed from the Bayley Scales of Infant Development - Second Edition, standardization version (BSID2, 1991) at 24 months, and (3) spontaneous child language production coded from videotapes at 24 months.

(1) Caregiver report of child language production was obtained from the 21-month telephone interview. Philip Dale, Ph.D. (developmental consultant for the Seattle Study) created this language interview, the MacArthur Toddler Talk Inventory (MTTI), from existing parent-report shortforms of productive language (Reznick & Goldsmith, 1989). The MTTI includes: a) a list of 123 words/phrases common for toddlers, grouped into categories such as activities, animals, food and drinks, and verbs, and b) examples of the 3 longest sentences the child has recently said. The MTTI yields 3 measures of reported child language production: 1) vocabulary (total number of words/routine phrases, with a maximum of 123 words/phrases; 2) grammatical complexity (maximum sentence length (MSL) derived from the 3 longest sentences); and 3) child's language age (a norm-referenced score, in months, corresponding to the child's vocabulary total score).⁶ The validity of maternal report of early child language has been adequately demonstrated in a variety of populations of children (see Fenson, Dale, Reznick, Bates, Thal, & Pethick, 1994) including use with substance-abusing mothers (Coggins, Wilkinson, McMahon, & Carson, 1992). There were no missing data on the MTTI.

⁵ Intercorrelations among the raw-score self-reported cocaine measures were also significantly correlated (r_s .22 to .88, $p_s < .05$ to $<.0001$); however, it is more appropriate to report the results of the log-transformed variables since the raw-score measures are highly skewed.

⁶ Dr. Philip Dale provided the data (see Fenson et al., 1994) from which to compute the language ages corresponding to the vocabulary total scores on the MTTI.

(2) The Bayley verbal score was an informal summary of verbal ability composed of selected BSID2 (1991) mental scale items. Example items include "names one picture," "points to 3 doll parts," and "understands 2 prepositions." The maximum score for this measure was 43. There were no missing data on the BSID2 verbal score.

(3) A sample of spontaneous child language production was obtained from the videotaped, 5- to 8-minute caregiver-child free play plus cleanup sequence. The child's spontaneous language was transcribed into computer format using the CHILDES Project procedures (MacWhinney, 1995). Each transcript was then analyzed using the CLAN programs (Child Language ANalysis; MacWhinney, 1995) to generate the following production measures: 1) vocabulary (number of different words produced during the session); and 2) grammatical complexity (mean length of morphemes per utterance (MLU) derived from the intelligible utterances produced during the session). In addition to the measures generated from the language transcripts, each transcriber rated the intelligibility of the child's language on a 1 to 5 scale, with a 1 indicating that most of the child's language was unintelligible (poor), a 3 indicating that at least half of the child's language was intelligible (fair), and a 5 indicating that most of the child's language was intelligible (good). (See Appendix C for the "Child Language Transcription and Coding Manual.")

Four transcribers, blind to the child's drug exposure history and the purpose of this study, were trained to high interrater reliability (mean $r = .96$ for vocabulary and $.98$ for grammatical complexity). For 16% of the sample, interrater reliability was checked periodically and consistently remained high ($r = .95$ for vocabulary and $.96$ for grammatical complexity). Twelve children (6%) had missing language data because the videotaped mother-child play sequence was incomplete or missing. The language sample data for children who did not speak during the mother-child play sequence ($n=5$) were included in the analyses, instead of considering these cases as missing data. The language data for

these 5 children were scored a zero, representing no language production when given the opportunity to talk.⁷

Toddler Outcomes: Quality of Play Behavior. Each 10-minute child-alone play sequence was coded for 14 qualitative dimensions of play behavior by 2 trained coders blind to the child's drug exposure history and the purpose of this study. The qualitative rating scales developed by Carol Rodning (Beckwith et al., 1994) were slightly modified for this study. The modified coding system includes a majority of Rodning's rating scales, several of Hagan's scales (a majority of which also overlap with Beckwith et al.), and rating scales developed for this study which were either not included or vaguely defined by the other two systems. The modified play coding system includes 14 dimensions of play, divided into two categories: global measures of play and measures of specific play behaviors.

The *global ratings of play behavior* focused on the entire 10-minute play session, whether or not the child played with the toys. The 7 global items were engagement with toys, attempts to get out of the room, aimless activity, overall affective tone, referencing the caregiver, affective tone directed toward the caregiver, and amount of frustration. The "affect towards the caregiver" and "referencing the caregiver" scales were included in the coding system as indicators of caregiver-child interaction, even though these behaviors were not the focus of the child-alone play task. The global behaviors were rated on a 5-point scale, with lower numbers indicating inappropriate behavior for children of this age. For example, a rating of 1 on the "engagement with toys" scale describes a child who did

⁷ It is important to note that the productive language outcomes generated from this study were valid measures of cocaine-exposed children's early language abilities. Although the spontaneous language samples were obtained from a relatively short observation period (5- to 8-minutes), 24-month vocabulary and MLU were moderately correlated with each other ($r = .64, p < .001$), with 21-month vocabulary and MSL ($r_s = .42$ to $.58, p_s < .001$), with the BSID2 MDI ($r_s = .41$ to $.61, p_s < .001$) and the BSID2 verbal score ($r_s = .31$ to $.55, p_s < .01$ to $p < .001$) (See Appendix F for correlation matrix).

not interact with the toys at all or less than 20% of the play session, whereas a rating of 5 describes a child who engaged with the toys for more than 80% of the play session.

The *specific play behavior ratings* focused only on the time during which the child played with the toys. The 7 specific play behavior items were combining toys, expansion of theme, toy selection strategies, transitions during play, mouthing of toys, immature play behaviors, and attention span. The specific play behaviors were rated on a 5-point Likert scale, with 1 indicating “atypical or immature behavior” and 5 indicating “typical behavior” for a two-year-old child. For example, a rating of 1 on the “combining toys” scale describes a child who mostly used one toy at a time during play (there may be 1 or 2 instances of combining toys), whereas a rating of 5 describes a child who usually combines several toys together and the majority of toy combinations are either functional or symbolic (there may be 1 or 2 instances of using only one toy at a time).

Coders were trained to interrater reliability (percent agreement within 1 scale point) of 90% or above on each of the 14 play behaviors. Interrater reliability was checked periodically on a total of 20% of the sample and remained at an overall level of 92% for the 14 rating scales (range 83% to 100%). There was one case of missing data for the play measures since this subject did not have any videotaped interaction data.⁸ (See Appendix D for the “Qualitative Ratings of Play Behaviors Coding Manual” which describes in detail each play behavior and the corresponding play behavior ratings.)

⁸ As with the language outcomes, it is important to note that the global and specific play behavior ratings generated from the child-alone play session were valid measures of the quality of cocaine-exposed children's play skills. Global play behaviors were moderately to highly intercorrelated ($r_s = -.22$ to $.83$, $p < .05$ to $p < .001$), positively related to the BSID2 MDI ($r_s = .24$ to $.33$, $p < .05$ to $p < .01$), positively related to level of spontaneous language at 24 months ($r_s = .27$ to $.44$, $p < .01$ to $p < .001$), and associated with the specific play behavior measures ($r_s = -.21$ to $.62$, $p < .05$ to $p < .001$). Specific play behaviors were moderately to highly intercorrelated ($r_s = .23$ to $.84$, $p < .05$ to $p < .001$), positively related to the BSID2 MDI ($r_s = .23$ to $.51$, $p < .05$ to $p < .001$), positively related to reported and spontaneous language ($r_s = .20$ to $.41$, $p < .05$ to $p < .001$), and associated with the global play behavior measures ($r_s = -.21$ to $.62$, $p < .05$ to $p < .001$) (See Appendix F for correlation matrix).

Toddler Outcomes: Developmental Status. The Bayley Scales of Infant Development - Second Edition, standardization version (1991) was administered during the 24-month laboratory visit to assess the child's overall developmental status at age 2. The BSID2 is administered in a structured, standardized manner and provides raw and scaled scores as measures of mental and motor performance of children between the ages of 1 to 42 months. Raw scores from the BSID2 mental and motor scales were converted into scaled scores, the Mental Developmental Index (MDI) and the Psychomotor Developmental Index (PDI), with a mean of 100 and a standard deviation of 16.⁹

Control for Confounds: Covariates. A covariate is a measure other than the independent variable which is significantly related to the dependent (i.e., outcome) measure, and thus can obscure or confound the relationship between the independent and dependent variable(s) (Tabachnick & Fidell, 1989). For this study, a specific covariate selection and reduction process was defined following previous literature (e.g., Jacobson & Jacobson, 1996) and discussion with statistical consultants and thesis advisors. In brief, zero-order correlations between 42 potential covariates (e.g., maternal demographics and postnatal environment) and 12 outcomes were examined for statistical and theoretical significance. This multi-step process resulted in a reduced set of specific covariates, listed in Table 3.

Potential covariate measures were gathered from questionnaires at study enrollment and at the 2-year laboratory visit. Maternal demographics such as age, years of education, parity, marital status and race were obtained from the Hospital Screening Questionnaire administered on the day following birth. Maternal substance use during pregnancy was obtained from the Postpartum Maternal Interview (PPMI) at study enrollment. In addition

⁹ The standardization version of the BSID2 was considered an appropriate developmental assessment tool as the items on the test were similar to the items on the final BSID2. Conversion of raw data to scaled scores was provided by The Psychological Corporation, San Antonio, Texas, since there are no published norms for the standardization version of the BSID2.

to assessing prenatal cocaine use, the PPMI also comprehensively assessed alcohol consumption, marijuana use, and cigarette smoking during the month prior to recognition of conception and during each trimester of pregnancy. Alcohol use was measured in total number of drinks, average number of drinks per drinking day, total number of absolute ounces of alcohol, total times alcohol was consumed, and total times binge alcohol use occurred (≥ 5 drinks on one drinking occasion). Marijuana use was measured in total number of days (frequency) and total number of estimated joints. Cigarette smoking was assessed in total number of packs. Other maternal factors such as number of prenatal visits and welfare status were also obtained from the PPMI. Estimated maternal IQ was obtained from the Shipley Institute of Living Scale (Zachary, 1991), a paper and pencil test of verbal and abstract thinking skills. The Shipley total score was converted into an estimated IQ score.

Postnatal environmental measures were obtained from the Modified HOME Inventory at 21 months and the Parental Interview (PI), a questionnaire developed for the Seattle Study, at 24 months. A standardized observational measure of the home environment (HOME, 1978) was modified for use as a phone interview. The modified HOME yielded two measures. First was a total score summarizing 4 subscales from the original HOME: organization of the environment, provision of appropriate play materials, maternal involvement with the child, and opportunities for variety in daily stimulation. Second was an informal measure of environmental stimulation, the total number of different toys the child has in their home. From the PI administered at the 24-month laboratory assessment, caregivers reported on the child's health and home environment over the past year, including the number and type of child illnesses, where and with whom the child has lived, the number and type of household changes, whether the caregiver was in an abusive situation, and the extent of the caregiver's licit and illicit substance use.

Data Analysis

The COC and NON-COC groups were fairly well matched, allowing for control of many confounding factors in the study design. Confounding factors not dealt with in the study design were adjusted statistically. The main analytic techniques used in this study include correlation, t-test, multiple regression, and chi-square. First, the distributions of all study measures were examined to make decisions about variable transformations (all highly skewed variables were log transformed), data reduction, and appropriate methods of analysis (see detailed sections on data reduction and data analysis below). From the large number of covariate candidates, a small set of high priority covariates were selected to create adjusted outcome measures and to enter into the regression models. Two alternative regression approaches were used to analyze the dose-response and main effects of prenatal cocaine exposure on toddler outcomes: an adjusted outcome strategy and a traditional hierarchical regression strategy, respectively. These strategies are described in detail below. T-tests were used to assess group mean differences on adjusted outcome measures. Finally, chi-square analyses were used to compare the two groups on the number of children falling below a clinically significant cutoff for selected measures in each outcome domain.

Data Reduction. Table 5 lists the reduced set of study measures. As previously mentioned, all cocaine dose measures were significantly intercorrelated. Log total number of grams used throughout pregnancy (prior pregnancy through third trimester) was most strongly associated with the other log cocaine use measures (r s .55 to .93, $p < .001$), and so was used as the predictor in the regression analyses. The bivariate grouping variable, COC/NON-COC, was used in group mean comparison t-tests.

A rank sum procedure (O'Brien, 1984) was used to reduce the large number (23) of outcome variables to a more manageable and interpretable number (12). The first step in the rank sum procedure was to compute a ranked variable from each outcome variable

(through SPSS). A low rank value was assigned to the lowest value for each outcome variable, thus a low rank score indicates poorer outcome. Mean ranks were used in the case of ties. Next, theoretically related ranked variables were summed to produce the final rank sum outcome measures. For example, the ranked play variables "affective tone towards the caregiver" and "referencing the caregiver" were summed together to produce the rank summed "interaction with caregiver" outcome measure. Large rank sum values indicate better performance on a particular outcome. Table 5 lists each rank sum outcome measure and describes which variables went into each rank sum measure. The BSID2 MDI was not included in the rank sum procedure since it is a standardized value and assesses a separate outcome domain. From now on, the term "outcome measures" refers to the rank sum variables and the Bayley MDI.

Covariate reduction was accomplished by examining the significance of zero-order correlations between 42 potential covariates and the 12 outcome measures. This process resulted in a reduced set of covariates. This set of covariates were then regressed on each outcome measure to determine which covariates remained significant for each outcome. Next, patterns of relationships between the reduced set of covariates (about 4 or 5 covariates depending on the outcome) and the measures within each outcome domain were examined to find the covariates consistent across the measures within each domain. That is, consistent covariates had significant regression slopes in relation to outcomes and the slopes were of the same sign within each outcome domain. The final set of covariates were entered into regressions in one analytic strategy and used to create adjusted outcomes for another analytic strategy. (See Appendix E for the step-by-step covariate selection and reduction procedures and Table 5 for the final set of covariates).

Data Analysis Strategies. The Outcome Adjustment approach was used to assess a dose-response model of prenatal cocaine exposure on 2-year child outcomes as well as group mean differences in outcome measures. In this approach, the significant final

covariates in the NON-COC group were used to compute “adjusted outcome” variables for the COC group. The rationale for this approach was that some dimensions assessed by covariates in the COC group may be directly related to cocaine use, so that covarying these effects will likely lead to statistical “over control” (Jacobson & Jacobson, 1996). In contrast, adjusting for the effects of covariates as they occur in the NON-COC comparison group is not confounded with the fact of cocaine use and all that is related to such behavior, and thus will more appropriately adjust study outcomes for potential confounds (F. Bookstein and P. Sampson, personal communication, 1996).¹⁰ For example, the significant covariates for the BSID2 MDI in the NON-COC group were: 1) total ounces of prenatal alcohol exposure throughout pregnancy, 2) mother uses medical coupons, 3) child gender, and 4) number of toys in the home at 21 months. The “adjusted MDI” score (computed for all cases regardless of group) = original MDI score - $\beta_1(\text{covar1}) - \beta_2(\text{covar2}) - \beta_3(\text{covar3}) - \beta_4(\text{covar4})$. The Outcome Adjustment approach allowed for two very straightforward analyses of the data. First, simple regression models analyzed log total grams of cocaine used throughout pregnancy on each adjusted outcome in the COC group only (n = 80), excluding the false-negative cases (i.e., false-negative cases were excluded from these analyses because their cocaine use values were imputed from regression analysis to begin with). Additional variables were not entered into the model since they were dealt with by study design or covariate adjustment. Second, t-tests were used to analyze group mean differences on the adjusted outcomes for the full sample (n = 200).

The Traditional Multiple Regression approach was used to assess the main effects and interactions of prenatal cocaine exposure on unadjusted child outcomes for the full sample of 200 cases. First, log total grams of cocaine used throughout pregnancy and child gender were entered into a regression for each outcome. The independent, main

¹⁰ Covariates for the NON-COC group were selected as described in the data reduction section and Appendix E.

effects of these variables were examined in relation to each other and each outcome. Next, a cocaine by gender interaction term was entered into the model to evaluate how the addition of this variable impacted the main effects of prenatal cocaine exposure and child gender on outcome. A cocaine by gender interaction term was created since gender was significantly related to most outcomes in both groups, and it has been associated with poor outcome in another polydrug-exposed sample (Beckwith et al., 1994). Lastly, other significant covariates were entered into each model to evaluate how the addition of these variables impacted the main effects and interaction of prenatal cocaine exposure and child gender on outcome.

TABLE I.2-Group Matching

Measures	COC			NON-COC			p-value
	%	<u>M</u>	<u>SD</u>	%	<u>M</u>	<u>SD</u>	
<u>Maternal demographics</u>							
Age (yrs)		25.31	5.01		23.62	5.02	.018
Education (yrs)		11.68	1.55		11.84	1.57	NS
Race (% Black)	39			29			NS
Log parity		1.16	0.38		0.96	0.31	.000
<u>Other prenatal exposures</u>							
Log marijuana frequency		1.74	1.86		1.29	1.90	NS
Log # cigarette packs		4.14	1.85		3.33	2.37	.008
Log alcohol ounces		2.77	1.95		1.85	1.55	.000
Any alcohol binge (%)	39			29			NS
<u>Child Characteristics</u>							
Gestational Age		39.19	2.14		39.53	1.57	NS
Gender (% female)	58			50			NS
Age at two-year assessment		24.01	0.17		24.00	0.0	NS

TABLE II.2-Study Measures: Cocaine Use and Child Outcomes

A. Maternal cocaine use during pregnancy

1. Frequency (number of times)
2. Total amount (number of grams)
3. Maximum amount at any one time
4. Average amount of cocaine per day
5. Any cocaine binge (≥ 1 gram at one time)

B. Child outcomes

1. Productive language
 - a. Caregiver report at 21 months
 1. Vocabulary
 2. Grammatical complexity (MSL)
 3. Language age
 - b. BSID2 verbal score
 - c. Spontaneous child language at 24 months from videotaped interaction
 1. Vocabulary
 2. Grammatical complexity (MLU)
 3. Language intelligibility
2. Global play behaviors from videotaped child-alone play
 - a. Engagement
 - b. Out of room
 - c. Aimlessness
 - d. Overall affective tone
 - e. Affect towards caregiver
 - f. Referencing caregiver

TABLE II.2 (continued)

-
- g. Frustration
3. Specific play behaviors from videotaped child-alone play
- a. Combining toys
 - b. Toy selection strategy
 - c. Expansion of theme
 - d. Transitions
 - e. Mouthing toys
 - f. Immature behaviors
 - g. Attention span
4. Developmental status using BSID2
- a. Mental Developmental Index (MDI)
 - b. Psychomotor Developmental Index (PDI)
-

TABLE III.2-Study Measures: Covariates

Maternal education
Maternal IQ
Maternal ethnicity
Number of prenatal visits
Log alcohol ounces
Log no. of cigarette packs
Medical coupons (welfare status)
Public assistance (welfare status)
Child gender
Number of toys in home at 21 months
Number of child illnesses from 12-24 months
Caregiver in abusive relationship from 12-24 months
Number of stressful moves from 12-24 months
Number of children ≥ 6 in home at 24 months
Number of types of family stressors at 24 months

TABLE IV.2-Cocaine Use During Pregnancy (Raw Scores)

Measures	Prior through 1st Trimester ^a			2nd through 3rd Trimester			Prior through 3rd Trimester ^a		
	%	<u>M</u>	<u>SD</u>	%	<u>M</u>	<u>SD</u>	%	<u>M</u>	<u>SD</u>
<u>Self-report for full COC sample (n=100)</u>									
Frequency		28.60	35.00		16.19	31.19		44.80	58.30
Amount (grams)		37.15	79.91		19.88	48.64		57.03	108.66
Maximum amount		1.61	2.08		0.97	1.81		1.85	2.16
Average amount/day		0.92	1.11		0.72	0.96		0.98	1.06
Any cocaine binge	54			29			59		
<u>Self-report for COC sample minus false-negative cases (n= 80)</u>									
Frequency		30.82	37.31		19.49	34.10		50.31	63.10
Amount (grams)		44.40	87.86		24.42	53.48		68.83	118.63
Maximum amount		1.50	2.12		1.11	2.00		1.80	2.23
Average amount/day		1.00	1.21		0.76	1.04		1.09	1.13
Any cocaine binge	53			35			59		

^a Prior = prior to pregnancy recognition.

TABLE V.2-Study Measures After Data Reduction Procedures

-
- A. Prenatal cocaine use
 - 1. Log total number of grams used throughout pregnancy
 - B. Outcome domains
 - 1. Productive language
 - a. Rank sum vocabulary (MTTI and spontaneous vocabulary)
 - b. Rank sum MLU (MTTI MSL and spontaneous MLU)
 - c. Rank sum language total (MTTI vocabulary and MLU, spontaneous vocabulary and MLU, BSID verbal score)
 - 2. Global play measures
 - a. Rank sum engagement (engagement, out of room, aimlessness)
 - b. Rank sum affective tone (affective tone and frustration)
 - c. Rank sum interaction with caregiver (affect towards and referencing caregiver)
 - d. Rank sum global play total (all global play measures)
 - 3. Specific play behaviors
 - a. Rank sum cognitive play (combining, selection strategies, expansion of themes, transitions)
 - b. Rank sum deviant play (mouthing and immature play behavior)
 - c. Rank sum attention span (attention span)
 - d. Rank sum specific play total (all specific play measures)
 - 4. Developmental status
 - a. BSID2 MDI
 - C. Covariates by analysis strategy and outcome domain
 - 1. For the adjusted outcome approach (adjustment based on non-cocaine group)
 - a. Productive language

TABLE V.2 (continued)

-
1. Welfare status (medical coupons)
 2. Child gender
 3. Number of toys in home at 21 months
 4. Number of illnesses from 12-24 months
 5. Number of children ≥ 6 in home at 24 months
 - b. Global play behaviors
 1. Maternal IQ
 2. Maternal race
 3. Number of illnesses from 12-24 months
 4. Mom in abusive relationship from 12-24 months
 5. Number of children ≥ 6 in home at 12-24 months
 6. Number of stressful moves from 12-24 months
 - c. Specific play behaviors
 1. Maternal IQ
 2. Child gender
 3. Mom in abusive relationship from 12-24 months
 4. Number of children ≥ 6 in home at 24 months
 - d. Developmental status - BSID2 MDI
 1. Welfare status (medical coupons)
 2. Child gender
 3. Log alcohol ounces consumed throughout pregnancy
 4. Number of toys in home at 21 months
 2. For the traditional regression approach (based on full sample)
 - a. Productive language

TABLE V.2 (continued)

-
1. Welfare status (public assistance)
 2. Child gender
 3. Log number of cigarette packs smoked throughout pregnancy
 4. Number of toys in home at 21 months
 5. Number of illnesses from 12-24 months
- b. Global play behaviors
1. Maternal race
 2. Child gender
 3. Mom in abusive relationship from 12-24 months
 4. Number of stressful moves from 12-24 months
- c. Specific play behaviors
1. Maternal IQ
 2. Maternal race
 3. Child gender
 4. Mom in abusive relationship from 12-24 months
- d. Developmental status - BSID2 MDI
1. Maternal IQ
 2. Log number of cigarette packs smoked throughout pregnancy
 3. Child gender
 4. Number of toys in home at 21 months
 5. Mom in abusive relationship from 12-24 months
-

Results

Sample description

Table 6 presents group comparisons on selected maternal demographics and substance use during pregnancy. Both groups of women were in their mid 20's. Although the COC group was slightly older than the NON-COC group (25 vs. 24 years, $p < .05$, respectively), this difference is not clinically meaningful and has been observed in many other samples (e.g., Beckwith et al., 1994; Chasnoff et al., 1992; Graham et al., 1992). Both groups of women completed approximately 12 years of education and performed within normal limits on a paper and pencil intelligence test (IQ estimated from the Shipley), even though the COC group scored approximately 4 points lower than the NON-COC group (90 vs. 94, $p < .05$, respectively). Similar proportions of women in the COC group (40%) and the NON-COC group (30%) were African-American, while the remainder of the sample was predominantly Caucasian. These demographic data underscore the success of group matching presented in the methods section.

Differences in demographic factors which had not been considered for group matching did exist between the two groups of women in this sample, and were similar to differences among the women in the Seattle Study (Carmichael Olson et al., 1995). A majority of women in the COC and NON-COC groups were single, divorced, or separated, but approximately twice as many women in the NON-COC group (29%) were married than in the COC group (13%). The women in the COC group had significantly more children and a significantly greater percentage of these women used public assistance as their main source of income than the NON-COC group. Lastly, the women in the COC group attended significantly fewer prenatal visits during this pregnancy than did the women in the

NON-COC group. Covariate adjustment was used for these demographic differences in data analysis.

Perhaps the most consistent finding in the cocaine effects literature is that cocaine-using women abuse other toxic substances during pregnancy in greater amounts than do comparison groups (e.g., Beckwith et al., 1994; Chasnoff et al., 1992). Efforts to match the COC and NON-COC groups on other prenatal exposures were partially successful in this sample. Table 6 illustrates that the two groups of women were similar in the average number of drinks consumed per drinking day, in the proportion who alcohol binged at any time, in the total number of days they used marijuana, and the total number of marijuana joints smoked throughout pregnancy. On the other hand, the women in the COC group smoked significantly more packs of cigarettes and consumed more alcohol (total number of drinks, total number of absolute ounces of alcohol, total number of times alcohol consumed, total times binged) than the NON-COC group. Prenatal exposure differences were dealt with by covariate adjustment in data analysis.

Table 7 presents group comparisons of postnatal environmental characteristics. Caregiver report of the *quality* of the home environment at 21 months of age, using a standardized telephone interview, revealed no differences between the two groups in a measure summarizing the areas of organization, provision of play materials, involvement with child, or variety in daily stimulation. However, caregiver report at 2 years of age revealed that the COC and NON-COC groups differed in the *structure* of the home environment. A higher percentage of children in the COC group were cared for by foster parents or relatives other than a biological parent(s), whereas almost all children in the NON-COC group were cared for by a biological parent. Approximately half the caregivers of the COC group were working either part-time or full-time outside the home, while

approximately three-fourths of the caregivers of the NON-COC group worked. A similar percentage of caregivers in both groups were in what they considered to be an abusive situation, and they reported a similar number of stressful moves within the past year. However, the caregivers of the COC group reported significantly more types of family stresses within the past year. Approximately three-fourths of caregivers for both groups of children reported alcohol use during the past year, and approximately one-quarter of caregivers for each group reported using marijuana within the last year. By the 2-year visit, only 26% of women in the COC group reported using cocaine within the past year. Most interestingly, 8% ($n = 7$) of the caregivers in the NON-COC group, the comparison group of non-cocaine users, reported using cocaine within the past year. At study enrollment, these women were Caucasian, in their early 20's, had completed 12 years of education, half were married and half were on public assistance. By the 2 year visit, all women used alcohol, half used marijuana, a majority were in an abusive situation, and all reported 2 or more family stressors within the past year.

Infant characteristics

Table 8 presents group comparisons of birth outcomes and infant growth at 24 months. At birth, the average gestational age of both groups of infants did not differ, but a significantly higher proportion of infants in the COC group were small for their gestational age compared to the infants in the NON-COC group (12% vs. 1%, $p < .05$, respectively). In addition, infants in the COC group were significantly smaller in weight, length, and head circumference at birth than infants in the NON-COC group. By 2 years of age,

however, the two groups of children no longer differed in physical growth measures such as weight, length, and head circumference.

Group comparisons of raw score child outcomes

Productive language outcomes. Table 9 presents raw score language outcomes for both the COC and NON-COC groups. At 21 months, on the MTTI, caregivers in the COC group reported an average vocabulary size of 43 words and level of grammatical development at the 2 to 3 word stage. The mean language age for reported vocabulary size was 22 months, commensurate with their chronological age. Normative data for MSL also indicate that the COC group was well within normal limits in grammatical development (Fenson et al., 1994). Caregivers for the NON-COC group reported language skills similar to those of the COC group. At 24 months of age, from a spontaneous language sample, the COC group exhibited an average vocabulary of 27 words and sentence length of approximately 1 to 2 words in an unstructured caregiver-child play situation. Language transcribers rated the children's language as fairly to mostly intelligible. Average MLU was within the normative range for grammatical development at 2 years of age (Miller, 1981). It is important to note the wide variability in vocabulary size for both groups of children at both 21 and 24 months, a finding typical of children this age (Bates, Dale, & Thal, 1995). The children in the NON-COC group exhibited similar language abilities in the unstructured caregiver-child play session. (See Appendix G for histograms of raw score outcomes.)

Global play behavior outcomes. Table 9 also presents raw score global play

behavior outcomes for the COC and NON-COC groups. The majority of global behaviors were rated a 4, on average, suggesting that the quality of cocaine-exposed children's global play behaviors were appropriate for their age (Beckwith et al., 1994). On average, children in the COC group engaged with the toys for more than half to approximately 3/4 of the 10-minute play session. They rarely exhibited aimless behaviors, such as walking around the room with no purpose, and rarely attempted to leave the room during the play session. Affectively during child-alone play, cocaine-exposed children most often displayed positive emotions (such as smiles, laughs, or joy) or were neutral (such as showing interest or flat affect) and only sometimes exhibited signs of frustration (such as whining or fussing). Although the children were supposed to play by themselves, they referenced their caregivers about 5 or 6 times during the 10-minute session, and when doing so, displayed both positive and negative affect (e.g., anger, crying) toward their caregivers. The NON-COC group was rated similarly on global play behaviors. (See Appendix G for histograms of raw score outcomes.)

Specific play behavior outcomes. Table 9 also presents raw score specific play behavior outcomes for both groups of children. The COC group demonstrated variability in the quality of specific play behaviors, with a range in ratings from a 2 (somewhat inappropriate for their age) to a 5 (appropriate for their age) in the child-alone play situation. The majority of specific play behaviors were rated a 3, suggesting that the quality of cocaine-exposed children's behaviors were somewhat lower than expected for their age (Beckwith et al., 1994; Belsky & Most, 1981). When engaging with toys, children in the COC group sometimes used one toy at a time and at other times combined several toys together. A majority of these toy combinations were rated as relational, such

as putting two plates together on the floor, a stage of play development somewhat more typical of younger children. When selecting which toys to play with, cocaine-exposed children were purposeful and deliberate in their choices some of the time, and random in their choices at other times. They also demonstrated both smooth and abrupt transitions between play acts. For example, sometimes they abruptly dropped the toy they were playing with before exploring it first, and at other times they explored the toy for some time before putting down the toy and smoothly moving onto a new toy. These behaviors suggest that the children in the COC group, on average, were in a transitional stage of play development in which exploration consisted of both immature and mature play behaviors.

The COC group demonstrated more difficulty expanding on initiated play themes relative to other specific play behaviors. For example, they may have put plates, cups and spoons on the floor as if to have a tea party, but did not expand on this "tea party" theme by pouring tea into the cups or feeding the dolls with the spoons. Thus, the length of their play sequences were short and unelaborated, behavior which is more typical of younger children. In addition, they sometimes engaged in exploration consistent with the behavior of younger children, such as throwing, kicking, and banging. The attention span of the COC group was variable; at times the children were easily distracted (usually by the door, the one-way mirror, a piece of tape stuck to the carpet, or the caregiver) and at other times they were absorbed and interested in their play activities. Commensurate with their age, however, the COC group exhibited very few instances of inappropriate mouthing (e.g., mouthing objects not intended for the mouth, or perseverative mouthing of objects). The NON-COC group was rated similarly on specific play behaviors. (See Appendix G for histograms of raw score outcomes.)

Developmental status. Table 9 also presents the standard scores for the BSID2 mental and motor scales for both groups of children. At two years of age, the cocaine-exposed children were functioning within normal limits ($M = 100 \pm 16$) on both the mental ($M = 87.12$) and motor scales ($M = 95.14$) of the BSID2. However, the average MDI score fell at the low-normal end of the BSID2 normal distribution. Although the groups did not differ on mean MDI score, a significantly larger percentage of children in the COC group (40%) scored greater than one standard deviation below the MDI standardized mean of 100 than the percentage of children in the NON-COC group (25%) ($\chi^2 = 5.13, p < .05$). (See Appendix G for histograms of raw score outcomes.)

Effects of prenatal cocaine exposure on child outcomes at age 2: Comparison of two analytic strategies

Adjusted outcome approach. Table 10 presents the adjusted outcome scores for the COC and NON-COC groups. (See Appendix H for histograms of adjusted outcomes.) Regression analyses for adjusted outcome measures in the COC group only (minus the false-negative cases) revealed no dose-response relationships between prenatal cocaine use throughout pregnancy and 24-month child outcomes, except for one global play measure. Contrary to expectations, children exposed to more grams of cocaine throughout pregnancy displayed more positive and/or neutral affect during child-alone play at age 2 ($F(1,77) = 4.03, p < .05$). Group difference t-tests on adjusted outcomes for the full sample yielded results similar to the adjusted outcome regression analyses. There were no group differences except on one global play measure. Contrary to expectations, the COC group spent a significantly greater amount of the 10-minute child-alone play session engaged with

toys than the NON-COC group ($t = -2.18, p < .05$).

Traditional regression approach. Table 11 presents the unadjusted outcome scores for the COC and NON-COC groups. Traditional multiple regression analyses on unadjusted child outcomes yielded results similar to the adjusted outcome approach. There were no main effects of prenatal cocaine use throughout pregnancy on unadjusted child outcomes. However, there was a significant cocaine by gender interaction for one global play measure. Rank sum caregiver interaction was significant ($F(3, 194) = 2.74, p < .05$) when the cocaine by gender interaction term was entered into the model ($t = -2.22, p < .05$), and remained significant ($t = -1.99, p < .05$) even after covariates were added to the model. Figure 1 illustrates group means for caregiver interaction. Examination of these means shows that the boys in the COC group ($M = 187.87$) were doing more poorly than either the girls in the COC group ($M = 223.00$), the boys in the NON-COC group ($M = 209.84$) or the girls in the NON-COC group ($M = 213.52$).

Clinically meaningful group differences on adjusted outcomes

Table 12 presents group comparisons on cutoffs for selected adjusted outcome measures. On the BSID2 mental scale, a larger proportion of children in the COC group (23%) scored 1.5 standard deviations below the MDI standardized mean of 100 than the percentage of children in the NON-COC group (12%) ($\chi^2 = 4.19, p < .05$). Exploratory ANOVAs revealed that children in the COC group who scored more poorly on the BSID2 had significantly lower scores on measures of spontaneous language ($F(1,92) = 25.85, p < .0001$) and exhibited more deviant play behaviors ($F(1,97) = 4.01, p < .05$) than children

in the COC group who scored within normal limits on the MDI. Amount of prenatal cocaine exposure was not related to having scored 1.5 SDs below the MDI mean, nor were any maternal demographic, child characteristic (e.g., gender, OFC, birthweight), or postnatal environmental variables. There were no significant differences between the percentage of children in the COC and NON-COC groups who scored below specified cutoffs on measures of language and play.

TABLE VI.3-Group Comparisons of Maternal Demographics and Prenatal Drug Use at Enrollment

Measures	COC			NON-COC			p-value ^a
	%	<u>M</u>	<u>SD</u>	%	<u>M</u>	<u>SD</u>	
<u>Maternal demographics</u>							
Age (yrs)		25.31	5.01		23.62	5.02	.018
Education (yrs)		11.68	1.55		11.84	1.57	NS
Maternal IQ (Shipley)		89.94	12.17		93.57	10.94	.027
Race (%)							NS
White/Hispanic	54			68			
Black	39			29			
Other	7			3			
Marital status (%)							.01
Single/divorced/separated	70			52			
Living as married	17			19			
Married	13			29			
Parity (no. of living children) ^b		2.42	1.30		1.77	1.05	.000
Multiparous (%)	69			50			.006
Welfare status (%)							
Public assistance	80			41			.000
Medical coupons	93			73			.000
No. of prenatal visits		9.86	4.82		12.54	4.61	.000

TABLE VI.3 (continued)

Maternal prenatal drug use^b

Alcohol

Total no. of drinks	222.08	382.78	75.72	245.72	.001
Average no. of drinks/ drinking day	3.34	3.04	2.79	2.91	NS
Total no. of ounces	101.47	181.73	39.66	159.92	.001
Total times binged	20.31	44.01	5.09	19.46	.002
Any alcohol binge (%)	39		29		NS

Marijuana

Total days used	36.61	69.95	32.97	72.37	NS
Total no. of joints	39.53	98.17	39.10	128.94	NS

Cigarettes

Total no. of packs	169.65	153.19	138.16	139.43	.01
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^a Independent sample t-test.^b Using a t-test on log scores, not raw scores.

TABLE VII.3-Group Comparisons of Postnatal Environment

Measures	COC			NON-COC			p-value ^a
	%	<u>M</u>	<u>SD</u>	%	<u>M</u>	<u>SD</u>	
<u>Postnatal environment at 21 months</u>							
Modified HOME inventory		17.34	2.45		17.83	2.51	NS
Total no. of toys child has		14.97	3.89		15.57	4.19	NS
<u>Postnatal environment at 24 months</u>							
<u>(children with main caregivers only)^b (n=91)</u>				<u>(n=92)</u>			
Who child lives with (%)							.000
Biological mother/father	74			98			
Foster parent(s)	14			0			
Grandparent(s)	4			1			
Other	8			1			
Caregiver in abusive situation (%)	22			24			NS
Caregiver works PT or FT	45			71			.002
Total no. of stressful moves ^c		0.31	0.65		0.26	0.57	NS
No. of type of family stressors		4.87	2.70		4.02	2.36	.025
Uses alcohol postnatally (%)	72			74			NS
Uses marijuana postnatally (%)	26			24			NS
Uses cocaine postnatally (%)	26			8			.000

TABLE VII.3 (continued)

^a Independent sample t-test.

^b Nine children in the COC group and eight children in the NON-COC group were brought to the 24-month lab visit by someone other than the child's main caregiver. Therefore, these non-main caregiver data were excluded from these analyses, as they may not have accurate knowledge of the child's day-to-day environment over the past year.

^c Using a t-test on log scores, not raw scores.

TABLE VIII.3-Group Comparisons of Growth Measurements at Birth and Two Years

Measures	COC			NON-COC			p-value ^a
	%	<u>M</u>	<u>SD</u>	%	<u>M</u>	<u>SD</u>	
<u>Infant birth outcomes</u>							
Gender (% female)	58			50			NS
Gestational age (weeks)		39.19	2.14		39.53	1.57	NS
Small for GA (%)	12			1			.03
Birthweight (grams)		3075.96	629.90		3339.11	511.28	.001
Birth length (cm)		48.62	3.19		49.76	2.73	.01
Head circumference (cm)		33.46	1.67		34.22	1.40	.001
<u>Child growth at 2 years</u>							
Weight (kg)		12.33	1.50		12.51	1.35	NS
Length (cm)		86.28	3.29		86.48	3.11	NS
Head circumference (cm)		48.46	1.49		48.60	1.41	NS

^a Independent sample t-test.

