Effects of Prenatal Tobacco Exposure
on Newborn Auditory
Information Processing Ability

by

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Abstract

Numerous physical and cognitive effects of prenatal tobacco-exposure have been well documented in the literature. Animal studies indicate that tobacco is a neuroteratogenic agent, although findings with humans have been inconsistent. Studies with human infants investigating the effects of tobacco-exposure during pregnancy have been marred by unreliable subject identification procedures, poor control over confounding factors, and invalid measures of CNS integrity. The literature on the physical and cognitive effects of prenatal tobacco-exposure is reviewed and a study comparing tobacco-exposed infants with a matched control group (N=48) at birth and at 3-weeks of age (N=18) on deficits of auditory information processing is presented. Maternal smoking was identified through self-report and verified using maternal saliva cotinine analyses. The reporting channel of maternal self-report of smoking status (i.e., self-administered questionnaire versus face-to-face interview) was assessed to determine if the method of reporting influenced the accuracy of mothers' self-report. Prenatal tobacco-exposure was associated with impairments in neonatal auditory information processing. Specifically, fetal tobacco exposure was found to interfere with newborns' ability to habituate to a sound source, but their ability to orient and recover responding to novelty was not consistently affected. A similar pattern of results was found at 3-week follow up, suggesting that the adverse effects of prenatal exposure last beyond the nicotine withdrawal period. The results imply that prenatal tobacco exposure is associated with impairments in information processing. These differences are discussed in terms of impairments in arousal regulation. These auditory processing deficits may be related to the language difficulties associated with prenatal tobacco exposure found in childhood.

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Effects of Prenatal Tobacco Exposure

On Newborn Information Processing

Nicotine Exposure: Prevalence and General Effects on Men, Women, and Children

The detrimental effects of smoking have been widely explored over the past four decades. The results of smoking can be devastating to the individual. In Canada there were an estimated 27,867 male and 13,541 female deaths in 1991 attributable to smoking (Health Canada, 1996). Smoking remains the number one preventable cause of death and disease in Canada. It is estimated that smoking prematurely kills three times more Canadians than car accidents, suicides, drug abuse, murder, and AIDS combined (Health Canada, 1996). Women and men who smoke are at increased risk for coronary heart disease, lung cancer, breathing problems (emphysema and chronic bronchitis) and cancer of the throat, mouth, larynx, esophagus, pancreas, kidney, and bladder (Health Canada, 1996). Women who smoke also have increased risks that men who smoke do not have. These risks include lower fertility, stroke, cancer of the cervix, osteoporosis, menstrual and menopausal problems. In addition the pregnancies of women who smoke are more likely to result in miscarriage, premature birth and stillbirth and the infants are at increased risk of low birthweight and sudden infant death syndrome (Health Canada, 1996).

Given that 25% of women in Canada smoke and that the prevalence is highest among women aged 20 - 44 years (26.2%), children are often the ultimate victims of women who smoke, both during pregnancy and following birth (Statistics Canada, 1997). As well as the above effects, it has been noted that smoking during pregnancy and in the home creates further risks to the child, such as impaired lung function; eye, nose and throat irritation; a greater likelihood of respiratory illness, including asthma, pneumonia, and bronchitis; up to three times the normal risk of heart disease; up to three and a half times the normal risk of chronic middle ear infection; and increased suffering allergies and other pre-existing conditions (Health Canada, 1996). Given the enormity of the health risks due to smoking during pregnancy, it is surprising to note that in Canada more than half (58%) of women smokers continued to smoke during their last pregnancy and almost three-quarters (74%) were regularly exposed to their own or their partners' smoke while pregnant (Health Canada, 1996). In Nova Scotia specifically, it has recently been reported by the Tobacco Control Unit that 27.6% of women delivering in 1997 reported smoking during pregnancy at hospital discharge (Nova Scotia Atlee Perinatal Database, 1999). Clearly, smoking during pregnancy has severe and detrimental effects on mothers who choose to smoke as well as on the children of smokers.

Effect of Prenatal Nicotine Exposure on Infant Physical Development

There are direct effects of prenatal exposure to nicotine on the physical development of the fetus. The most well documented effect is low birth weight (Ahlborg & Bodin, 1991; Castro, Azen, Hobel, & Platt, 1993; Rush & Callhan, 1989; Streissguth, 1986; Streissguth, Sampson, Barr, Bookstein, & Carmichael, 1994). In an early report (Butler, Goldstein, & Ross, 1972) maternal smoking was associated with an average reduction of 170 grams in birthweight. In another study maternal tobacco use was associated with an average decrease in birthweight of 200 grams (Castro, et al., 1993).

Cigarette smoking during pregnancy has also been identified as a risk factor for sudden infant death syndrome and fetal mortality. Haglund and Cnattingius (1990) in a study of 279,938 live births in Sweden found that the overall rate of SIDS was 0.7 per 1000. A clear dose-response relation by amount smoked was observed. Smoking up to nine cigarettes per day doubled the risk of SIDS and smoking 10 or more cigarettes per day nearly tripled the risk of SIDS compared to nonsmokers (Haglund & Cnattingius, 1990). Butler et al. (1972) reported a 28% increase in late fetal and neonatal mortality rate even after adjustment for other variables, such as maternal parity, socioeconomic status, maternal age and height, as well as gender and gestational age of the infant.

It is known that nicotine readily crosses the placenta and enters the bloodstream of the fetus. However, there is no clear evidence that maternal cigarette smoking produces any type of organic damage in the embryos and fetuses. Possible effects of cigarette smoking that might damage the brains of fetuses and embryos include the direct toxic effects of tobacco, low maternal food intake, and chronic or intermittent hypoxia (Naeye, 1992). Naeye (1992) reports that there are over 4,000 constituents in tobacco and only a few have been tested for their biologic activity and, therefore, almost nothing is known about their individual effects on the developing fetus. Also, there is no evidence that poor nutrition deprives fetuses of nutrition when women smoke during pregnancy. In fact, women who smoke during pregnancy report higher caloric intake than nonsmokers (Papoz, Eschwege, & Pequinot, 1982), although, the nutritional value of this increased intake is not known. One mechanism by which cigarette smoke may damage the developing brain of the fetus is hypoxia. Women who smoke during pregnancy have increased placental vascular resistance (Howard, Hosokawa, & Maguire, 1987) which could be a direct effect of nicotine (Naeye, 1992). Increased vascular resistance may restrict blood flow to the placenta and reduce the amount of oxygenated blood to the fetus (Howard et al., 1987). When a pregnant woman smokes a cigarette, her blood pressure is reduced for five to 15 minutes, which reduces the flow of oxygenated blood from the uterus to the placenta (Lehtovirta & Forss, 1978; Morrow, Ritchie, & Bull, 1988). It has been found that infants born to smoking mothers have more carboxyhemoglobin in their blood at birth than infants born to nonsmokers (Cole, Hawkins, & Roberts, 1972). Carboxyhemoglobin can lead to fetal hypoxia because it replaces oxyhemoglobin that normally releases oxygen to the fetal cells. This in utero oxygen deprivation may interfere with the developing fetal brain and contribute to later cognitive deficits.

In addition to the indirect effects of nicotine on the developing fetal brain through decreased oxygen and nutrient supply, nicotine readily crosses the blood-brain barrier and has been shown to interfere directly with fetal brain development. Animal studies have shown that prolonged fetal exposure to nicotine results in an increase in the number of nicotinic cholinergic binding sites (Navarro et al., 1989; Slotkin, Orband-Miller, & Queen, 1987), reduces neuronal proliferation (Navarro et al., 1989) and differentation (Slotkin Greer, Faust, Cho, and Seidler, 1986), delays cell maturation (Navarro et al., 1989; Slotkin et al., 1986), and increases levels of dopamine and norepinephrine in the forebrain (Lichtensteiger, Ribary, Schlumpf, Odermatt, & Widmer, 1988). The metabolism of central catecholamine systems has been shown to remain disturbed into adulthood among rats prenatally exposed to nicotine (Lichtenstriger et al., 1988). The interference of prenatal nicotine exposure in the early biochemical events that regulate the growth and development of the CNS may result in various functional and/or structural abnormalities of the CNS (Nash & Persaud, 1988). It has been speculated that catecholamine disturbances induced by prenatal exposure to nicotine may be linked to both behavioral and learning problems (Lichtensteiger et al., 1988). In young rats, lesions of the dopamine system have been shown to result in motor hyperactivity and decreased performance while lesions of the norepinephrine systems have produced learning deficits (Raskin, Shaywitz, Cohen, & Anderson, 1984, as cited in Lichtensteiger et al., 1988).

Although, it should not be assumed that the results of these animal studies will generalize to the human population, the evidence suggests that prenatal exposure to nicotine may interfere with fetal brain development. If these effects do occur in humans, it is possible that any disturbances in normal brain development may be evident through deficits in higher order brain processes.

Effect of Prenatal Nicotine Exposure on Infant and Child Cognitive Development

Measurable deficits in cognitive functioning of infants and children born to smoking mothers have been identified over the past two decades. Cigarette smoking during pregnancy has been related to the following behavioral and performance measures: poor auditory habituation and orientation, and lower mental and motor scores in infancy; decrements in reading, arithmetic, general abilities and IQ; and learning difficulties, hyperactivity, impulsivity and neurological soft signs in childhood (Streissguth, 1986). However, most of these studies have not adjusted for alcohol and other drug use as well as potential psychosocial confounding variables, such as socioeconomic status, maternal education, postnatal exposure to cigarette smoking, and /or birth order, which have been previously identified to impact on these same outcomes (Streissguth, 1986).