TABLE IX.3-Group Comparisons of Raw Score Child Outcomes

Measures	COC		NON-COC	
	<u>M</u>	<u>SD</u>	<u>M</u>	<u>SD</u>
<u>Productive language</u>				
21m MTTI vocabulary	42.62	24.63	40.25	25.56
21m MTTI MSL	2.69	1.34	2.57	1.32
21m MTTI language age (mo.)	21.69	3.66	21.36	3.80
24m vocabulary	26.78	16.20	27.33	16.62
24m MLU	1.49	0.54	1.61	0.50
24m intelligibility	3.90	0.97	3.71	1.01
24m BSID2 verbal score	16.79	6.17	16.21	7.08
<u>Global play behaviors</u>				
Engagement	4.20	1.23	4.30	1.10
Out of room	3.90	1.23	3.72	1.29
Aimlessness	4.00	0.89	4.09	0.81
Overall affect	4.21	1.21	4.31	1.10
Affect to caregiver	2.94	0.96	3.00	0.85
Referencing caregiver	4.35	0.95	4.37	0.93
Frustration	3.67	1.36	3.74	1.34
<u>Specific play behaviors</u>				
Combining toys	3.35	1.02	3.35	0.94
Toy selection strategies	2.74	1.23	2.85	1.14
Expansion of themes	1.65	0.73	1.69	0.73

TABLE IX.3 (continued)

Transitions	2.68	1.28	2.76	1.15
Mouthing toys	4.52	0.75	4.54	0.76
Immature behaviors	3.42	1.14	3.50	0.98
Attention span	3.08	1.42	3.19	1.29
<u>Developmental status</u>				
BSID2 MDI	87.12	15.84	89.58	14.95
BSID2 PDI	95.14	17.28	96.23	14.53

TABLE X.3-Group Comparisons of Adjusted Child Outcomes

Measures	COC		NON-COC	
	<u>M</u>	<u>SD</u>	<u>M</u>	<u>SD</u>
<u>Productive language</u>				
Vocabulary	171.51	112.99	145.11	96.01
MLU	235.36	96.58	221.74	90.30
Language total	552.08	234.78	502.02	198.49
<u>Global play behavior</u>				
Engagement*	152.79	155.24	111.79	104.86
Affective tone	17.29	119.61	-5.89	88.81
Interaction with caregiver	140.71	76.42	133.53	64.81
Global total	306.69	284.68	239.43	192.50
<u>Specific play behavior</u>				
Cognitive level	350.92	216.37	338.24	169.23
Deviant play	183.30	87.65	183.62	77.46
Attention span	34.04	67.13	28.23	47.73
Specific total	568.17	333.27	550.01	251.80
<u>Developmental status</u>				
BSID2 MDI	87.95	14.30	90.62	12.95

* Group difference is significant at $p < .05$, per t-test.

TABLE XI.3-Group Comparisons of Unadjusted Child Outcomes

Measures	COC			NON-COC		
	%	<u>M</u>	<u>SD</u>	%	<u>M</u>	<u>SD</u>
<u>Productive language</u>						
Vocabulary		209.98	107.01		201.88	107.83
MLU		205.67	98.02		204.65	101.88
Language total		521.86	231.95		509.97	233.66
<u>Global play behavior</u>						
Engagement		317.35	136.31		316.50	126.58
Affective tone		208.05	105.17		214.84	105.39
Interaction with caregiver		208.30	74.93		211.68	71.84
Global total		730.78	250.80		743.02	244.99
<u>Specific play behavior</u>						
Cognitive level		419.98	209.20		433.66	195.78
Deviant play		210.09	89.58		214.65	85.04
Attention span		103.88	62.50		108.47	56.69
Specific total		733.96	325.24		756.77	299.65
<u>Developmental status</u>						
BSID2 MDI		87.12	15.84		89.58	14.95

TABLE XII.3-Clinically Meaningful Differences in Selected Adjusted Outcome Measures

Measures	Percent (%) below cutoff	
	COC	NON-COC
<u>Productive language (bottom quartile)</u>		
Vocabulary	22	27
MLU	26	23
Language total	25	25
<u>Play behaviors (bottom quartile)</u>		
Global play total	24	26
Specific play total	27	22
<u>Developmental status</u>		
> 1 SD below MDI mean+	38	27
> 1.5 SDs below MDI mean*	23	12

+ Group differences is significant at $p < .10$, per chi-square.

* Group differences is significant at $p < .05$, per chi-square.

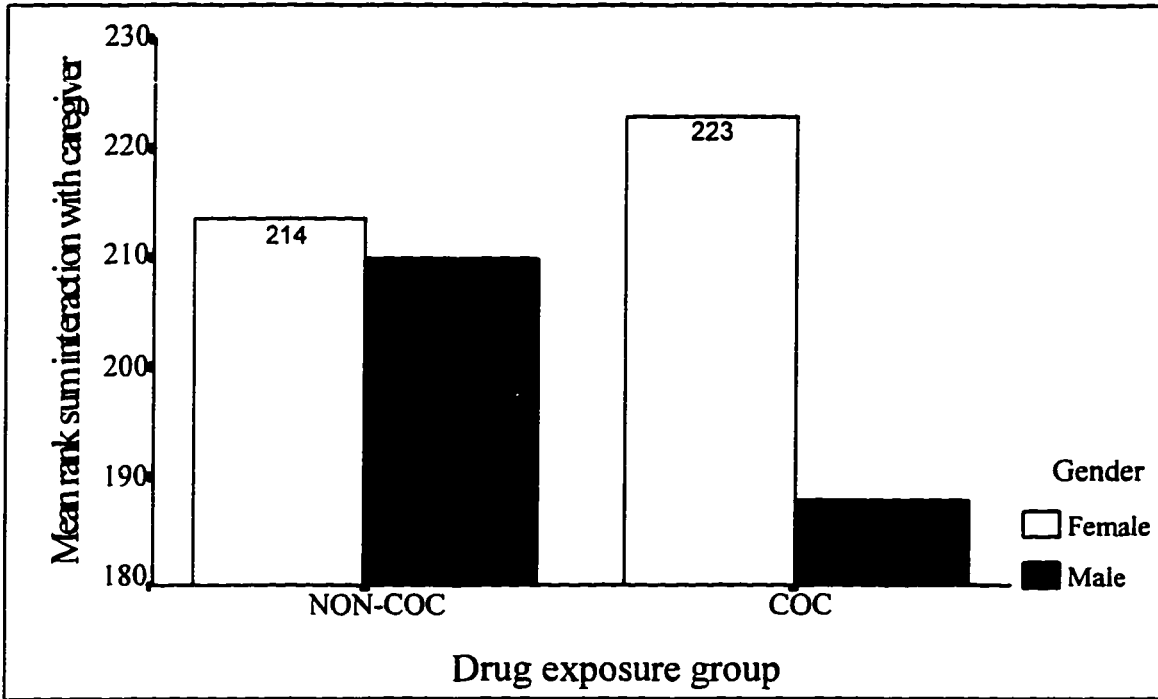


FIGURE 1: Rank Sum Interaction with Caregiver.

Discussion

This study of prenatal cocaine effects on two-year representational abilities (language and play) and global cognitive skills is one of only a few so far to attempt to systematically handle the methodological challenges plaguing this field of research. The main objective of this study was to determine if cocaine has an adverse impact on toddler representational abilities and developmental status, independent of other risk factors associated with maternal cocaine use and developmental outcome. A complex study design and innovative data analysis strategy were employed to accomplish this goal. Substantial effort was made in both the larger Seattle Study cohort and the subsample presented here to design a study with: sample size of sufficient power to detect expected effects, optimal sample retention, lack of examiner bias, accurate self-report of cocaine use throughout pregnancy (with verification via a biological marker), and control for confounding risk factors known to affect child development. An innovative data analysis strategy, including a complex covariate selection process and a check via two alternative statistical approaches, was employed to analyze independent cocaine effects on 2-year child outcome. One statistical approach examined dose-response and group difference models on covariate-adjusted outcomes, while the other approach examined a main effects model through traditional multiple regressions on unadjusted outcomes.

A Dose-Response Effect of Prenatal Cocaine Exposure

It was hypothesized that cocaine effects would be more likely to impact certain highly-exposed children, rather than the group as a whole. Such subtle individual differences may be obscured by a group difference approach. A dose-response analysis of the relationship between exposure and outcome, controlling for confounding factors, would be more likely to reveal such subtle cocaine effects. For example, dose-response

relationships between cocaine exposure and child outcome have been reported in a subsample of neonates from the Seattle Study (Martin et al., in press) and in one other sample of cocaine-exposed newborns (Tronick et al., 1994). In the current study, however, dose-response analyses did not detect a relationship between amount of cocaine exposure and specific two-year developmental skills. That is, the most highly-cocaine exposed toddlers did not necessarily exhibit the worst performance in early productive language abilities, quality of play or general developmental status. As expected, there were no group differences on 2-year adjusted outcomes. Traditional regression analyses corroborated these null results, but also showed that postnatal environmental factors (considered covariates in the analyses) were more significant contributors to variability in 2-year outcomes than prenatal cocaine exposure.

One possible reason for null results may arise from a decrease in cocaine use (self-reported) from the prior/first trimester to the second/third trimester of pregnancy that generally characterizes this sample (see Table 4). Some women may have decreased their cocaine use after learning they were pregnant, resulting in a mean decrease in cocaine use over time and potentially a decrease in cocaine's effects on development. Very few studies have evaluated duration or timing of cocaine exposure on child outcome, an interesting area for future research considering that cocaine's hypothesized effects on brain development may be dependent on gestational exposure factors such as duration and timing (Mayes, 1994; Volpe, 1992). Two studies presented at a recent infancy conference reported a relationship between first trimester cocaine use and poor developmental outcome (Jacobson & Choido, 1996; Richardson & Day, 1996). Findings from the Seattle Study suggested that cocaine use throughout all 3 trimesters of pregnancy accounted for impairment in volitional movement in 4-month old infants (Swanson, 1992). Exploratory analyses of the duration (exposed or not exposed throughout pregnancy) of cocaine exposure in the present study were not associated with 2-year developmental outcome. This result may be due to a

decrease in cocaine use over time (although the women used throughout pregnancy), the age or measures assessed, or mediating postnatal environmental factors. Hence, the story of cocaine's potential subtle effects on long-term developmental functioning is more complex than group mean difference studies can detect, particularly if these effects are via the duration, amount, frequency, or timing of exposure, and/or mediating factors.

Another possible reason for null results may be that mediating postnatal environmental influences on developmental outcome were possibly overcontrolled (Jacobson & Jacobson, 1996) or inappropriately chosen as confounding instead of mediating variables (Jacobson & Jacobson, 1996; Neuspiel, 1995). A comparison of adjusted and unadjusted outcomes (Tables 10 and 11) illustrates that although the two groups of children were not significantly different on a majority of the outcome measures, the covariate adjustment process (i.e., adjustment for maternal demographics and postnatal environment) appears to have had a greater impact on the NON-COC group relative to the COC group. Whereas the unadjusted play behavior outcomes of the COC group were slightly lower than those of the NON-COC group, the adjustment process resulted in slightly higher adjusted play outcome scores for the COC group relative to the NON-COC group. This comparison suggests that the confounds typically associated with developmental outcome may have a differential effect in the COC and NON-COC groups. For example, more highly cocaine-exposed children in this sample were more likely to be cared for by someone other than the biological mother, and these home environments were more likely to be characterized by less stress, less violence, and no postnatal illicit substance use. Protective factors such as the structure and quality of the home environment may have mediated the adverse effects of high cocaine exposure. Because such factors were controlled for (or overcontrolled) in this study, potential cocaine effects mediated by these risk and/or protective factors would not have been detected in the statistical analyses. It is important to reiterate, however, that the main goal of this study was to detect an

independent effect of prenatal cocaine exposure on child outcome, a goal which required controlling for all other potential influences, including the postnatal environment.

Prenatal Cocaine Effects on Specific Developmental Skills

It was also hypothesized that cocaine would be more likely to impact important, specific developmental skills in early childhood that are predictive of later developmental competence, rather than emerge as deficits on global skills measured by standardized assessments. Language and play, important representational skills in the second year of life which have predictive significance for later cognitive and social/emotional functioning, were assessed in unstructured, naturalistic contexts to reveal hypothesized cocaine effects. Global cognitive skills were assessed by the standardized Bayley Scales of Infant Development - Second Edition (standardization version).

Early Productive Language. The hypothesis that cocaine effects would emerge as deficits in specific developmental skills was not confirmed for the early expressive language skills of vocabulary and grammatical complexity. In fact, cocaine-exposed children (as well as the comparison group) did not appear delayed in these early language skills; vocabulary and grammar were within the normal range for two year olds, with no group differences on the number of children falling below language cutoffs (i.e., the bottom quartile on adjusted rank sum language outcome distributions for the full sample). In addition, there was wide variability in vocabulary size, a finding consistent with studies of language development in normally developing children (Fenson et al., 1994) and atypical populations (Bates et al., 1995).

Research on the language development of cocaine-exposed children is in an exploratory and early phase of systematic investigation. Vocabulary size and mean sentence length were specifically assessed in this study because they are typical measures of early productive language skills in the infancy and toddler periods. Only one other study

of cocaine-exposed children evaluated these same language skills (Mentis & Lundgren, 1995), but results were difficult to interpret because of serious methodological limitations (e.g., very small sample size of 5 children and an ambiguous comparison group), and were therefore in need of replication. The present findings of no differences between groups on measures of vocabulary and MLU, and no specific effects of prenatal cocaine exposure on these early productive language skills, support the preliminary results reported by Mentis & Lundgren (1995).

Although prenatal cocaine exposure may directly or indirectly affect brain structures associated with language (typically in the left hemisphere), brain plasticity or redundancy in the neural substrates underlying language skills may explain the findings of undisrupted early expressive abilities (Feldman, 1994; Levy, Amir, & Shalev, 1994). The robust nature of the progression of grammatical development has also been noted in other atypical populations of children with biological etiology, such as children with Autism (Tager-Flusberg, 1994) and preschoolers who experienced prenatal or perinatal unilateral brain injuries (Feldman, 1994; Levy et al., 1994). Thus, a toxic insult to the brain, such as prenatal exposure to cocaine and/or other drugs, also may not disrupt the acquisition of early expressive language skills, particularly in the area of early grammatical development. On the other hand, any potential effects of prenatal drug exposure on early language development may be mediated by the postnatal environment, as has been documented in both normal and at-risk populations (Bee, Barnard, Eyres, Gray, Hammond, Spietz, Snyder, & Clark, 1982; Bates, et al., 1995; Morisset, Barnard, Greenberg, Booth, & Spieker, 1990). Alternatively, other components of language and communicative development, particularly those that are more closely tied to social interactions such as communicative intentions, discourse patterns, and narrative abilities, may be more sensitive to toxic effects, or to the interaction of these effects with the postnatal environment, but

have yet to be systematically explored in samples of cocaine-exposed and other polydrug-exposed children.

Quality of Play. The hypothesis that prenatal cocaine exposure would adversely affect another representational skill, quality of play behaviors during child-alone play, was also not confirmed in this study. The most highly-cocaine exposed children did not necessarily exhibit the most immature play behaviors, nor did more cocaine-exposed toddlers fall below specified play behavior cutoffs than non-cocaine exposed toddlers. In fact, both cocaine-exposed and non-cocaine-exposed toddlers exhibited global play behaviors appropriate to a child-alone play context, such as engaging the toys for a majority of the play session, mostly displaying positive and/or neutral affect, and sometimes displaying signs of frustration.

Yet there were a few *subtle* signs of disruption in the quality of play behaviors for both groups of children in this study, similar to Beckwith et al.'s (1994) findings of immature play in polydrug-exposed toddlers. Several of the specific play behaviors were rated somewhat lower than the global play behaviors (see Table 9), suggesting more difficulty in how the children engaged with the toys despite the amount of engagement or their affective tone during play. For example, their toy combinations were typically relational, a transitional form of play linking early exploration with more developmentally advanced play (Belsky & Most, 1981), they rarely expanded or elaborated on initiated play themes, they randomly selected toys and abruptly transitioned between play acts. Importantly, however, these subtle play deficits can not be attributed specifically to prenatal cocaine exposure since both groups of children were rated similarly on all play behaviors. Instead, subtle deficits in how the child engaged their environment through play may reflect an effect of polydrug-exposure, the postnatal environment, the play context (child-alone play), or a combination of these factors. Although this study was not designed to evaluate these influences on play behavior, exploratory analyses suggest that children living with a

non-biological caregiver (and thus in a less stressed home environment), irrespective of group status, were rated higher on specific play behaviors.

One tentative adverse effect of cocaine was observed in the quality of interaction with the caregiver. Cocaine-exposed boys were judged to have more negative interactions with their caregivers than any other group. This finding is particularly intriguing because the nature of the task required the children to play by themselves. Yet both groups of children frequently initiated some form of interaction with their caregivers, and in doing so, cocaine-exposed boys appeared to be more negative affectively (and maybe physically) in those interactions. This result needs to be interpreted with caution as it was the only significant adverse cocaine effect finding from all three data analysis techniques. However, this finding does accord with recent theory that cocaine effects may emerge in regulatory behaviors, such as arousal, affect, and attention, mediated by dopamine-rich brain structures (Lester et al., 1995).

Developmental Status. The hypothesis that prenatal cocaine exposure would not emerge as deficits in global cognitive skills assessed by a structured developmental test was partially confirmed in this study. Cocaine-exposed children performed within normal limits on the mental and motor scales of the BSID2, as did the non-cocaine-exposed group, although the mean MDI was shifted toward the low normal range of the standardized distribution (for both unadjusted and adjusted scores). Highly-cocaine-exposed children did not show the worst performance on the BSID2, nor were there group differences in mental and motor performance. The low-average MDI score for both groups is somewhat lower than other cocaine/polydrug-exposed samples (this may be a function of the new Bayley which was not used in earlier cocaine studies), but consistent with reports of no cocaine effects on global cognitive skills measured by standardized assessments in samples of infants (Jacobson & Chiodo, 1996; Mayes et al., 1996), toddlers (Chasnoff et al., 1992; Graham et al., 1992), and preschool-age children (Griffith et al., 1994).

A subgroup (23%) of cocaine-exposed children exhibited general cognitive delays on the BSID2 (scores greater than 1.5 SDs below the standardized MDI mean), whereas only 12% of the non-cocaine exposed children scored below the MDI cutoff. This subgroup was not necessarily comprised of the most highly cocaine-exposed toddlers, as might be expected, nor did maternal demographic factors, child weight or head circumference, or postnatal factors (e.g., structure or quality of home environment) explain poor performance between groups on the MDI. Compromised performance on overall language and deviant play (adjusted) measures was noted for this subgroup of cocaine-exposed children with cognitive delays relative to the subgroup of cocaine-exposed children with normal MDIs. Importantly, however, compromised performance in these skills does not appear to be specific to prenatal cocaine exposure since similar language and play decrements were also found for the subgroup of non-cocaine-exposed children who scored below the MDI clinical cutoff. Chasnoff et al. (1992) found similar results on the BSID MDI for a subgroup of 2-year-old cocaine/polydrug-exposed children and a subgroup of non-cocaine/polydrug exposed children in comparison to a drug-free control group, but this deficit in cognitive skills was not detected on the Stanford-Binet Intelligence Scale at age 3 (Griffith et al., 1994).

These results suggest that there may be a subset of polydrug-exposed children vulnerable to developmental delay, but compromised development is likely not attributable to specific effects of prenatal cocaine exposure. Instead, the biological risk posed by prenatal drug exposure (including cocaine) may be one factor contributing to this vulnerability, in addition to interacting with a variety of other risk factors in explaining compromised developmental functioning. A transactional approach, which assesses the bidirectional contributions of biological vulnerability and environmental context in determining developmental outcome, would be needed to explore this complex relationship. For example, a path analysis of Chasnoff and colleagues' data found that drug effects on 3-

year IQ were mediated through a biological factor (head growth), an environmental factor (quality of the home setting) and a behavioral factor (perseverance) (Azuma & Chasnoff, 1993). The present study suggests that poor language skills may also be a contributing factor to poor performance on tests of global mental skills, particularly tests with a large number of verbal items such as the new Bayley.

Performance in Structured Versus Unstructured Situations. Independent effects of prenatal cocaine exposure were not exhibited in skills measured via unstructured contexts (play and language) or in skills measured in a structured context (global cognitive skills). However, the unstructured child-alone play situation did reveal subtle signs of immature play for both groups of children, supporting the notion that an unstructured situation in which the child's behavior is not supported or guided is sensitive to polydrug and/or environmental effects. Beeghly and Tronick (1994) argue that drug effects are likely to be expressed during another type of unstructured situation, mother-child interaction, particularly in the mutual regulation of interactions between a drug-exposed child and a caregiver who continues to abuse drugs. For example, face-to-face interactions between cocaine/polydrug-exposed infants and their mothers were less well regulated and characterized by negative affect in comparison to unexposed dyads (Tronick, Olson, Weinberg, Beeghly, Cabral, Rose-Jacobs, Frank, & Zuckerman, 1995). Compromised performance for a subgroup of children in the present study was also noted on the structured BSID2 assessment, irrespective of cocaine exposure. The BSID2 may be more sensitive to polydrug effects than its predecessor, the BSID, as the BSID2 contains more varied cognitive and verbal items, particularly for the older age ranges, than does the BSID.

The two assessment techniques yielded complementary findings. While the BSID2 revealed that a small subgroup of children may have a general developmental delay, the unstructured child-alone situation revealed subtle signs of disruption in how the children engaged the environment, behaviors not easily captured by a structured, standardized

assessment. It appears that both assessments are valid, and perhaps necessary, methodologies for examining drug effects on development. Importantly, both methodologies should probably be used in conjunction with one another to obtain a more complete picture of developmental functioning.

Conclusions

Given cocaine's hypothesized effects on the developing fetal brain and corresponding postnatal behavior, the present study was designed to detect an independent effect of prenatal cocaine exposure on specific representational abilities and global cognitive skills at age 2, controlling for other factors confounded with maternal cocaine use. The representational abilities of language and play were specifically chosen as they are salient developmental skills in the toddler period with predictive validity for future developmental functioning. Hypothesized independent effects of prenatal cocaine exposure, including a dose-response relationship, on 2-year developmental skills were not confirmed in this study. The failure to detect a real effect (Type II error) is a possible reason for null findings in this study and in the field of human behavioral toxicology in general (Jacobson & Jacobson, 1996). However, this study reduced the possibility of Type II error by establishing a sufficient sample size ($n=200$) to detect cocaine effects, oversampling the highest exposed children in the COC group, verifying maternal self-report of cocaine use with a biological marker (RIAH), and carefully constructing the NON-COC group to control for other risk factors confounded with maternal cocaine use. Therefore, the null results of prenatal cocaine exposure are likely valid findings for the developmental outcomes measured at 2 years of age.

These results suggest a "cautious optimism" regarding cocaine effects on child development at age 2. And yet, these results also highlight the need to examine developmental outcome of drug-exposed children in terms of the complex interplay

between a biological risk factor, such as prenatal exposure to cocaine (and other toxic substances) and the risk and protective factors in the social context in which development occurs. In particular, environmentally mediated outcomes such as language and play may be more appropriately assessed from such a transactional approach to cocaine effects. Factors that should be considered in a transactional approach include, but are not limited to, infant characteristics (prenatal cocaine exposure, infant temperament, and associated biological vulnerability), postnatal environmental characteristics (structure and quality of the caregiving context), and caregiver characteristics (psychosocial functioning and parenting behaviors) (Alessandri, Sullivan, Bendersky, & Lewis, 1995; Lester, LaGasse, Freier, & Brunner, 1996; Mayes & Bornstein, 1995). The transactional approach is a challenge to the drug effects field, but a challenge that needs to be acknowledged and implemented in order to reveal the complex, yet potentially subtle, effects of prenatal cocaine exposure on child development.

Future Directions

Perhaps the most important message from this study was that research questions/hypotheses dictate the study design, measures and analyses, and consequently limit the conclusions that can be drawn from the results. This study was designed to detect an independent, dose-response effect of prenatal cocaine exposure. As such, this study was able to address the issue of whether or not cocaine (independent of other confounds) has adverse effects on particular developmental skills at age 2; a important question in the field of fetal drug effects as very few outcomes beyond the first year of life have been investigated in drug-exposed children. This study could not, however, address transactional issues such as postnatal environmental or caregiver interactional influences on child development; important questions in the field of developmental psychology which are currently gaining momentum in the drug effects field as well, particularly in research on human subjects (Lester et al., 1995; Mayes & Bornstein, 1995).

The second generation of fetal drug effects research is moving beyond asking whether or not cocaine adversely affects development, to asking how and through what mechanisms the biological vulnerability posed by prenatal cocaine exposure interacts with the social and cultural context to determine individual differences in developmental outcome. This reconceptualization of cocaine effects necessitates a reconceptualization in the methodology used to assess these influences. The methodological challenges that plagued the first generation of research continue to exist, but lessons learned from these early studies will help to refine the choice of study design, sample characteristics, and outcome measures in future research on cocaine effects.

One challenge for future research is designing studies which assess hypothesized transactional influences. Transactional studies are prospective and longitudinal in design, and for the population of drug-exposed children should begin at birth and continue up to a

designated age of interest, preferably school age or beyond. These studies must adequately and appropriately assess a variety of risk and protective factors that potentially attenuate or mediate poor developmental outcome. Selection of these factors will depend on the outcome(s) of choice, but are likely to include prenatal factors (maternal substance use, pregnancy complications, nutritional status, prenatal visits), maternal demographics (age, education, race, ethnicity, parity, marital status), infant characteristics (gender, temperament, prematurity), maternal/caregiver psychosocial status over time (level and severity of stress, psychopathology), and postnatal environment over time (quality of stimulation and caregiver responsiveness, structure of family, including multiple caregiving placements, domestic violence). For example, mutual regulation of dyadic interaction in infancy is multiply determined by the clarity of cues the child exhibits to the caregiver and the caregiver's ability to read and respond to those cues (Beeghly & Tronick, 1994). For the cocaine-exposed dyad, mutual regulation may be particularly impaired if prenatal drug (cocaine) exposure affects the child's ability to clearly display cues and/or the caregiver has difficulty reading and responding to the child's cues due to continued substance use, stress, or psychopathology (or a combination of these factors). Thus, the assessment of transactional influences among various risk and protective factors is needed to determine the possible etiology and maintenance of impaired mutual regulation in the cocaine-exposed dyad.

A second challenge for future research concerns sample composition issues. Sample composition differences between studies of play in drug-exposed samples illustrate this particular methodological challenge. For example, both Beckwith et al. (1994) and Hagan (1995) had small sample sizes, recruited predominantly African-American women, and offered no information about the pattern of maternal substance use during pregnancy in either the target or comparison groups (therefore, some of the comparison toddlers may have been substance-exposed). On the other hand, the present study assessed a large

sample of children born to predominantly low-income, Caucasian women for whom the pattern of substance use during pregnancy was assessed for both cocaine-exposed and non-cocaine-exposed groups. Consequently, interpretation and assimilation of findings from these studies is difficult and may only be generalizable to the population from which the sample was drawn.

Future studies in this field need to carefully select and define how many and who comprises the sample, for both the target group and the control/comparison group(s), to help clarify interpretation and generalization of results. For example, no difference findings from small sample studies or studies with high sample attrition are particularly difficult to interpret because you do not know who is in the sample. In the case of high sample attrition, no difference findings between groups could solely be due to the fact that the "healthiest" or most highly motivated individuals from both groups remained in the study. Thus, in determining the number of subjects to be followed in a longitudinal study, a power analysis should be used to determine a sample size with sufficient power to detect hypothesized effects, allowing for sample attrition at each time point. Power analyses may need to be calculated for each outcome measure, or at least one outcome measure at each time point in the longitudinal design, to determine a sufficient sample size.

Selection of appropriate comparison group(s) depends on the study question. For example, if cocaine effects are hypothesized to emerge via transactional influences with the environment, then several comparison groups are needed to determine if the developmental trajectory of cocaine-exposed children is different from other high-risk children. One comparison group, for instance, would include women who were matched to the target group on prenatal use of other toxic substances (e.g., alcohol, marijuana, and tobacco), maternal demographics (e.g., age, education, ethnicity) and environmental factors (poverty, violent neighborhood, family structure). A second, yet necessary, comparison group would include women matched for the same maternal demographic and

environmental factors, but who did not use toxic substances (or used very little) during pregnancy. This control group is necessary to evaluate the influence of high-social risk on developmental outcome, independent of maternal substance use and prenatal substance exposure.

A third challenge for future research in the cocaine effects field concerns measurement of appropriate developmental outcomes (Mayes, 1996; Zuckerman, 1996). Guided by recent theory of how cocaine can potentially alter brain functions which mediate aspects of behavior regulation, such as arousal, affect, and attention, several new paradigms have been developed to assess these specific developmental skills. For example, Lewis and colleagues (Bendersky, Alessandri, & Lewis, 1996) have begun to use a face-to-face paradigm with cocaine-exposed infants to assess affective and arousal modulation following removal of a pleasant stimulus (the mother's smiling face). Preliminary findings suggest that cocaine-exposed infants have particular difficulty recovering once upset by the removal of the stimulus. Beeghly, Brown & Tronick (1993) have developed a self-regulatory play paradigm for toddlers and preschoolers in which the child proceeds through a series of play episodes, separately with the caregiver and a stranger (research staff member). The hallmark play episode, a perturbed play situation, consists of the stranger bouncing around in a somewhat disorganized, yet affectively positive fashion without looking at or responding to the child. The child's physical, affective, social, and communicative behaviors are rated before, during and after this slightly stressful, perturbed play sequence. Preliminary findings suggest that this paradigm differentiates the play behaviors of middle-class, inner-city and drug-exposed samples (Beeghly, 1993, personal communication).

Appropriate developmental outcomes in the school age period with potential sensitivity to cocaine effects include peer relations and neuropsychological functioning. For example, impairments in affect, attention, arousal and/or communication may be

observed in peer group entry situations where the child is required to successfully negotiate entry into an already established peer group, cooperate with peers once entry is granted and/or cope with possible peer rejection if entry is denied (Beckwith, Crawford, Moore, & Howard, 1995). Finally, neuropsychological functioning in school age children and adolescents is an unexplored, yet intriguing area for future research. Neuropsychological skills such as memory, behavioral inhibition, and sustained attention are the skills hypothesized to be impacted by prenatal cocaine exposure. Standardized assessment batteries for evaluation of neuropsychological functioning currently exist (e.g., Halstead-Reitan).

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Appendix A. Models of Cocaine Effects on Fetal Brain Development and Annotated Bibliography.

Pharmacology of cocaine . Cocaine is a stimulant drug which affects both the peripheral nervous system (PNS) and central nervous system (CNS) by blocking the reuptake of released monoaminergic neurotransmitters (dopamine (DA), norepinephrine (NE) and serotonin) (Mayes, 1992, 1994; Volpe, 1992). The monoamines accumulate in the synaptic area and activate the dopaminergic, adrenergic, and serotonergic neurotransmitter systems resulting in the physiologic effects of increased heart rate and blood pressure in the PNS and the neurophysiologic effects of increased neuronal excitability in the CNS (Gingras et al., 1992; Mayes, 1992). The increased activation of DA is responsible for the euphoria or "high" that accounts for the strong reinforcing qualities of the drug. Alterations in serotonin may account for the sleep cycle disturbances accompanying cocaine use, while the increased activation of NE causes excitation of the sympathetic nervous system including hypertension, tachycardia, and vasoconstriction. The development of catecholaminergic (DA and NE) neurons occurs between the 7th and 17th weeks of gestation. This is an early-appearing system which plays a critical role in several phases of brain development including cell proliferation, neuronal growth, and synaptogenesis (Mayes, 1994; Volpe, 1992).

Direct effects of prenatal cocaine exposure on fetal development . Mayes (1994) highlights three critical caveats about the neurobiology of prenatal cocaine exposure. First, the susceptibility of different brain regions and different neurological functions to cocaine may vary at different times in prenatal and postnatal development. Second, cocaine does not appear to specifically impact one brain area or function, but instead, generally impacts "neurotransmitter-regulated patterns" of fetal brain development (p. 123). Third, prenatal and/or postnatal compensatory brain mechanisms may offset potential impairments in basic neurobehavioral functions due to prenatal cocaine exposure.

Cocaine readily and rapidly crosses the placenta and the blood-brain barrier (Gingras et al., 1992). The placenta does not protect the fetus from the distribution of drugs due to maternal drug use during pregnancy. In early gestation, drugs that distribute to the fetus remain there until the levels in the mother's blood are low enough to set up appropriate concentration gradients that will draw the drugs out of the fetal compartment. In later gestation, the fetal liver can biotransform some drug molecules, but the fetal kidneys will excrete the waste products back into the amniotic fluid.

The direct effect of prenatal cocaine exposure is on the release and metabolism of the monoaminergic neurotransmitters in the CNS and their influence on fetal brain development (Mayes, 1994). Because neurotransmitters (NT) operate together, it is expected that effects on one NT would induce alterations in other NT within a given neural circuit. Although prenatal exposure to cocaine may cause increased levels of NT initially, long-term exposure to cocaine could lead to decreased levels of NT (Gingras et al., 1992).

Cocaine exposure during critical or vulnerable periods of fetal brain development (typically during 2nd and 3rd trimesters) may place the fetus at risk for abnormal development of neurotransmitter systems, abnormal neuronal growth and differentiation, altered migrational events, altered synaptogenesis or abnormal glial cell function (Gingras, et al., 1992; Kosofsky, Wilkins, Gressens, & Evrard, 1994; Mayes, 1994; Volpe, 1992). Thus, cocaine may produce functional alterations in developing brain structures (Mayes, 1994). Postnatally, DA and NE are involved in modulating several neuropsychological functions, such as activity level, attention, and the regulation of anxiety or other emotional states (Mayes, 1992). Disruption or alteration in the functioning of these neurological structures may lead to disruptions in the development of their corresponding neuropsychological behaviors (Lester et al, 1995). Disruption in brain development may be more common than suspected because conventional techniques may not detect the abnormalities (Volpe, 1992).

Studies of cocaine's direct effects on the brain:

1. Shih, Conc-Wesson, & Reddix (1988). Examined auditory brainstem responses (ABR) to determine peripheral and brainstem auditory dysfunction of drug-exposed infants (selected for cocaine-exposure, but no control for other exposures or risk factors in analyses). Drug-exposed neonates showed prolonged interpeak latencies and prolonged absolute latencies compared to drug-free neonates, suggesting neurologic impairment that warrants further audiologic and neurologic follow-up.

2. Ward, Bautista, Buckley, Schuetz, Wachsman, Bean, & Warburton (1989). Two month old infants of cocaine-abusing mothers had elevated circulating plasma NE levels in comparison to controls, but no difference in adrenergic receptor density or affinity despite elevated levels of circulating NE in exposed infants. These findings are consistent with sympathetic NS tone, but whether it is a direct effect of cocaine exposure or via indirect effects of hypoxia is unknown.

3. Anderson-Brown, Slotkin, & Seidler (1990). Prenatal cocaine exposure inhibited DNA synthesis (cell maturation) in the cerebellum, cerebral cortex, and midbrain plus brainstem of rats from 1-15 days of age; this effect was not secondary to ischemia nor to local anesthesia, suggesting a direct effect.

4. Dow-Edwards, Freed, & Fico (1990). Examined glucose metabolism of 45 brain structures in 60-day-old male offspring of cocaine-treated rats. Alterations in glucose metabolism (decrease) were found in 2 cortical structures (primary somatosensory and motor) and 14 subcortical structures (e.g., substantia nigra, pars compacta and caudate nucleus, nucleus accumbens and zona incerta). Of all brain areas analyzed, the hypothalamic structures contained the greatest concentration of nuclei showing significant decreases in metabolic activity. Subcortical sensory systems as well as the size of selected cortical and subcortical structures were not affected by prenatal cocaine exposure. DA-rich regions of the forebrain that showed decreased glucose metabolism did not have altered

binding to a DA antagonist. The authors suggest that prenatal cocaine exposure can cause permanent neurological effects in the functional activity of the neuronal pathways mediating motor, limbic, and neuroendocrine function at doses below those which produce growth retardation and terata.

5. Dow-Edwards, Freed-Malen, & Hughes (1993). Cocaine was administered to rats on P11-20 when forebrain, hypothalamus, and cortex are undergoing synaptic maturation. 60-day-old male and female rats were examined for brain glucose metabolism. In cocaine-treated females, 18/45 structures (motor and limbic) showed increased metabolic activity. In cocaine-treated males, there was no effect on motor or hypothalamic structures, but 2/17 limbic structures showed decreased metabolic activity and 2/11 sensory structures showed increased rates. Results suggest gender differences in long-term metabolic activity, and timing of cocaine exposure produces different metabolic effects.

6. Kosofsky, Wilkins, Gressens, & Evrard (1994). Prenatal cocaine exposure in mice showed a direct effect on fetal brain and body growth which permanently alters neocortical cytoarchitecture in exposed offspring. Results show that brain growth is compromised, glial fascicle density is decreased, glial defasciculation is delayed the radial organization of the neuropil is altered, with thinning of the axonal-dendritic bundles, and the final position of neurons is altered, with disruption and imprecision of horizontal lamination.

7. Dow-Edwards (1995). Cocaine's effects on the developing brain may be gender specific. Prenatal cocaine exposure in rats alters brain glucose metabolism in male rats, whereas female rats appear to exhibit most of the behavioral abnormalities. Postnatal cocaine exposure in rats (approximately 3rd trimester in humans) affects brain glucose metabolism in female rats, whereas both genders show behavioral alterations.

Indirect effects of prenatal cocaine exposure on fetal development. NE-related vasoconstrictive effects is an important, indirect mechanism of action in producing

developmental toxicity (Dow-Edwards, 1995). Maternal cocaine use causes constriction of the uterine and placental vasculature which leads to a decrease in utero-placental blood flow, and therefore, a decrease in oxygen and nutrients to the fetus. Cocaine distribution to the fetus may also have direct vasoconstrictive effects on fetal CNS and PNS (Gingras, et al., 1992). Maternal vasoconstriction and fetal vasoconstriction can cause fetal hypoxemia, malnutrition, hypertension, tachycardia and various cerebral lesions or abnormalities. The 'hypoxic profile' of the fetus has not been adequately documented or reproduced to show that the neurobehavioral effects are the result of the hypoxia produced by cocaine (Dow-Edwards, 1995).

Studies of cocaine's indirect effects on the brain:

1. Dixon and Bejar (1989). A significantly higher percentage of cocaine/polydrug-exposed, term neonates (35%) were found to have cerebral injury than drug-free, well neonates (5%), but not different from drug-free infants at risk for hypoxicischemic encephalopathy. Lesions in the drug-exposed group were intraventricular hemorrhage, echodensities associated with necrosis, and cavitory lesions; lesions were focused in the basal ganglion, frontal lobes, and posterior fossa. Lesions are most likely due to vasoconstrictive effects of stimulant drugs.

2. Woods, Plessinger, Scott, & Miller (1989). Prenatal cocaine exposure in fetal lamb was related to a decrease in utero-placental perfusion. Fetal oxygen pressures fell significantly and remained low.

3. Fantel, Person, Burroughs-Gleim, & Mackler (1990). Cocaine exposure in vitro in D10 rat embryos caused prompt and significant decreases in heart rates and significant reductions in measures of growth and development and diameters of the vitelline arteries. Cocaine also significantly inhibited the activity of the terminal electron transport system of the mitochondria of embryos. Placental vasoconstriction limits the ability of

embryos to meet the increased glucose demands induced by hypoxia. Authors suggest that compromised energy supplies form the basis of the developmental toxicity of cocaine.