Detrimental effects of prenatal exposure to nicotine on newborn neurobehavioral functioning have been examined and the results have been inconsistent (Fried & Makin, 1987; Jacobson, Fein, Jacobson, Schwartz, & Dowler, 1984; Picone, Allen, Olsen, & Ferris, 1982; Richardson, Day, & Taylor, 1989; Saxton, 1978). The most frequently employed measure of newborn neurobehavioural functioning is the Neonatal Behavioral Assessment Scale (NBAS; Brazelton, 1984). This scale consists of items assessing 27 newborn behaviors and 20 reflexes, typically summarized according to seven cluster scores: Habituation, Orientation, Motor Behavior, Range of State, State Regulation, Autonomic Stability, and Abnormal Reflexes. Saxton (1978) published the first report using the NBAS to investigate the neurobehavioral functioning of infants prenatally exposed to nicotine. Infants of mothers who smoked more than 15 cigarettes per day had decreased scores on auditory habitation and two measures of auditory orientation and were more difficult to console than control infants. The infants were all of normal birthweight and were matched for socioeconomic status, maternal age, and parity.

Picone et al. (1982) replicated the results of Saxton (1978), employing the NBAS at 2 days, 3 days, and 2 weeks to assess newborn neurobehavioral performance. It was found that maternal cigarette smoking significantly affected habituation, orientation, and autonomic regulation (e.g., tremors and startles). Specifically, when the habituation and orientation scores were divided into their auditory and visual components, there were clear effects on the auditory responsiveness of the infant. Infants were more likely to habituate to auditory stimuli, but were less likely to orient to the source of the sound. These infants also had poorer autonomic regulation, (e.g., more tremors and startles) than non-exposed infants. However, alcohol and caffeine consumption were not controlled in this study and it was not clearly stated what other variables were considered.

In a prospective study of 250 infants, Fried and Makin (1987) investigated neonatal behavioral correlates using the NBAS. The findings of previous studies (Picone et al., 1982; Saxton, 1978) were supported by this study. Fried and Makin (1987) found that maternal cigarette smoking was associated with increased tremors and poorer auditory habituation as compared to a group of controls. However, 18.8 % of the subjects also used marijuana and 40.8% used alcohol (moderately to heavily). Therefore, it is not clear whether the effects of nicotine exposure were compounded by the interaction with these two other drugs. However, the effects of smoking on the NBAS differed from the effects of both alcohol and marijuana, and the effects of nicotine remained after controlling for alcohol and marijuana use.

Two other studies employing the NBAS failed to find nicotine-associated deficits in infants' performance on the NBAS (Jacobson et al., 1984; Richardson et al., 1989). Jacobson et al. (1984) found a similar relationship between smoking and poorer auditory habituation and orientation but this pattern failed to reach significance after controlling for other variables (e.g., SES and caffeine consumption). However, the previously mentioned decrease in irritability found by Fried and Makin (1987) was replicated. Richardson et al. (1989) conducted a prospective study regarding the effects of prenatal substance use (alcohol, marijuana, and tobacco) on the neonatal behavior of 373 full-term infants. They failed to find any significant effects of irritability, habituation, or orientation. However, 75% of the subjects had missing data on the habituation cluster. The only significant predictor of NBAS performance was NBAS examiner. It was not clearly stated which possible confounding variables were considered in their analysis.

In summary, the studies investigating newborn neurobehavioral functioning employing the NBAS have provided inconsistent evidence regarding the specific detrimental effects of prenatal nicotine exposure, particularly with regard to auditory stimuli. Some researchers have found impairments in auditory habituation and orientation, while others have not. In many of these studies the methodology employed while using the NBAS was not fully discussed. It has been shown that the NBAS is extremely sensitive to examiner effects (Richardson et al., 1989) and, therefore, differing methodologies may account for some of these discrepant findings. It was also not clear from the majority of studies what specific confounding variables were considered. Many of the studies were investigating the effects of tobacco along with marijuana, alcohol, and/or caffeine and, therefore, the specific effects of nicotine cannot be reliably ascertained. Although the data are not entirely consistent there is evidence that nicotine may selectively affect the development of the newborn's auditory system

Studies following children prenatally exposed to nicotine into early and middle childhood have provided evidence for small, but consistent deficits of prenatal nicotine exposure on later cognitive functioning. Several extensive longitudinal studies as well as individual initiatives have provided equivocal evidence regarding the specific detrimental effects of nicotine exposure on the cognitive functioning of children.

Longitudinal Studies

The first longitudinal investigation of the effects of cigarette smoking on the infant was the British National Child Development Study (Butler & Goldstein, 1973; Rush & Callahan, 1989; Streissguth, 1986; Streissguth et al., 1994). This study collected data on over 16,000 live births during one week in 1958. This study was not originally intended to investigate the effects of maternal smoking; however, data regarding the smoking behavior of all participants was gathered at delivery or shortly after, along with a number of other variables. These children were followed up at age seven and eleven (Butler & Goldstein, 1973). At age seven, the children born to mothers who smoked showed an average decrease in reading ability of four months compared to those born to nonsmokers. This finding was still evident after controlling for mothers' age, socioeconomic status, number of children in the household, and sex of the child. At age eleven the same pattern was observed. The average difference among children whose mothers smoked more than ten cigarettes per day compared to nonsmokers was a three month decrement in general ability, four month decrement in reading comprehension, and five months decrement in mathematics (Rush & Callahan, 1989; Streissguth, 1986; Streissguth et al., 1994). Another research team followed up the same children at age 16 and found that children born to smokers were one-eighth of a standard deviation lower in reading and one-fifth of a standard deviation lower in mathematics (Fogelman, 1980, as cited in Streissguth, 1986). Although these decrements were small they were highly significant in the sample of 6000 children. However, it should be noted that in this series of studies several important variables were not considered, the most important being alcohol consumption. It is not clear, therefore, whether the effects observed were a direct result of nicotine exposure or some other related variable, such as alcohol consumption.

The next longitudinal initiative was the Perinatal Collaborative Study (Broman, Nichols, and Kennedy, 1975; Hardy and Mellits, 1972; Naeye and Peters, 1984; Nichols and Chen, 1981). This study was conducted in the United States beginning in 1960. This project periodically followed 58,000 pregnancies until age seven. Several researchers have participated in this initiative with mixed findings. A well-controlled study conducted by Hardy and Mellits (1972) matched 88 infants of women who smoked 10 or more cigarettes per day during pregnancy on race, gender, date of delivery, maternal age, and maternal schooling with 88 control subjects born to nonsmokers. These infants were followed up at age seven and eleven. At follow-up the children were administered the Stanford-Binet IQ Scale, Wechsler Intelligence Test for Children, Wide Range Achievement Test, and Bender Gestalt Test. Of the cognitive measures, only the spelling scale of the Wide Range Achievement Test was significantly lower among children prenatally exposed to nicotine. However, the exposed children performed worse than the non-exposed on all subtests, although still within the average range. Because the sample size was small in this investigation it is unlikely that minimal effects could be observed. Broman, Nichols, and Kennedy (1975) reported a small (1.0 point) decrement in intelligence of children at age four born to smoking mothers. However, this difference was no longer significant after adjustment for socioeconomic status, race, and gender. Nichols and Chen (1981) examined 29,889 children at age seven for signs of minimal brain damage (MBD). Maternal smoking during pregnancy was significantly related to all three components of MBD, learning difficulties, hyperactivity-impulsivity, and neurological soft signs. Specifically, children born to women who smoked more than 20 cigarettes per day were 25% more likely to have learning disabilities, 44% more likely to have severe learning disability, 28% more likely to show hyperactivity-impulsivity, 32% more likely to show severe hyperactivity-impulsivity, and 15% more likely to have neurological soft signs. However, this study did not control for social differences among smokers and nonsmokers.

Finally, Naeye and Peters (1984) investigated the cognitive development of seven-year-olds. They found significant decrements in spelling and reading scales on the Wide Range Achievement Test of children born to smokers as compared to nonsmokers. Again, as with the British National Child Development Study, alcohol consumption was not controlled.

We are, therefore, left with the lingering problem of some other variable(s) (alcohol consumption; postnatal exposure to nicotine, etc.) confounding the results of these studies.

The third prospective study was the Seattle Longitudinal Study (Streissguth, Barr, & Martin, 1983; Streissguth et al. 1994). This study investigated the effects of nicotine and alcohol exposure on infants, and follow-up groups of four and seven year olds (Streissguth et al. 1994). Infants were assessed at Day 1 using the NBAS (Streissguth, Barr, & Martin, 1983) which revealed a significant association between nicotine and poorer habituation (Streissguth et al. 1994). However, by 8 months of age there were no significant associations between prenatal nicotine exposure and infant development as measured by the Bayley Scales of Infant Development (Streissguth et al., 1994).

Streissguth et al. (1994) reported no differences between children prenatally exposed to nicotine and those not exposed on either the full scale, verbal, or performance IQ scores on the Wechsler Preschool and Primary Scale of Intelligence (WPPSI) at age four. At age seven, the same children were tested using the WISC, WRAT, the Stroop test, and an attention/vigilance task. Significant differences were not found for the full scale, performance or verbal IQ scores of the WISC. The children did differ, however, as in the study by Naeye and Peters (1984), on the spelling subtest on the WRAT but in this study the children did not differ on the reading or arithmetic subtests. On the Stroop test, children born to smokers performed significantly worse on the word reading subtest, but not the color naming subtest. Children born to smokers also exhibited longer reaction times on the attention/vigilance task compared to children born to nonsmokers. The findings from this series of studies, which controlled for alcohol exposure as well as other social variables, indicates that there are small but measurable effects in the spelling ability and reaction time of children prenatally exposed to nicotine. These studies do not, however, provide support for previous reports of the association between prenatal exposure to nicotine and later intelligence.

The final longitudinal initiative was the Ottawa Prenatal Prospective Study (Fried and Makin, 1987; Fried & Watkinson,1988; Fried & Watkinson, 1990; Fried, O'Connell, & Watkinson, 1992) begun in 1978. In a series of studies, Fried and colleagues examined a group of children at birth and followed them periodically at 12 and 24 months, 36 and 48 months, and 60 and 72 months to assess areas of cognitive and language development.

Fried and Makin (1987) examined 250 infants exposed prenatally to alcohol, tobacco, and marijuana. The infants were assessed between days 3 and 6 using the NBAS. Infants born to smoking mothers exhibited poorer auditory habituation and increased tremors.

At 12 and 24-month follow-up, 217 children at 12 months, and 153 children at 24 months, were assessed at home using the Bayley Scales of Infant Development. At 24 months, the children were also administered the Reynell Developmental Language Scales and the Home Observation Measure of the Environment (Fried & Watkinson,1988). The Bayley test consists of three scales: the Mental Developmental Index (MDI) the Psychomotor Developmental Index (PDI); and the Infant Behavior Record (IBR). Of the three drugs considered, (i.e., alcohol, marijuana, and tobacco), cigarette smoking was the only one that showed significant effects. At 12 months, prenatal exposure to tobacco was associated with lowered MDI scores and with auditory related items as assessed by the IBR (Fried & Watkinson, 1988). Prenatal exposure to tobacco assessed at 24 months continued to be related to some auditory items, but it was no longer significantly associated with MDI scores or the two Reynell Language Scores. The authors report that the influence of postnatal environmental factors may have obscured any significant associations between prenatal exposure to tobacco and cognitive functioning at 24 months (Fried & Watkinson, 1988). Maternal nicotine consumption was negatively related to the HOME measure, suggesting that the home environment of smokers is different from nonsmokers. Fried and Watkinson (1988) report that the smoking mother may have a lifestyle that includes less maternal/child involvement, which may play a role in the child's early cognitive development.

At 36 and 48-month neurobehavioral follow-up, 133 36-month-olds and 130 48-month olds were assessed using the McCarthy Scales of Children's Abilities and the Reynell Developmental Language Scale (Fried & Watkinson, 1990). At age four the children were also administered two motor behavior tests and the Peabody Picture Vocabulary Test (Fried & Watkinson, 1990). In both three and four year olds one significant discriminant function resulted which maximally separated the heavy smokers from the nonsmokers with the light smokers in between. The primary variable responsible for discrimination at age three was the verbal subscale of the McCarthy, which was negatively related to smoking. At age four the primary variables responsible were three language related tests; the Peabody Picture Vocabulary, the McCarthy verbal subscale, and the Reynell expressive component, all negatively related to smoking. These effects remained significant after controlling for other variables including: the home environment, alcohol and marijuana use, family income, mothers weight and pregnancy weight gain, age, education, nutrition, gender of the infant, birthweight, and length of gestation. Overall, the heavy smoking groups had poorer verbal skills than either the light or non-smoking groups (Fried & Watkinson, 1990).

These children were again assessed at 60 and 72-months of age using the McCarthy Scales of Children's Abilities and the Peabody Picture Vocabulary Test (Fried, O'Connell, & Watkinson, 1992). The results were consistent with those reported at ages three and four. At ages five and six years, one discriminant function again maximally separated the heavy smokers from nonsmokers with light smokers in between. At age five the primary variables responsible for the discrimination were the McCarthy General Cognitive Index and Verbal Subscale, and the Peabody Picture Vocabulary Test, which were all negatively related to smoking. At age six, the variables contributing to the discriminant function were the Peabody Picture Vocabulary, the McCarthy Motor, Memory, Verbal and Quantitative subscales, and the General Cognitive Index. In summary, discriminant function analyses revealed an association between prenatal cigarette smoking and lower cognitive, receptive language, and expressive language scores at ages three, four, five, and six (Fried & Watkinson, 1990; Fried et al., 1992).

The results of these longitudinal initiatives do not provide definitive evidence of direct effects of prenatal exposure to nicotine on later cognitive development. However, the Ottawa Prenatal Prospective Study provides support for small, but measurable, deficits in cognitive functioning, particularly verbal skills, of children born to smokers. This investigation was one of the best-controlled and carefully constructed series of studies reviewed. The effects reported by Fried and colleagues remained after control of other possible confounding variables, including alcohol exposure, which has been named as an essential control variable (Streissguth et al., 1994). One of the most difficult confounds to control is the home environment of the child. It is known that women who smoke reportedly drink more coffee, are more anxious, change jobs more frequently, have less formal education, and divorce more often than women who do not smoke (Naeye, 1992). It is difficult, if not impossible, to separate the direct effects of prenatal nicotine exposure from this ever-growing list of environmental influences. What is clear from these studies is the need for more carefully controlled longitudinal initiatives. Naeye (1992) suggests that further research should attempt to follow children born in the same family in which the mother smoked during one pregnancy but not the other. He suggests this would help to reduce the number of possible confounds and provide clearer support to the direct and detrimental effects of prenatal nicotine exposure on the cognitive development of children.

Sexton, Fox and Hebel (1990) conducted a well-controlled prospective study of the effects of prenatal exposure to nicotine on cognitive functioning. At age three, 101 children of mothers who smoked throughout their pregnancy and 263 children of mothers who never smoked (or quit smoking early in pregnancy) were assessed using the McCarthy Scales of Children's Abilities and the Preschool Version of the Minnesota Child Development Inventory (MCDI). The results indicated that children of smokers performed at a lower level, although still above average, on the General Cognitive Index of the McCarthy Scales than children of nonsmokers (mean 102.3 vs. 107.5 respectively). A dose response effect was also observed, indicating that the higher the level of thiocyanate (an indicator of nicotine exposure) in the mother at the eight-month, the lower the cognitive functioning of the child at age three. The mothers' responses to the MCDI were consistent with those of the McCarthy. Overall, children born to smokers received lower scores than those born to nonsmokers, and in particular on two subtests measuring cognitive ability (Sexton et al., 1990). These results remained after controlling for several factors including, social and background characteristics, maternal behaviors during pregnancy (including alcohol consumption), maternal time available to the child, and child's characteristics.

Recent publications have identified an association between maternal smoking and risk for attention-deficit hyperactivity disorder (ADHD). Milberger, Biederman, Faraone, Chen, and Jones (1996) found that 22% of children with ADHD had a maternal history of smoking compared with 8% of non-ADHD children. This association remained after adjustment for socioeconomic status, alcohol use, parental IQ, and parental ADHD status. Significant differences were found in IQ between those children whose mothers smoked during pregnancy and those whose mothers did not smoke. Those whose mothers smoked during pregnancy scored on average 9 IQ points lower than those whose mothers did not smoke during pregnancy (Milberger et al., 1996).

Summary

In summary, the results of these longitudinal investigations and individual initiatives provide support for specific detrimental effects of prenatal exposure to nicotine on the later cognitive functioning of children. However, not all reports are consistent. There are several factors that may influence the discrepant findings of these researchers. The number one difficulty in this research is control for possible confounding variables. While the majority of the studies reviewed attempted to control for an impressive amount of variables (e.g., postnatal exposure to cigarette smoke; maternal age, IQ, height, occupation; birth weight, paternal smoking; home environment; number of siblings, etc.), there is always the problem of the lingering influential variable that the researchers failed to identify.

Following children from birth to eleven years of age, in some cases, is a massive undertaking and there are far too many environmental influences to attempt to control. Therefore, the studies in which consistent deficits were found are even more remarkable given the adversity encountered in this line of research. It is quite possible that the effects attributable to prenatal nicotine exposure are actually under-representations of the true effects due to the excess of possible intervening variables.

Identification of Women Who Smoke During Pregnancy

The valid identification of women who smoke during pregnancy is central to all studies attempting to explore the physical or cognitive effects of smoking on the newborn. However, the identification of smoking poses special problems. The harmful effects of smoking in general and on the fetus in particular have been known for the past four decades. Due to the wide publication of the detrimental effects of smoking during the 1980s and 90s, women who are pregnant are *hyper-aware* of the negative social sanctions regarding smoking during pregnancy. This knowledge can lead to substantial underreporting of smoking behavior due to social desirability factors.

The usual form of gathering information regarding smoking or other behaviors in the general population has been self-report. Generally, self-report has been found to be valid for behaviors that are not socially undesirable or if the individuals have no reason to minimize or maximize their occurrence (Patrick et al., 1994). However, studies involving pregnant women have been identified as high-demand conditions and, as such, there is substantial pressure to underreport smoking behavior (Walsh, Redman, & Adamson, 1996). While it is acknowledged in the literature that self-report is not the "gold standard," it has been used for lack of other more appropriate or valid measures of smoking status for a number of reasons, including the fact that self-report is the most economical and reliable way of gaining information regarding an individual's behavior on a daily basis.

In their review of smoking cessation studies, Velicer, Prochaska, Rossi and Snow (1992) concluded that self-reported smoking is generally accurate, but they noted that high-risk individuals (such as adolescents or pregnant women) might be an exception. Patrick et al. (1994) report that bias is increased wherever social desirability is greatest, as is the case with pregnant women. Most of the reviews investigating the accuracy of self-reported smoking status have deliberately excluded pregnant women from the analysis, which may impact the accuracy of reviews regarding the reliability and validity of self-report in pregnant women.