4. Webster, Brown-Woodman, Lipson, & Ritchie (1991). Examination of cocaine-exposed rat fetuses showed that 40% of the fetal brains were damaged, and that the damage appears to be due to hemorrhage from the fetal vessels and ischemia. Cerebral damage included bilateral necrosis and cavitation in the cortex, hemorrhage and ectopic outgrowths in the corpus striatum, bilateral cavitation in the brainstem and vacuolization in the lens of the eye. Temporary constriction/occlusion of the uterine vessels of the pregnant rats produced a similar type and distribution of damage. Authors conclude that the brain damage associated with prenatal cocaine exposure results from a constriction/occlusion mechanism (i.e., vasoconstriction).

5. Little & Snell (1991). Although brain growth (measured as head circumference) of cocaine-exposed infants was similar to that of alcohol-exposed infants, an asymmetrical pattern characterized both groups in which head circumference was reduced proportionately more than birthweight.

6. Prenatal cocaine exposure associated with increased rate of congenital malformations (limb deformities, cardiac malformations, ocular impairments, anomalies of the urinary tract), but not independently of other drugs (e.g., Bingol, Fuchs, Diaz, Stone, & Gromisch, 1987; Dixon, 1994). Most likely malformations are due to the vasoconstrictive effects of cocaine on blood flow to developing organ systems.

Appendix B. Intercorrelations Among Log-Transformed Prenatal Cocaine Use Measures (n = 100)

	Maximum grams			Frequency			Total grams		
	P1 ^a	2/3 ^b	P3 ^c	P1	2/3	P3	P1	2/3	P3
Grams/day P1	.75			.46			.64		
Grams/day 2/3	.85			.58			.76		
Grams/day P3		.72			.31 ^d			.58	
Maximum grams P1				.52			.69		
Maximum grams 2/3				.57			.72		
Maximum grams P3					.38			.62	
Frequency P1							.89		
Frequency 2/3								.93	
Frequency P3									.89

^aP1 = prior to recognition of conception through 1st trimester

^b2/3 = 2nd through 3rd trimester

^cP3 = prior through 3rd trimester

d $p < .01$, otherwise all other r 's are $p < .001$.

Appendix C. Language Transcription Manual

CHILD LANGUAGE TRANSCRIPTION AND CODING MANUAL

I. OUTLINE OF LANGUAGE TRANSCRIPTION AND CODING PROCEDURES

A. The child's language during the videotaped 5 to 8 minute caregiver-child free play plus clean-up sequence is to be transcribed continuously, from the beginning of the caregiver-child free play until the end of the clean-up sequence. The first 10 minutes of the taped session consists of a child-alone play sequence from which quality of child play behaviors will be coded. The following 5 - 8 minutes of the taped session is the caregiver-child free play plus clean-up sequence.

B. Watch the videotaped sequence once to get a general idea the child's verbal intelligibility. Intelligibility will be rated on a 1 to 5 scale. Record the intelligibility rating in the appropriate column on the transcription checklist sheet.

- 1 = most (90%) of the child's language is unintelligible
- 2 = between 1 and 3
- 3 = half of the child's language is unintelligible
- 4 = between 3 and 5
- 5 = most (90%) the child's language is intelligible.

C. Watch the videotaped sequence a second time to transcribe the child's language following the rules outlined below.

1. Macros have been created on the PC to facilitate language transcription. Use the Alt key plus one of the following macro codes to obtain frequently typed material.

Alt +:	Information to appear on screen:
H	Header tiers (obligatory @ tiers at beginning of transcript)
C	*CHD: (main tier identifier)
M	%com: (comment tier identifier)
E	@End (obligatory @ tier at end of transcript)

2. Begin transcription when there is a clear indication that the caregiver-child play sequence is going to start. For example, the mother may get up out of the chair and say, "do you want to play with mom?" Or the caregiver may just walk over and sit down next to the child. The caregiver-child play session usually starts sometime after the timer on the screen reaches 10 minutes. Do not transcribe any child language before the caregiver-child play session starts. End the transcription when the Examiner comes into the room or the screen goes blank.

3. Use a %com tier to indicate when cleanup starts within the language transcript.

4. Record the total length of the caregiver-child play sequence (i.e., the total of both play and cleanup) on a %com tier on the second to last line of the chat transcript and in the appropriate column on the language transcription checklist. Record the time in minutes and seconds.

D. Save and retrieve chat transcripts.

1. Save the transcript in text format. On the PC, use CTRL - F5, choose 1 (DOS), then 1 (save) again, to save in DOS text format. Enter complete filename including directory pathway (i.e., c:\nida24m\chat\filename.cha). Do not use F10 to save chat transcription files!!

2. To retrieve a previously saved chat file, use F5 to get into the directory listing. Choose 7 to change directories (type in: c:\nida24m\chat). Use the arrow keys to highlight the appropriate filename. Choose 1 to retrieve the file (you will see a brief message at the bottom of the screen, "DOS text conversion," that lets you know the file was saved in text format, if you do not see this message, make sure to re-save the file in text format using CTRL - F5). If you have made corrections or additions to this file, you must re-save the file in text format using CTRL - F5. If you have not made any corrections or want to exit the file after having saved it, choose F7, type 'n' to "save document" (if you type 'y' to this save command, the document will not be saved in text format) and type 'y' or 'n' to "exit WP". Typing 'n' to exit will bring up a blank screen, and typing 'y' will exit the program and return you to the main menu.

E. Use CLAN analyses to check the chat files for spelling and morpheme break errors and chat transcript accuracy. Make sure the main menu is opened up to the NIDA24m\CHAT directory before you run any CLAN programs since the files you want to check are in this directory. First, run the FREQ program to check for spelling and morpheme breaks (see CLAN rules and addendums below). Second, use the CHECK program to check the accuracy of the transcript (see CLAN rules and addendums below or taped to side of filing cabinet).

II. CHAT TRANSCRIPTION FILE FORMAT

A. GENERAL INFORMATION

The CHAT (Codes for Human Analysis of Transcripts) transcription procedures to be used on this project are similar to those outlined in The CHILDES Project (MacWhinney, 1991) and The Slice Project Transcription Manual (Dale, 1991). Each videotaped language sample will be transcribed into a computer word processor according to the CHAT transcription format and rules outlined below while viewing the videotaped interaction. This transcription format will permit the use of the CLAN (Child Language ANalysis) programs to analyze the transcripts. The CHAT format and the CLAN programs were developed as part of the CHILDES (Child Language Data Exchange System) project at Carnegie-Mellon University (MacWhinney, 1991).

Any word processor that can save files in text format can be used to enter the language transcripts into CHAT format. For example, word processors on MS-DOS machines such as Word Perfect or MSWord and word processors on Macintoshes such as MacWrite or MSWord can be used to type the language samples into CHAT format. Each transcription file will be saved as a text file and named according to the following

convention: RRF#####.cha. The #'s are for the child's ID number and the extension .cha indicates that the file is a chat transcription file.

The CHAT system was designed to be as flexible as possible. Following is an example of a CHAT-formatted transcription file for the RRF study. The six lines in the transcript beginning with @ are required for every file. For this project, transcripts will only include an orthographic, not a phonetic, transcription of the child's utterances, including both spontaneous and imitative utterances. The utterances of the child's conversational partner (usually the mother) will not be transcribed. In addition to transcription of the child's utterances, each utterance will also be coded (coding scheme to be decided upon).

@Begin	[beginning of transcript]
@Participants: CHD Amy Child	[child's first name]
@ID: RRF2010.cha	[ID# as written on videotape]
@Sex of CHD: female	[sex of child]
@Coder: Susan	[coder's first name]
*CHD: why is-'nt daddy come-ing?	[child tier]
%com: Father usually picks up child around 4 pm.	[comment tier]
*CHD: he-'ll be here soon.	[child tier]
%com: start of cleanup.	[start of cleanup sequence]
*CHD: allgone.	[child tier]
%com: time 6:30.	[total length of play sequence]
@End	[end of transcript]

B. MAIN TIERS

The "main tier" is the most important. These are the lines of the actual utterances and begin with an asterisk (*) and the first three letters of the name of the speaker followed by a colon, e.g., *CHD: for the child. Additional tiers (called dependent tiers, which will be elaborated on later in this manual) are used for several purposes. Additional tiers such as %com lines (a comment line) are used to add information to clarify the main tier. Other dependent tiers contain specific codes (%cod:) for the main tier.

The utterance itself begins in column nine. That is, there are three spaces after the colon (e.g., *CHD:---utterance.). Words that begin sentences are not capitalized; only proper names, kinship terms, and letter names (Mommy, Grandma, A) are capitalized. Each utterance is to be transcribed onto a separate line (or separate main tier). If the utterance is longer than a single line, it is necessary to space over to column 9 of the next line to type out the rest of the utterance.

C. PUNCTUATION

Each utterance should end with one of the following five punctuation:

. ? ! +... +/.

The +... is used for an incomplete but not interrupted utterance (trailing off without finishing a sentence). The +/ marks the end of an utterance which is incomplete because another speaker began to talk and interrupted the first speaker.

On the main tier line, there are other punctuation marks which carry specific meanings:

- [/] retracing without correction; speaker begins sentence, stops, and repeats earlier material without change, e.g., "I wanted [/] I wanted to invite Margie."
- [//] retracing with correction; speaker begins sentence, stops, changes material but maintains same idea, e.g., "I wanted [//] I thought I wanted to invite Margie."
- [#] pause within utterance.
- [?] previous word is unclear, transcriber's best guess is provided.
- xxx whole utterance is unintelligible.
- xx marks unintelligibility of a word within an otherwise intelligible utterance.
- www material not transcribed, e.g., sound effects, laughter, etc., use sparingly.
- () non-completion of a word, e.g., (a)bout, (th)em.
- suffix marker, e.g., dog-s, walk-es.
- + compound or rote form marker, e.g., Star+Wars, woof+woof+woof.
- ' contraction marker, hyphen is also needed to mark morpheme break, e.g., Bob-'is for Bob's and do-'nt for don't.

Sometimes the intended meaning of a word becomes clear a little later when the child produces a clear version of it, yet the first attempt is still unintelligible on its own. In this case, the first attempt should remain xxx.

D. DEPENDENT TIER MARKERS

In the CHAT system, provision is made for including any of a large number of additional representations of each utterance, such as phonetic, morphological, pragmatic and others. These additional tiers, called dependent tiers because they are dependent on the main tier, are marked with a percentage (%) sign. Multiple dependent tiers can follow an asterisked main tier. The spacing on the @ lines and the dependent tiers is not as crucial as it is on the main tiers.

- %com: comments made by the observer/examiner and/or transcriber.
- %exp: explanation of the identity of deictic words (e.g., that, he, and it) when not clear from the content of the utterance, and other explanations such as sound effects.
- %cod: specified code for pragmatic, semantic, phonological coding, etc.

III. CHAT TRANSCRIPTION RULES

A. GENERAL INFORMATION

1. The general goal is to get an accurate, but orthographic, representation of what the child said. Be careful not to infer the presence of word endings or morphological markers when they are actually not there. Similarly, do not attempt to transcribe phonological errors exactly. False starts, dysfluencies, and revisions should be recorded in square brackets, e.g., "I mean [//] I need to go home." The [/] and [//] are used when entire words are repeated. False starts and dysfluencies of individual words are indicated in square brackets such as "[wh-wh-] where he go?"

2. The division of the child's stream of speech into utterances should rely primarily on intonation (a falling contour signalling the end of one utterance) and breath contour (two phrases produced seamlessly in one breath group constitute one utterance) rather than the grammatical structure. For example, "you look at that one; I look at this one" consists of two clauses which could each stand as separate sentences; however, when produced in one breath group with no intonation fall after the first clause, it consists of a single utterance.

3. Often the identification of a particular word is doubtful, and the choice is between transcribing it as xx or as a word followed by [?]. If you are fairly sure that this portion of the utterance corresponds to one word, and you have some confidence that you can identify the word, it is preferable to transcribe the word followed by [?], rather than use xx. In addition, whole utterances are often unintelligible. When this occurs, listen to the utterance no more than 5 times to try to decipher the words. If the utterance remains unintelligible after having listened to it 5 times, transcribe the utterance as xxx.

4. Catenatives should be transcribed as single words, e.g., "wanna," "hafta," "gonna," and "gotta." But slang forms should be expanded, e.g., "c'mon" as "come on," "shoulda" as "should have," "cause" as "because," "posta" as "supposed to," "kinda" as "kind of."

5. Words need to be transcribed in a consistent pattern. For this reason, elliptical forms such as 'em should be transcribed as "them," etc. The following standardized forms should be used:

hmm	hmm?	yeah
okay	whee	oops
you (for ya)	huh?	

6. There are a number of two syllable expressions that express positive and negative meaning. Rather than transcribing them precisely, they are classified and transcribed as APOS or ANEG

APOS:	includes uh-huh and mm-hmm (stress on second syllable).
ANEG:	includes huh-uh and hmm-mm (stress on first syllable), as well as uh-oh, oh-oh, etc.

7. Onomatopoeic words should be considered as words rather than sounds if they have clear syllabic shape, with vowels and consonants, and are conventional within English, e.g., "zoom, ring, ding, woof." Purely vocalic sound effects, e.g., the "oo-oo" of a siren, or laughter, or animal noise, are marked www on the main tier and an %exp tier is added to identify the sound:

*CHD: www.
%exp: siren noise.

8. Words such as "ah," "oh," and "um" are sometimes used as words with distinct meaning, e.g., "ah" meaning "I understand that now," and are sometimes used as fillers while thinking of the next word. When they are used as a word with meaning, they are transcribed as regular words. When they occur in an utterance as a filler, they are placed in square brackets, and thus not counted for CLAN analyses, e.g., "I went [um] to the store."

B. MORPHEME DIVISION

1. Compounds. Words which can be spelled either as one word or two are generally transcribed as one, e.g., "allgone," "alldone," "boyfriend/girlfriend," "backyard," and "kittycat," "peekaboo," "rockabye," "dammit." Certain compound words are treated as one word by transcribing them with a +. Be careful not to overuse the + sign for every word that seems like a compound word. The following are examples of appropriate cases for the + sign:

school+bus	ice+cream	fire+engine	pine+cone
peanut+butter	french+fry	fire+hydrant	teddy+bear
Cabbage+Patch	green+bean	t+shirt	hot+dog
show+and+tell	fire+truck	tree+house	bunny+rabbit
time+out	baby+doll	meow+meow	look+it
thank+you	bye+bye		
no+no+no (when produced in a single breathgroup; treat as self-repetitions when in separate utterances)			

Some of these may also be transcribed simply as one word, e.g., hotdog or pinecone. The child's own name, as opposed to all other names, should be treated as one word with +, e.g., Jimmy+Smith. Titles of TV shows, books, etc., should also be transcribed as one word, e.g., "Sesame Street" as "Sesame+Street."

2. Morpheme Breaks. A limited division of words into morphemes, appropriate for children at this level, is indicated on the main tier. Contracted auxiliaries and negations are transcribed using a hyphen to indicate the morpheme boundary, and then a fairly full form of the contracted element:

he'd transcribed as	he-'had or he-'d (for he would)
she's	she-'has or she-'is
they'd	they-'had
how'd	how-'did
we'll	we-'ll
I'm	I-'m
they're	they-'re
can't	can-'nt
doesn't	does-'nt
let's	let-'us
we've	we-'ve
won't	will-'nt

Note that because it is important that each root and ending be spelled consistently, the word as a whole may not be spelled in the conventional way, e.g., can't is transcribed as can-'nt, so that it can be related to other uses of can and to other negative contractions.

Whether or not to separate bound morphemes (i.e., suffixes, as opposed to contractions) with a hyphen depends on the nature of the suffix. Some bound morphemes are derivational affixes (ones which change part of speech, such as the -er of farmer, the -ed of tired, and the -en of broken). These derivational affixes are not separated with a hyphen. Similarly, reflexive pronouns such as himself and myself should be left as one

morpheme. On the other hand, most inflectional affixes, such as the noun plural -s, the present progressive -ing, the comparative -er, and the past tense -ed (which add meaning to the stem, without changing the part of speech) should be distinguished as a separate morpheme. Overregularized suffixes are credited, as in come-ed. Exceptions: Irregular past forms of verbs (broke, went), irregular plurals (feet, mice), irregular auxiliaries (might, should), irregular 3rd person singulars (does), and diminutives (doggy, Mommy) are not analyzed into separate morphemes.

The following markers are used on the main tier to show separate morphemes:

-ed	past tense, e.g., walk-ed
-es	third person singular, e.g., walk-es
-ing	progressive, e.g., walk-ing
-'s	possessive, e.g., Mary-'s
-s'	plural possessive, e.g., baby-s'
-s	plural, e.g., shoe-s
-er	comparative, e.g., big-er
-est	superlative, e.g., small-est

Again, note that the transcription may differ from the conventional spelling of the word, e.g, walk-es. The most difficult part of this coding is to distinguish certain ambiguous endings, particularly -ed (which may be the regular past tense, as in "he walked," or the verb-to-adjective suffix, as in "he is tired"; only the former would be divided) and -ing (which may be the progressive ending, as in "he is swimming," or the gerundive, as in "swimming is fun;" again, only the former would be divided). See attached sheet titled, "Standard Forms for Affixes" for additional types of bound morphemes.

IV. CLAN ANALYSIS OF CHILD LANGUAGE

Once a child's language sample has been transcribed into CHAT format and saved as a text file, it can then be analyzed using the CLAN programs. The following commands demonstrate how to analyze the child's language (*CHD tiers in the CHAT transcripts) using the CLAN programs. See the CHILDES Project book for complete details on each CLAN program, their corresponding options, and additional types of linguistic analyses.

A. Run **FREQ** to check spelling and morpheme breaks. The **FREQ** program outputs a alphabetical list of all the words the child spoke during the free play session. Use the pause and enter keys to keep the output from scrolling by the screen too fast. Use this list to check for spelling and morpheme break errors. If errors are found, go back to the transcript and correct the errors. Remember to re-save the transcript in text format.

freq +t*chd filename

B. **CHECK** accuracy of transcripts. The **CHECK** program will check the transcript for proper CHAT format. Errors are outputed to the screen. Use the pause and enter keys to keep the output from scrolling by the screen too fast. See addendum for more explicit instructions on how to use **CHECK**.

check -g2 +d filename

C. VOCABULARY. To obtain the total number of words a child produced in the original transcripts (.cha files), from all the children separately, stored in one file, use the freq command:

```
freq +t*chd *.cha > filename
```

This freq command executes a frequency of all the children's (*chd) words and redirects (>) the output for each individual file (*.cha) to one large file. This command doesn't combine the analyses from all the .cha files into one analysis, but it does store the freq analysis of each individual .cha file into one larger file for easier access.

D. UTTERANCES. To determine the total number of utterances a particular child produced use the lines command:

```
lines +t*chd filename
```

This lines command will place numbers next to each child utterance in the specified filename. To get the total number of utterances for a different filename, run the command again, but change the filename.

To determine the total number of utterances each child produced in their individual transcripts, but have the separate analyses stored into one large file use the command:

```
lines +t*chd *.cha > filename
```

E. MEAN LENGTH OF UTTERANCE (MLU). To obtain the MLU of the child's language from the CHAT files use the mlu command:

```
mlu +t*chd *.cha +f
```

The mlu command calculates the mean length of utterance of the child tiers, for all of the .cha files (*.cha) separately and sends the results of each transcript to a corresponding file with the extension .mlu.

To place the results of each individual .mlu file into one larger file use the following command:

```
mlu +t*chd *.cha > filename
```

Appendix D. Play Development Literature and Play Coding Manual

In terms of developmental level of play (i.e., the cognitive component of play), two-year-olds are able to engage in a variety of symbolic or pretense play behaviors (of which there are several levels from self directed pretense to substitution pretense). Simple manipulation tends to decrease linearly from the middle of the first to the middle of the second year while pretense play increases linearly (Belsky & Most, 1981). Relational play is a transitional form of play which links early exploration with more developmentally advanced pretense play (Belsky & Most, 1981). As the ability to symbolize advances, pretense play becomes a) more decentered such that children are able to apply pretend schemes to other people and inanimate objects and not just themselves, and b) more decontextualized such that play behaviors are mentally generated before action, and thus become more independent of available objects and context (e.g., substitutions) (Belsky & Most, 1981; McCune-Nicolich, 1981). Most published play coding systems focus on the quantitative assessment (frequency counts, time sampling, etc.) of the developmental level of play (e.g., Belsky & Most, 1981; McCune-Nicolich, 1981; Tamis-LeMonda & Bornstein, 1994). This was not the desired focus of the current study.

In general, most two-year-olds should be exhibiting symbolic play, but the level of their play skills is influenced by the social context (alone or with another) and, when playing with another, by the partner's availability and involvement. Developmental level and length of symbolic play is raised when a child is interacting with an appropriately available and involved social partner (usually the mother) than playing alone (Fiese, 1990; Slade, 1987). Maternal play is related to toddler play concurrently (Tamis-LeMonda & Bornstein, 1991, 1994), and associations between domains of mother-child interaction (social, didactic, and control) and child pretense play are specific (e.g., combination of social and didactic domains relates to pretense play) (Vibbert & Bornstein, 1989).

At the time of the dissertation proposal, the only published studies of play in drug-exposed children were by Beckwith, Rodning and colleagues (1989, 1994). Although their studies contained many design flaws, the play coding system appeared valid for assessment of two-year-old's play, including both quantitative measures of the developmental level of play and rating scales of the quality of play behavior in a 16-minute child-alone play session. Their data suggested an atypical pattern of play behavior in polydrug-exposed toddlers. Using Beckwith and colleagues' play coding system, a pilot study of play behaviors in 20 highly-drug exposed two-year-olds from the Seattle Study cohort was conducted to determine if this system could be used with the current data to measure disrupted play (McConville, 1994). The drug-exposed toddlers did show deficits in play behaviors. In addition, the quantitative (frequency counts) and qualitative (rating scales) measures provided similar information about the toddler's play skills, suggesting only one type of coding need be done. Recently, Hagan (1995) used a modified version of Beckwith et al.'s (1994) qualitative rating system (modified for use with caregiver-child interaction) and did not replicate findings of disrupted play behaviors in cocaine/polydrug-exposed toddlers, at least when the children played with their mothers (rather than alone, as in the Beckwith et al. study).

Based on this literature review, the play coding system for this study was chosen according to several priorities. First, the coding system would be similar to Beckwith et al.'s (1994) system in order to replicate or refute the findings of disrupted play in polydrug-exposed toddlers. Second, either the quantitative or the qualitative measures would be used in this study but not both, due to the intensity of training and coding required for 200 subjects, and the fact that McConville's study suggested that similar results obtained from both measures. Third, a coding system which included some measures of behavior regulation in order to comment on behaviors (e.g., affect, attention) hypothesized to be affected by prenatal cocaine exposure (Lester et al., 1995; Mayes, 1994,

1996). Therefore, the play coding system developed for this study was a qualitative rating system of 14 play behaviors, which included rating scales from both Beckwith and Rodning's and Hagan's systems, in addition to rating scales developed for this project which were either not included or vaguely defined in the other two coding systems.

QUALITATIVE RATINGS OF PLAY BEHAVIORS CODING MANUAL*

This coding system was adapted from the play coding systems used by Rodning, Beckwith, & colleagues (1989; 1994) and Hagan (1995). Portions of this system are either additions or modifications to their coding systems, and are denoted with an asterisk (*).

This qualitative coding system is designed to assess the quality of two-year-olds' play behaviors during a 10 minute, child-alone play session. This system does not assess absolute frequency of play behaviors during the play session, although many of the qualitative items are frequency based. The coding system is divided into two parts, global ratings and specific behavior ratings, with a total of 14 items.

Each subject's play session must be watched in its entirety (i.e., full 10 minutes or more) at least once to rate both the global and specific behaviors. For some subjects, either the entire play session or particular parts of the play session will need to be watched more than once in order to accurately assess the quality of the child's play behaviors. It is up to the coder to decide how many times to watch the play session or parts of the play session. Regardless of how many times a play session is watched, each subject must receive a rating for each of the global and specific play behavior items. Following is a description of the rating scale for each play behavior.

A. GLOBAL RATINGS* (These ratings focus on the entire play session, whether or not the child is playing with the toys.)

1. **ENGAGEMENT WITH TOYS*** - Is the child engaged or involved with the set of toys for a majority of the 10 minute session? Engagement with toys can be either immature or mature play behaviors as well as verbal behavior, as long as the child is actively engaging with the toys. For example, throwing the toys would be considered engagement.

Engagement with toys may occur by or with the caregiver and by the one-way window. On the other hand, a child who walks around the room without purpose, stands next to the caregiver or the door/window without playing with the toys, or just holds onto a toy without manipulating it would not be counted as engagement with toys. The coder must determine approximately how much time the child is engaged with the toys.

1 = child not engaged with toys at all or less than 20% (2 minutes) of the time.

3 = child engaged with the toys for at least half of the play session.

5 = child engaged with the toys for almost all of the time or more than 80% of the time.

2. **ATTEMPTS TO GET OUT OF THE ROOM*** - Does the child indicate that s/he wants to get out of the room, either by going to the door and trying to open it, engaging the caregiver to open the door, or vocalizing that s/he wants out? The coder must determine approximately how often this behavior occurs during the play session.

1 = child continually tries to get out of the room; child almost seems to persevere on achieving this goal even though caregiver has said otherwise.

3 = child occasionally tries to get out of the room (a few times), but is able to resume play with toys by him/herself or if caregiver requests such behavior.

4 = child tries to get out of room once and is able to resume play, unless this one occurrence is at the end of the play session such that the child may not have time to resume play.

5 = child never tries to get out of room.

3. **AIMLESS ACTIVITY*** - Does the child demonstrate aimless behaviors, such as walking around the room with no purpose in mind? The child may seem "lost" in this situation, such that the child just sits or walks around without knowing what to do (i.e., playing or exploring the toys). On the other hand, does the child seem purposeful in his/her exploration of the toys and/or the room?

1 = child frequently aimless; child seems "lost" in this situation for a majority of the play session.

3 = child occasionally aimless, approximately half the time.

4 = child rarely aimless; maybe one or two instances of aimless activity during the play session.

5 = child never aimless or without purpose during the play session; the child's activity is in the service of purposeful (and planned?) behavior.

4. **OVERALL AFFECTIVE TONE*** - In general, does the child appear to be happy, unhappy, or neutral during the play session. A happy rating would be characterized by a child who appears to be enjoying him/herself, evidenced by laughter, smiling, clapping, singing. An unhappy rating would be characterized by a child who displays excessive whining, crying, pouting, anger, sadness. A neutral rating would be characterized by a child who is neither happy nor unhappy; the child may have flat affect or a continued look of interest.

1 = almost all affect is negative (anger, crying, sadness), almost no positive affect.

3 = half the time the child displays negative affect, half the time the child displays positive or neutral affect.

5 = almost all affect is positive (smiles, laughs, joy) or neutral (flat affect, interest); child almost never displays negative affect during play session (only one or 2 instances of brief negative affect).

5. **REFERENCE THE CAREGIVER*** - Does the child reference or acknowledge the caregiver's presence in the room and how often? Referencing the caregiver may be in the form of looking at the caregiver, talking to the caregiver, or walking over to the caregiver. Referencing includes both initiating interaction with the caregiver and responding to the caregiver's initiations. This rating excludes the quality of the reference to the caregiver, but instead focuses on the frequency of references.

1 = child never references the caregiver during the play session.

2 = child rarely references the caregiver, maybe 1 or 2 times.

3 = child occasionally references the caregiver, approximately 3 to 4 times during the play session.

4 = child references the caregiver 5 or 6 times.

5 = child often references the caregiver, 7 or more times during the play session.

6. **AFFECTIVE TONE DIRECTED TOWARD THE CAREGIVER*** - This item rates the quality of the child's references toward the caregiver. Are the child's references to the caregiver negative (whiny, fussy, pouty, aggressive, angry), positive (smiles, laughs, joy) or neutral (neither negative or positive, but mostly flat affect). If the child never references or engages with the caregiver, rate this behavior as not applicable (7).

- 1 = child is mostly negative towards the caregiver.
 3 = child is sometimes negative/sometimes positive with the caregiver, or mostly neutral.
 5 = child is always positive with the caregiver.

7. AMOUNT OF FRUSTRATION* - This item rates the amount of frustration displayed by the child, with the caregiver or toys, during the play session. Frustration includes whining, fussing, crying, struggling in a negative way with a toy, acting aggressive or hostile toward the toys or the caregiver.

- 1 = child frequently displays frustration during the play session.
 3 = child sometimes displays frustration during the play session.
 4 = child rarely displays frustration during the play session; only 1 or 2 instances.
 5 = child never displays frustration during the play session.

B. SPECIFIC PLAY BEHAVIOR RATINGS (These ratings focus on the times that the child is engaged with the toys, particularly during specific play acts. A play act is defined as a block of time spent engaged in a particular activity; the amount of time spent in a particular play act may vary. The coder must determine when the child has finished one activity and has moved on to the next activity. Play acts can range from simple manipulative or relational play to higher levels of functional or symbolic play.

8. NUMBER OF TOYS IN A SINGLE PLAY ACT - Does the child mostly play with just one toy at a time (one block, one tea cup, one car) or does the child consistently combine several objects together (several blocks, tea set toys, gas station and cars) during play? The coder must determine whether the child uses the toys one at a time or combines several toys at a time. Examples of combining toys are putting the dolls in the crib, feeding the dolls from the bottle or spoons, pushing the small car through the gas station, pouring from the teapot into the cups, putting the lid on to the pot to cook, placing the plates, spoons, and/or cups out as if setting the table. To receive a rating of 5 on this item, the majority of the child's toy combinations must be either functional or symbolic. If the majority of the child's combinations are relational, give the child a rating of 3 on this item.

- 1 = child mostly uses just one toy at a time during play; there may be 1 or 2 instances of combining toys.
 3 = child sometimes uses one toy at a time and sometimes combines several toys during play or the majority of the child's combinations are relational.
 5 = child usually combines several toys together and the majority of toy combinations are either functional or symbolic; there may be 1 or 2 instances of using only one toy at a time.

9. EXPANSION OF THEME - How often does the child expand on themes (e.g., tea party theme) that were initiated during the play session, in either a verbal or physical way? One theme may be having a tea party. This theme could involve making the tea, pouring it into cups, stirring it, drinking it, and maybe even sharing it with the dolls. Another theme may be putting a doll to bed. This theme could involve laying the doll into the crib, covering the doll with a blanket, saying "night-night," and kissing the doll. In each of these examples, the child has initiated a theme (e.g., feeding or night-night) and the child expands the original play behavior into a sequence of behaviors within the theme. A child who starts themes, such as putting the doll into the crib, but never expands them into a sequence of behaviors would receive a 1 or 2 on this item. A child who starts themes and frequently expands them would receive a 4 or 5 on this item. To receive credit for

expanding an initiated theme, the child must do 3 or more related steps in the sequence of the theme (e.g., put out cups, pour tea, and drink would be given credit for expansion, but put out cups and pour tea would not get credit for expansion).

1 = child never expands on play themes.

3 = child sometimes expands on play themes, approximately half of the initiated themes.

5 = child usually expands themes; more than 80% of initiated themes.

10. TOY SELECTION STRATEGIES - When the child is choosing toys within a particular play act or between play acts, does the child appear to be doing so in a deliberate manner or are these behaviors random? Does the child deliberately look for and pick up toys after finishing with something else, or does the child just randomly go about picking up toys and putting them down without demonstrating purpose in choosing them? The child must demonstrate purpose in choosing toys to receive a high score.

1 = the child mostly selects toys randomly; there is no apparent purpose in selection; may be 1 or 2 instances of purposeful selection.

3 = half the time the child's selection strategies are random, half the time purposeful and deliberate.

5 = the child's search for toys is deliberate and purposeful most of the time; may be 1 or 2 instances of random selection.

11. TRANSITIONS DURING PLAY - How does the child transition from one play act to the next during the play session? Abrupt transitions include behaviors such as frequently dropping toys as though the child forgot about holding them, picking up and putting down or dropping toys without exploring them first, or spending little time engaged in different play acts before moving on to another play activity. Smooth transitions include behaviors such as thinking about what to do before doing it, spending a moderate amount of time engaged in different play acts, or thoughtful completion of an activity before moving on to the next activity. The key concept here is planned, organized actions versus unplanned, disorganized actions.

1 = most transitions are abrupt (e.g., quickly moves from one activity to another or frequently drops toys); may be 1 or 2 instances of smooth transitions.

3 = child sometimes has abrupt transitions, half the time.

5 = most transitions are smooth and seem planned and organized (e.g., the child rarely drops toys and spends some time engaged with the toys); may be 1 or 2 instances of abrupt transitions.

12. MOUTHING OF TOYS - Does the child exhibit inappropriate mouthing of toys, such as mouthing the car or blocks (unless child pretends blocks are pieces of food)? Does the child appear to be inappropriately mouthing the cup, bottle or spoon, e.g., perseveratively or for an extended amount of time? This type of exploration is typically seen in younger infants, but is considered to be inappropriate and immature for toddlers.

1 = child does a lot of inappropriate mouthing.

3 = child does some inappropriate mouthing.

4 = child does a little inappropriate mouthing.

5 = child never exhibits inappropriate mouthing.

13. IMMATURE PLAY BEHAVIORS - Does the child seem to throw, swing, toss, kick, or bang a lot of the toys? Does the child pick up and put down toys without really exploring them first? Each of these behaviors is immature or developmentally inappropriate for toddlers.

1 = the child exhibits a lot of immature play behaviors; they predominate the play session.

3 = the child exhibits some immature play behavior; explores objects appropriately at least part of the time.

4 = the child exhibits a little immature play behavior, only a few instances.

5 = the child never exhibits immature play behaviors.

14. ATTENTION SPAN - In general, is the child absorbed and interested in the play activities (as evidenced by being focused and persistent), or is s/he easily distracted (evidenced by fleeting attention from one activity to the next, or by distraction of things in the environment such the window, door, mother)?

1 = the child is easily distracted while engaging with the toys; more than 80% of the time.

3 = the child is attentive half the time; the child is easily distracted half the time.

5 = the child is absorbed and interested while engaging with the toys; more than 80% of the time.

**QUALITATIVE RATINGS OF PLAY BEHAVIORS
CODING SHEET**

ID # _____ **CODER:** _____ **DATE:** _____

A. GLOBAL RATINGS

1. ENGAGEMENT WITH TOYS _____
2. ATTEMPTS TO GET OUT OF THE ROOM _____
3. AIMLESS ACTIVITY _____
4. OVERALL AFFECTIVE TONE _____
5. REFERENCE THE CAREGIVER _____
6. AFFECTIVE TONE DIRECTED TOWARD CAREGIVER _____
7. AMOUNT OF FRUSTRATION _____

B. SPECIFIC PLAY BEHAVIORS

8. NUMBER OF TOYS IN A SINGLE PLAY ACT _____
9. EXPANSION OF THEME _____
10. TOY SELECTION STRATEGIES _____
11. TRANSITIONS DURING PLAY _____
12. MOUTHING OF TOYS _____
13. IMMATURE PLAY BEHAVIORS _____
14. ATTENTION SPAN _____

Appendix E. Procedures for Covariate Selection and Reduction to Compute Adjusted Outcome Measures

1. For each group (COC, NON-COC, and full sample), correlate covariates by child outcome.
 - a. Maternal demographics by child outcome (16 variables, e.g., age, educ, parity, IQ, prenatal drug use).
 - b. Infant characteristics by child outcome (8 variables, e.g., BW, gender, gest age).
 - c. Postnatal environment by child outcome (18 variables, e.g., abuse, drug use, stressors).
 - d. Covariates were chosen by precedence/literature (42 possible covariates chosen).
2. Examine the correlation matrices for each group for significant associations between covariates and outcomes.
 - a. Highlight each significant correlation (any at $p < .10$).
 - b. A covariate is considered important if it has at least two significant correlations with any outcomes.
3. Look for patterns of relationships between covariates and outcomes.
 - a. From the correlation matrices, create a written list of significant covariates and the outcomes they are related to for each sample.
 - b. Using this list, note which covariates from the COC and NON-COC groups are the same, and which ones are different, from the full sample.
 - c. From the 42 variables initially identified as possible covariates, 25 were selected as important (related to outcome).
 - d. Compare the significant covariates for the 3 groups, particularly the covariates of the COC and NON-COC groups.
4. Further reduction of covariates.
 - a. Eliminate any covariates from the list of 25 that are redundant with each other (i.e., the covariates are highly correlated with each other, greater than .5).
 - b. Eliminate any covariates that are not correlated at least $p < .05$ with outcome (look back at the original correlation matrices).
 - c. Eliminate any covariates that overcontrol for confounding (e.g., birthweight, gest age, mother-child interaction, e.g., Jacobson & Jacobson, 1996)
 - d. Important covariates were ones consistent across all 3 groups, and any additional ones that were significant for the NON-COC group (since the NON-COC group data is used to create the adjusted outcome scores).
 - e. 13 covariates remained after reduction.
5. Stepwise regression for selection of final covariates within the NON-COC group only.
 - a. Run forward and backward regressions on each outcome variable using the 13 covariates as the IV's for the NON-COC group only. Print out the final step of each regression output (includes significance of model and variables in and not in the equation) and the residual plot and partial residual plots. Plots are generated through the plots option in the regression command of SPSS.
 - b. Examine final step of the forward and backward regression output for each outcome. Do the two analyses yield the same selection of covariates?

- c. Examine residual plots of both forward and backward regressions for multivariate outliers (large standardized residuals, $> \pm 3$). If outlier(s) are found, rerun the regressions excluding the case(s). Compare the values of the “variables in the equation” section of the output for the model including and excluding the outlier(s). Do the values differ greatly? If not, the outlier(s) can remain in the regression analyses. If the two models differ greatly, then the regression analysis from which covariate coefficients are used for this outcome will have to be run with and without the outlier(s).
- d. Examine partial residual plots to determine the degree of association between each significant covariate and each outcome.
- e. How many and which of the 13 covariates remain significant for each outcome? Create a list of final significant covariates for each outcome by outcome domain (language, specific play, global play, and bayley).

6. Forced entry regression analyses to obtain covariate coefficients for outcome adjustment.

- a. By each outcome domain, use the list of final significant covariates and the regression output from #5 to examine the patterns of relationships between the covariates and the outcome measures in that domain. Which covariates are consistent across the measures within each domain? That is, consistent covariates have significant regression slopes in relation to outcome measures and the slopes are of the same sign within each outcome domain. In addition, a “consistent covariate” must also be significantly related to two or more of the measures within the outcome domain.
- b. The final covariates for each outcome measure (approximately 4 or 5 depending on outcome domain) are then entered into a forced entry regression analysis for the non-cocaine group only. There should be one final regression analysis for each outcome measure which lists the covariates entered into the analysis and their unstandardized B coefficients and significance level.
- c. The unstandardized B coefficients of each covariate for each outcome are used to compute an “adjusted outcome” score for all cases regardless of group membership. Even if a covariate becomes non-significant in this forced entry regression, the B coefficient is still used to compute the adjusted outcome scores. For example, the significant covariates for the BSID2 MDI in the NON-COC group are: 1) total ounces of prenatal alcohol exposure throughout pregnancy, 2) mother uses medical coupons, 3) child gender, and 4) number of toys in the home at 21 months. The “adjusted MDI” score (computed for all cases) = original MDI score - $\beta_1(\text{covar1}) - \beta_2(\text{covar2}) - \beta_3(\text{covar3}) - \beta_4(\text{covar4})$. An adjusted outcome score is computed in this manner for each language, play, and developmental status outcome measure.