Many studies have examined the influence of different variables regarding self-report of smoking status in adolescents (see Patrick et al., 1994, for a review). Adolescents, like pregnant women, have a desire to underreport their smoking behavior, and adolescents have been shown to consistently underreport their smoking status (Patrick et al. 1994; Martin & Newman, 1988; see Aguinis, Pierce, & Quigley, 1993, for a review). However, the use of an objective measure of tobacco use has been found to increase the accuracy of adolescents' self- reports. Bauman and Dent (1982) found that adolescents reported significantly greater amounts of smoking if they were informed that a biochemical measure would be employed (exhaled carbon monoxide levels) before completing the questionnaire.

The findings from studies investigating the validity of self-report in adolescents are comparable to those involving pregnant women. Self-report is the most commonly employed measure of smoking status in studies with pregnant women. However, due to the reporting bias generally found with this population, these studies have also used some form of collateral confirmation of these self-reports. Studies employing biological markers with pregnant women have reported deceptions of smoking status ranging from 7.4% to 50% (Fox, Sexton, Hebel & Thompson, 1989; Secker-Walker, Vacek, Flynn, & Mead, 1997; Walsh et al., 1996). Ford, Tappin, Schluter, and Wild (1996) compared pregnant self-reported smokers to smokers identified using serum cotinine analysis. They found that of the cotinine-validated smokers, 22% denied smoking. Further, half of the mothers who replied to the questionnaire systematically underreported the amount they smoked.

In another study using midwives as collateral informants, as well as questionnaire and urinalysis, the conservative estimate of the proportion of midwife identified nonsmokers who could be reclassified as smokers as a result of urinalysis was 7.4%, the medium estimate was 8.8%, and the worst-case scenario was 15.2% (Walsh et al., 1996). Fox et al. (1989) investigated the accuracy of self-report of prepregnancy smoking status over time, during the 18th week (test) and again at 8 months (retest). They found that over 50% of the women reported discrepant prepregnancy smoking behaviors at test and retest. They report that of those who changed their estimates the changes were usually small. However, they did not employ an objective measure so the deceivers could not be identified.

The findings of deception in studies involving pregnant women are not universal. Secker-Walker et al. (1997) found an 87-92% agreement between self-reported smoking status and two biochemical measures (exhaled carbon monoxide and urinary cotinine). They report that these findings are in agreement with other studies assessing smoking behavior in the general population (Patrick et al. 1994; Secker-Walker et al., 1997). However, it is also cautioned that there may be some error in the biochemical measures that would incorrectly classify a smoker as a nonsmoker, thereby influencing the agreement between deceivers and the biochemical measure.

While there is some disagreement in the literature regarding the accuracy of self-report of smoking status in pregnant women, there is evidence that the use of a biochemical marker increases the accuracy of identifying gestational smokers. Along with the use of biochemical markers, several other factors have been found to influence the accuracy of self-reported smoking behavior, such as issues regarding the construction and administration of the self-report questionnaire.

Factors Influencing Validity of Self-Reports

Due to the exclusion of pregnant women from the meta-analytic reviews regarding factors influencing self-reports, the majority of studies discussed in the following section have used adolescents. However, the social desirability factors are at least as strong in pregnant women as in adolescents so it is believed that these factors will readily translate into the pregnant population.

Biological measures

Objective biological measures have been found to increase the validity of self-report of smoking status among pregnant women (Fox et al., 1989; Secker-Walker et al., 1997; Walsh et al., 1996). Biochemical measures of smoking have become commonly used in smoking research. The three most commonly used biochemical markers in this area are carbon monoxide (CO), thiocyanate (SCN), and cotinine.

The evaluation of a marker is assessed in terms of sensitivity and specificity, false positives and false negatives (Dolcini, Adler, & Ginsberg, 1996; Velicer et al. 1992). Sensitivity refers to the proportion of "true smokers" who are classified as smokers by the biological measure; a highly sensitive test has a low rate of false negatives (i.e., classifying true smokers as nonsmokers). Specificity refers to the proportion of "true nonsmokers" who were classified as nonsmokers by the biological measure. Therefore, a highly specific test has a low rate of false positives (i.e., classifying true nonsmokers as smokers).

Carbon Monoxide and thiocyanate have been successfully used as biochemical markers in the discrimination of self-reported smoking status with sensitivities of 84 -85% and specificities of 79 - 84%. However, both of these markers have limitations which make them a less desirable choice. Both CO and SCN are present in certain environmental sources, such as air pollution (CO) and certain foods (SCN) and are less sensitive to light smoking. As a result these biochemical markers are falling out of favour as the marker of choice (Jarvis et al. 1987; Velicer et al. 1990).

Although nicotine is a primary component of tobacco, it cannot easily be used as a marker due to its short half-life of 30 minutes (Rychatarik & McGillicuddy, 1998). Instead, cotinine, a direct metabolite of nicotine can be measured in blood, saliva and urine. Cotinine has an estimated half-life of 15 to 40 hours (Jarvis et al. 1987; Rychatarik & McGillicuddy, 1998; Velicer et al. 1990). Because cotinine is a direct metabolite of nicotine and is not influenced by other environmental factors, its sensitivity and specificity have typically been very high, ranging from 90% to 98%. Velicer et al. (1990) reports that even light and intermittent smokers are detected with a high degree of certainty. Cotinine has the ability not shown by other biochemical markers of being able to detect smokeless tobacco use, such as snuff or nicotine patches. This can aid in the identification of individuals who are not "smokers" per se, but who still ingest nicotine. Cotinine is viewed as the single best measure of smoking and hence has been named the measure of choice for assessing smoking status (Dolcini et al. 1996; Jarvis et al. 1987; Patrick et al. 1994; Rychatarik & McGillicuddy, 1998; Velicer et al. 1990). Self-reports of smoking validated by cotinine plasma, saliva, and urine biochemical markers have been found to have higher specificity and sensitivity than those reports validated by other biochemical tests (Patrick et al. 1994).

Construction and Administration of Questionnaire

Dolcini et al. (1996) outline four limitations to the self-report questionnaire. First, it has been reported that the clarity and specificity of questions assessing smoking status affects the accuracy of self-report (Dolcini et al., 1996) and the association with a biochemical marker. Patrick et al. (1994) report that one of the most unmeasured study characteristic is the specific wording of questions regarding smoking status. Very few studies reported this information despite the fact that there is evidence that questionnaire responses are heavily influenced by how a question is phrased and the order in which the questions are asked. Individuals, particularly those who smoke lightly or sporadically, are likely to classify themselves as nonsmokers if a broad categorization, such as smoker or nonsmoker is employed. It is recommended that specific questions about smoking behavior be used. The second limitation is the time frame. Asking about specific time frames versus usual habits appears to yield more accurate reports (Dolcini et al., 1996). In addition, it is important that the time frame be geared to the half-life of the biochemical measure employed. It will not be beneficial to ask about smoking behavior over the past two weeks when the biochemical measure can only validate smoking behaviors for the past 24 hours.

The third limitation noted was reporting channel (i.e., whether the information was gathered through self-administered questionnaire or through face-to-face interviews). Dolcini et al.(1996) report that there is no study directly examining this difference. However, Luepker, Pallonene, Murray, and Pirie (1989) compared the validity of self-report obtained by telephone with that obtained in face-to-face interviews in a sample of adolescents. They found that 35% of those who labeled themselves as quitters on the telephone labeled themselves as smokers in the face-to-face condition.

The results from Patrick et al.'s (1994) meta-analytic review suggests that interview administered questionnaires yielded higher estimates of sensitivity and specificity than did self-administered questionnaires among a sample of adolescents. Interviews identified more of the smokers correctly and classified nonsmokers more accurately. This may reflect smokers' awareness of sensory cues about smoking (e.g., stained teeth, fingers, visible cigarettes or smoke odor) that would be obvious to an interviewer. Patrick et al. (1994) conclude that more respondents may attempt to hide smoking behavior in a self-administered questionnaire even when biochemical validation is known. Face to face interviews appear to gather more accurate self-reports than do self-administered questionnaires. However, direct evidence assessing the discrepancies between self-report and interview administered questionnaires was not presented.

A final factor influencing the validity of self-report of smoking status is anonymity or confidentiality. Dolcini et al. (1996) report that anonymity can be used to increase honesty. Anonymity may reduce the social pressure to underreport smoking and increase agreement with biochemical measures. There is mixed evidence as to whether adolescents promised anonymity report more accurate self-reports than those promised confidentiality. Murray and Perry (1987) found evidence for increased honesty under conditions of anonymity. In contrast, Akers, Massey, Clarke, and Lauer (1983) found no differences in validity of smoking when comparing non-anonymous, confidential questionnaires to anonymous questionnaires. However, it has been suggested that assuring individuals of confidentiality and, if possible, anonymity should increase the accuracy of self-reports (Dolcini et al., 1996). If anonymity is not possible, special attention should be paid to issues of confidentiality.

Summary

In summary, several factors must be considered when identifying gestational smokers. These factors include the use of biochemical measures, the construction of the specific questions, and the method of administration. In any study where the reliable identification of smokers and nonsmokers is crucial to the aims of the study, and in a high-risk population such as pregnant women, it is recommended that a biochemical measure be employed to validate self-reports (Patrick et al., 1994). It is, therefore, important to employ a biochemical measure with high sensitivity and specificity. Cotinine, a primary metabolite of nicotine has the highest sensitivity and specificity (Patrick et al. 1994; Jarvis et al., 1987; Velicer et al. 1990). Cotinine is becoming the biochemical measure of choice in studies investigating smoking.

The construction of the questionnaire is also important. The careful wording of questions and the time frame of the biochemical measure chosen must be evaluated.

Cotinine has an estimated half-life of 15 to 40 hours (Jarvis et al. 1987; Velicer et al. 1990; Rychatarik & McGillicuddy, 1998); therefore, questions regarding smoking status must reflect this length of time. The method of administration also impacts on the reliability and validity of self-reports. It is not clear, but it has been suggested that self-reports of smoking status are more reliable with face-to-face interviews rather than self-administered questionnaire.

Information Processing in Neonates

Conventional tests of infant intelligence, for example the Bayley Scales of Infant Development, are based on variations in the growth of early sensorimotor abilities and are often used to predict later developmental problems (Fagan & Singer, 1983). However, these tests were not developed to measure intellectual functioning. They were intended to provide a description of normal infant ability and as such offer no predictive validity for later intelligence, at least prior to 18 to 24 months of age (McCall, 1979; McCall & Carriger, 1993).

Conventional tests for assessing newborns were developed to identify infants at risk and in need of intervention, and their emphasis is on assessing neurological integrity and the overall behavioral organization and physiological condition of the infant and his or her influence on the parent-infant relationship (Brazelton, 1984). As with the measures of infant development, these newborn assessment procedures were developed for describing the behavior and ability of normally functioning infants. The standard tests, widely in use, are composed of items that tap the development of sensory and motor skills, functions which are not related to intelligence later in life and, therefore, would not be expected to be early indicators of intelligence (except in specific cases such as infants with multiple congenital abnormalities; Fagan & Singer, 1983). However, the NBAS has measures of orientation and habituation (which have been associated with later intelligence as will be discussed in the following section) and has been the most widely used screening instrument for newborn information processing ability over the past two decades.

The NBAS has several limitations, which undermine the usefulness of this measure for assessing cognitive ability. The inability to reliably predict later cognitive functioning may be a result of the relatively uncontrolled method used with the NBAS. In the typical procedure for the NBAS, the experimenter both holds the infant and delivers the stimulus (e.g., shakes a rattle), within the peripheral field of vision of the infant. This may influence the head turning response given by the infant, by both the physical movements of the examiner and visual cues seen by the infant. Examiner effects have been found to have an extreme impact on the results of the NBAS. Richardson et al. (1989) found that the most reliable predictor of performance on the NBAS was the NBAS examiner. The development of an appropriate method to test newborn cognitive ability was essential to the continuation of this line of research. Varying results were being reported due to the discrepant methodology employed in different investigations (Fagan & Singer, 1983).

Muir and Field (1979) criticized the NBAS for lack of methodological control and provided controlled conditions that improved the NBAS orientation and habituation procedures. Because experimenter bias influenced the results of the NBAS to such a great extent, Muir and Field reduced these effects by first preventing the experimenter from knowing the location of the sound source by tape-recording the auditory stimuli and using headphones to deliver the stimuli to both ears of the experimenter, simultaneously. Second, they eliminated visual cues by presenting the stimuli through stereo speakers to the infant. Third, they modified the method of holding the infant to permit free movement of the head to the left and right. Using this technique, Muir and Field reliably demonstrated that neonates were capable of orienting to auditory stimuli under highly controlled conditions.

With the development of more appropriate tests for measuring newborn orientation to stimuli, habituation and recovery to novelty (primarily with visual stimuli) began to be investigated as potential predictors of infant cognitive ability (Fagan, 1970; Fagan & Singer, 1983; McCall & Carriger, 1993). These investigations were based upon the early work of Sokolov (1963) on the orienting reflex. Briefly, he suggested that a novel stimulus initially provokes an orienting response (reflex) and with repeated presentation of the stimulus a neuronal model of the stimulus is created. This representation increases in accuracy until it retains information about the stimulus. Subsequent presentation of the stimulus is compared in memory to this neuronal model. If the comparatory stimulus matches the neuronal model it will fail to elicit or actually inhibit the orienting reflex. If the stimulus is mismatched it will elicit the orienting reflex (Bornstein, 1989; Clifton & Nelson, 1976; Cohen, 1991). The key process in this theory is the creation of a neuronal model upon which further comparisons are based. This implies that the infant is encoding, retrieving, comparing and, consequently, actively processing the incoming stimuli.

There are two processes involved in this model that have been associated with infant cognitive ability. The first process is habituation, which is usually measured by the amount of time an infant spends looking at a repeated visual stimulus. Once the infant begins to lose interest in the stimulus, habituation is said to have occurred. More efficient styles of information processing are characterized by faster habituation and less looking time at the stimulus (Bornstein & Sigman, 1986; McCall, 1989). The second process is recovery to novelty, which is measured by the amount of time the infant spends looking at the novel as compared to the familiar stimulus. Either greater amounts of looking time at the novel stimuli or lesser amounts of looking time at the familiar stimulus are characteristics of more efficient styles of information processing (Bornstein & Sigman, 1986; McCall, 1989).

It has been hypothesized that the infant's ability to recognize a previously seen stimulus may involve processes similar to those tapped in later intelligence tests, and consequently may validly reflect early intelligence (Fagan &Singer, 1983). To predict later intelligence it is necessary to measure behaviors during infancy that are similar in kind or tap the same processes known to be related to later intelligence (Fagan & Singer, 1983). For example, on later intelligence tests children are asked to discriminate among stimuli, to retain new information, to identify similarities and to define words. While infants cannot define words, Fagan and Singer (1983) suggest that they can exhibit discrimination, retention and identification. These three skills can be reliably demonstrated in infant habituation and recovery to novelty paradigms. The infant must be able to retain information about the familiarized stimulus (gathered during habituation) in order to discriminate the novel stimulus from the familiarized stimulus and identify it as similar or different. Failure to habituate or recover responding implies a breakdown in the formation (retention) of the neuronal model of the initial stimulus or a failure in the discrimination process between the familiar and novel. The ability of an infant to perform these three tasks is hypothesized to be related to later intellectual functioning and, therefore, infants with deficits on these tasks are thought to be at risk for developmental delay (Fagan & Singer, 1983).

Several researchers have employed the habituation and recovery to novelty paradigm in assessing newborns with visual and auditory stimuli and have repeatedly shown that infants from birth through 36 months will habituate to repeated presentation of a stimulus and recover responding to a novel stimulus (Bornstein, 1989; Bornestein & Sigman, 1986; Clifton & Nelson, 1976; Fagan & Singer, 1983; Swain, Zelazo & Clifton, 1991; Tarquinio, Zelazo, & Weiss, 1990; Tarquinio, Zelazo, Gryspeerdt, & Allen, 1991; Weiss, Zelazo, & Swain, 1988; Zelazo, Weiss, Randolph, Swain, & Moore, 1987). Infant habituation and recovery paradigms have been used as tools to make predictions about the continuity of intelligence from infancy to later childhood (Bornstein, 1989; Cohen & Parmelee, 1983; Fagan & McGrath, 1981; Fagan, 1970; Lewis & Brooks-Gunn, 1981; Sigman, Cohen, Beckwith, & Parmelee, 1986; see Bornstein & Sigman, 1986; Fagan & Singer, 1983; McCall & Carriger, 1993; for reviews). Using infant controlled procedures with visual stimuli, moderate correlations (ranging from .29 to .66, mean = .44) have been repeatedly documented between infant habituation and recovery to novelty responses and later childhood intelligence (Bornstein & Sigman, 1986; McCall & Carriger, 1993).

Selective Receptor Adaptation vs. Information Processing

It has been established in the literature that habituation-recovery paradigms are moderately predictive of later intelligence (Bornstein, 1989; Cohen & Parmelee, 1983; Fagan, 1970; Fagan & McGrath, 1981; Fagan & Singer, 1983; Lewis & Brooks-Gunn, 1981; Sigman et al., 1986; see Bornstein & Sigman, 1986; McCall & Carriger, 1993 for reviews). However, despite this evidence researchers attempting to demonstrate this information processing ability in neonates have been criticized by proponents of the selective receptor adaptation (SRA) model (Dannemiller & Banks, 1983; 1986). This model posits that habituation occurs in infants under 3 or 4 months of age due to selective receptor adaptation at the cortical level. Therefore, decreases in attention to a repeated visual (or auditory) stimulus were hypothesized to result from fatigue of feature-selective neurons. Recovery of attention to either novel visual or auditory stimuli occurs because a different set of nonfatigued neurons is activated by the novel stimulus (Dannemiller & Banks,1983). However, this theory has fallen out of favour as more researchers provide either contradictory or inconsistent evidence. Zelazo and colleagues, employing auditory stimuli, have provided evidence that a selective receptor adaptation model cannot account for habituation and recovery to novelty (Swain et al., 1991; Tarquinio et al., 1991; Tarquinio et al., 1990; Weiss et al., 1988; Zelazo et al.,1987). In contrast to the SRA model, an information processing model has been posited which assumes that habituation and recovery to novelty can be accounted for by a relation between an internal representation of an old stimulus and characteristics of a new one (Weiss et al., 1988). Attention is influenced, in part, by the stimulus-schema discrepancy.