7. Dose-response relationships and group differences of adjusted outcome measures.

- a. Dose-response relationships are analyzed using the adjusted outcomes for the cocaine-exposed group only, minus the false-negative cases, through regression.
- b. Group differences on adjusted outcomes are analyzed using t-tests for the full sample.

Appendix F. Correlations Among Outcome Measures For COC Group

	<u>Raw Score Productive Language Outcomes</u>			
	21m Vocab	21m MLU	21m Lang Age	24m MLU
<u>Productive Language</u>				
21m Vocabulary	--	.99***	.58***	.53***
21m MLU	--	--	.71***	.42***
21m Language Age	--	--	--	.53***
24m Vocabulary	--	--	--	.64***
24m MLU	--	--	--	--
<u>Developmental Status</u>				
BSID2 MDI	.61***	.50***	.62***	.61***
BSID2 Verbal	.48***	.46***	.49***	.55***

+ p < .10, * p < .05, ** p < .01, *** p < .001.

Raw Score Global Play Behavior Outcomes

	Engagement	Out of Room	Aimless	Affect	Affect	Reference	Frustration
					Caregiver	Caregiver	

Global Play Behaviors

Engagement	--	.45***	.70***	.74***	.59***	-.22*	.70***
Out of Room	--	--	.45***	.54***	.40***	-.35***	.56***
Aimlessness	--	--	--	.54***	.38***	-.18+	.54***
Overall Affect	--	--	--	--	.76***	-.30**	.83***
Affect to Caregiver	--	--	--	--	--	-.07	.73***
Referencing Caregiver	--	--	--	--	--	--	-.33**

Specific Play Behaviors

Combining	.54***	.40***	.50***	.56***	.54***	-.15	.51***
Selection Strategies	.48***	.33**	.41***	.50***	.45***	-.23*	.50***
Expansion of Theme	.32**	.27**	.30**	.36***	.33**	-.05	.33**
Transitions	.49***	.37***	.36***	.51***	.46***	-.24*	.53***
Mouthing	.17+	.14	.15	.10	.07	-.23*	.26**

Immature Behaviors	.27**	.32**	.28**	.39***	.31**	-.21*	.40***
Attention Span	.62***	.42***	.48***	.57***	.48***	-.29**	.60***
<u>Productive Language</u>							
21m Vocabulary	.12	.02	.02	.19+	.17	-.01	.11
21 MLU	.09	.04	.05	.14	.12	-.04	.10
21m Language age	.12	.02	.02	.19+	.16	-.02	.11
24m Vocabulary	.33**	.27**	.19+	.44***	.39***	-.10	.35**
24m MLU	.20+	-.02	.09	.28**	.29**	.06	.20+
<u>Developmental Status</u>							
BSID2 MDI	.24*	.19+	.18+	.30**	.31**	-.13	.33**
BSID2 Verbal	.19+	.13	.11	.28**	.22*	-.07	.25*

+ p < .10, * p < .05, ** p < .01, *** p < .001.

Raw Score Specific Play Behavior Outcomes

	Combining	Selection	Expansion	Transition	Mouthing	Immature	Attention
	Strategies of Theme				Behaviors		Span

Specific Play Behaviors

Combining	--	.73***	.69***	.71***	.16	.57***	.58***
Selection Strategies	--	--	.61***	.83***	.28**	.66***	.79***
Expansion of Theme	--	--	--	.59***	.13	.49***	.49***
Transitions	--	--	--	--	.28**	.72***	.84***
Mouthing	--	--	--	--	--	.23*	.35***
Immature Behaviors	--	--	--	--	--	--	.56***

Productive Language

21m Vocabulary	.23*	.28**	.27**	.20+	.09	.23*	.17+
21m MLU	.21*	.25*	.28**	.20*	.11	.22*	.16
21m Language age	.23*	.28**	.26**	.19+	.08	.23*	.17+
24m Vocabulary	.39***	.37***	.35***	.35**	.07	.38***	.27**
24m MLU	.30**	.35**	.41***	.22*	-.06	.30**	.14

Developmental Status

BSID2 MDI	.40***	.49***	.35***	.51***	.23*	.47***	.37***
BSID2 Verbal	.31**	.39***	.21*	.37***	.24*	.41***	.32**

+ p < .10, * p < .05, ** p < .01, *** p < .001.

Unadjusted Outcome Measures

	MLU	Lang	Engmt	Affect	Cargvr X	Global	Cog	Deviant	Attn	Specific	MDI
Vocabulary	.81***	.95***	.23*	.28**	.26*	.31**	.41***	.29**	.25*	.39***	.70***
MLU	--	.91***	.18+	.23*	.24*	.26*	.37***	.24*	.16	.34**	.57***
Language	--	--	.25*	.30**	.27*	.34**	.45***	.33	.28**	.44***	.75***
Engagement	--	--	--	.69**	.16	.88***	.53***	.30**	.60***	.54	.27**
Affect	--	--	--	--	.32**	.88***	.56***	.39***	.60***	.58***	.34**
Caregiver Int.	--	--	--	--	--	.52***	.26*	.01	.17	.20*	.20+
Global	--	--	--	--	--	--	.59***	.33**	.63***	.59***	.35***
Cognitive	--	--	--	--	--	--	--	.62***	.78***	.97***	.50***
Deviant	--	--	--	--	--	--	--	--	.56***	.78***	.45***
Attention span	--	--	--	--	--	--	--	--	--	.85***	.37***
Specific	--	--	--	--	--	--	--	--	--	--	.51***

+ p < .10, * p < .05, ** p < .01, *** p < .001.

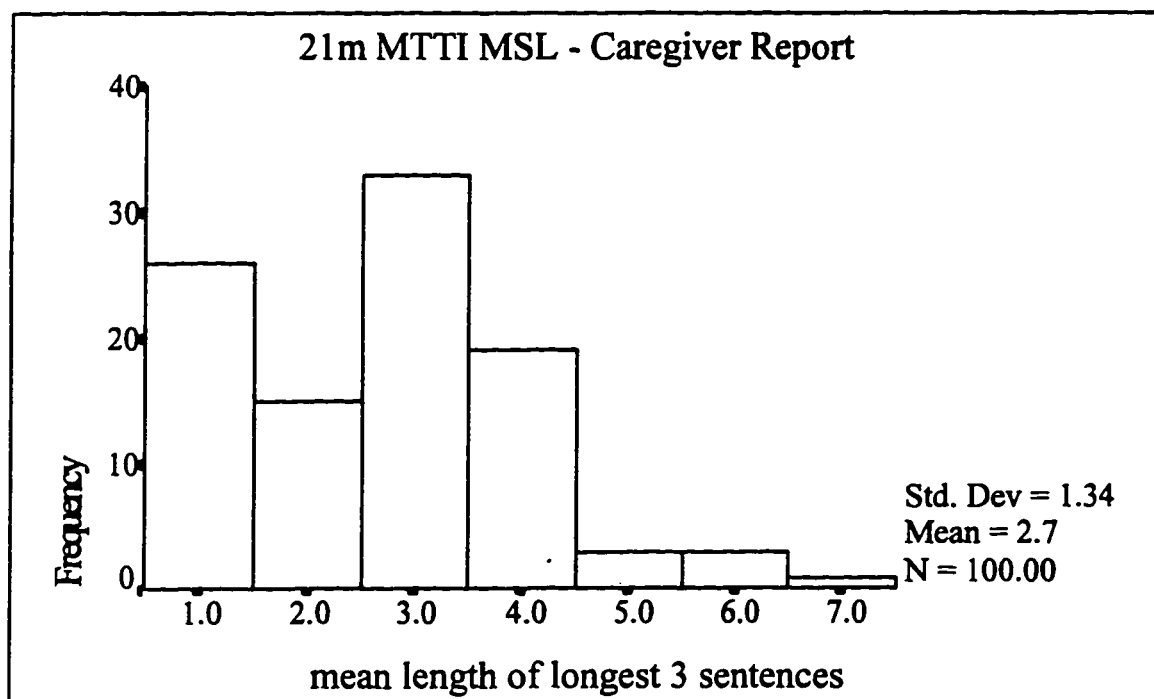
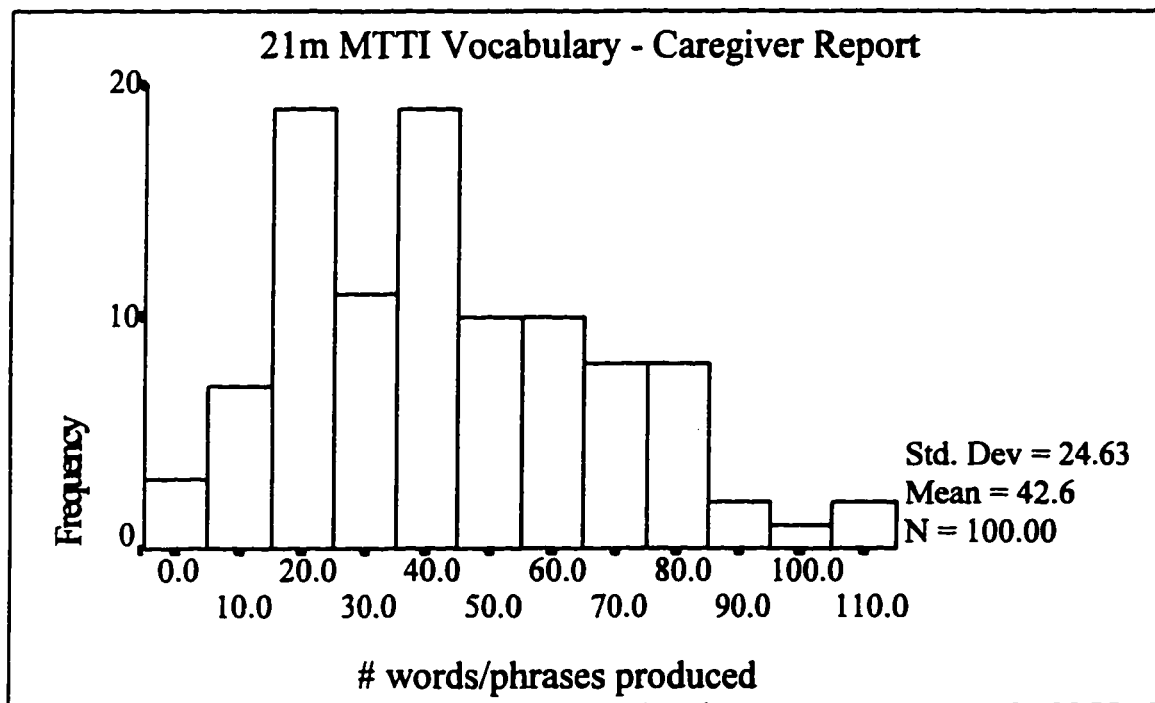
Adjusted Outcome Measures

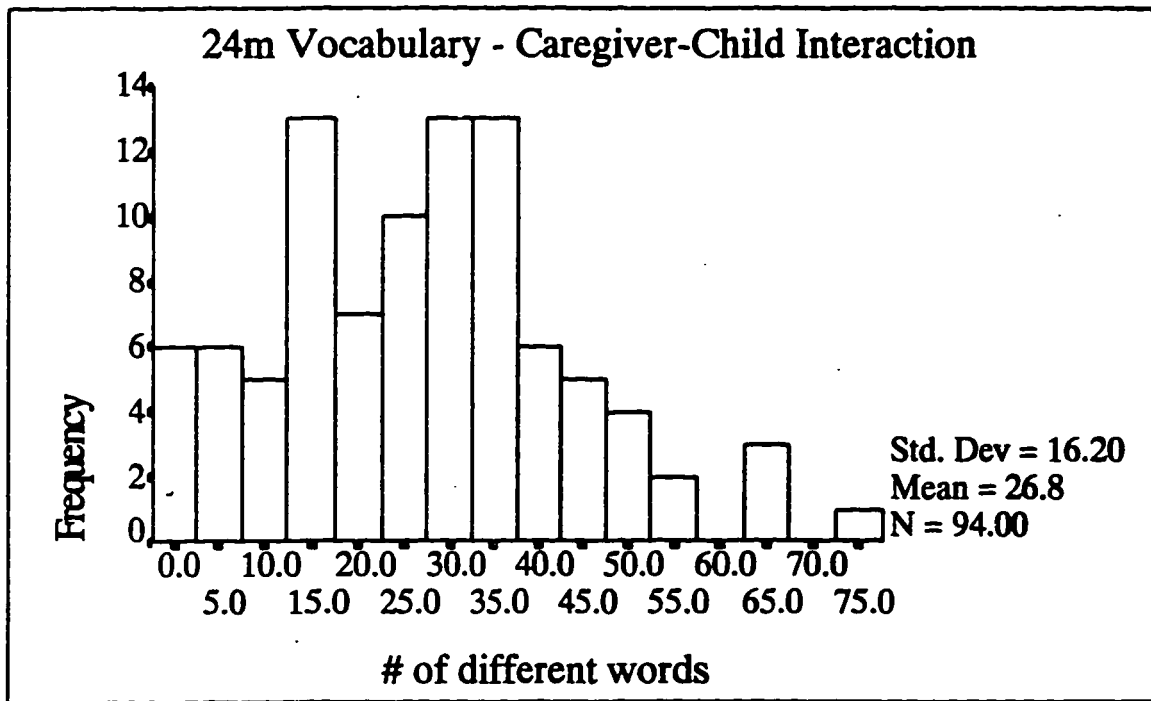
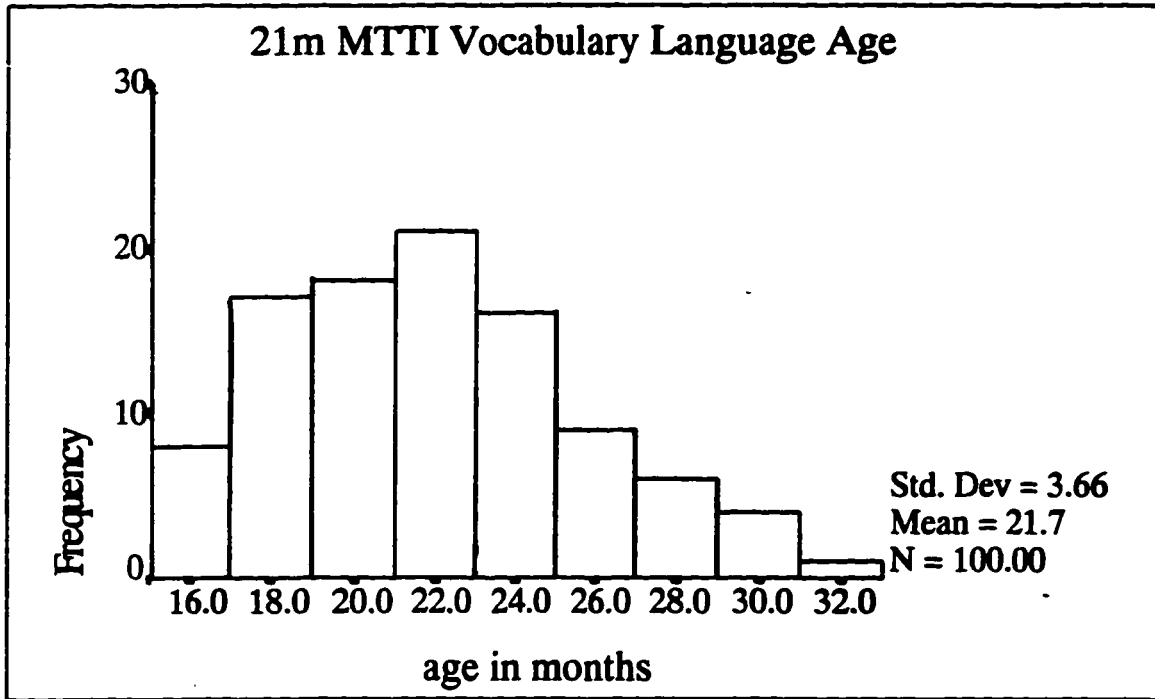
	MLU	Lang	Engmt	Affect	Cargvr X	Global	Cog	Deviant	Attn	Specific	MDI
Vocabulary	.80***	.95***	.24*	.24*	-.10	.18+	.44***	.31**	.33**	.43***	.59***
MLU	--	.91***	.18+	.19+	-.06	.14	.42***	.29**	.26*	.40***	.52***
Language	--	--	.22*	.23*	-.09	.17	.47***	.36***	.36***	.47***	.66***
Engagement	--	--	--	.77***	.17+	.91***	.53***	.17+	.59***	.51***	.12
Affect	--	--	--	--	.29**	.91***	.57***	.26*	.59***	.56***	.18+
Caregiver Int	--	--	--	--	--	.48***	.15	-.14	.07	.07	.05
Global	--	--	--	--	--	--	.56***	.16	.58***	.52***	.15
Cognitive	--	--	--	--	--	--	--	.59***	.81***	.97***	.40***
Deviant	--	--	--	--	--	--	--	--	.53***	.75***	.39***
Attention span	--	--	--	--	--	--	--	--	--	.87***	.28**
Specific	--	--	--	--	--	--	--	--	--	--	.42***

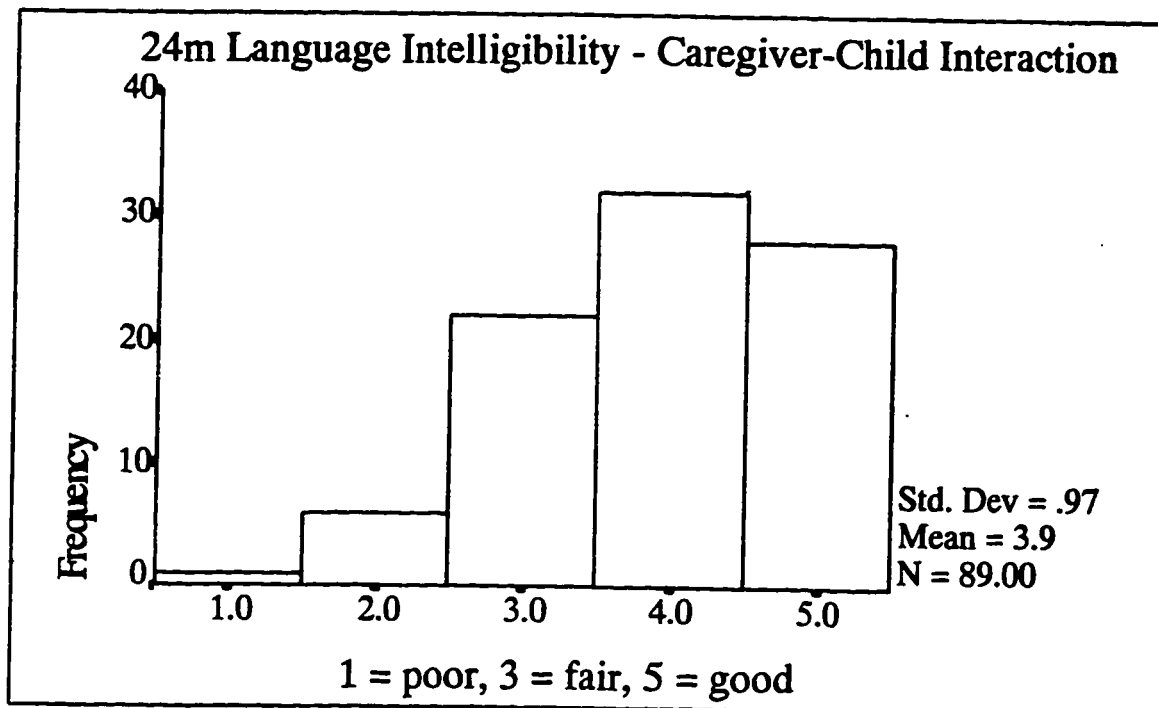
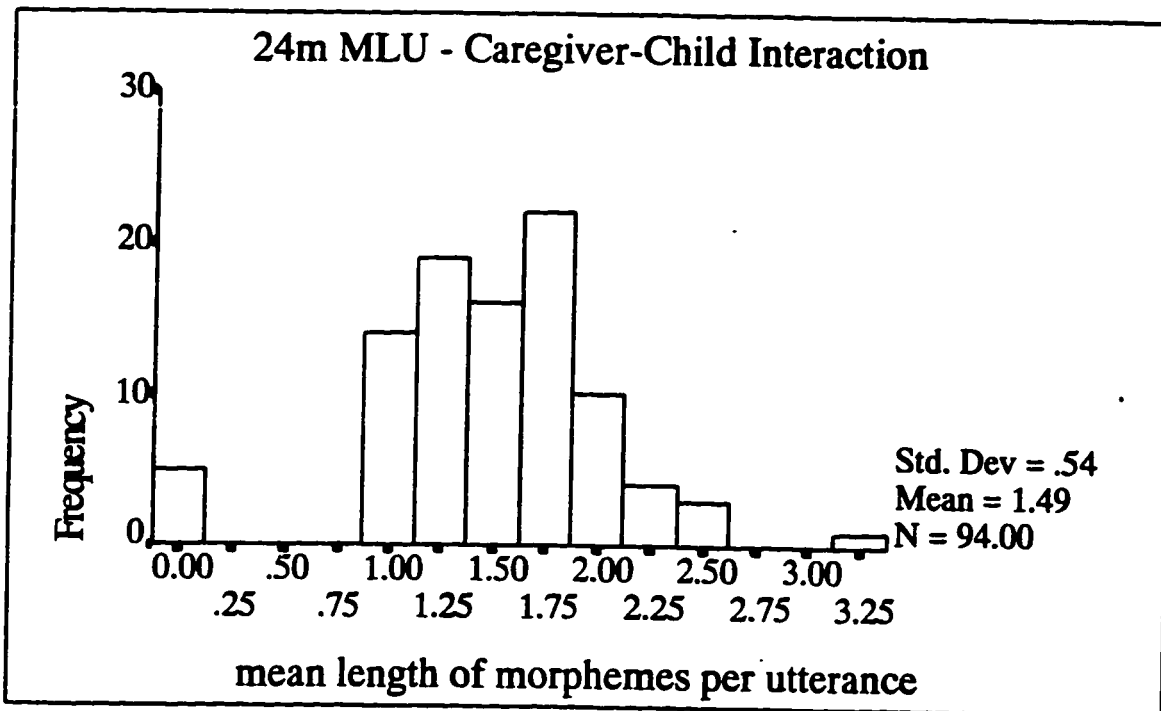
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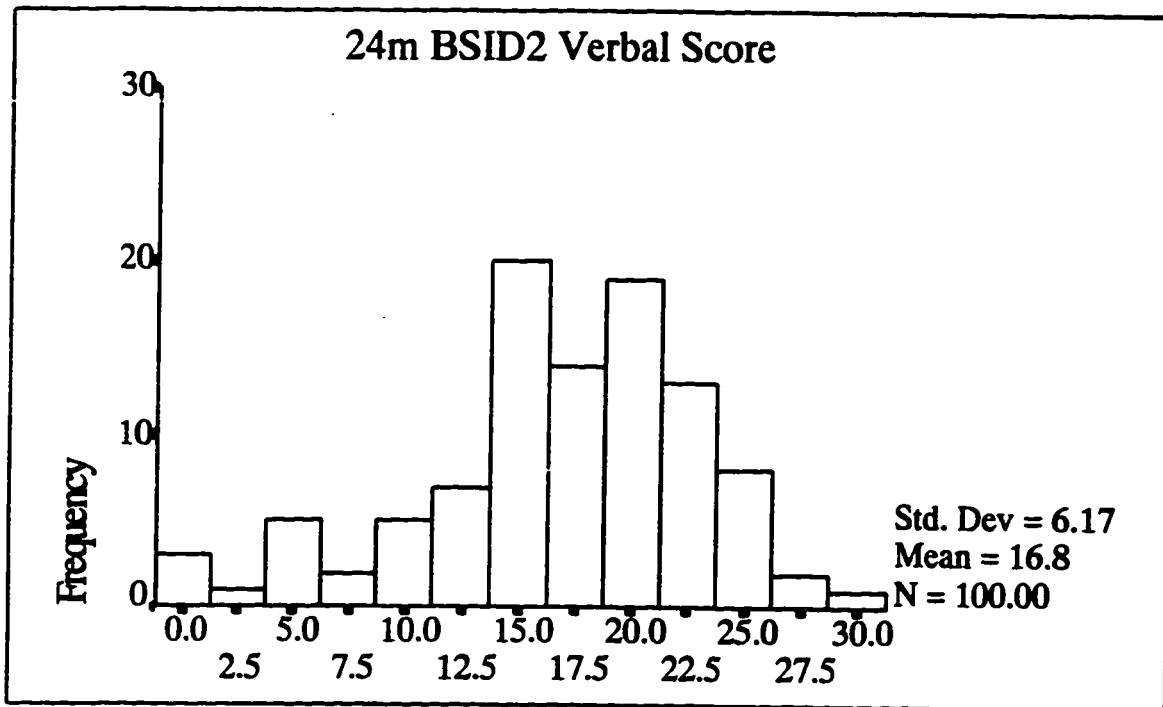
Appendix G. Histograms of Raw Score Child Outcomes by Group.

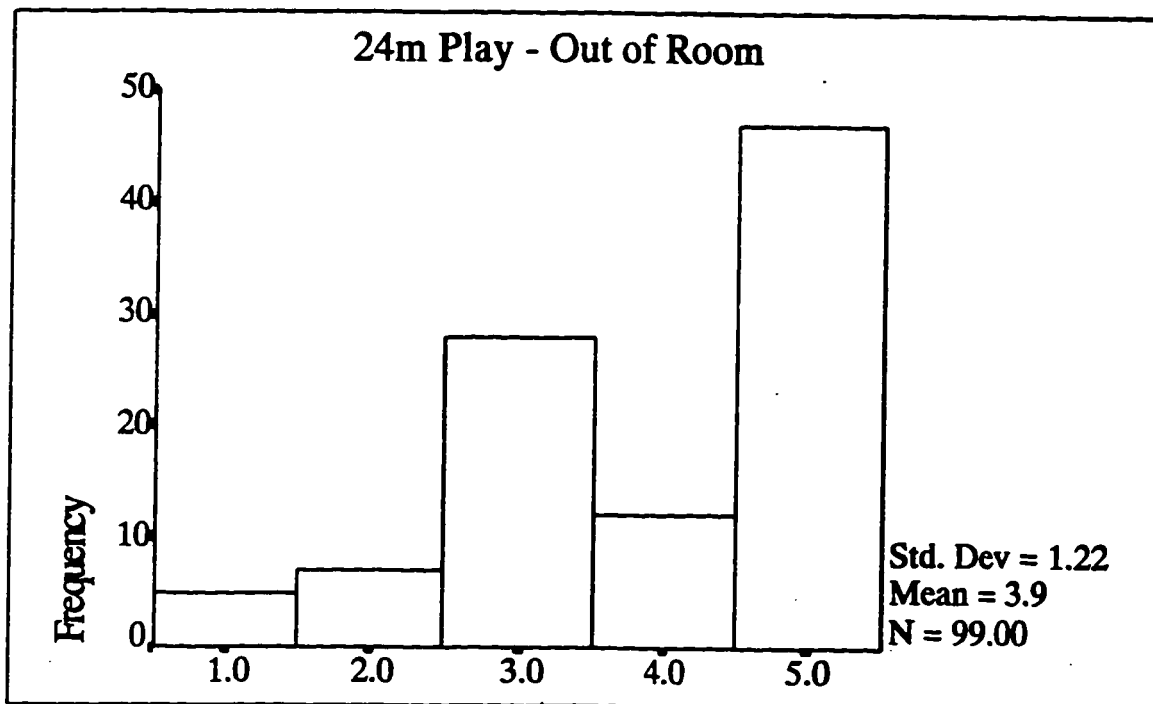
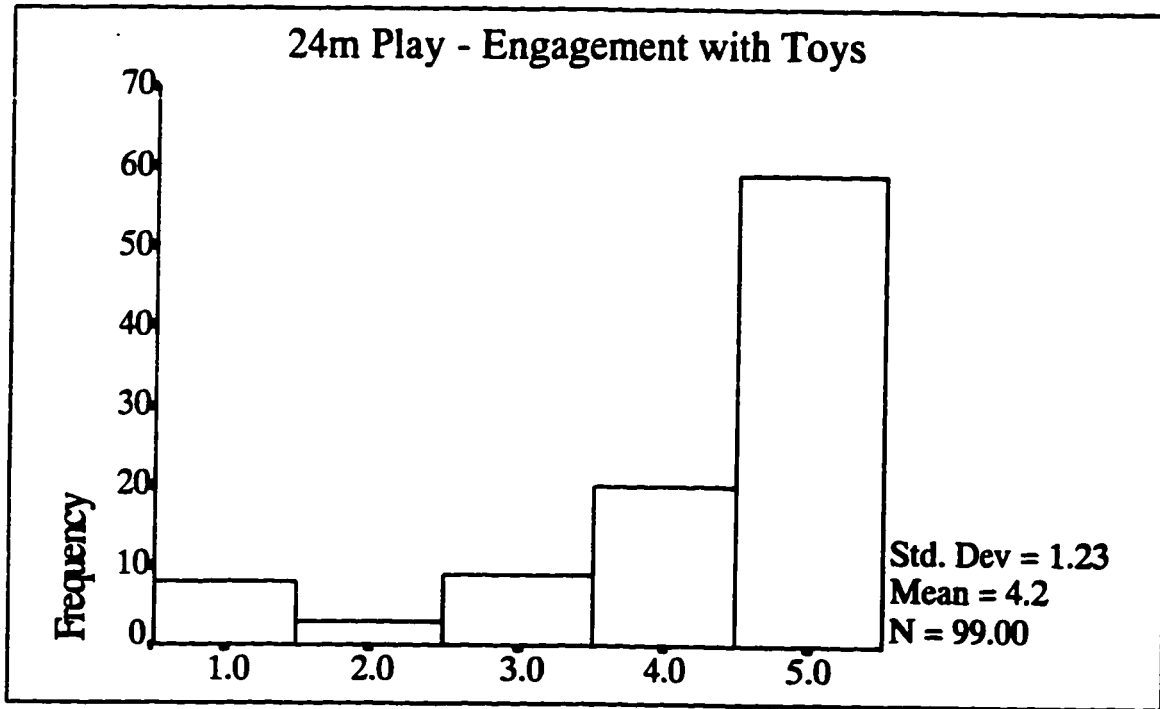
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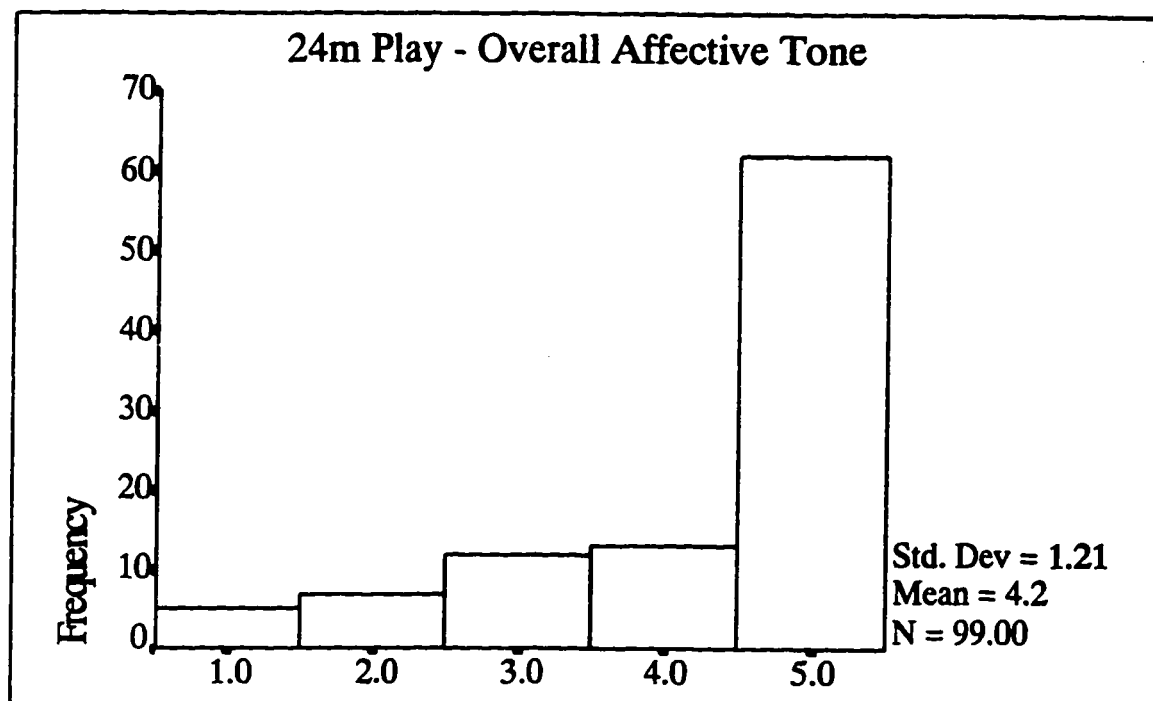
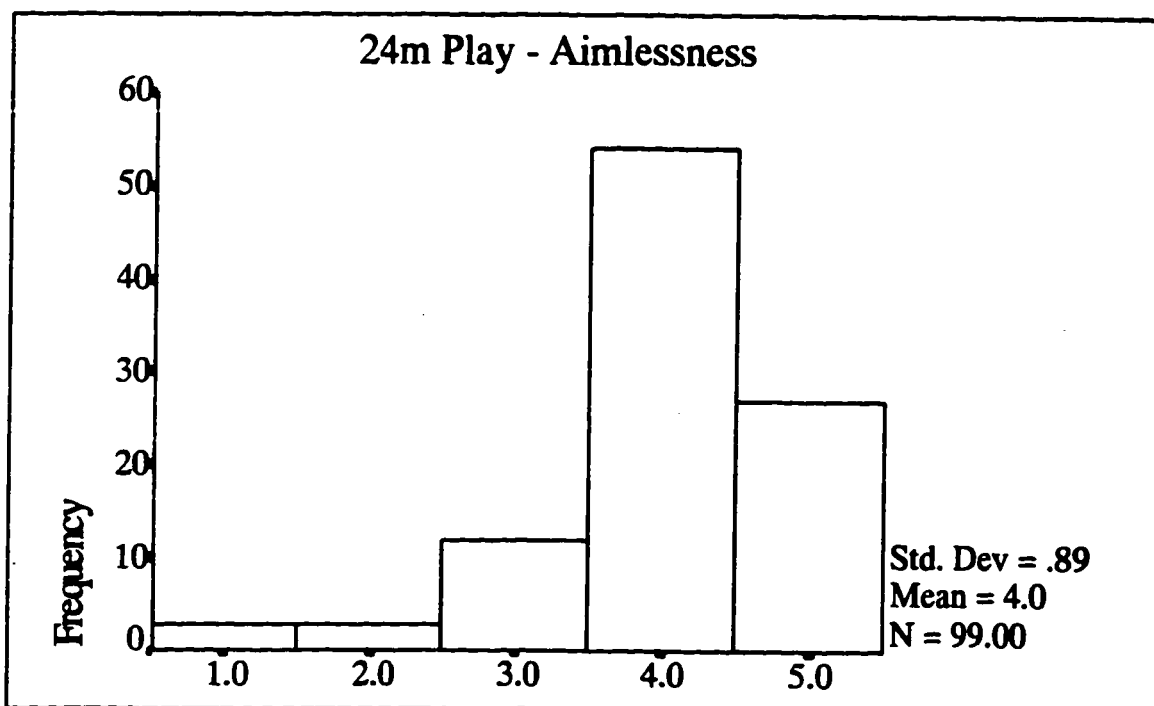


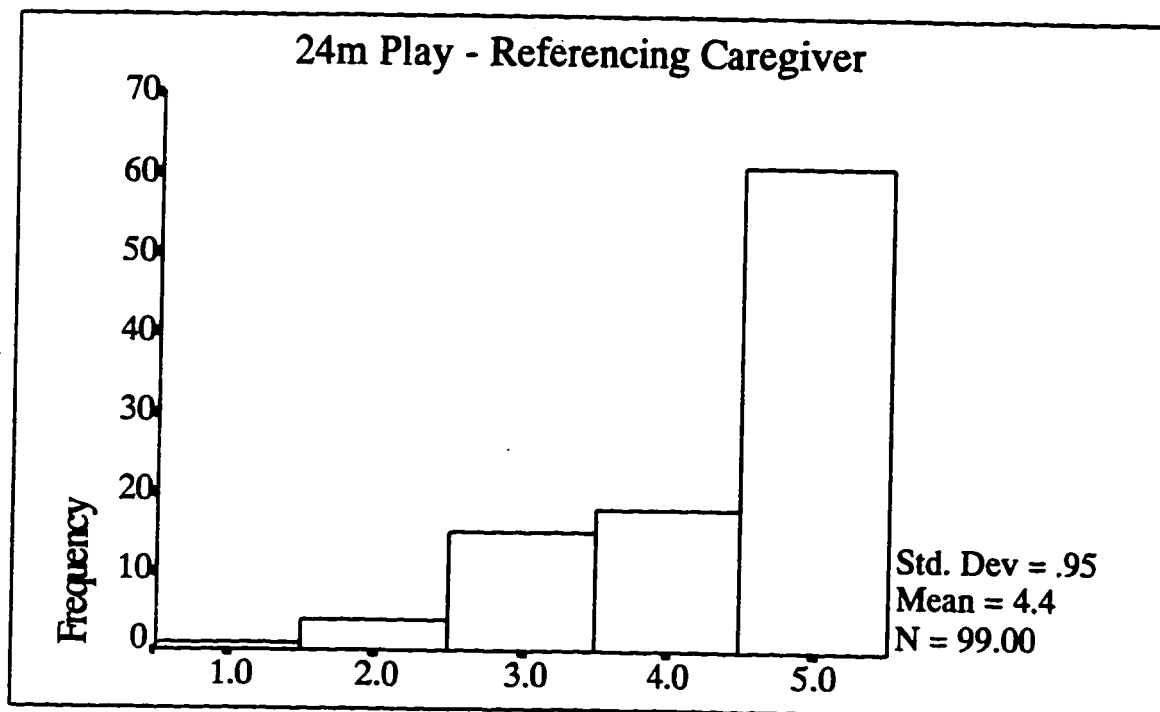
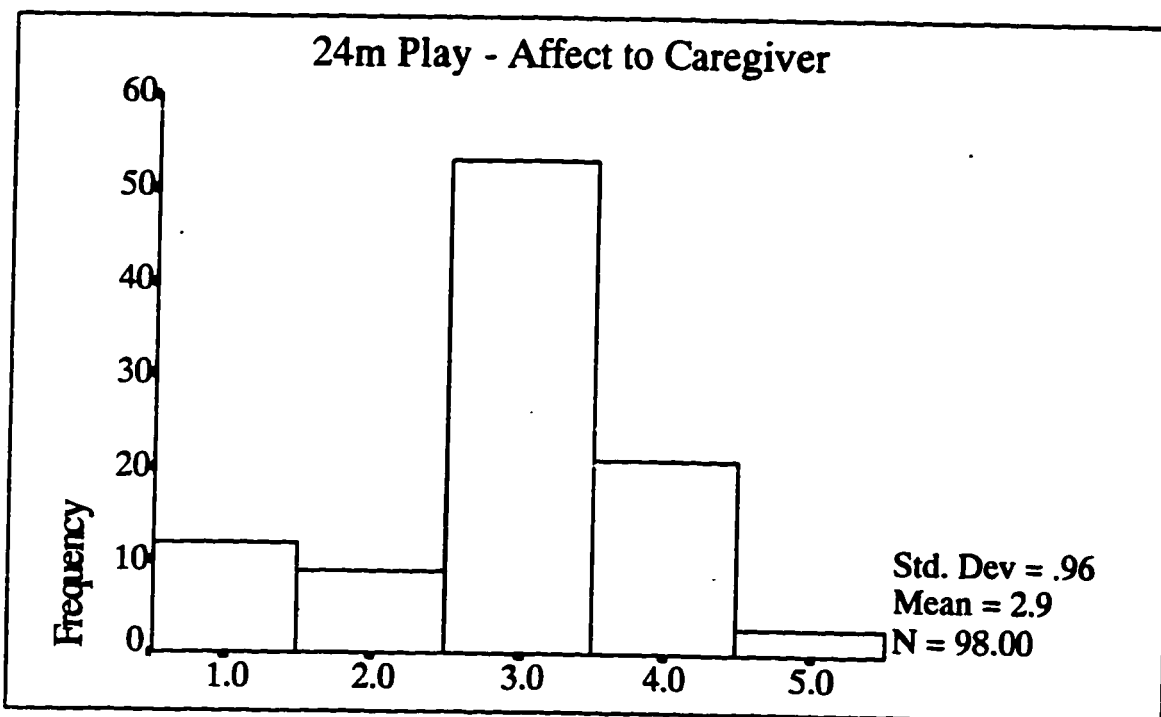