Auditory Information Processing

In the information processing procedure developed by Zelazo and colleagues, auditory stimuli are presented in the controlled conditions developed by Muir and Field (1979). The partial infant controlled auditory information processing procedure consists of three phases: 1) familiarization phase, 2) recovery phase, and 3) dishabituation phase. In the familiarization phase, an infant is presented with an auditory stimulus which is repeated every 2 seconds in trials of 30-second blocks. The primary dependent measure is infant head turns toward and away from the sound source. Infants initially exhibit high levels of head turning toward the sound source. After repeated presentations of the same stimulus, the infant's head turning response typically declines and the infant begins to turn away from the sound source. This procedure continues until predetermined criteria for orientation and habituation are met. Then a novel stimulus will be presented in the recovery phase. During this phase, infants will recover responding to novelty and will again exhibit high levels of head turning toward the novel sound source. After repeated presentations, infants' responses will decline and they will actively turn away from the now redundant sound source. Following habituation to the novel stimuli, the original familiarized stimulus will be presented in the dishabituation phase and again infants will recover responding.

Zelazo and colleagues (Swain et al., 1991; Tarquinio et al., 1991; Tarquinio, Zelazo, & Weiss, 1990; Weiss et al., 1988; Zelazo et al., 1987) through a series of studies employing the auditory information processing procedure, have provided evidence of active information processing in neonates as young as 24 hours old. Brody, Zelazo, and Chaika (1984) demonstrated that neonates would not only orient to an auditory stimulus but would habituate if a sufficient number of trials were presented. Further, they demonstrated that neonates would recover responding to a novel sound compared to a redundant sound heard by control infants and the neonates would also recover responding to the original stimulus following the introduction of the novel stimulus (dishabituation). Brody et al. (1984) suggests that this finding in itself does not refute the SRA model, but the stimuli employed in the study provide contradictory evidence. Brody et al. employed rattle sounds as auditory stimuli and suggested that the sound of the rattle was too diffuse to fit an SRA interpretation easily.

Brody et al. (1984) extended the habituation, orientation and recovery paradigm to speech sounds using the information processing procedure. The stimuli in this study were two infrequently occurring words ("tinder" and "beagle") recorded on a tape loop by a female experimenter. Replicating the findings of Brody et al. (1984), the neonates in this study reliably turned toward the word presented and habituated to repeated presentations of the same word. Further, the neonate recovered responding to a novel word and after presentation of the novel stimulus, recovered responding to the original familiarized stimulus. This study confirms that neonates have the capacity to reliably orient to lateral sounds and to habituate and recover responding to speech sounds. Again, this study does not provide direct evidence against the SRA model but as with the rattle sound the stimuli used in this study are too complex to fit neatly into patterns of auditory receptors.

Further evidence contradicting the SRA model came from a study conducted by Zelazo et al., (1987) who examined the effects of delay on retention of habituated head turning. From an information processing perspective it was hypothesized that the length of the delay during which habituation remained would provide an indication of the length of the neonates' memory. Delays of 10, 55, 100, and 145s following habituation were employed. It was found that habituation was retained after delays of 55s, but not 100 or 145 seconds. This finding appears to contradict the SRA model, as recovery following neuronal adaptation would usually occur after milliseconds not minutes. However, Dannemiller and Banks (1983) proposed that to refute the SRA model, habituation should remain after hours. Zelazo et al.(1991) suggest that the reasoning behind this lengthy delay is not clear and that this study provides evidence for memory in the infant, thereby supporting the information processing view.

Three further studies provide evidence in support of the information processing view. Weiss et al. (1988) assessed newborns for their recovery of head turning toward auditory stimuli presented at different levels of fundamental frequency and found that the largest discrepancy (28%), the one furthest away from the original stimulus and which would be expected to excite a new set of neuronal responding, produced the least recovery (Weiss et al., 1988). Tarquinio et al. (1991) investigated the effect of delay on neonates' response to decreased sound pressure level. The results revealed generalization of habituation to the decreased sound pressure level following a 55-second delay, but recovery occurred following a 10-second delay (Tarquinio et al., 1991). It was proposed that newborns retain the phonetic properties of the stimulus and categorize the lower volume sound as familiar and that this reflects evidence for neonatal memory (Tarquinio et al., 1991). Another study conducted by Swain et al. (1993) demonstrated that neonates appeared to retain memory for a specific sound over a 24 hour period when presented with the same sound over two days. These data imply that infants, shortly after birth, have the capacity to create mental representations (i.e., encode and store information about past experiences) (Swain et al., 1993).

One of the most convincing and robust lines of evidence in support of the information processing view is the finding that infants not only habituate to repeated presentation of a stimulus, which could be accounted for by neuronal fatigue, but they actively turn away from the sound source. The systematic turning away from redundant stimuli has been reliably and repeatedly demonstrated (Swain et al., 1991; Tarquinio et al., 1991; Tarquinio et al., 1990; Weiss et al., 1988; Zelazo et al., 1987). This implies that the infant has processed the auditory information and is involved in an active comparison between the stimulus and their mental representation of the stimulus.

Practical Implications

The practical implications of the auditory information processing procedure developed by Zelazo and colleagues were demonstrated when Zelazo, Weiss, Papageorgiou, and Laplante (1989) employed the information processing procedure in discriminating among neonates born at normal, moderate or high risk for developmental delay. They found that recovery of head turning to a novel word and to the return of a previously familiarized word discriminated among normal neonates and those at risk for developmental delay. Zelazo et al. (1989) found that orientation and habituation during the familiarization phase did not differentiate among the groups. However, infants who did not reach the criteria for orientation were excluded from the analyses which may obscure any possible differences between the groups on the measures of orientation and habituation. During the recovery phase, in response to the novel stimuli, normal infants exhibited the highest level of recovery of head turning to the novel stimulus, followed by the moderate risk group and the high-risk group exhibited the lowest level of recovery. Neither, the moderate- or high-risk infants recovered to initial orientation levels. Following habituation to the novel stimulus, infants were presented with the original familiarization stimulus for a second time (dishabituation phase). The percentage of head turns toward the previously familiarized stimulus again discriminated among the groups.

Potter, Zelazo, Stack, and Papageorgio (2000) employed the auditory information processing procedure to examine the effects of prenatal exposure to cocaine and tobacco on the information processing abilities of neonates. Neonates were presented with auditory stimuli (either "tinder" or "beagle") and their head turns toward and away from the stimuli served as the primary dependent measure. Neonates were presented with one stimulus during the familiarization phase until criteria for orientation and habituation were met. They were then presented with a novel word, again until orientation and habituation were achieved. Following the response to novelty, the neonates were presented again with the previously familiarized word (dishabituation). Recovery of localized head turning to a novel stimulus following repeated exposure to the previous stimulus discriminated between infants prenatally exposed to cocaine and non-exposed infants. In addition, fetal cocaine exposure was associated with impaired habituation to the familiarization stimulus, whereas orientation was not affected. Both groups turned systematically toward the stimulus during the familiarization phase, indicating orientation. However, during the last part of that phase, the non-exposed infants systematically turned away from the stimulus while the cocaine-exposed infants turned randomly toward and away from the stimulus (Potter et al., 2000).

Turning away from redundant stimuli is a robust finding that has been demonstrated repeatedly with normal infants during habituation and implies active processing of the stimulus (Swain et al., 1991; Tarquinio et al., 1991; Tarquinio et al., 1990; Weiss et al., 1988; Zelazo et al., 1987). Failure to turn away from the stimulus during the familiarization phase implies a breakdown or lack of processing.

Further, the cocaine exposed infants failed to recover responding to the novel stimulus (Potter et al., 2000). They continued to turn randomly; that is, their responses did not change with the introduction of the novel stimulus. However, the control infants did change their responses with the introduction of the novel stimulus. During the final trials of the familiarization phase, the control infants were actively turning away from the stimulus, whereas with presentation of the novel stimulus the control infants systematically turned toward the stimulus, i.e., their responses changed with the changing stimulus. During the dishabituation phase differences were also noted between the exposed and non-exposed infants. Fetal cocaine exposure was associated with a lack of recovery to the previously familiarized stimulus (dishabituation). The control infants performed as expected and recovered responding to the previously familiarized stimulus. These findings suggest that prenatal exposure to cocaine interferes with the infants' ability to process auditory stimuli and implies a break down in the creation and use of mental representations.

Potter (1996) also discovered differential patterns of responding using the auditory information processing procedure with infants prenatally exposed to tobacco. The procedure was identical to that used with the cocaine-exposed infants. Infants born to smokers exhibited deficits on a number of information processing measures relative to controls. In the first half of the familiarization phase, infants prenatally exposed to nicotine exhibited lower levels of head turning toward the stimulus, implying poorer orientation. In the second half of the familiarization phase, exposed infants exhibited higher levels of head turning toward the stimulus, implying poorer habituation (Potter, 1996). Infants exposed to tobacco were less likely to orient and habituate to the familiarization stimulus and those who did achieve orientation and habituation required more trials to do so relative to controls. There were no group differences in the level of head turning toward the novel stimulus or in habituation to the novel stimulus. Infants whose mothers smoked during pregnancy did not recover responding during the dishabituation phase. They exhibited lower levels of head turning toward the sound source, turned randomly toward and away from the dishabituation stimulus and required a greater number of trials compared to controls to reach orientation (Potter, 1996). The results indicate that prenatal exposure to tobacco interferes with newborn auditory information processing ability, which may impact later cognitive functioning, particularly in the area of language development and verbal ability.