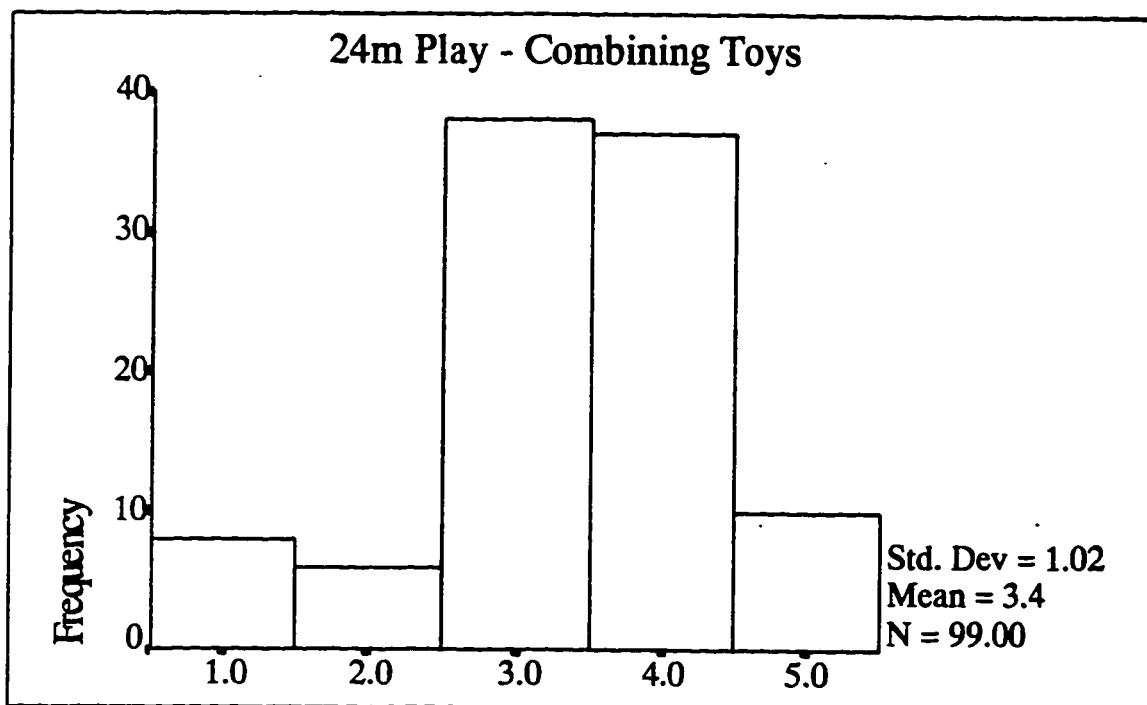
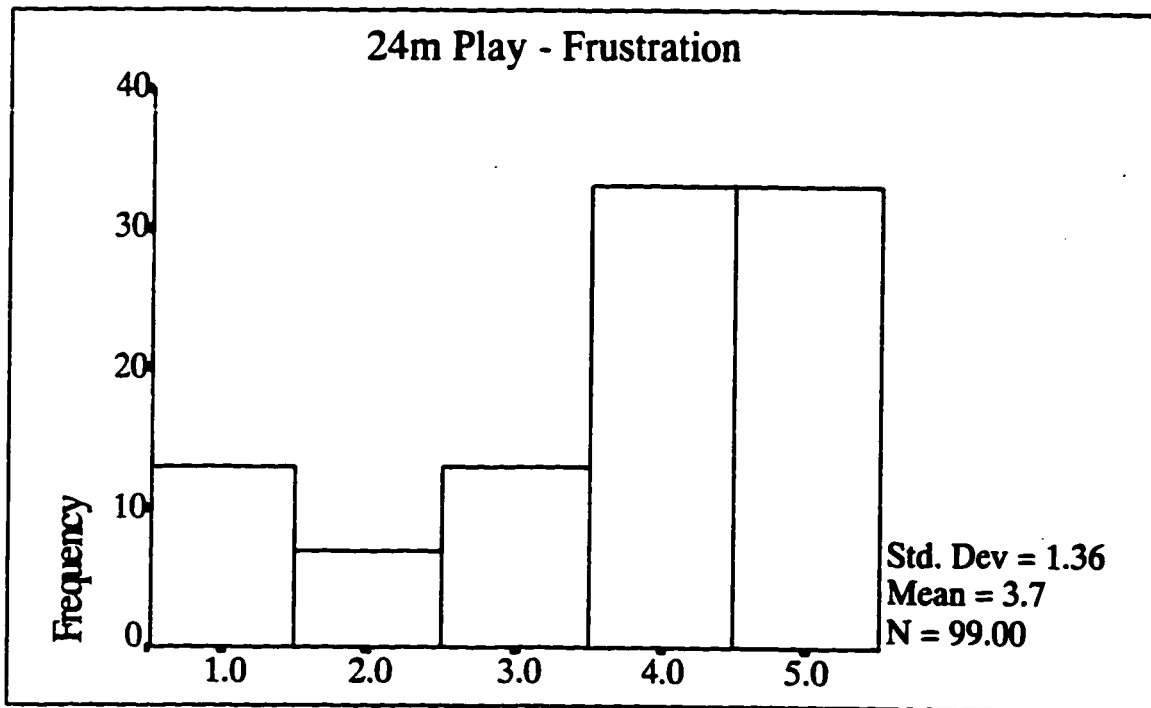


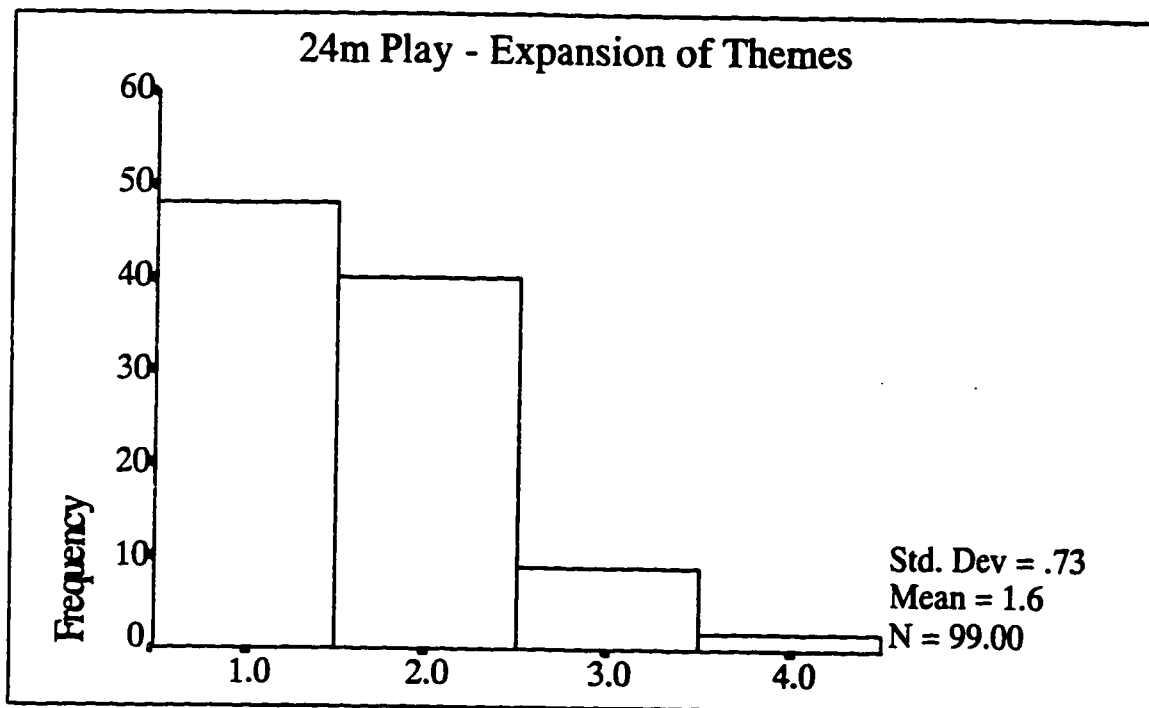
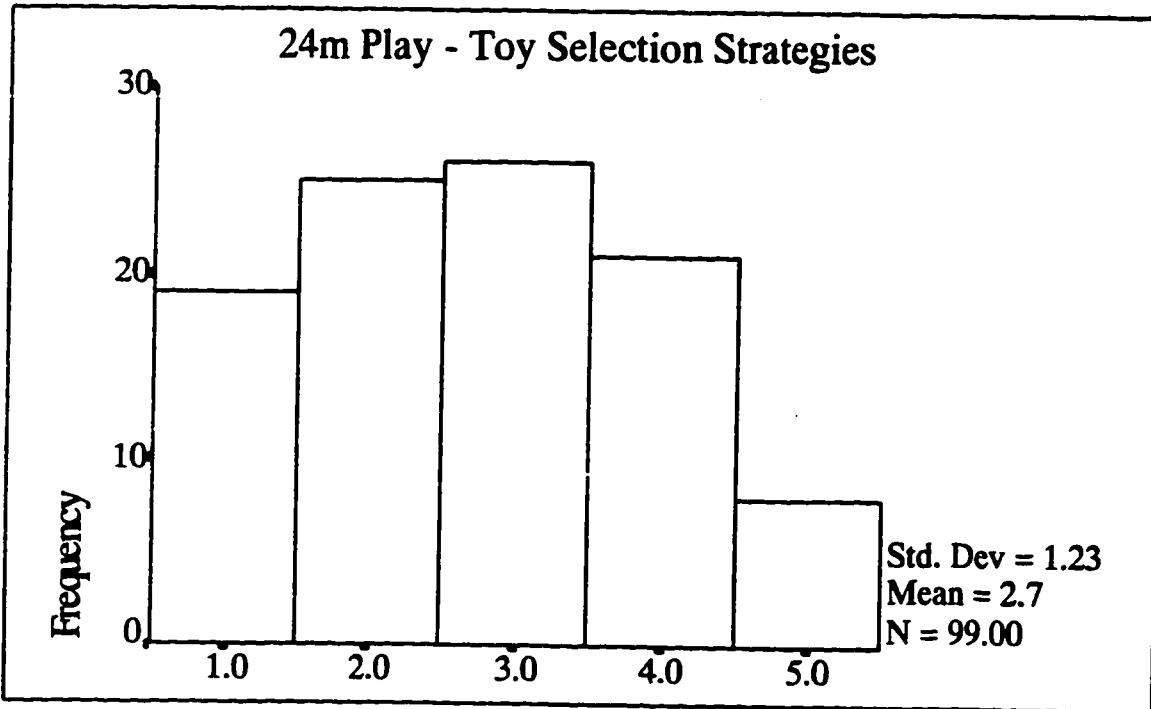


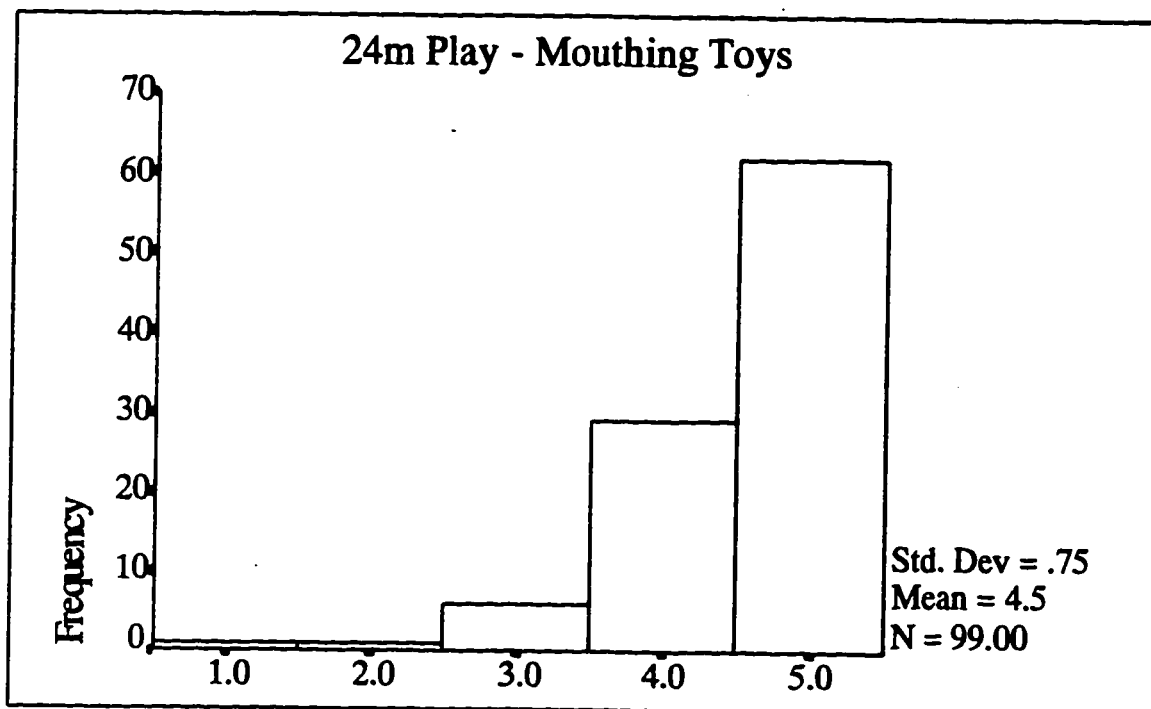
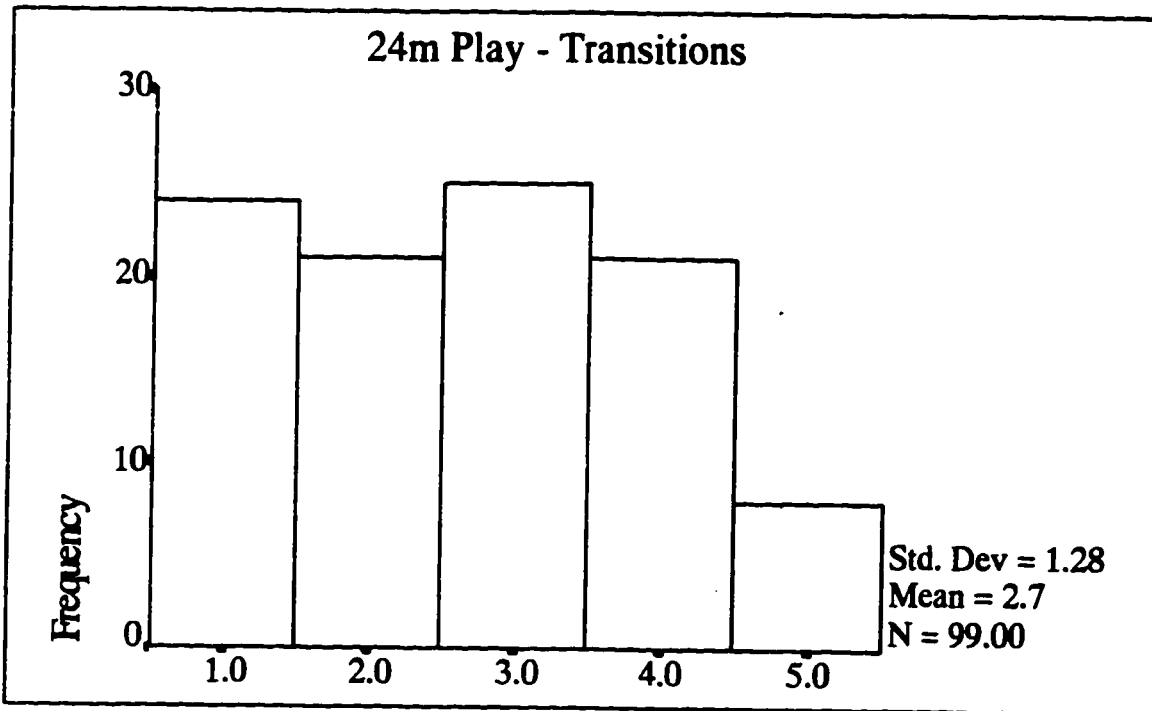


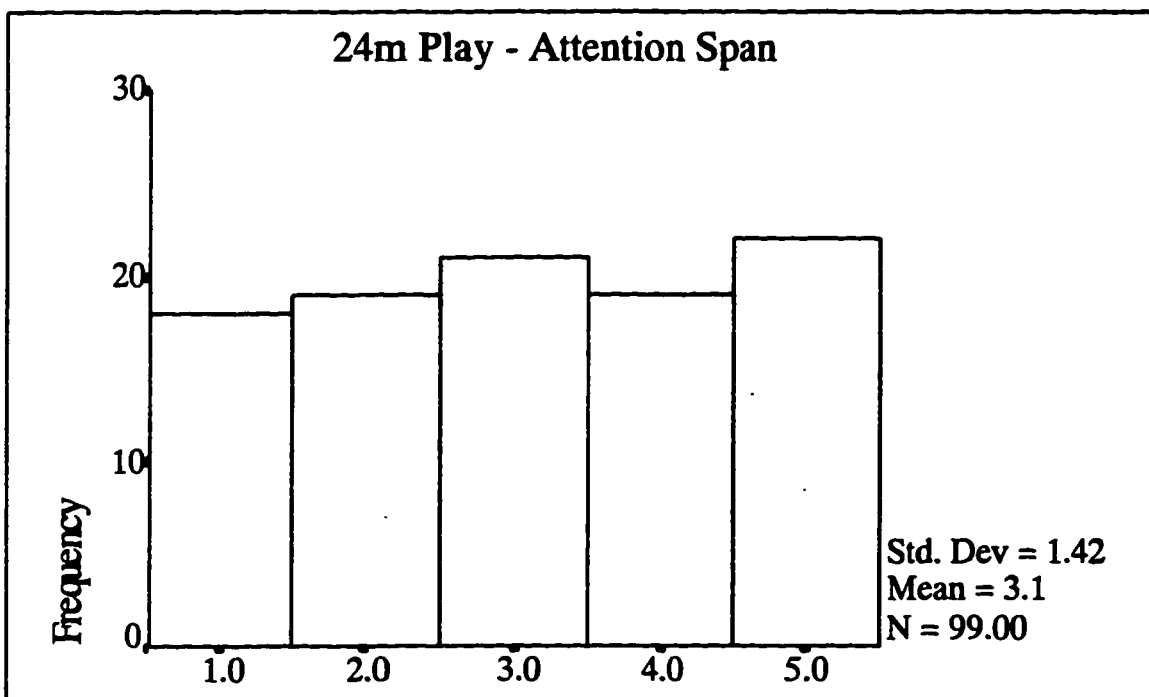
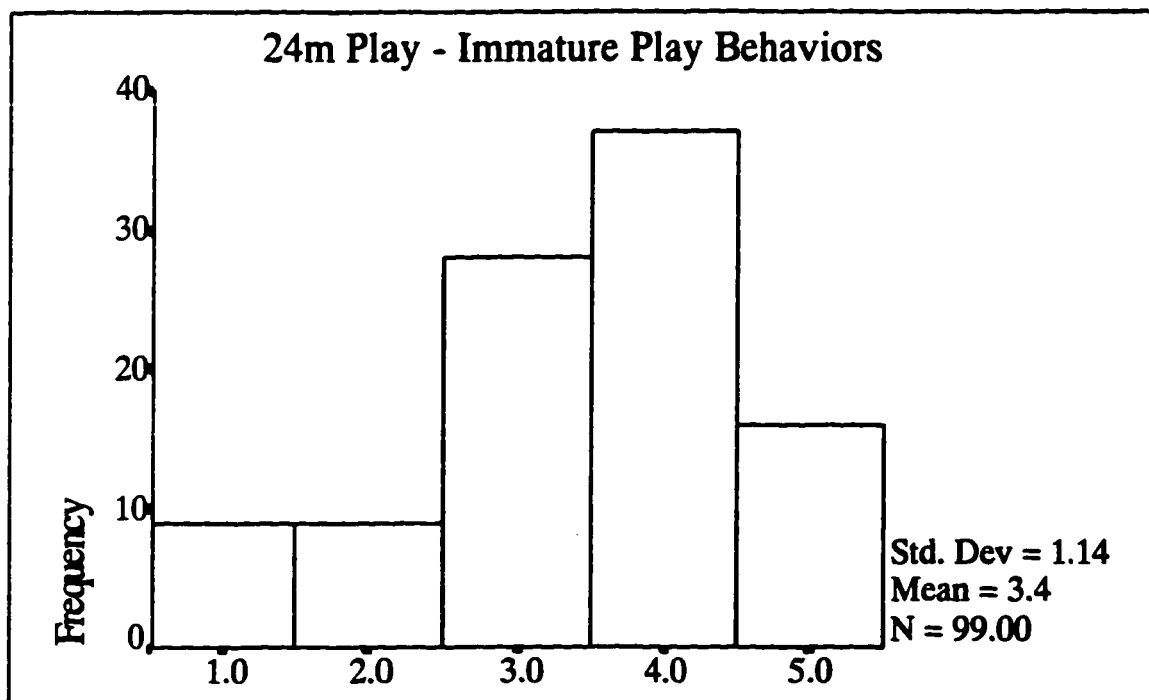


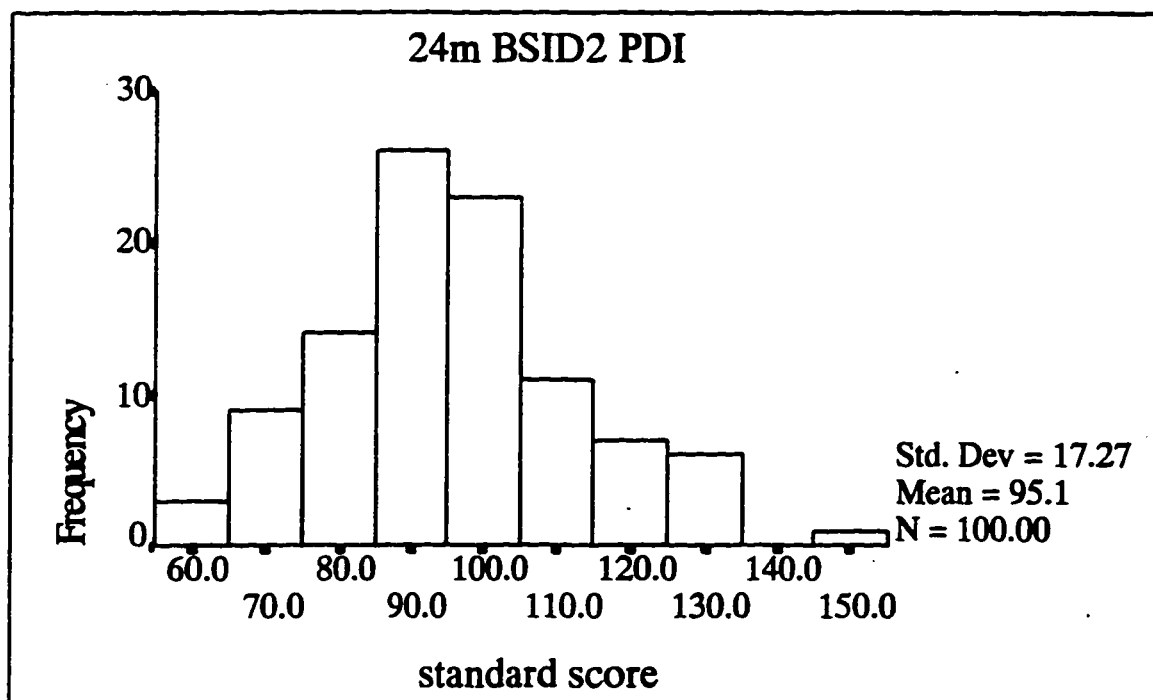
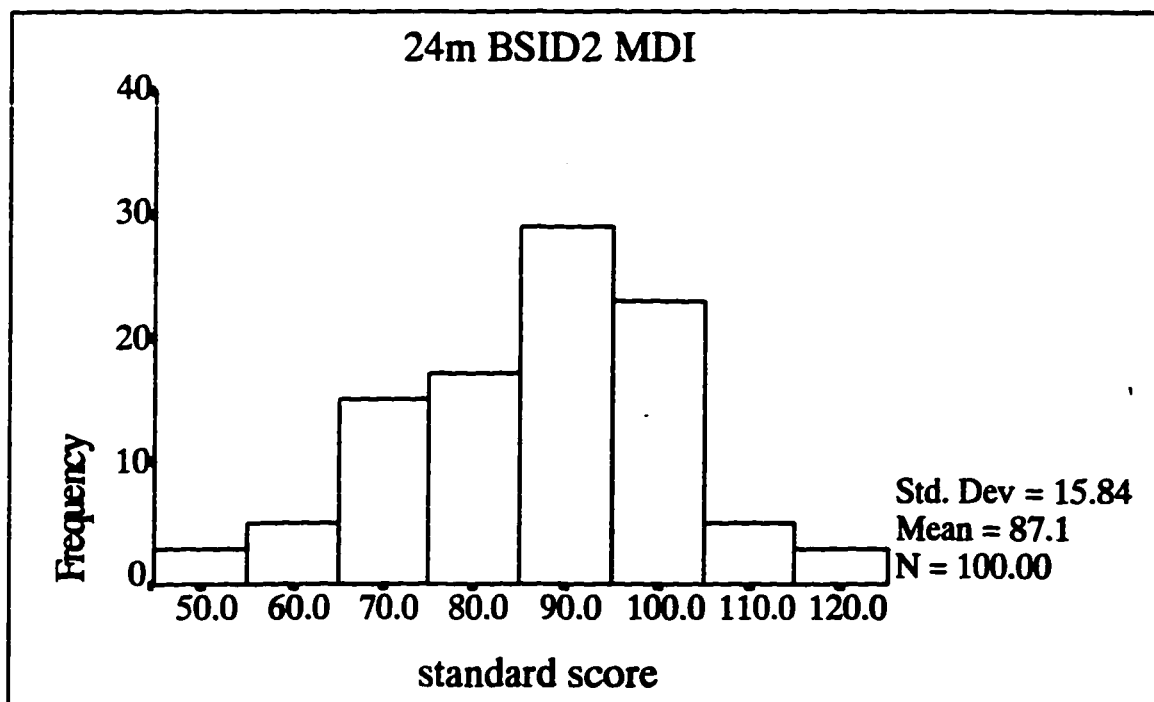




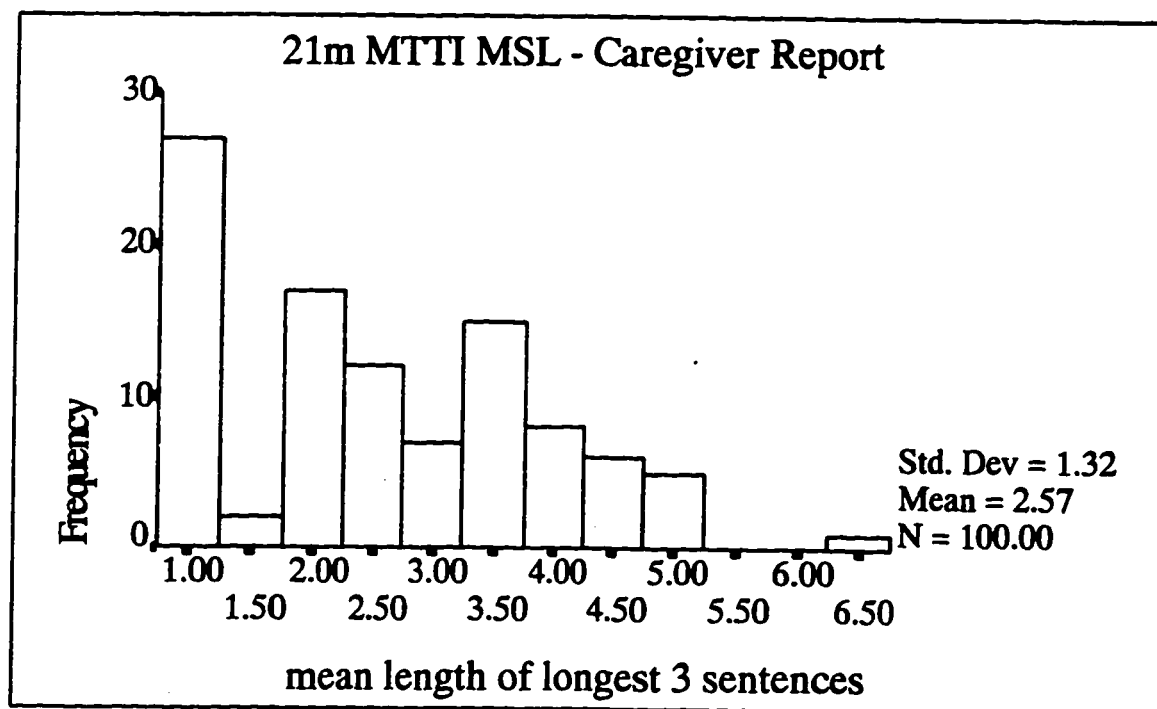
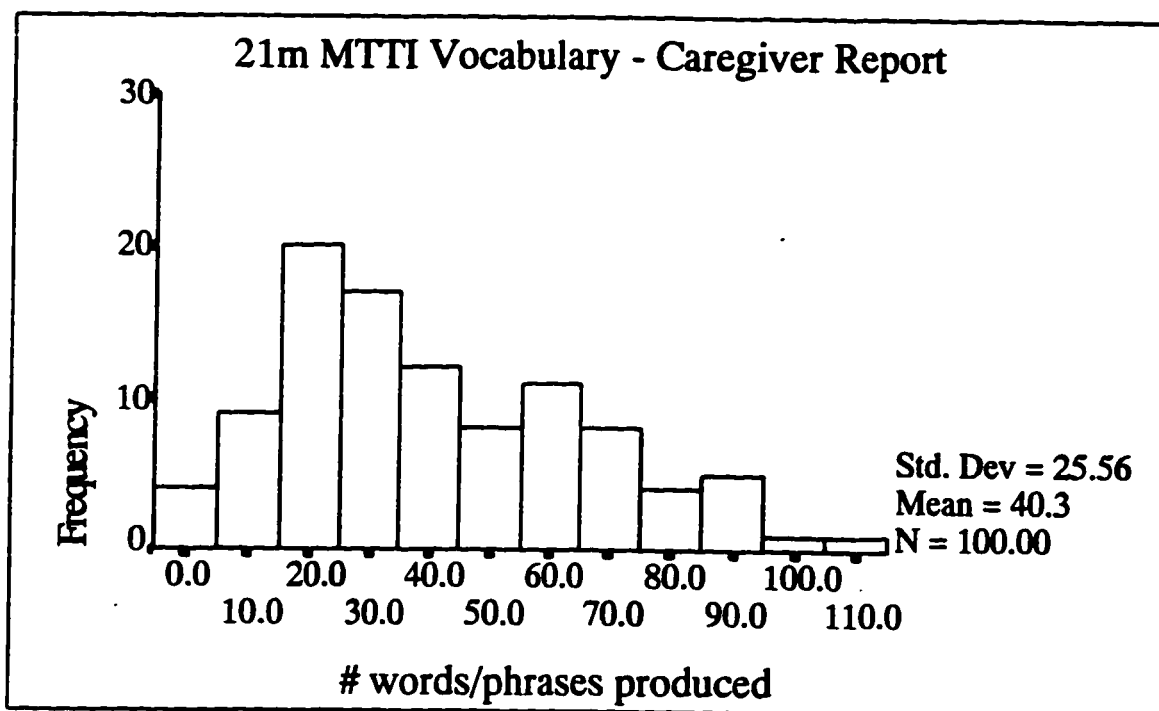


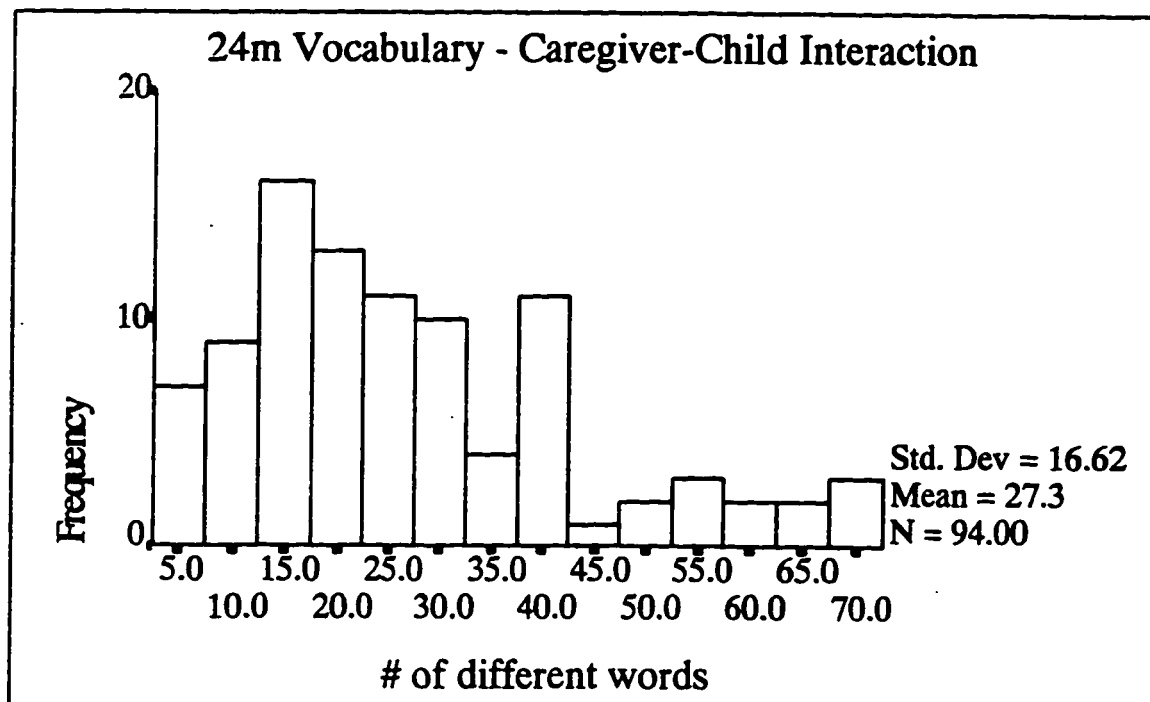
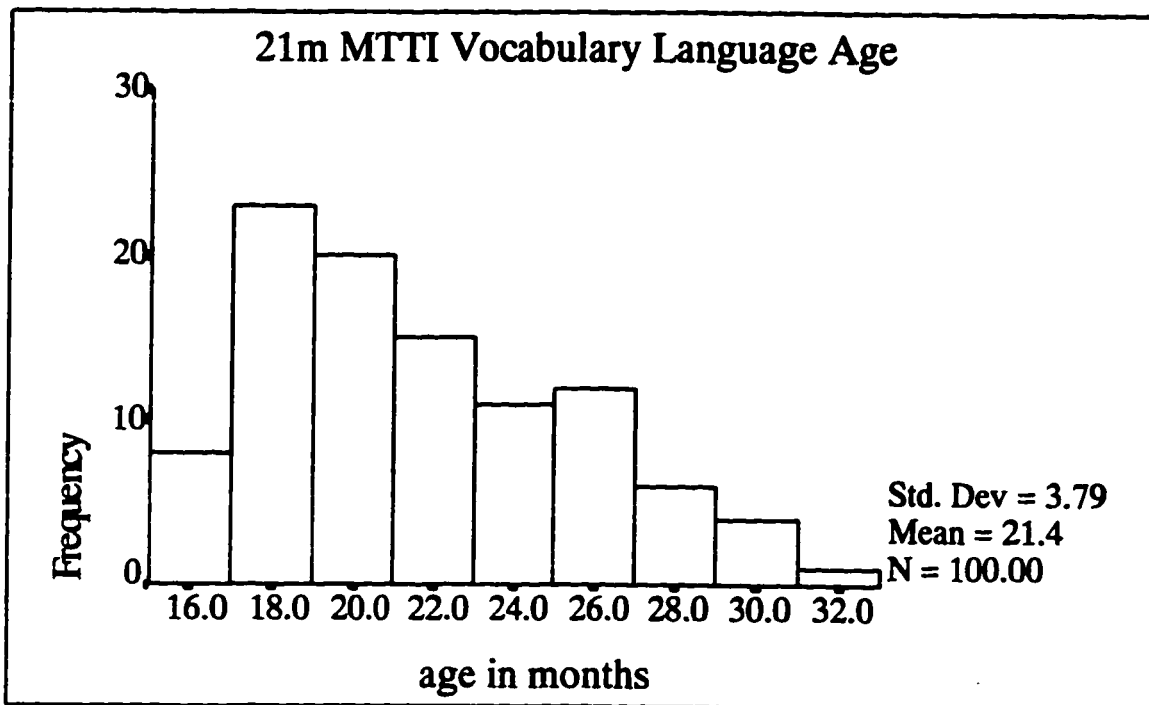


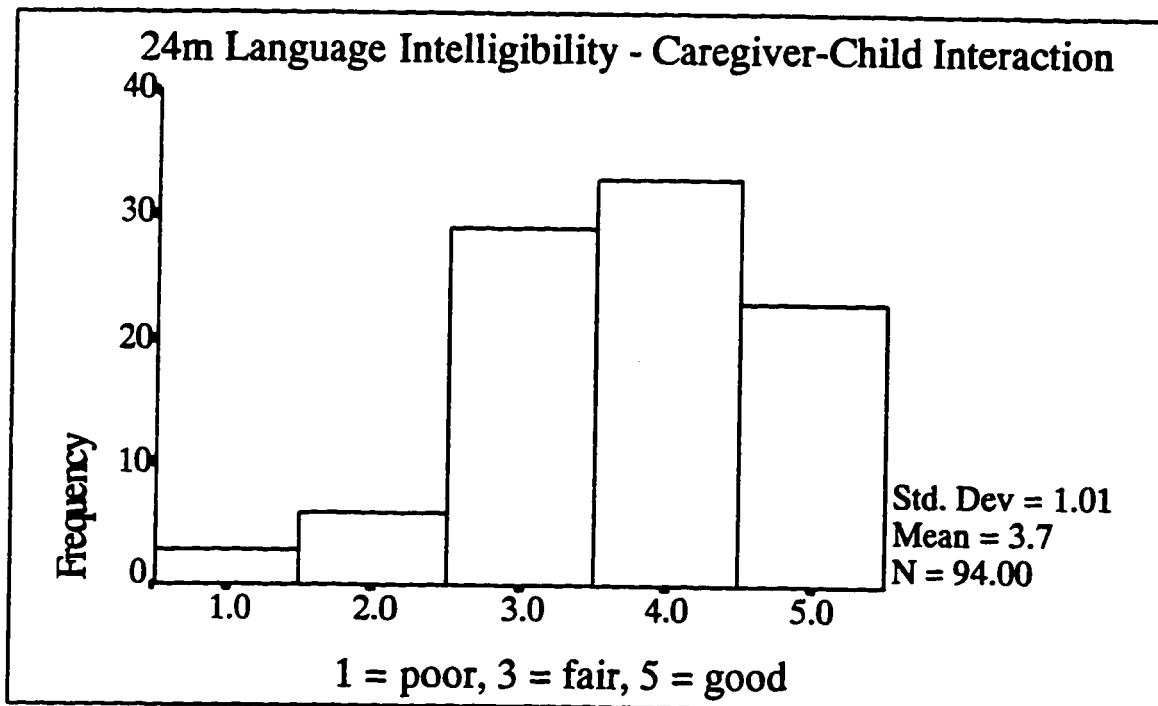
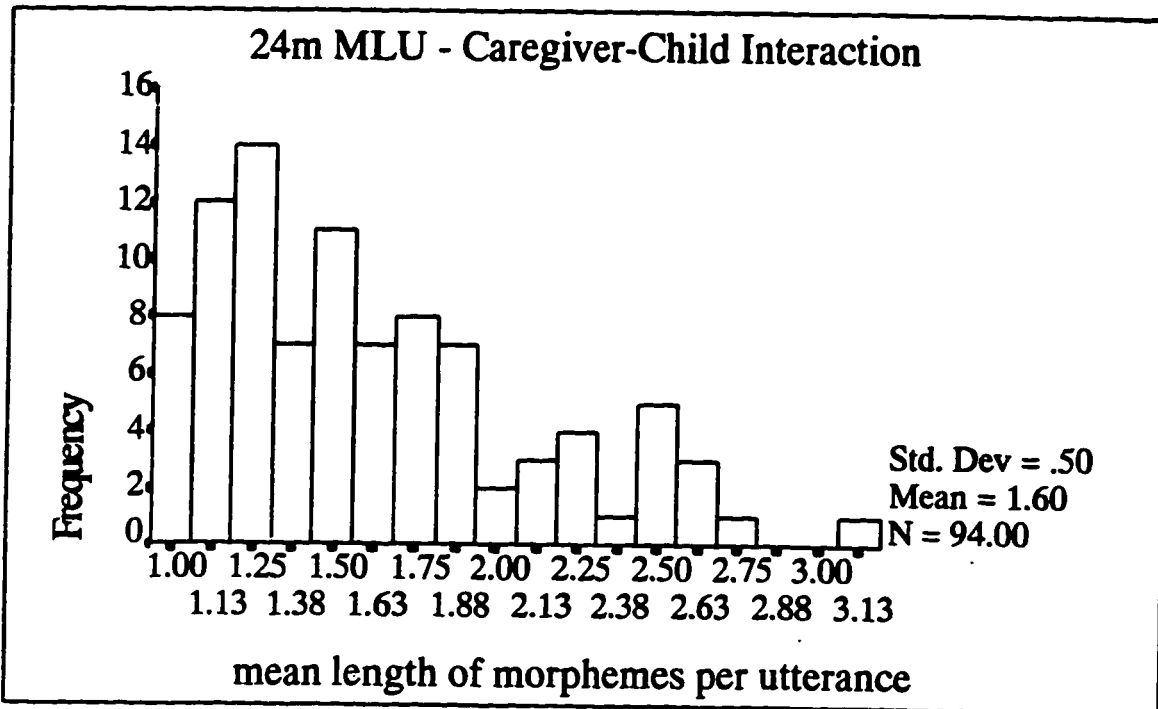


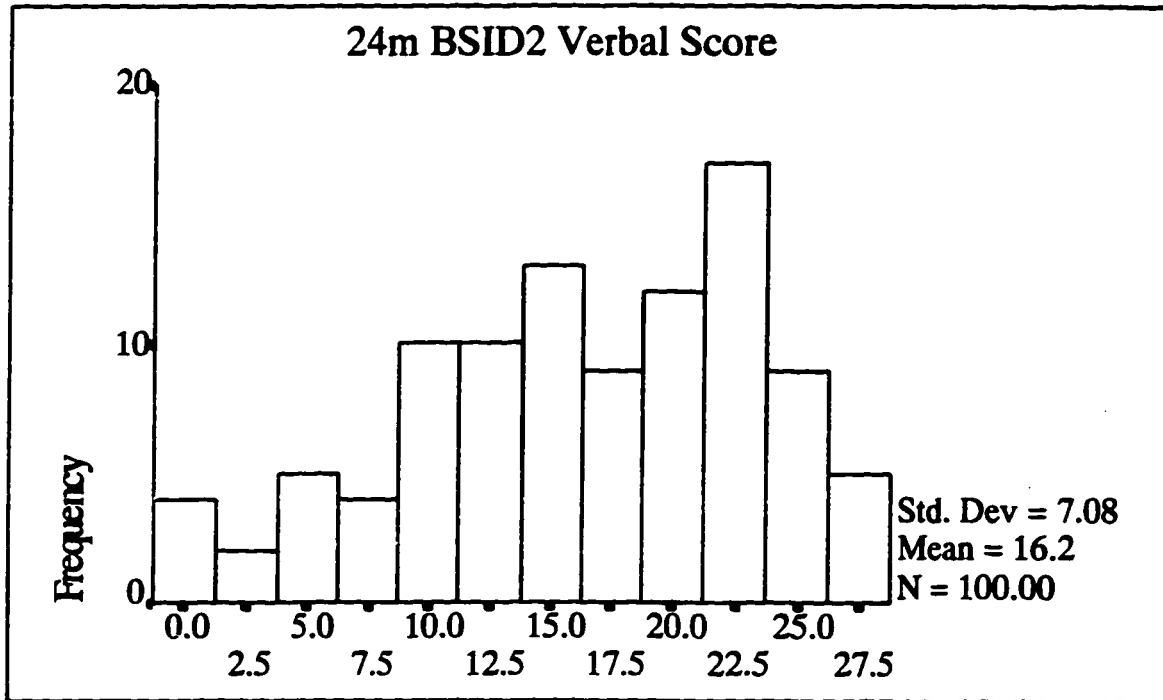


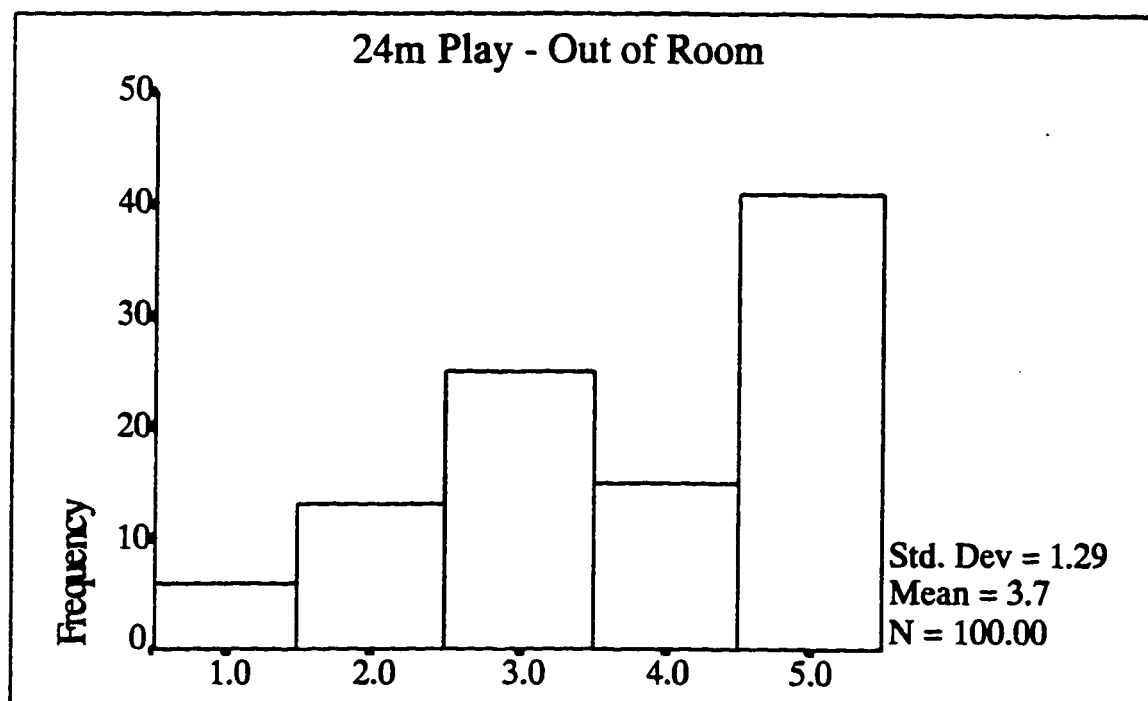
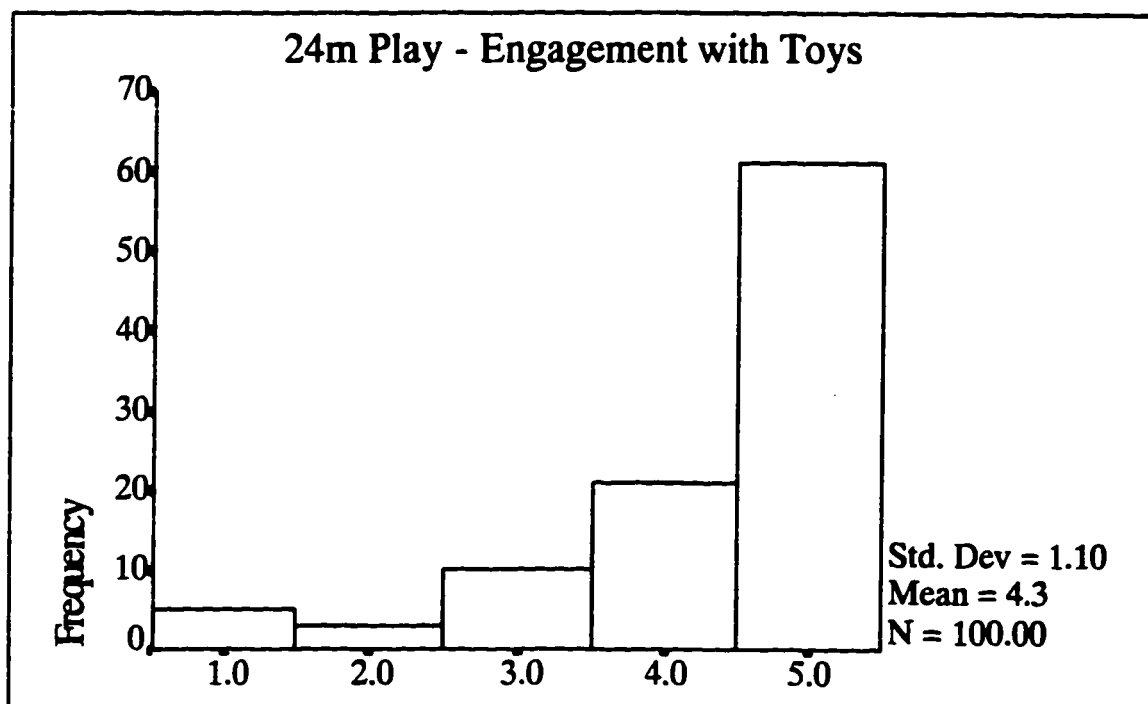
NON-COC GROUP.

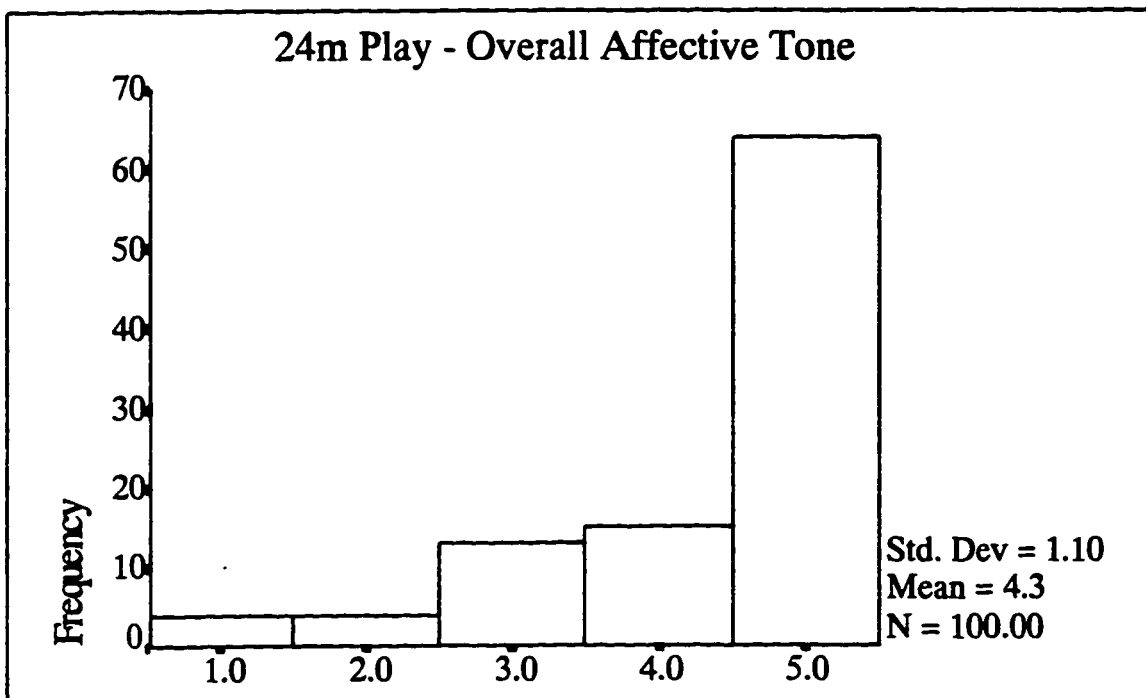
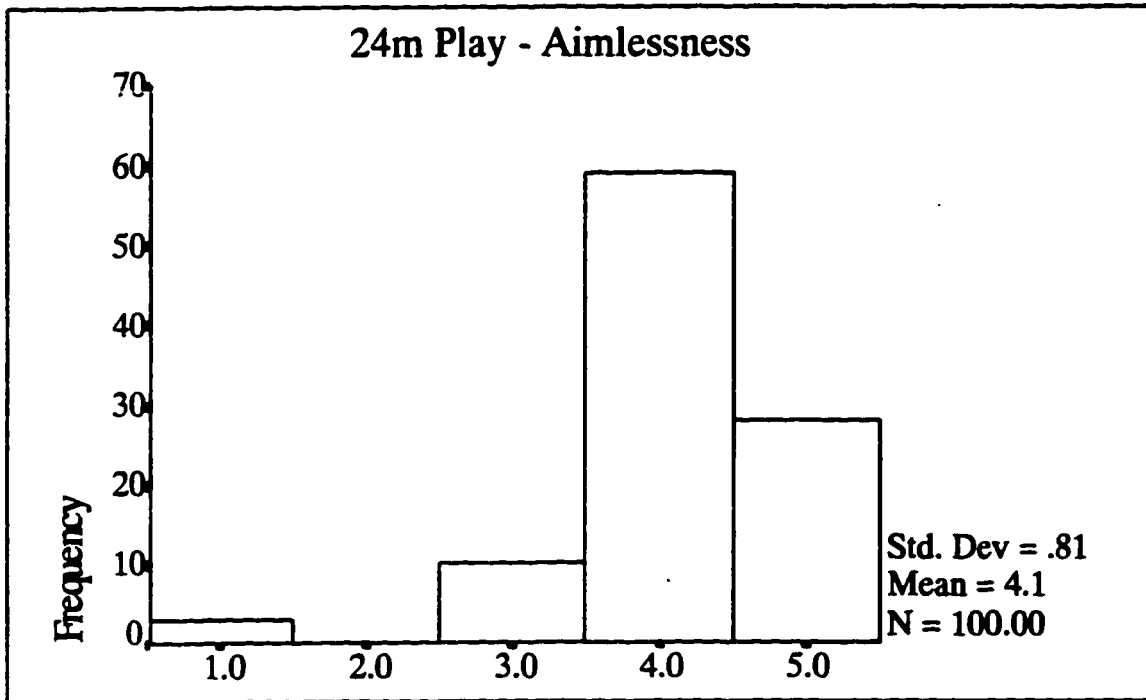


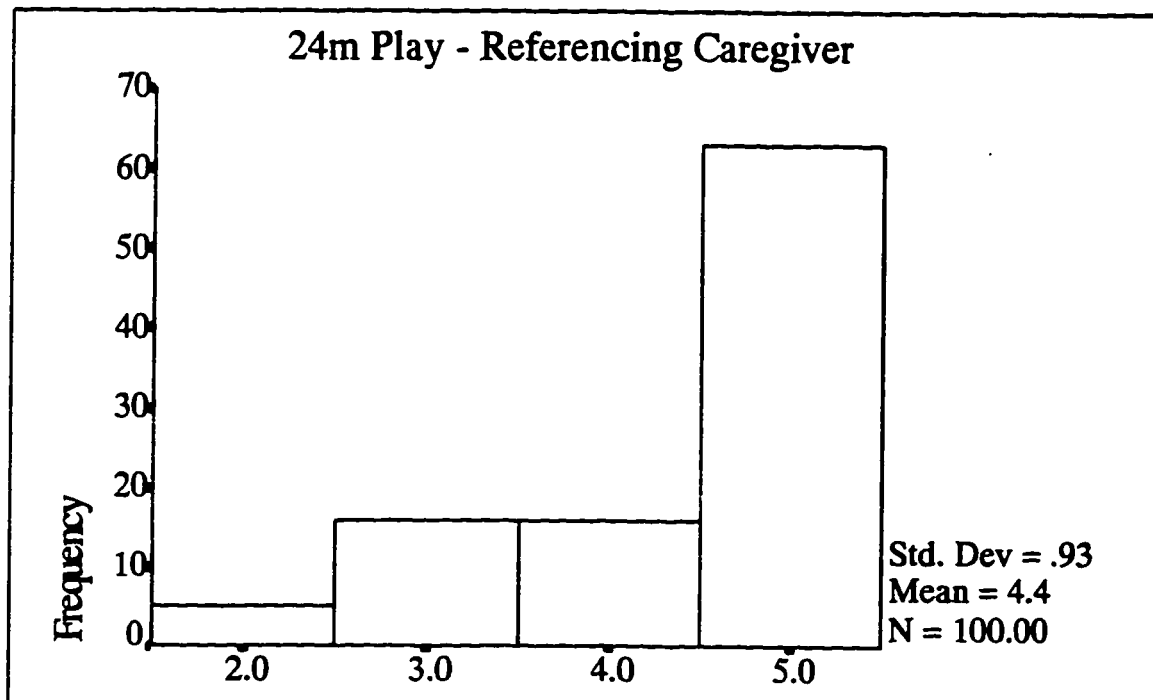
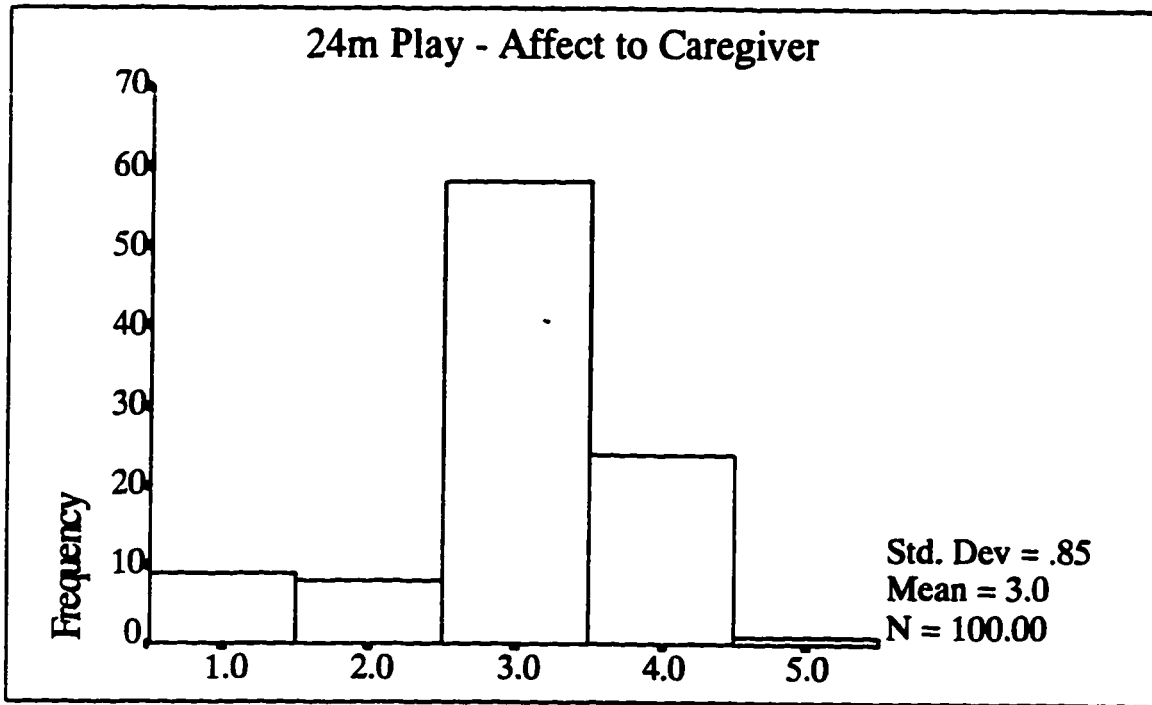


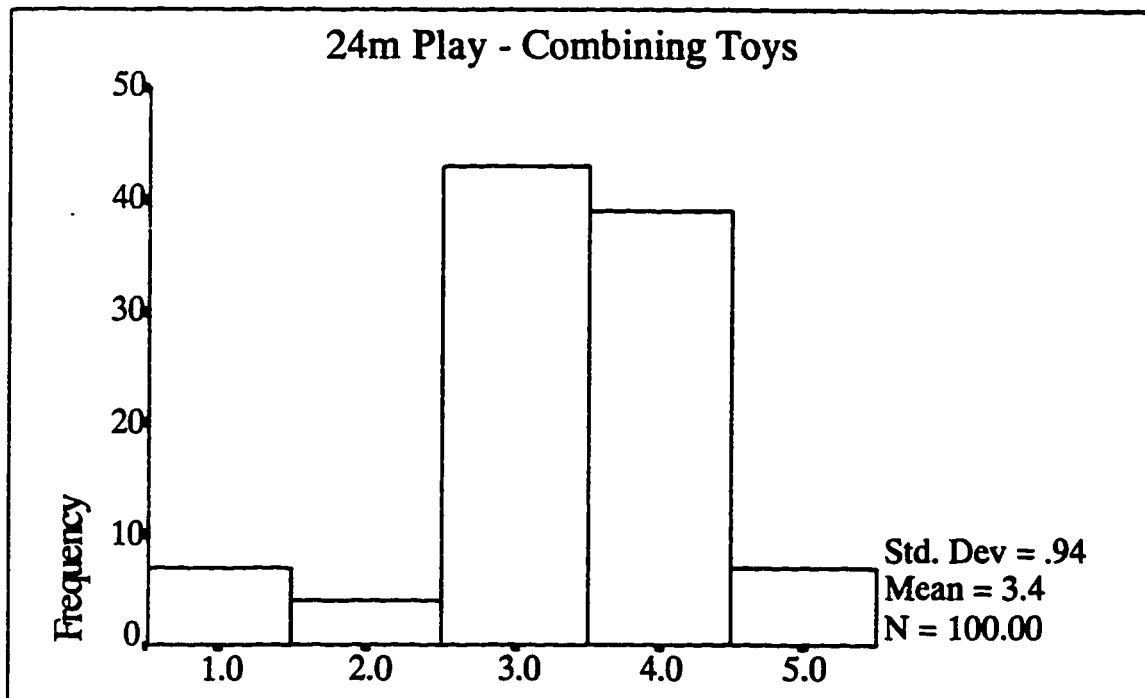
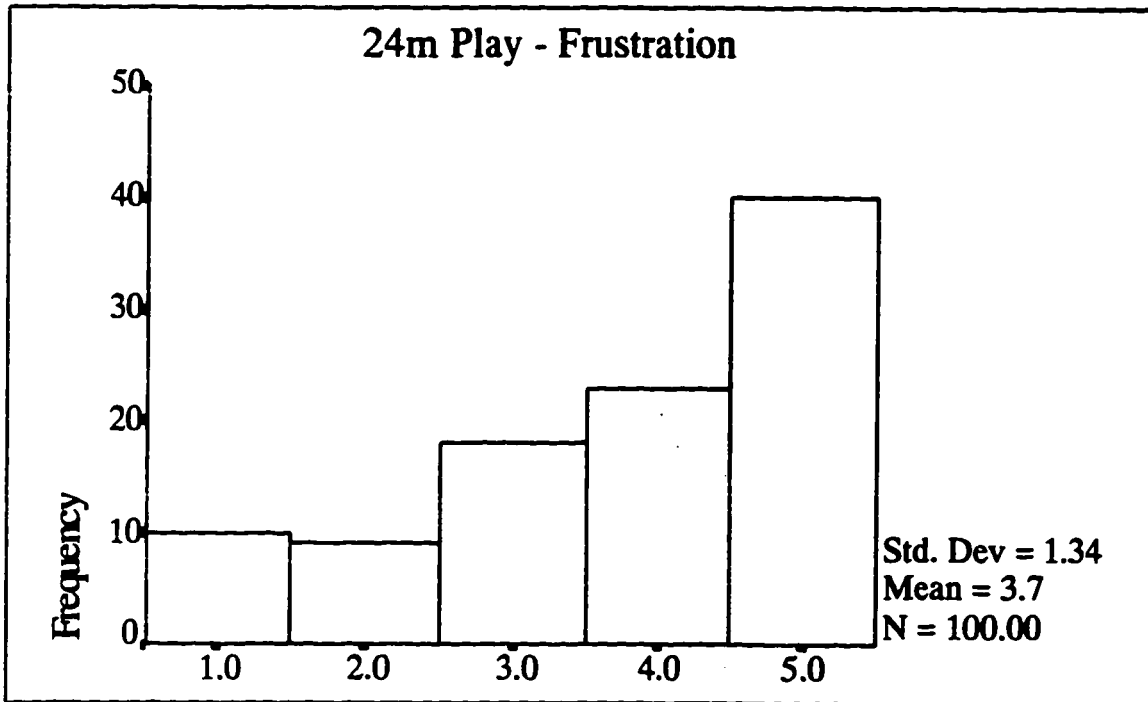


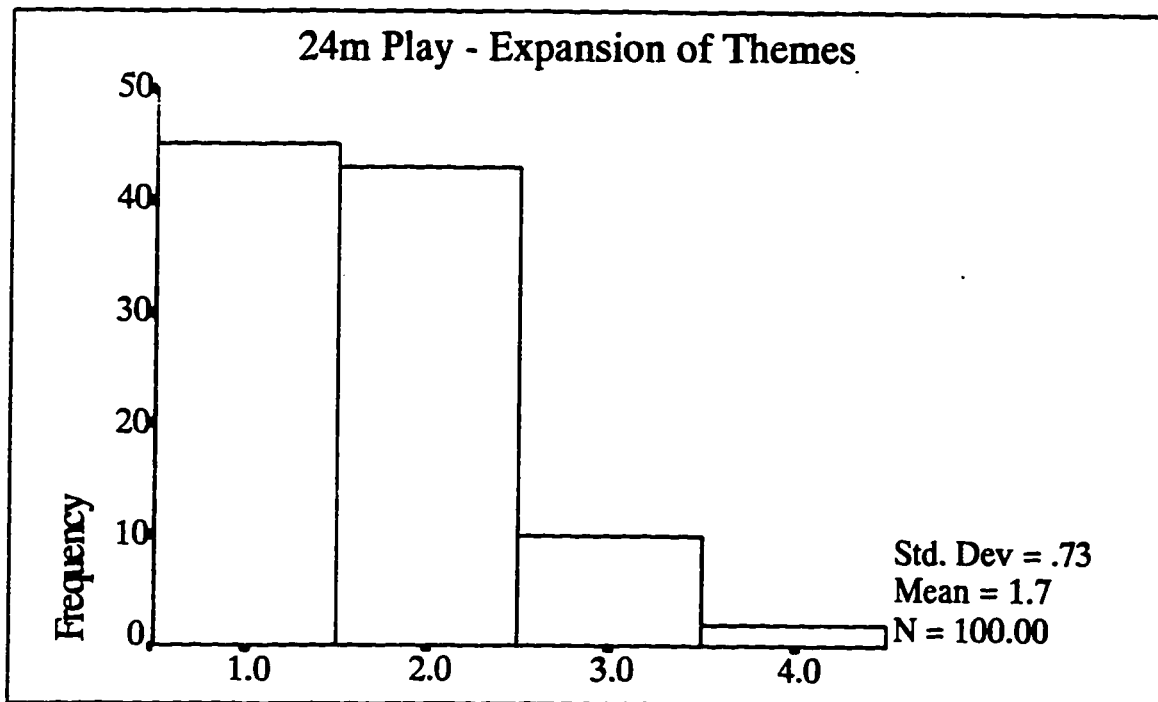
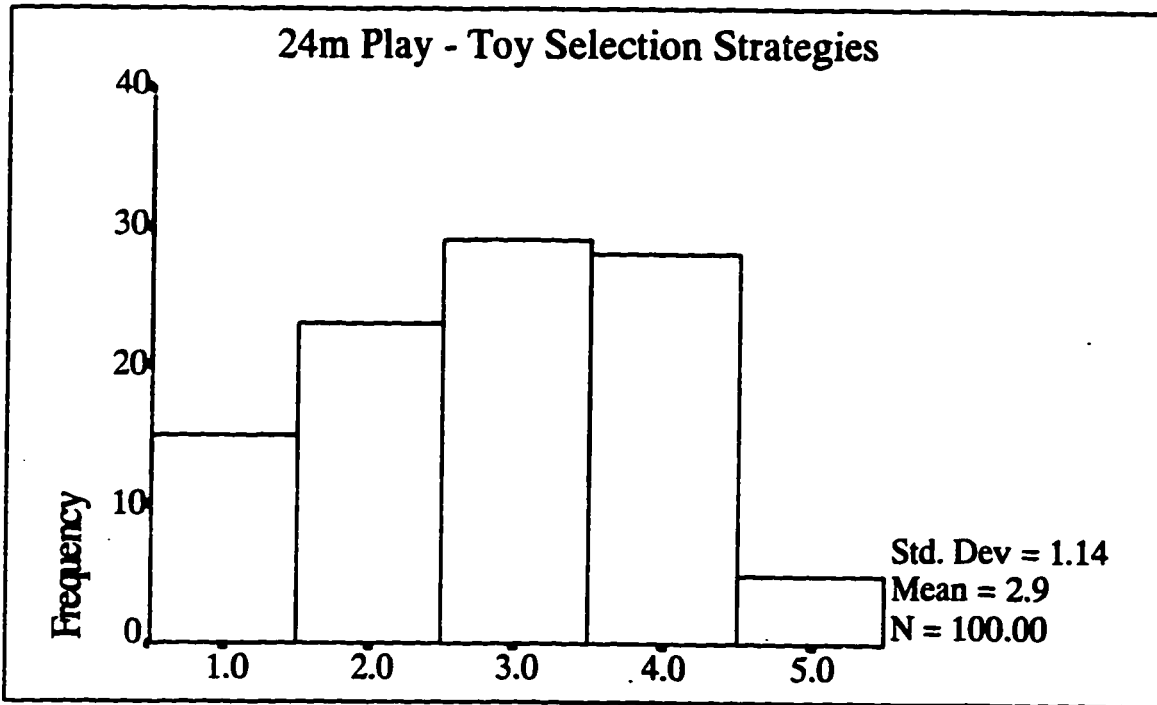


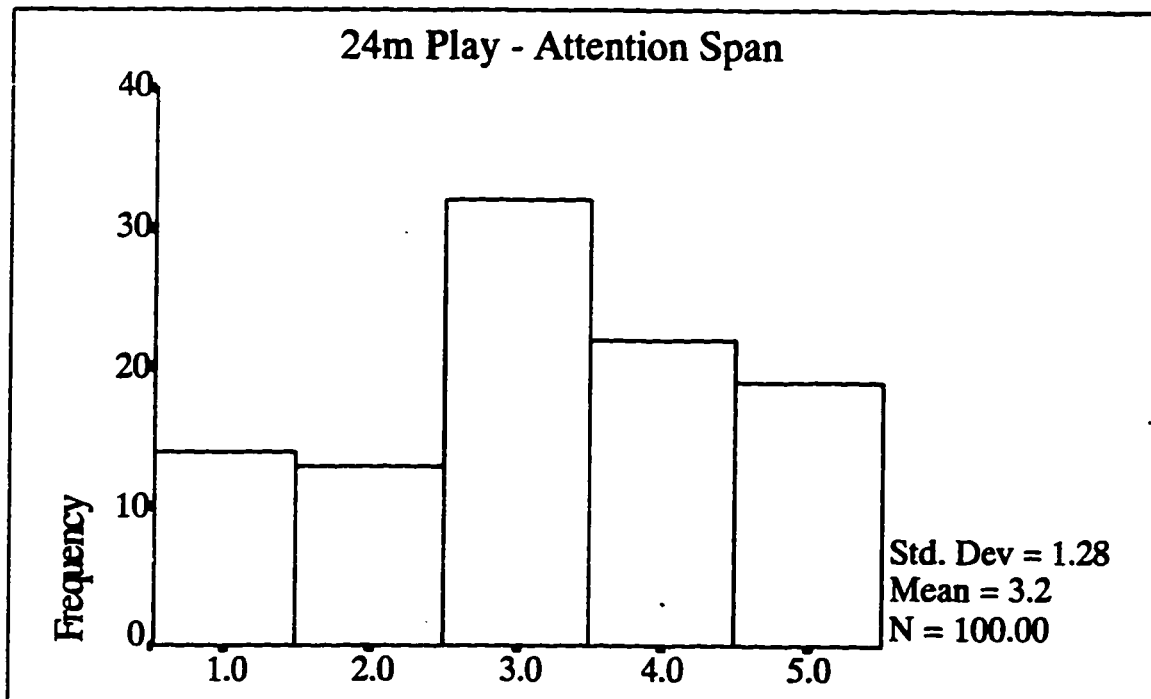
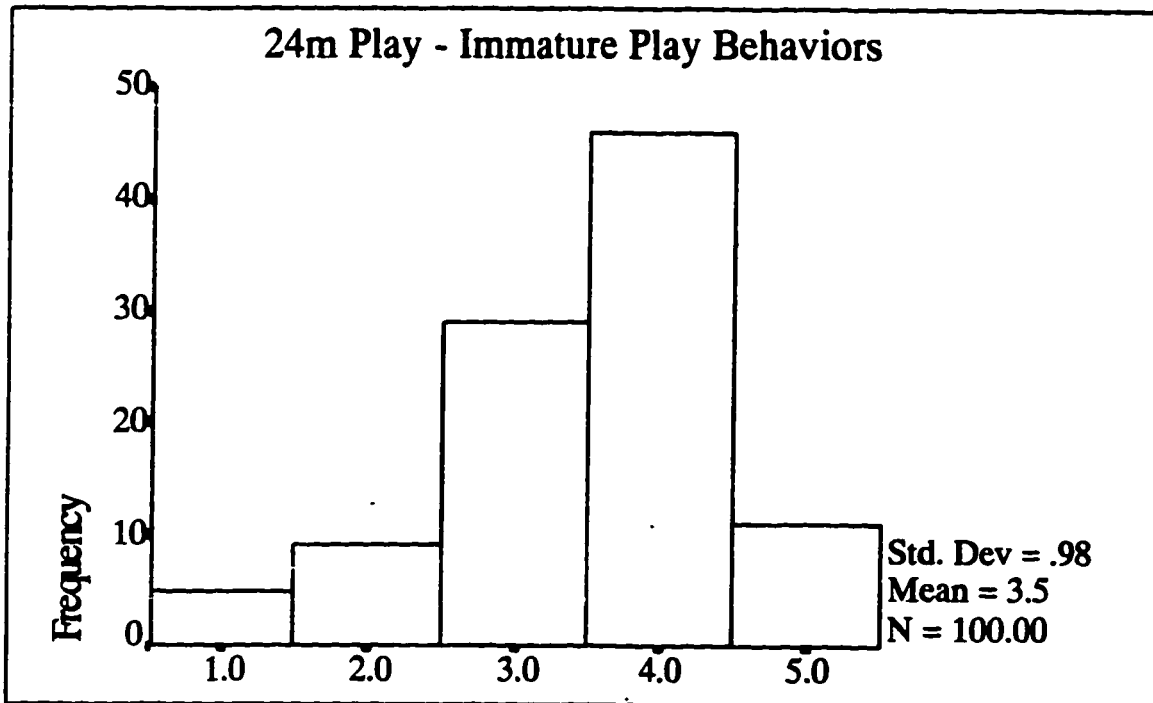