The results of these investigations (Potter et al., 2000; Potter, 1996) attest to the validity of the auditory information processing procedure in discriminating between infants who were prenatally exposed to two different substances (tobacco and cocaine) and a control group. The results demonstrate that exposure to these substances interferes with infants' ability to perform the three skills necessary in the habituation- recovery to novelty paradigm, discrimination, retention and identification (Fagan & Singer, 1983). These three skills have been associated with performance on later tests of intelligence and it is hypothesized that infants with deficits on these skills are at risk for later cognitive delays (Fagan & Singer, 1983).

These studies (Potter, Zelazo, Stack, & Papageorgio, 2000; Potter, 1996; Zelazo, Weiss, Papageorgiou & Lalante,1989), along with the others previously reviewed (Swain, Zelazo & Clifton, 1991; Tarquinio, Zelazo, Gryspeerdt & Allen, 1991; Tarquinio, Zelazo & Weiss, 1990; Weiss, Zelazo & Swain, 1988; Zelazo, Weiss, Randolph), provide support for the validity of this procedure in assessing differences in auditory information processing abilities among neonates at varying levels of risk for later cognitive delay.

Outline of Current Research

Control for Confounding Variables. Generally, questions asked to determine the effects of prenatal exposure to nicotine have focused on a cause and effect relationship between exposure and subsequent deficits in the infant or child, such as, does and/or can nicotine use during pregnancy cause learning disabilities (cognitive deficits) in children? These types of questions tend to leave out the influence of important confounding factors, including psychosocial variables and other prenatal correlates (Streissguth, 1986). Streissguth (1986) recommends that the appropriate question to be asked when investigating the possible detrimental effects of nicotine exposure on the cognitive abilities of infants is: "Is there a relationship between nicotine exposure in utero and subsequent learning disabilities (cognitive deficits) in the offspring after consideration of other related variables?" (p. 30). This question assumes that there are other possible variables impacting on the observed effects on children prenatally exposed to nicotine and takes them into account when analyzing the data. It is, therefore, important to the current study to investigate and control for as many of these potential confounding variables as is possible. Of course, even the best controlled study will fall victim to the influence of potential unidentified variables; however, in any study investigating the effects of prenatal exposure to nicotine, possible confounding variables identified in the literature (e.g., maternal education, maternal age, weight gain during pregnancy, socioeconomic status, infants' gestational age, infants' birthweight, Apgar score, and other substance use) should be assessed and controlled for as well as possible.

Rationale

It has been found that children born to smokers suffer from more physical difficulties and relatively lower scores on some cognitive measures, particularly long-term language impairment, than children born to non-smokers (Fried et al., 1992; Fried & Watkinson, 1990; Fried & Watkinson, 1988). It is not clear whether the effects are a result of prenatal exposure to nicotine or some combination of prenatal and postnatal exposure to maternal smoking and other psychosocial factors. Although deficits have been found in both verbal and nonverbal behaviors, the verbal behaviors are affected most strongly by prenatal exposure to nicotine. Maternal smoking is related to deficits in responsiveness to auditory stimuli on the NBAS (Fried & Makin, 1987; Richardson et al., 1989). These findings suggest that prenatal exposure to nicotine might selectively impair auditory functioning. However, the NBAS does not measure central processing of auditory information, so it is not known if the deficits are a result of reduced auditory threshold or impairments in central processing of auditory information. There are, however, no reports that infants born to smokers are more likely to be hearing impaired so it is likely that the deficits are a result of impairments in the processing of auditory information.

Due to the small, but measurable, harmful effects which have been associated with smoking on the developing fetus, particularly in the area of cognitive development, it is important to determine if the detrimental effects are present at birth. Along with the various psychosocial confounds involved in the isolation of the effects of prenatal exposure to nicotine (e.g., socioeconomic status, maternal IQ, number of siblings, and maternal age), postnatal exposure to nicotine is potentially the most detrimental. Therefore, the detection of information processing deficits in the neonate would provide further support for the effects of prenatal exposure to nicotine on the developing fetal brain.

Using the information processing procedure it has been found that infants at high risk for developmental delay do not differ from those not at risk on measures of habituation to the original stimulus, but do show differences in response to a novel stimulus and to the recovery of responding to the original stimulus, (Zelazo et al. 1989). However, in the Zelazo et al. (1989) study infants who did not reach the criteria for orientation were excluded from further analyses, thereby possibly obscuring any differences on the measures of orientation and habituation. Conversely, Potter (1996) found differences between infants prenatally exposed to nicotine and a control group on measures of orientation and habituation in the first phase, and orientation in last phase of the procedure, as discussed earlier. The discrepant findings may be a result of methodological differences or true differences in the information processing ability of infants prenatally exposed to nicotine and those at risk for developmental delay for other reasons. These differences may also be a function of nicotine withdrawal. It is possible that the effects observed by Potter (1996) may have been due to nicotine withdrawal and, as a result, may be transient. If effects of prenatal exposure to nicotine in neonates are discovered and continue to be found following the period of nicotine withdrawal, firmer conclusions regarding the direct effects of prenatal nicotine exposure on the developing fetus can be ascertained.

To accurately assess the potential detrimental effects of nicotine exposure on the infant, it is crucial that maternal smokers be identified accurately. It has been suggested in the literature that maternal smokers are a population with considerable pressure to underreport their smoking status (Walsh et al., 1996). Due to this reporting bias, several factors must be considered when assessing the status of maternal smokers. These factors include the use of a biochemical measure to validate the self-report; careful attention to the construction of the questions, including using specific questions and appropriate time frames; the reporting channel, i.e., self-administered questionnaire or face-to-face interview; and the guarantee of strict confidentiality if not anonymity.

The present study has several objectives. The first objective is to ascertain whether reporting channel (i.e., self-administered questionnaire or face-to-face interview) influences the reliability and validity of identifying gestational smokers. Mothers will either receive a self-administered questionnaire or participate in an oral interview of the same questionnaire. Mothers' responses will be verified by saliva cotinine analysis. The second objective is to employ the information-processing paradigm developed by Zelazo and colleagues to test the auditory information processing ability of neonates prenatally exposed to nicotine compared to a non-exposed control group. Finally, the infants will be re-tested at approximately three weeks of age to determine if any effects discovered at birth remain following the period of nicotine withdrawal.

Hypotheses

It was hypothesized that women who were interviewed in a face-to-face condition would provide more accurate self-reports of smoking status, as verified by maternal saliva cotinine analysis, than women who completed a self-administered questionnaire. While there is some disagreement in the information processing procedure regarding the expected pattern of response of the nicotine exposed infants, it was hypothesized that infants prenatally exposed to nicotine would show differences in information processing ability in each phase of the procedure (i.e., familiarization, recovery, and dishabituation), at initial testing and at three week follow-up.

Method

Participants

All participants were recruited from the obstetric unit of the Valley Regional Hospital, Kentville, Nova Scotia, between February and May 2000. All mothers who were on the obstetric unit on the days of testing were approached to participate in the study. One hundred and seventy potential participants were approached during the 4 month time frame of the study. Of those approached, one hundred and seven agreed to participate, resulting in a participation rate of 63 %. All infants participating in the study had 5 minute Apgar scores of 9 or10.

Tobacco - Exposed Group. Twenty-four tobacco-exposed neonates were tested on the information processing procedure. Smoking status was determined initially via self-report and verified by maternal saliva cotinine analysis.

Control Group. Eighty-three infants without a documented history of nicotine exposure were tested on the information processing procedure. The control group was identified as non-smoking through self-report and maternal saliva cotinine analysis. These infants formed a pool from which 24 matched controls were selected for the nicotine-exposed infants. Three of the 83 potential control neonates were excluded from the pool because of untestable state (i.e., one was sleeping, and two were rooting throughout the procedure). Six participants were excluded because of exposure to second hand smoke on a daily basis and two were excluded due to the detection of cotinine in the mothers' saliva (examination of raw data revealed that these mothers were exposed to second hand smoke two to six times a week). From the 72 remaining potential controls, the closest match for each nicotine-exposed neonate based on birthweight (BW), gestational age (GA), and age at testing (TA) was selected.

Subject Matching Procedure.

Matching criteria were chosen to allow matching of the maximum number of infants possible while remaining within one standard deviation of the nicotine-exposed group means. The control infant who was the closest match was selected for each nicotine-exposed infant according to the following matching criteria: a) BW within 398 g (.98 of one SD); b) GA within 1 week (.73 of one SD); and c) TA within 15 hours (.99 of one SD).

Tobacco-exposed newborns were matched with potential controls according to BW, followed by GA, and TA, respectively. If more than one potential control could be matched with a tobacco-exposed infant on a given variable, the one with the closest match on the subsequent variable was chosen. Eight of the tobacco-exposed newborns had more than one potential control by the time the last matching variable was reached. In these cases, the closest match on all possible variables was chosen as the control. The raw data for each of the three matching variables for the 24 tobacco-exposed/matched control pairs is shown in Table 1. Of the 24 matched pairs, 19 matched on all three variables and all of the pairs matched according to the criteria of two of the three variables. Sex was not included as a matching variable because previous research has shown no sex differences on the information processing procedure. However, in both the tobacco-exposed group and the matched controls, there were 12 males and 12 females.