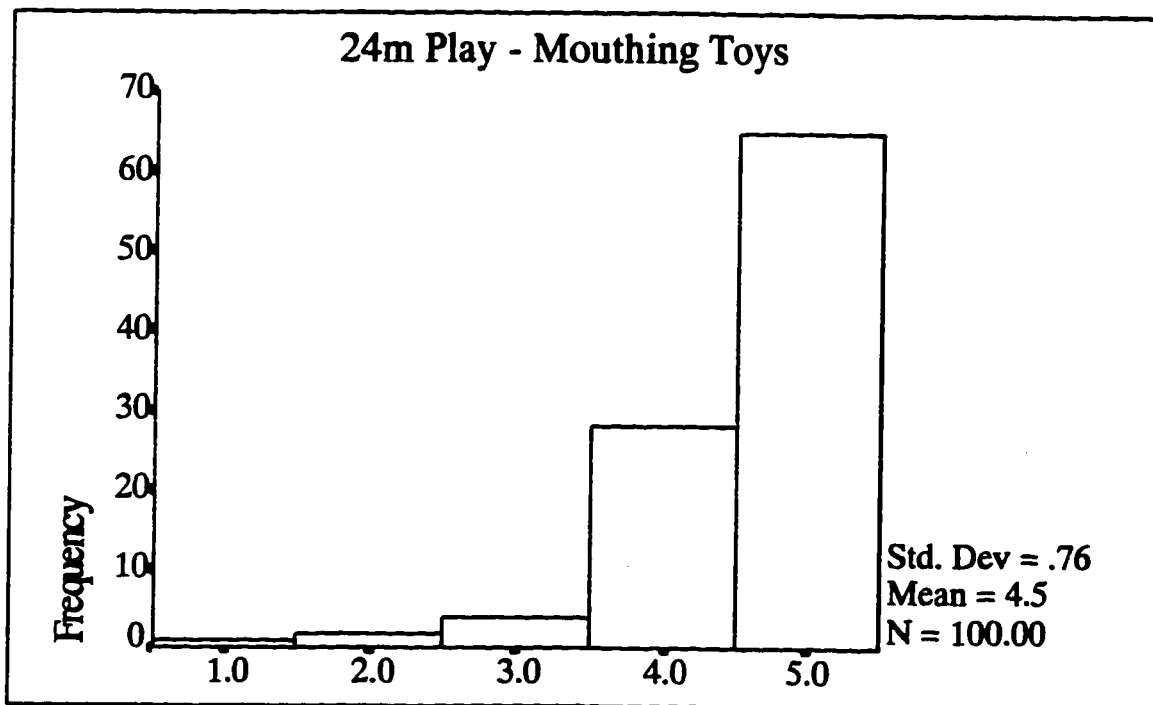
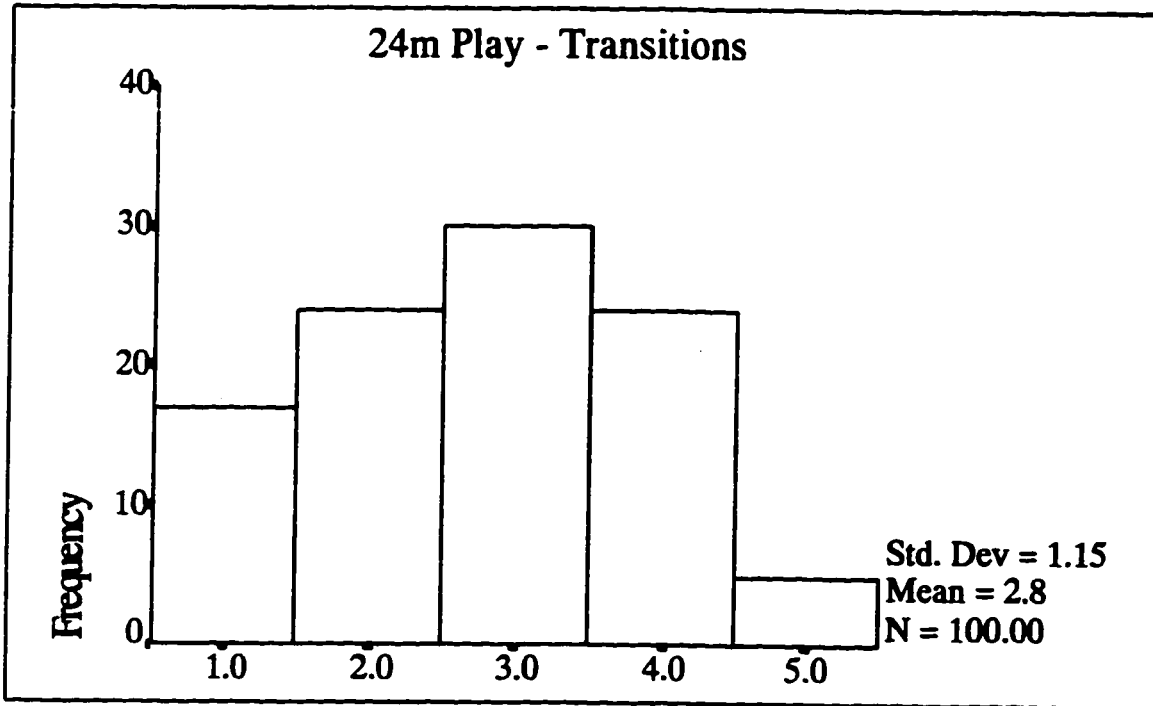


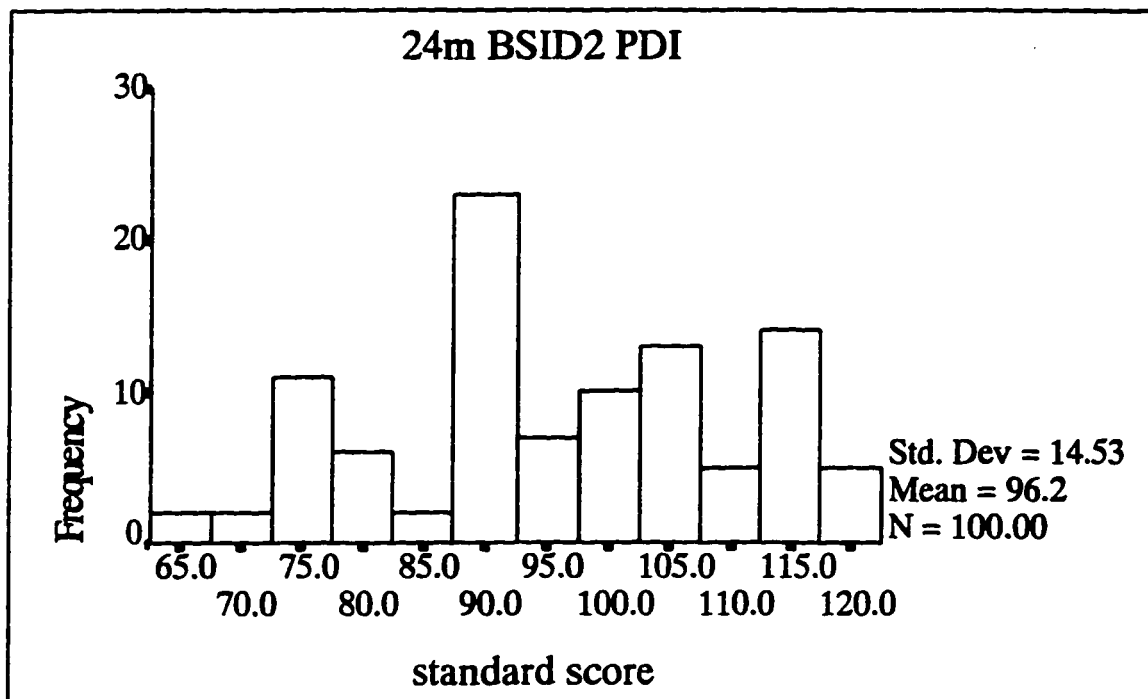
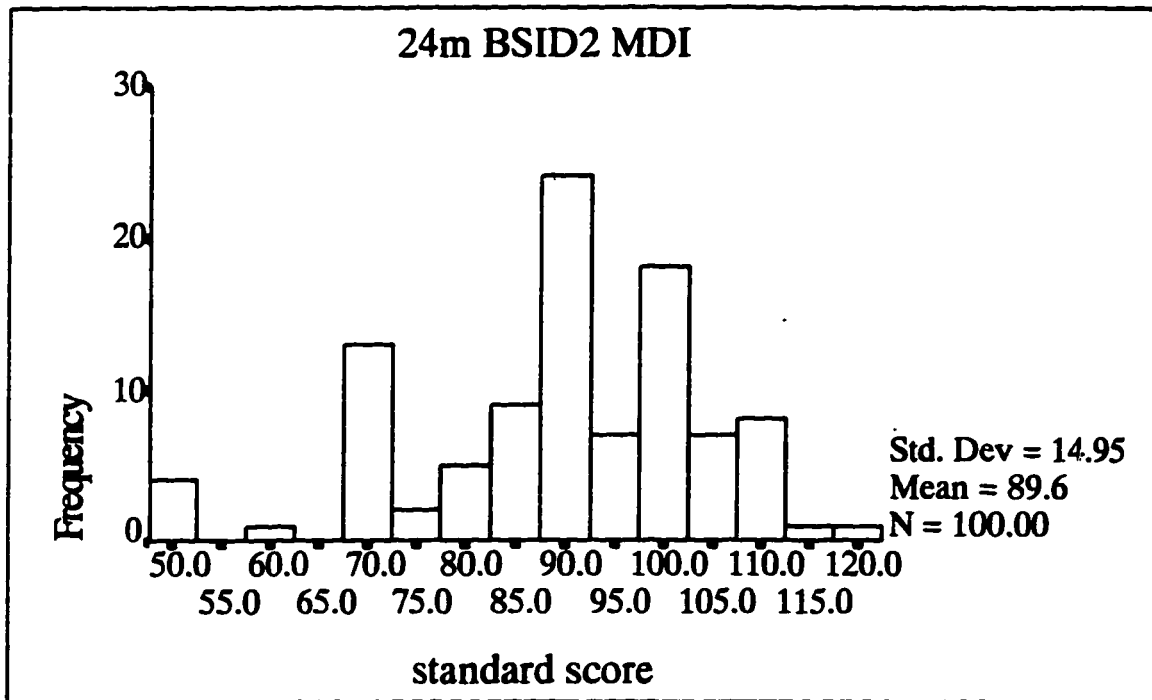






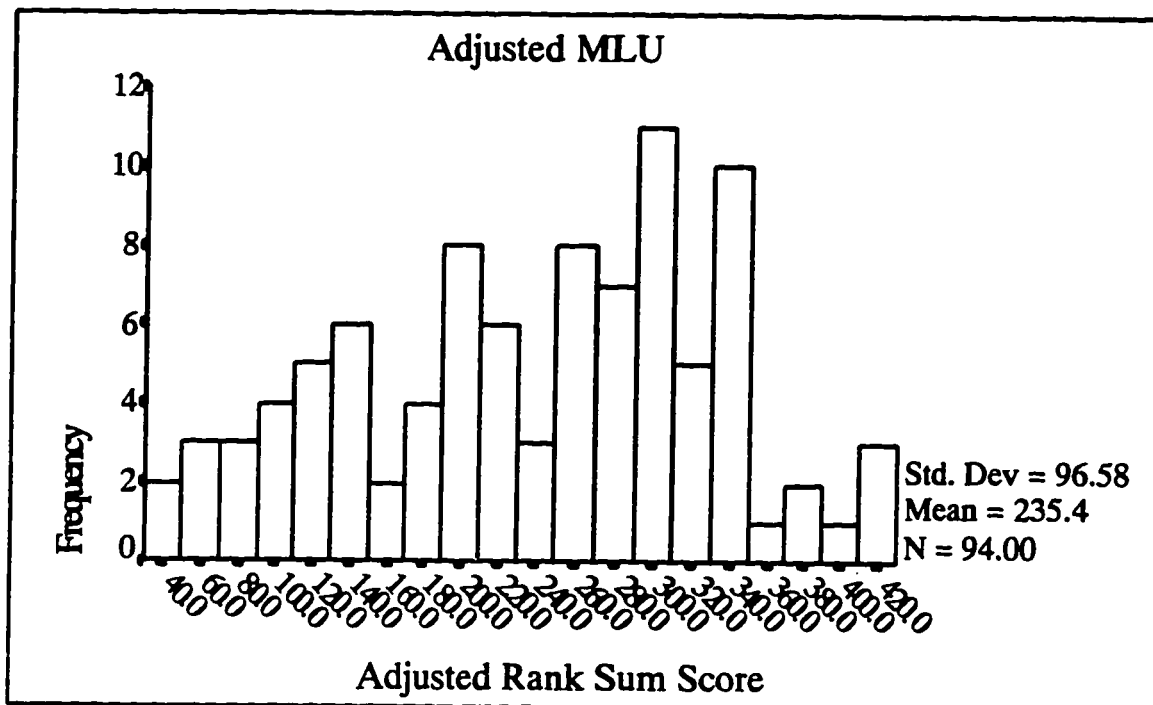
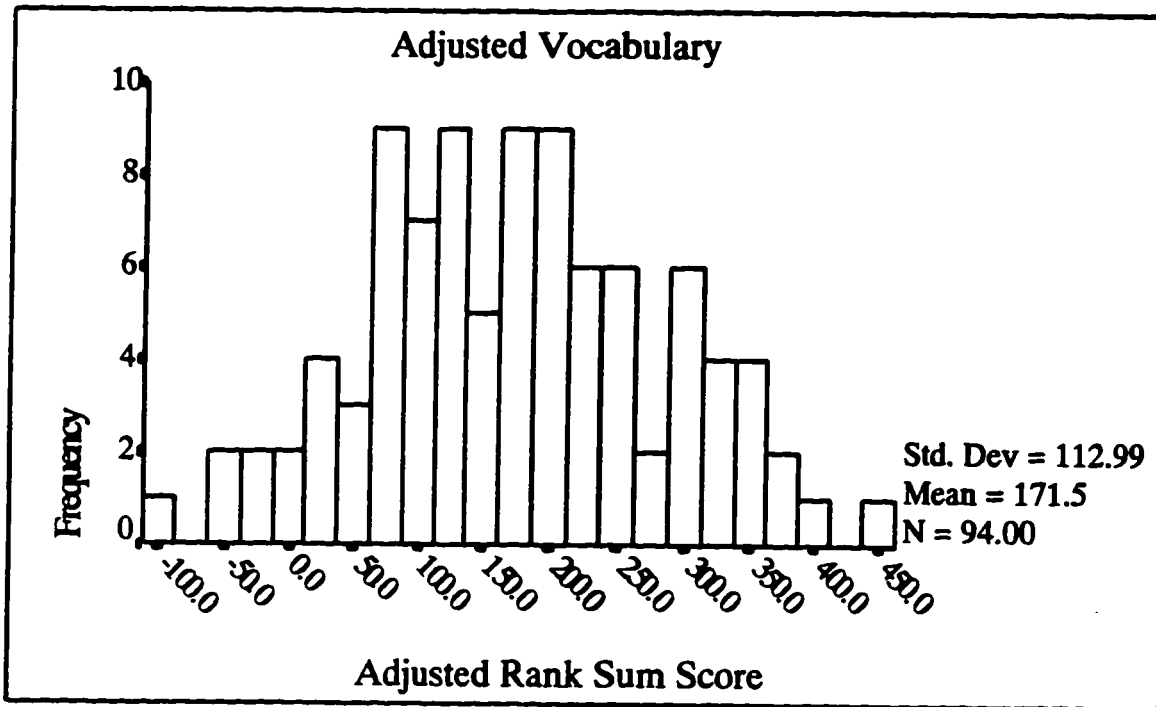


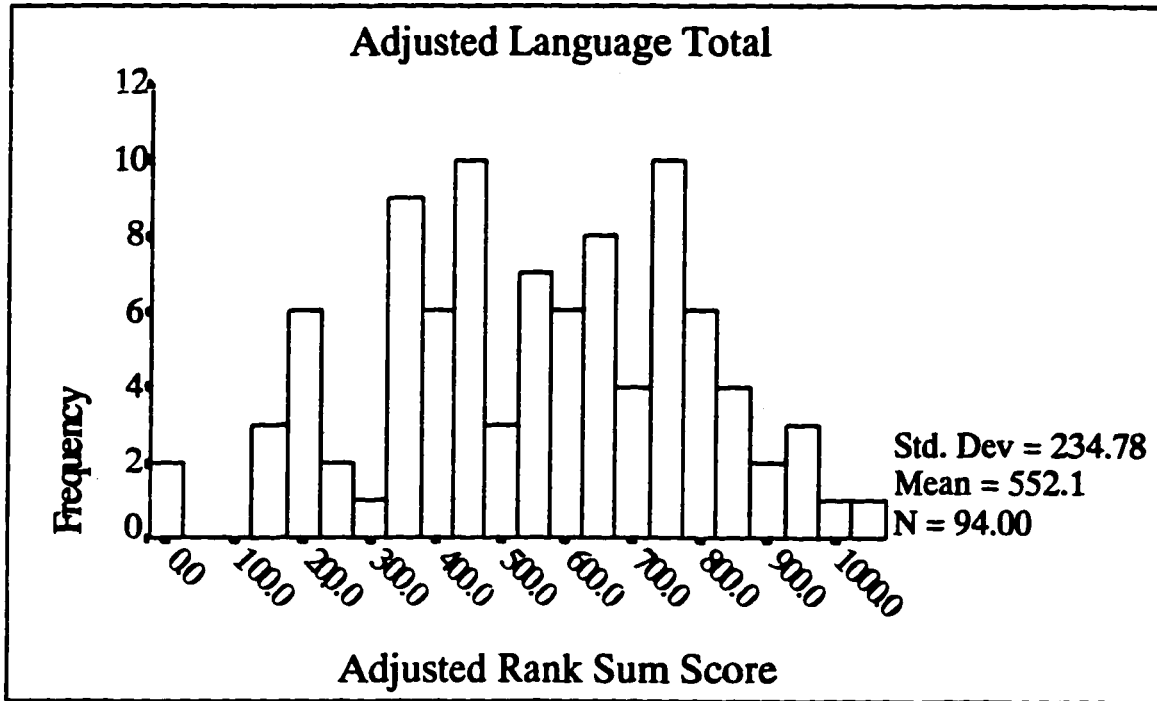


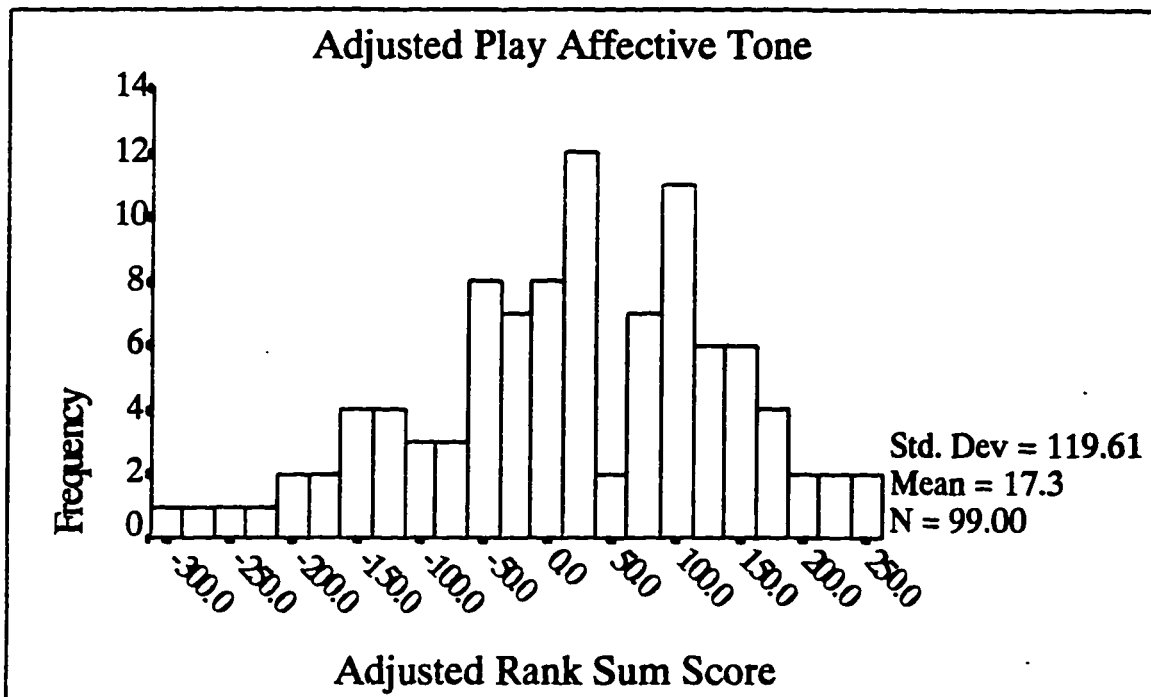
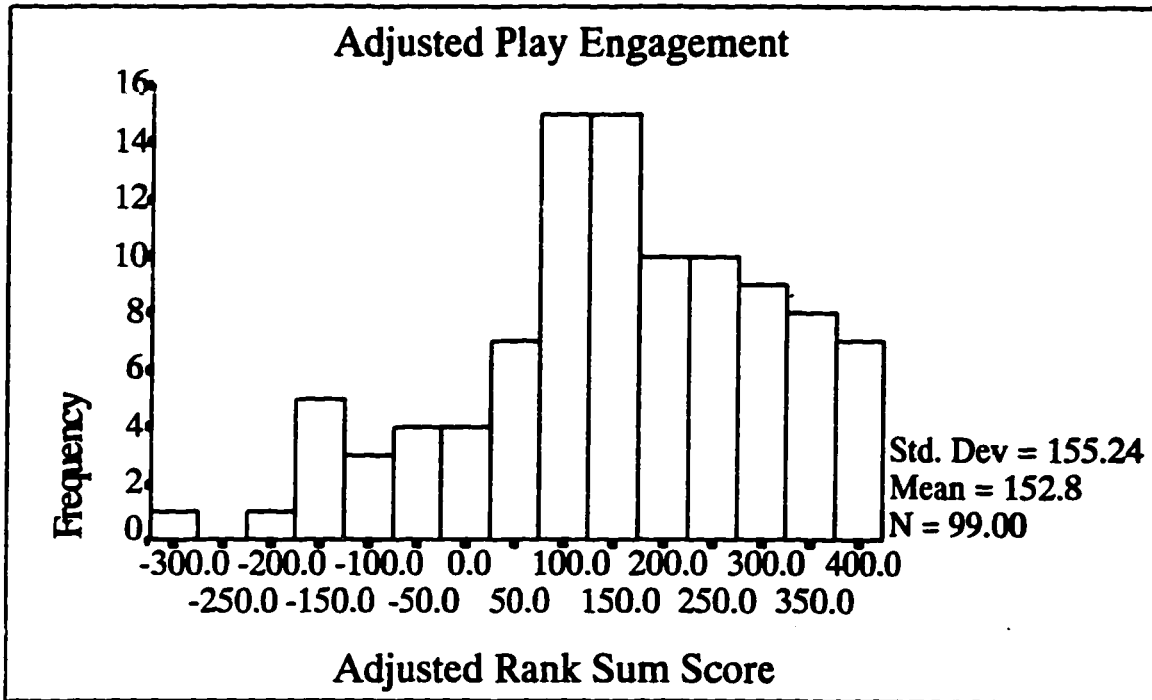


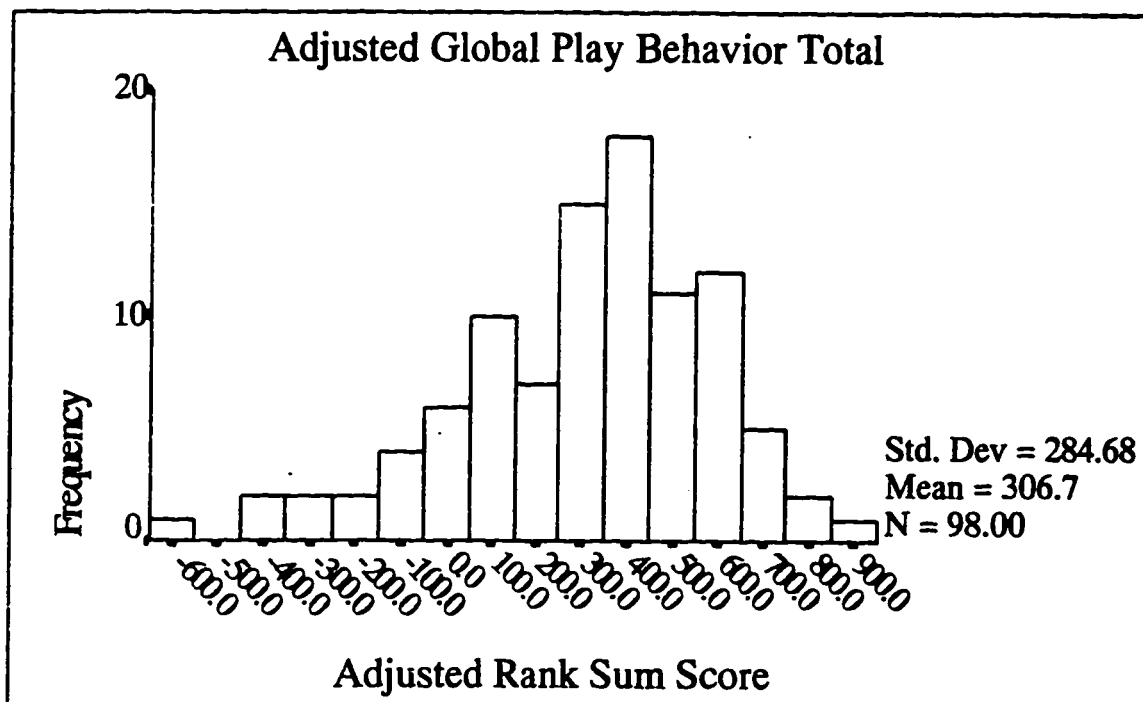
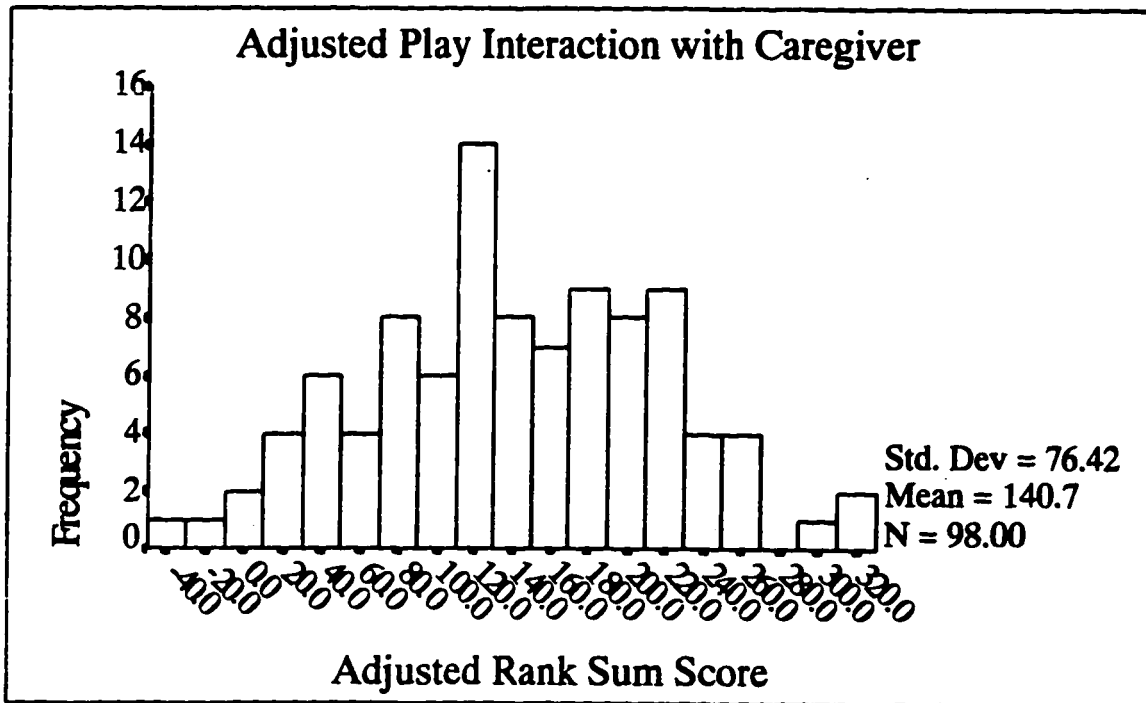
Appendix H. Histograms of Adjusted Child Outcomes by Group.

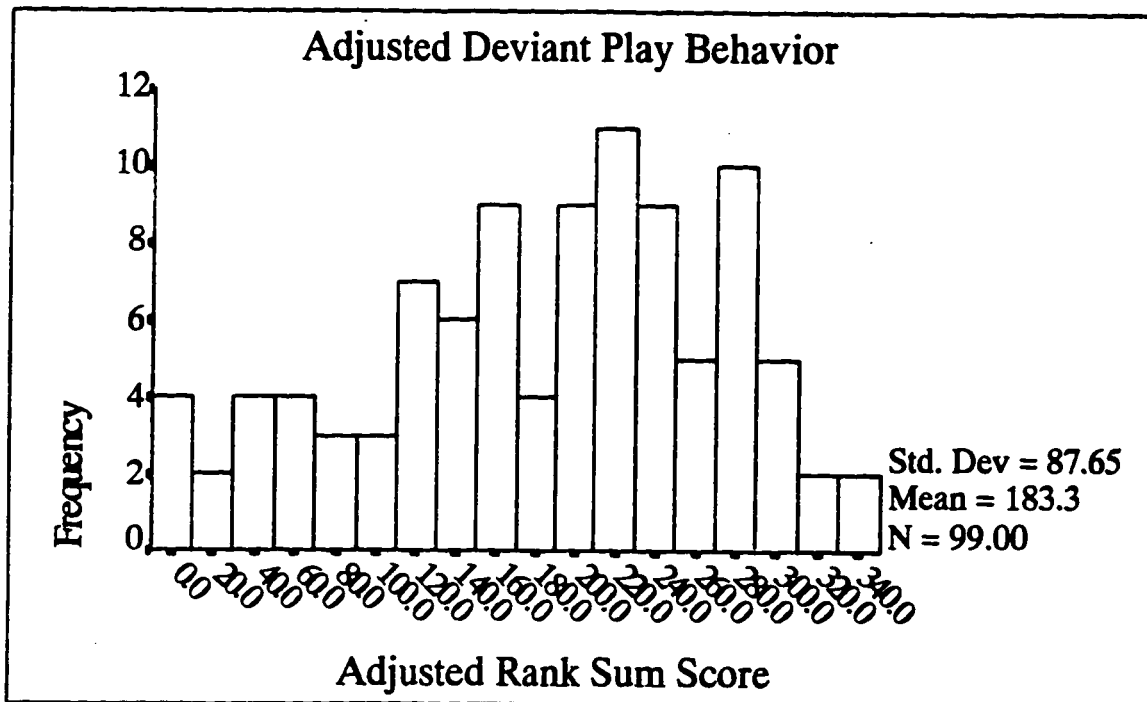
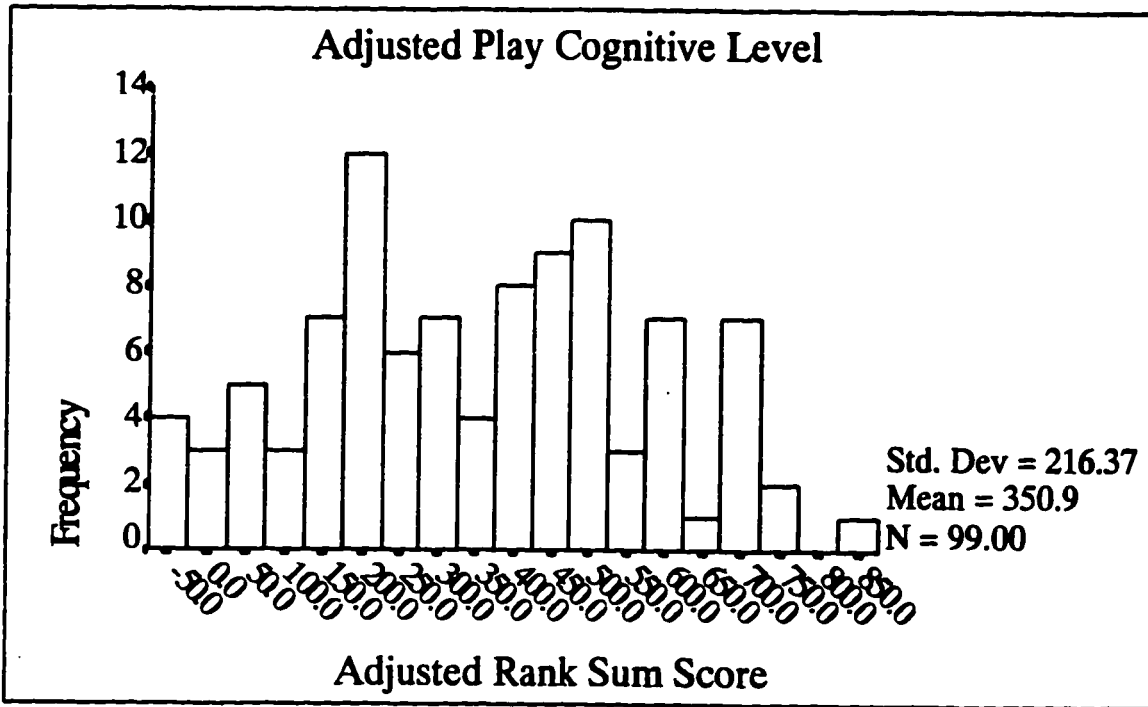
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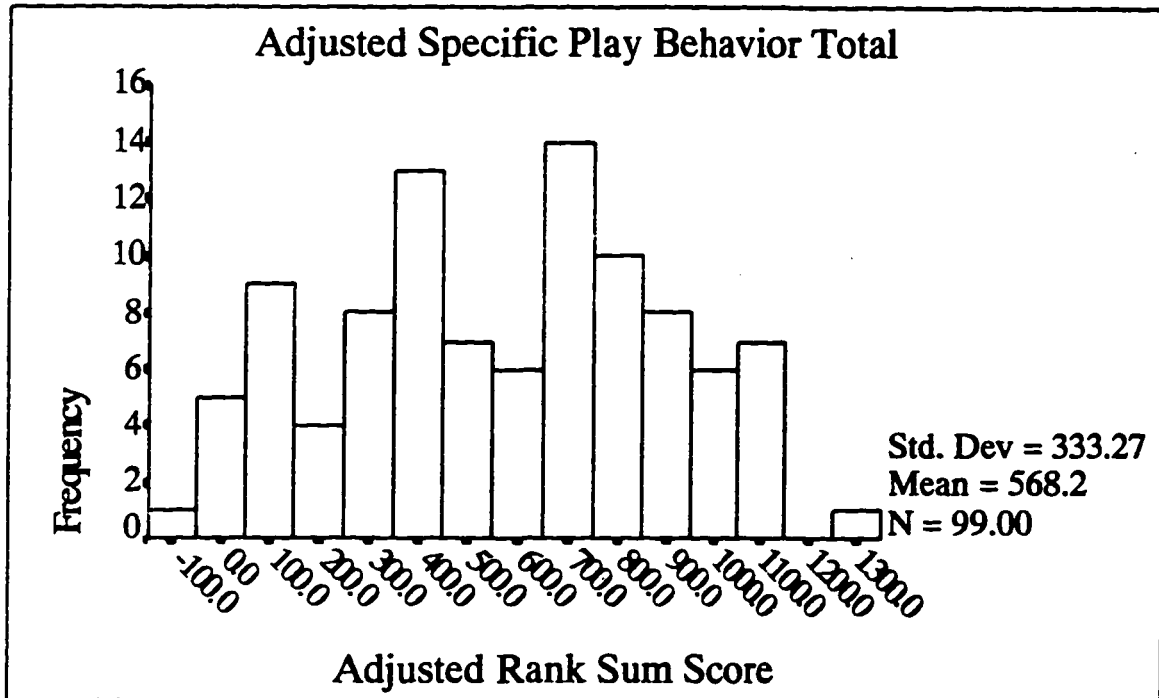
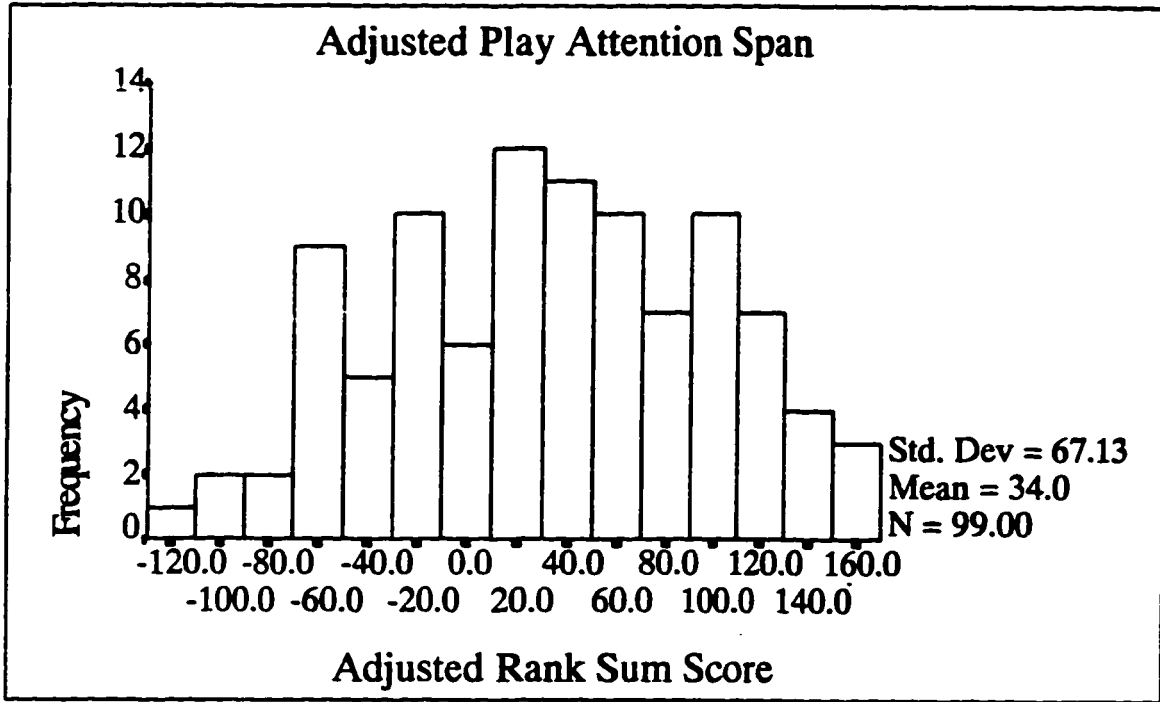


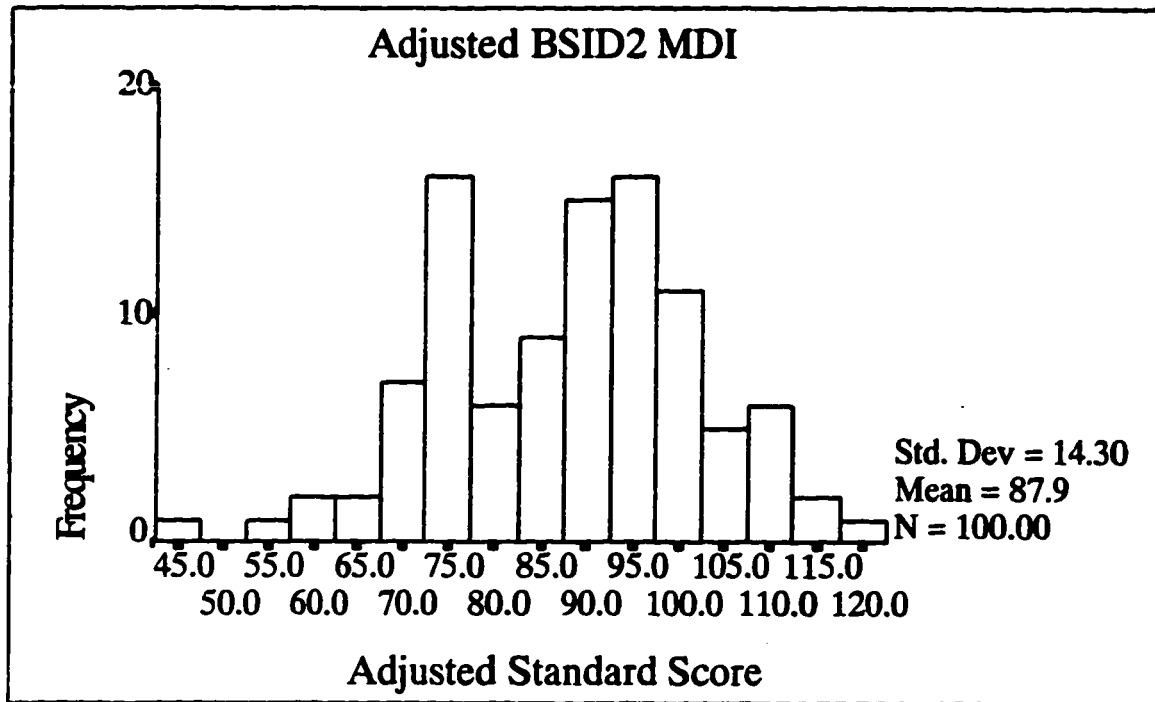




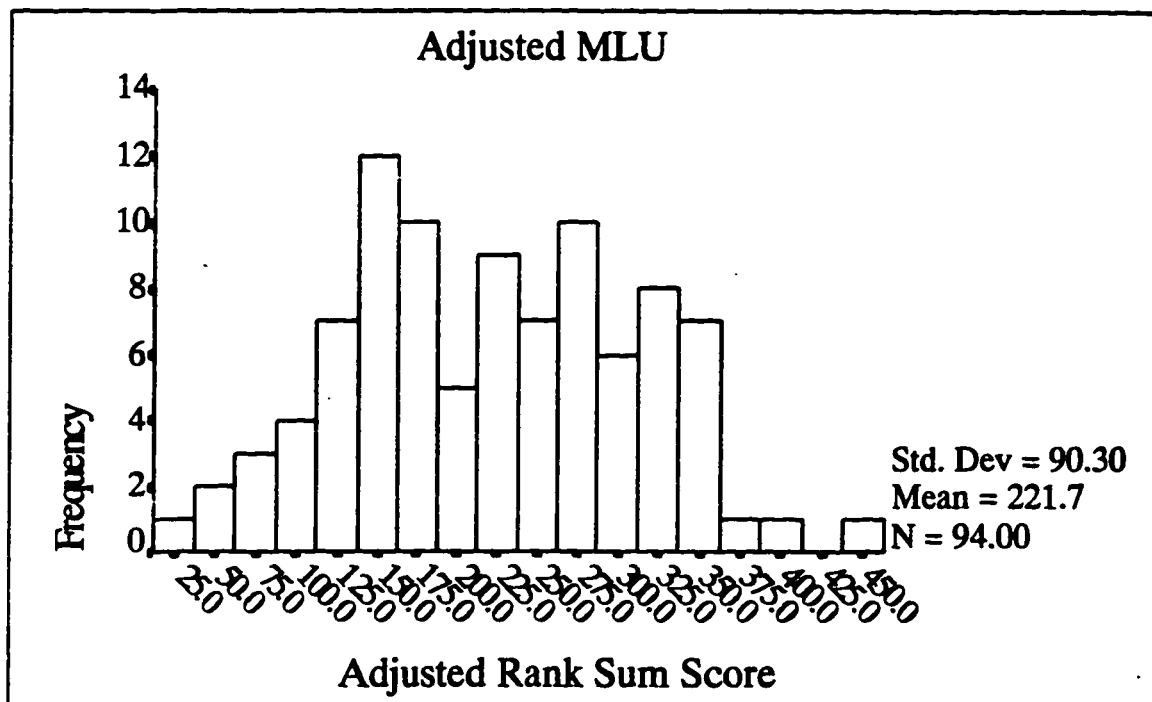
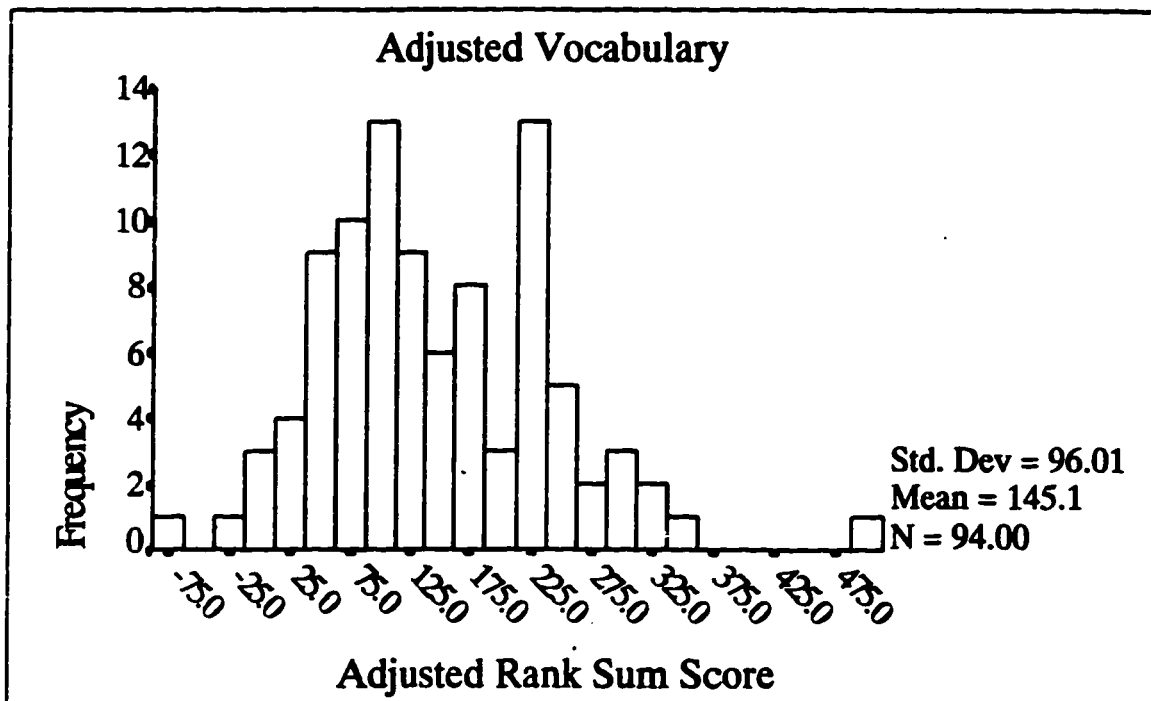


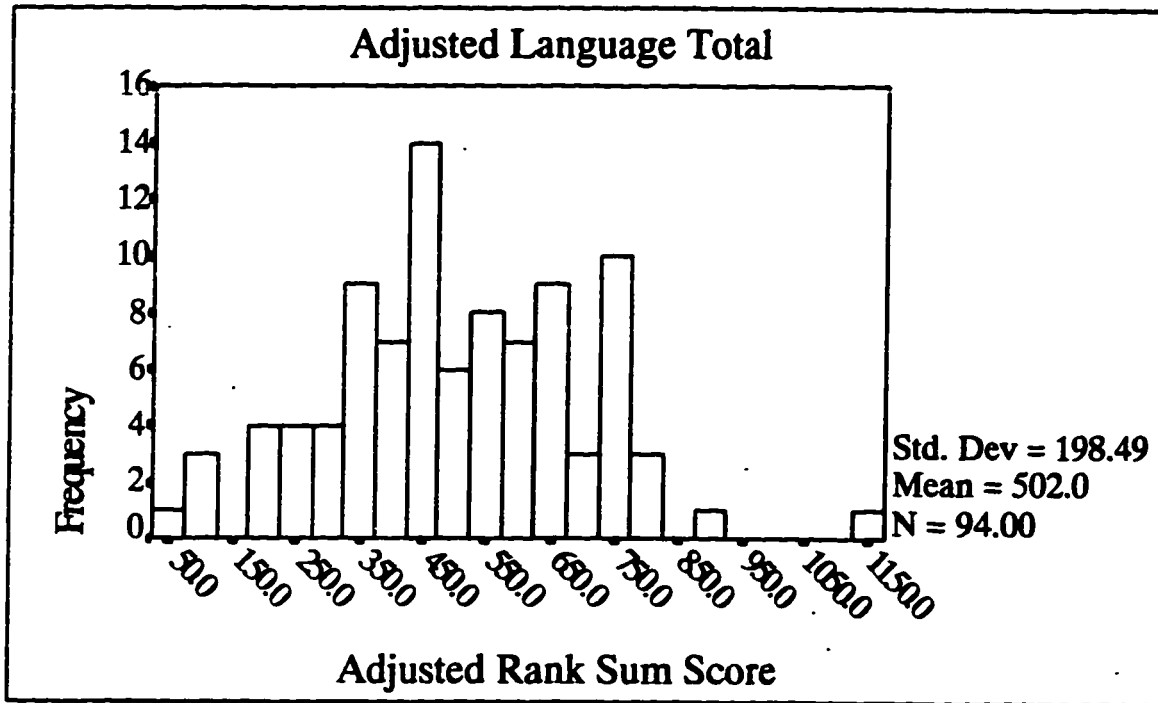


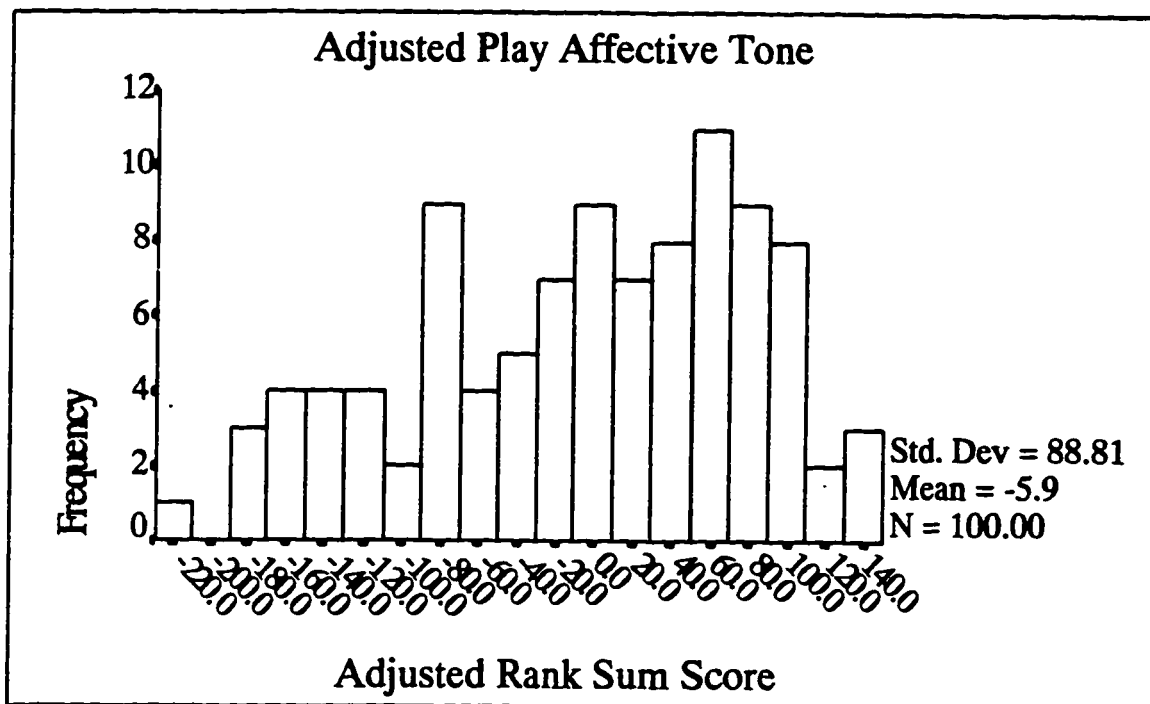
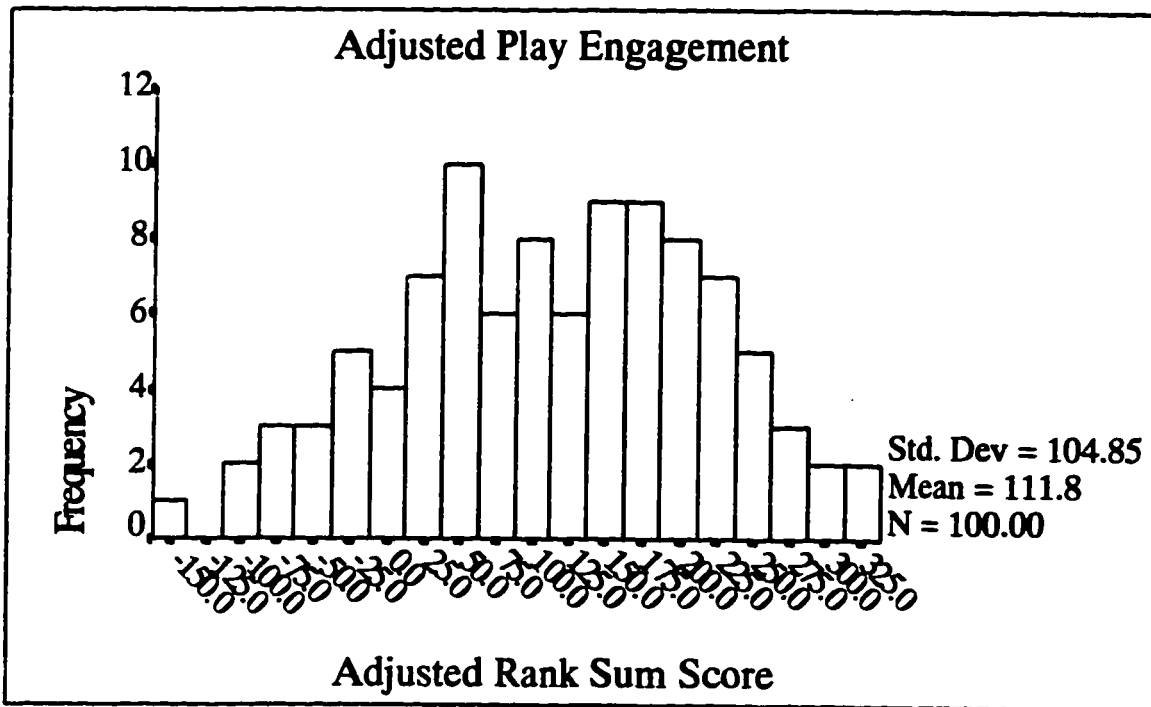


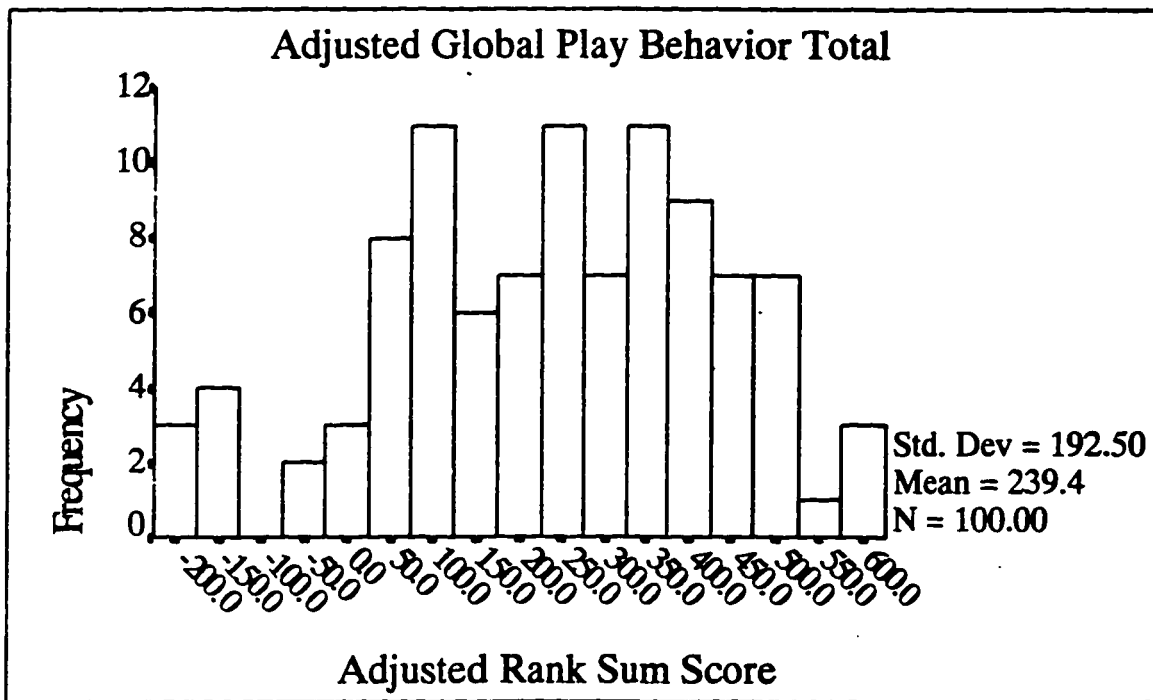
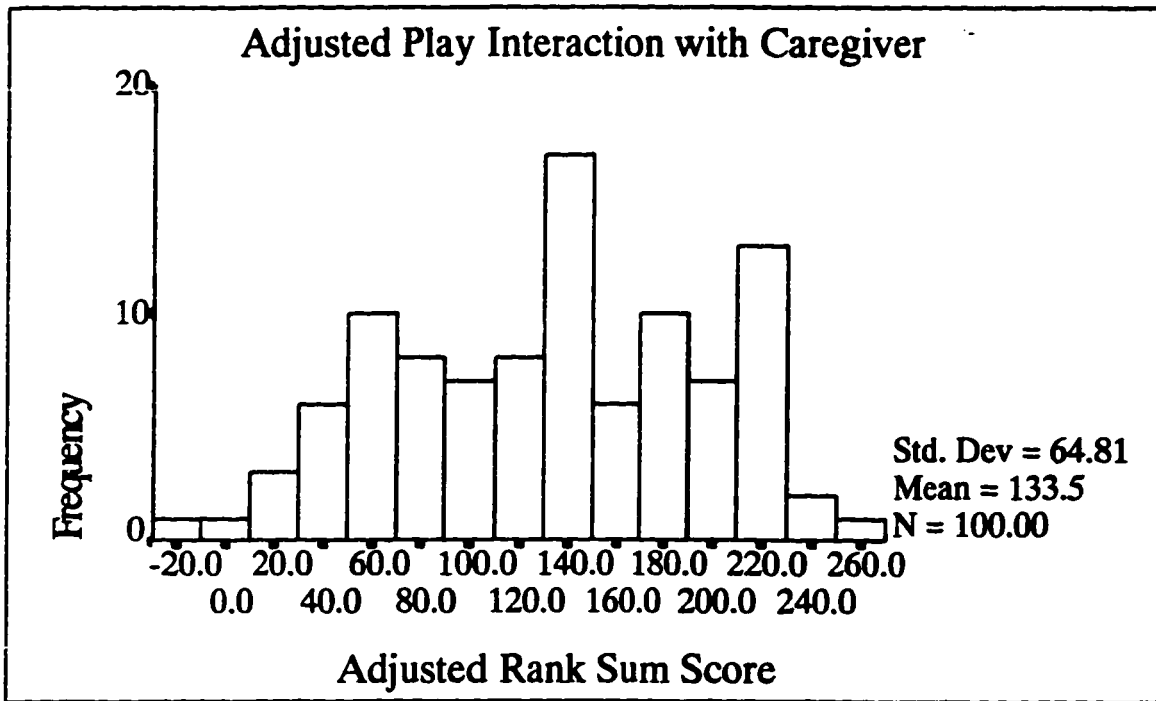


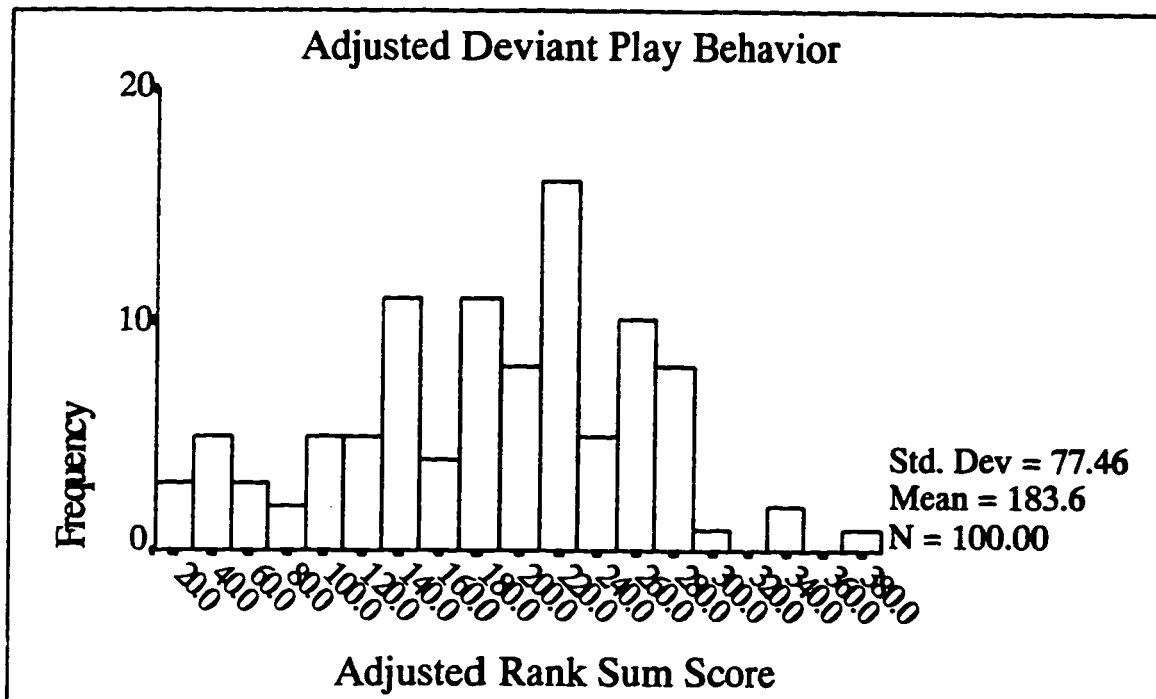
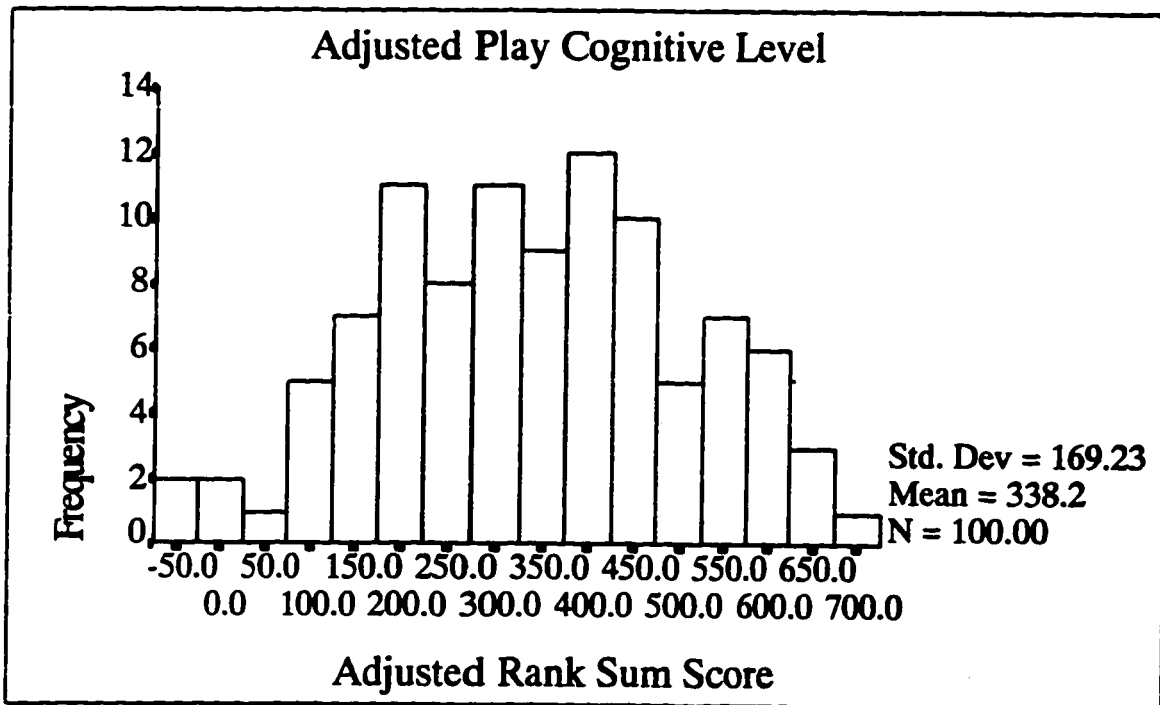
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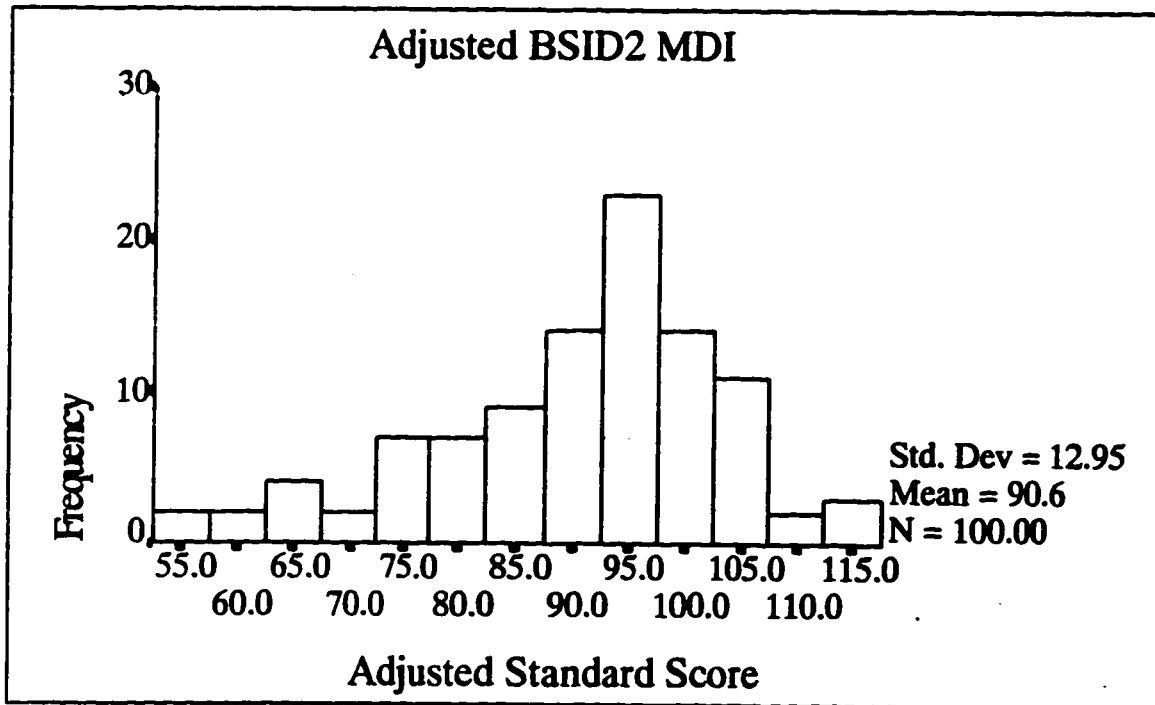


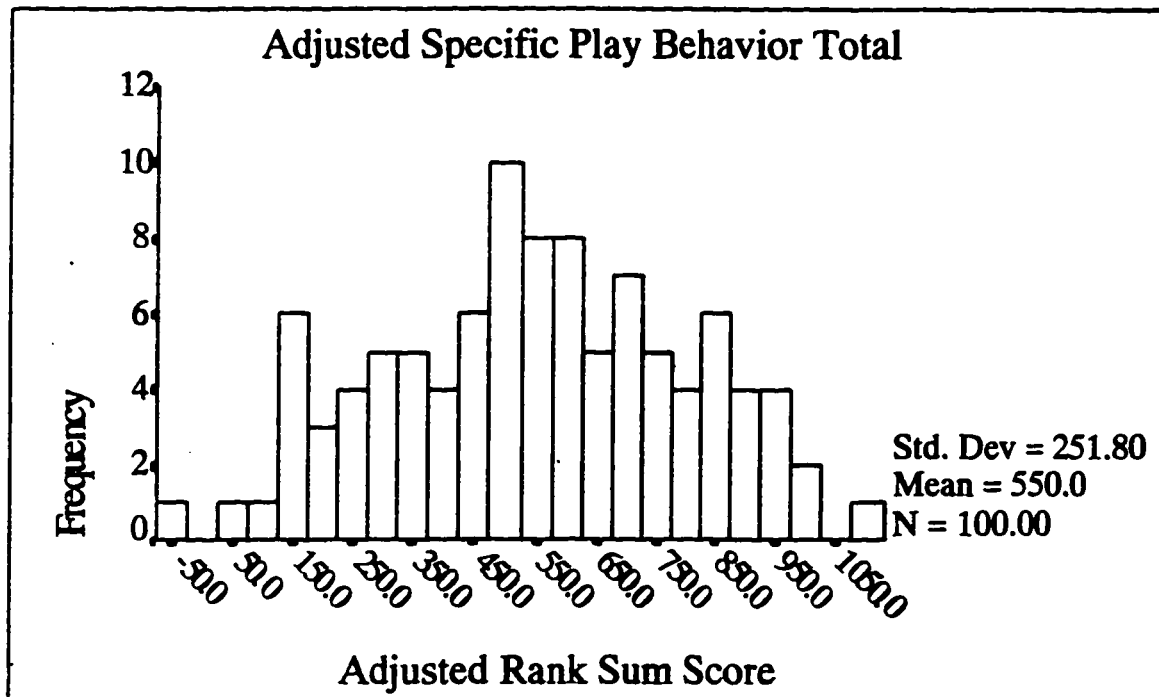
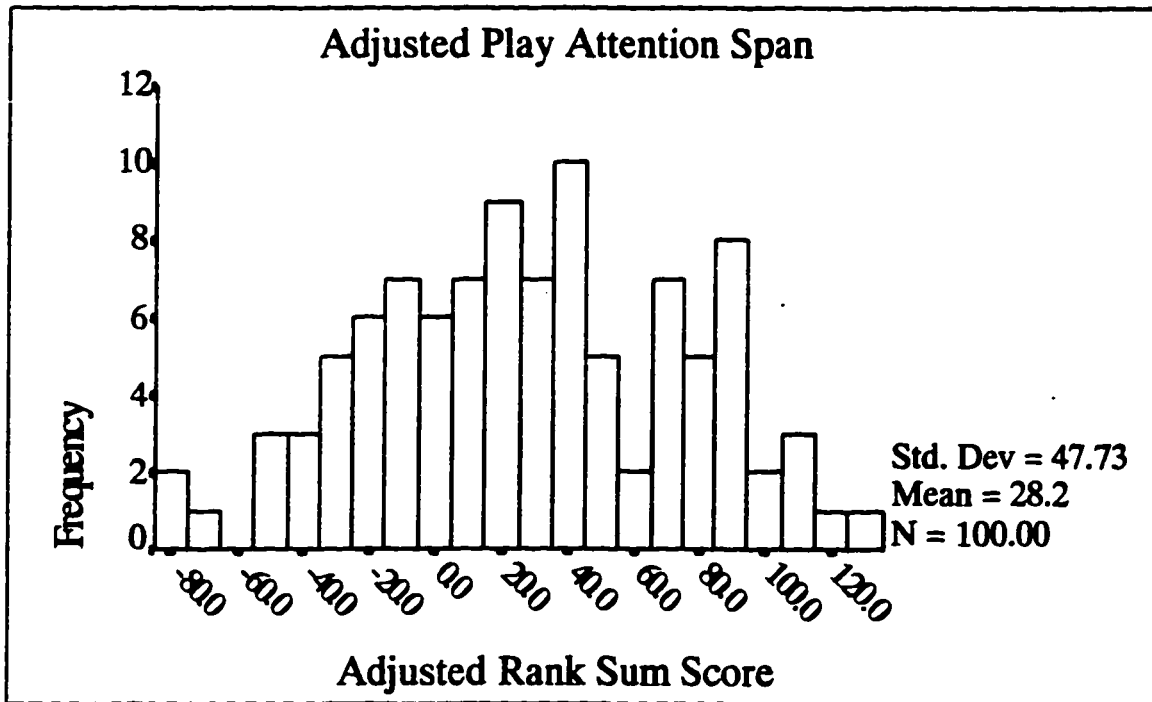












Vita

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EDUCATION:

- 1989 University of California, San Diego, La Jolla, CA, B.A.
Psychology, Cum Laude
- 1993 University of Washington, Seattle, WA, M.S.
Developmental Psychology
Thesis: "Developmental Changes in Internal State Language: Evidence From Linguistically Precocious Toddlers and Their Mothers."
- 1996 University of Washington, Seattle, WA, Ph.D.
Major: Developmental Psychology; Minor: Child-Clinical Psychology;
Breadths: Speech and Hearing Sciences and Physiological Psychology
Dissertation: "A Prospective Study of Prenatal Cocaine Exposure: Language, Play, and Global Cognitive Abilities in 2-Year-Olds."
(Chairperson of the Supervisory Committee: Professor Philip S. Dale)

HONORS AND AWARDS:

- 1995 Dissertation Award: The Graduate Student Research Fund, University of Washington
- 1996 Competitive Dissertation Award: The Gatzert Child Welfare Fellowship, University of Washington

PROFESSIONAL ORGANIZATIONS:

- | | |
|----------------|---|
| 1991 - present | Student Member, Society for Research in Child Development |
| 1994 - present | Student Member, American Psychological Association |
| 1996 | Student Member, International Society for Infant Studies |

RESEARCH EXPERIENCE:

1989-90 Research Assistant, University of California, Los Angeles, Neuropsychiatric Institute, Los Angeles, CA. Longitudinal study of the social and emotional development of children with Autism and Down syndrome. Supervision of laboratory research (recruitment, scheduling, videotaping); administration of a standardized language assessment for preschoolers; and observational assessment and coding of child affect from videotapes.

1992-1996 Graduate Research Associate, MOMS Project, Department of Obstetrics & Gynecology, University of Washington, Seattle, WA. Longitudinal study on the effectiveness of comprehensive drug and alcohol treatment for chemically-dependent women and their young children, maternal and child follow-up component. Supervision of undergraduate students; creation, management and analysis of large and complex computer database (includes data screening, editing, merging, univariate and multivariate analyses); observational assessment and coding of maternal involvement during play with their infants; co-authored publications and presentations of results.

1995-1996 Graduate Research Associate, Prenatal Cocaine Exposure Project, Department of Psychiatry and Behavioral Sciences, Fetal Alcohol & Drug Unit, University of Washington, Seattle, WA. A study focusing on the effects of prenatal cocaine exposure on toddler representational abilities (play and language) and global cognitive abilities. Observational assessment of the quality of toddler play; transcription of early child language; training and supervision of undergraduate and matriculated students; management and analysis of a large and complex computer database; co-author of upcoming publications and presentations. (Dissertation data was obtained from this project).

TEACHING EXPERIENCE:

1989 Undergraduate Teaching Assistant, Undergraduate Statistics, Department of Psychology, University of California, San Diego.

1990 - 1991 Graduate Teaching Assistant, Child Development, Department of Psychology, University of Washington.

1991 - 1992 Graduate Teaching Assistant, Psychology as a Social Science, Department of Psychology, University of Washington.

1995 Three-day workshop, "Early Childhood Development: An In-depth Overview for a Native American Residential School." Pierre Indian Learning Center, Pierre, South Dakota.

RECENT INVITED TALKS:

Toth-Sadjadi, S., & Muchmore, M. Internal State Language. Emotional Development graduate seminar, University of Washington, Seattle, WA. February 1995.

Toth-Sadjadi, S. Internal State Language. Developmental Psychology undergraduate course, University of Washington, Seattle, WA. April 1995.

Toth-Sadjadi, S. Prenatal Cocaine Exposure. Child Behavior Disorders undergraduate course, University of Washington, Seattle, WA. June 1995.

CLINICAL EXPERIENCE:

1993-1994 Co-Therapist, FAST TRACK Project, Department of Psychology, University of Washington, Seattle, WA. Longitudinal prevention and intervention study for young school-age children at high risk for developing conduct disorder. Co-conducted weekly social skills training sessions according to the social/emotional intervention program of the PATHS Curriculum developed at the University of Washington.

1993-1995 Psychometrist, CDC Secondary Disabilities Project, Department of Psychiatry & Behavioral Sciences, Fetal Alcohol and Drug Unit, University of Washington School of Medicine, Seattle, WA. Clinical study of the secondary disabilities of fetal alcohol-affected individuals (e.g., school, legal, and mental health problems). Administration of multiple psychological instruments to alcohol-affected children, adolescents, and adults, and report writing of assessment results.

MANUSCRIPTS:

Toth-Sadjadi, S. Developmental changes in internal state language: Evidence from linguistically precocious toddlers and their mothers. Unpublished master's thesis, University of Washington, Seattle, WA, 1993.

Toth-Sadjadi, S. The development of internal state language in linguistically precocious toddlers. In E. Clark (Ed.), The Proceedings of the Twenty-fifth Annual Child Language Research Forum. Stanford, CA: CSLI. 1993.

Toth-Sadjadi, S., & Dale, P. S. Sources of influence on the development and use of internal state language in young children selected for linguistic precocity. Under editorial review.

Stewart, K., Carmichael Olson, H., Toth-Sadjadi, S., & Richardson, P. The validity of the movement assessment of infants screening test for infants with prenatal polydrug exposure. Under editorial review.

Toth-Sadjadi, S., Carmichael Olson, H., & Hanna, E. Predictors of decline in developmental scores among infants born to substance-abusing women. Manuscript in preparation.

PRESENTATIONS:

Toth, S. The internal state language of linguistically precocious toddlers. Western Psychological Association, Portland, OR. April, 1992.

Toth-Sadjadi, S. The development of internal state language in linguistically precocious toddlers. Twenty-fifth Annual Child Language Research Forum, Stanford, CA. April, 1993.

Toth-Sadjadi, S., Muchmore, M., Greenberg, M. T., & Dale, P. S. Linguistic communication between developmentally delayed children and their mothers. American Psychological Association, Los Angeles, CA. August, 1994.

Muchmore, M., & Toth-Sadjadi, S. Expressive language, internal state language, and discourse patterns in developmentally delayed preschoolers and their mothers. Society for Research in Child Development, Indianapolis, Indiana. March, 1995.

Toth-Sadjadi, S., Carmichael Olson, H., Hanna, E. Predictors of decline in developmental scores among infants born to substance-abusing women. International Conference of Infant Studies, Providence, Rhode Island, April 1996.

Carmichael Olson, H., Toth-Sadjadi, S., Hanna, E. Substance abusing women and their young infants: Early child outcome and sources of vulnerability. International Conference of Infant Studies, Providence, Rhode Island, April 1996.