<u>Procedure</u>

Mothers were approached and invited to participate in the study within 48 hours of giving birth. The study was described to each potential participant and signed consent (Appendix A) was received for the researcher to access the mother's hospital chart, for her newborn to participate in the information processing procedure, and for the mother to be contacted approximately three weeks later for retest. At this time a saliva sample was collected from the mother. To investigate the influence of reporting channel on the accuracy of self-reports, mothers were given a questionnaire, either through a face-to-face interview with the researcher or as a self-administered questionnaire. The choice of interview or self-administration was done as randomly as possible; however, mothers who were in private rooms or alone in a double room were more likely to participate in the face-to-face interview, while those with others in the room were asked to complete the questionnaire themselves to ensure confidentiality. Mothers were not fully informed of the questionnaire/interview manipulation; however, following administration of the questionnaire either through face-to-face interview or self-administration, the mothers were debriefed regarding the true purpose of the manipulation (see Appendix B for debriefing procedure). The questionnaire contained demographic questions concerning mother's age, marital status, household income, infant's sex, date of birth, time of birth, and pregnancy weight gain, among others (Appendix C). The questionnaire also asked about smoking before and during pregnancy, exposure to second hand smoke during pregnancy, and alcohol consumption during pregnancy. Data concerning Apgar scores and birthweight were collected from hospital records.

Table 1

Raw data on Subject Matching for Tobacco-Exposed Infants and their Matched Controls

Birthweight (g)		Gestational Age (weeks)		Test Age (hours)	
Smoker	Control	Smoker	Control	Smoker	Control
2881	3096	39	40	35	46
2894	2578	37	38	31	18
2923	3061	37.5	38.5	7	14
2963	3062	39	40	13	25
2990	2768	40	35.5*	13	19
3029	2770	39	42*	23	10
3041	2855	39.5	38.5	25	40
3046	3082	39	40	12	42
3098	3443	39	40	30	98*
3119	3517	38	39	42	42
3141	3024	41.5	40	14	14
3148	3546	37	39*	16	24
3200	3511	42.5	39*	19	34
3204	3404	39	39	50	52
3394	3661	38.5	38	12	10
3457	3612	39.5	40	27	36
3491	3677	39	40	14	24
3530	3693	41	40	33	28
3548	3671	40	40	30	20
3563	3489	40	40	71	73
3881	3874	41.5	41	17	17
4001	3811	40	40.5	31	22
4050	3664	40	39	45	48
4342	4039	40	40	14	16

*Matched control subject is outside the limits of the matching criterion for that particular variable.

The data concerning the use of alcohol during pregnancy is summarized in Table 2. Alcohol consumption was low among all mothers, with 37.5% of the tobacco-exposed group and 33.3% of the control group reporting any alcohol use. Of the mothers who reported any alcohol use during pregnancy, 78.6% reported that this use was a one-time occurrence or occurred prior to knowledge of pregnancy. Of those who reported alcohol use throughout pregnancy, this was usually less than one glass of wine or one beer once a month. The highest amount of alcohol consumption reported was five or more drinks, reported by one control and two smokers; in all cases this occurred prior to knowledge of the pregnancy.

Infant Testing. Testing took place in the infant nursery at the Valley Regional Hospital. For the majority of tests the nursery was empty of other infants. The few times other infants were in the nursery, they were sleeping at the time. Infants were brought into the room, usually asleep, and awakened. If the infant was still sleepy, a series of reflexes were elicited (Moro, Babinski, and Stepping) to ensure an alert, inactive state. If the infant did not achieve this state he/she was returned to the mother and the testing was attempted later that same day. Following the wake-up procedure, the auditory information processing procedure began. The infant was held over a warming table by one experimenter (the holder) at a 45 ° angle between vertical and supine positions, with the infant's head and shoulders supported in the right hand and its lower back and buttocks in the left hand, as recommended by Muir and Field (1979). The stimuli were delivered from a set of computer speakers placed approximately 20 cm from the infant's ears. A second experimenter (the coder) coded the infant's head turning responses using a numeric

Table 2

Number Of Smokers And Control Mothers Who Drank Alcohol During Pregnancy

	Smokers (n=24)	Controls (n=24)
Alcohol use throughout pregnancy	1 (4%)	2 (8%)
Any alcohol use during pregnancy	8 (33%)	6 (25%)
No alcohol during pregnancy	16 (67%)	18 (75%)

keypad connected to a laptop computer. Head turns were coded when the infant rotated the sagittal midline of the head about 45° to either side. To reduce the probability of spurious turns, the conservative criterion of 45° was chosen, relative to the criteria of 6° and 15° used by Muir and Field (1979) and Clifton et al. (1981), respectively. Stimuli were presented at a safe sound pressure level of 72 decibels in a left-right-right-left order with the starting direction counterbalanced across infants. Each trial had a duration of 30s or until the infant exhibited a 3s head turn in either direction. Inter-trial intervals varied for each infant depending on the amount of time required to regain an alert state in cases where the infant had fallen asleep or become fretful. However, inter-trial intervals were generally 5 seconds in length, during which time the holder recentered the infant's head. One of three responses was possible for each trail: 1) head turn toward the stimulus, 2) head turn away from the stimulus, or 3) no head turn. The amount of time the infant spent sleeping and/or fretting was also recorded. The computer program kept a running total of the duration of each trial, each phase, and the total testing procedure. In order to eliminate experimenter bias, both the holder and the coder wore headphones, which delivered both stimuli mapped on top of each other and played repeatedly. The coder controlled the beginning of each trial and was thus aware of the stimuli being delivered and the changes from one phase to the next, however, the coder was not aware of the direction of the sound source. The experimenters were occasionally aware of group membership due to the interview component of the study design. The headphones served to reduce experimenter bias during the testing phase.

The experimental procedure consisted of three phases in a partial infant-controlled design: 1) Familiarization Phase: the familiarization trials were presented until criteria for orientation and habituation were attained or for 16 trials if the infant failed to orient or habituate; 2) Recovery Phase: a novel word was presented until orientation and habituation were attained or for 12 trials if the infant failed to re-orient or re-habituate; 3) Dishabituation Phase: the originally familiarized word was presented until the criterion for orientation was attained or for 9 trials if the criterion was not met. The criterion for orientation in each phase was defined as three turns toward the sound within four consecutive trials, and habituation required three successive trials in which no turn or turns away from the sound occurs after orientation (Zelazo, et al. 1989). The orientation and habituation criteria and the maximum number of trials in each phase were chosen based upon previous research with this procedure (Zelazo, et al. 1989). The principal dependent variable was head turns toward and away from the stimulus in each phase of the experimental procedure.

Apparatus and Stimuli

Auditory stimuli consisted of two words (tinder and beagle) presented through computer speakers placed approximately 20 cm from the infant's ears at a sound pressure level of 72 decibels. Output volume levels were checked with a sound pressure level meter at the beginning of each testing day. Each word was recorded by a female experimenter and was repeated in a consistent volume and intonation. Each word was approximately one second in duration and was repeated at a rate of one word every 2 seconds. The words *tinder* and *beagle* were chosen as test stimuli because of their low frequency of occurrence, comparable length, and phonetic content. These words were also identified previously as discriminable by older infants and neonates (Brody et al., 1984). Infants' responses were coded using a numeric keypad attached to a laptop computer. Four possible infant responses were coded on the keypad: right head turn, left head turn, fretting, and sleeping. A computer program written in Visual Basic was used to present the sound stimuli and keep track of the duration of the infants' responses, the duration of each trial, attainment of criteria for orientation and habituation, and the transition between phases.

Study Design

A multivariate design with one between-group independent variable (tobacco-exposed/control) and three measures of central information processing (orientation, habituation, and recovery to novelty) was employed to assess whether prenatal exposure to nicotine had an adverse effect on neonatal information processing. Multivariate and univariate analysis of variance, χ^2 tests, and t tests were used to assess group differences and within-group effects on the following measures of information processing: a) orientation to the stimuli in each of the three phases, b) habituation to the familiarization and novelty phase stimuli, and c) recovery of responding to the stimuli in the novelty and dishabituation phases. Multivariate analysis was also used to assess between group differences on several matching and control variables. These analyses consisted of a) three matching variables (BW, GA, and TA) and three demographic control variables (income, INC; maternal age, MA, and maternal education, ED), b) the percentage of time infants were in a positive state during the testing procedure, and c) the overall percentage of head turns toward the stimulus.

Data Reduction

As was done in previous studies conducted by Zelazo and colleagues (e.g. Potter et al., 2000; Zelazo et al., 1989) the following preparation of the data for analysis was conducted:

1) The trials in the familiarization and novelty phases were first divided into two equal or nearly equal blocks of trials. Generally, the first block represented orientation trials and the second block, habituation trials, with some overlap in the middle. When a trial block was made up of an uneven number of trials, turns toward the sound source were included in the first trial block, with turns away from the stimulus or no turns included in the second block. Trial blocks were used to assess changes in response patterns between phases (within group variable).

2) The two trial blocks in the familiarization phase were then subdivided again, resulting in four equal or nearly equal quartiles. Again, when a quartile was made up of an uneven number of trials, head turns toward the stimulus were included in quartiles near the beginning of the phase and head turns away or no turns were included in quartiles near the end of the phase. Reducing the trial blocks to quartiles was done to allow for changes in the direction of head turning to be assessed within each phase (within group variable). Therefore, in the following pages, with respect to the familiarization and novelty phases, the term “trial block” always refers to one half (or nearly one half) of the total trials in that phase and the term quartile always refers to one quarter (or nearly one quarter) of the trials of that phase.

For the dishabituation phase, a trial block of the first three to six trials was used in the data analysis. These trials were chosen because previous research indicated that infants would normally orient within six trials at this phase in the procedure (Zelazo et al., 1989). If the infant oriented in less than six trials, thus terminating the procedure, then the trial block was made up of that number of trials; i.e., if an infant oriented in three trials then the procedure was over and the dishabituation phase trial block consisted of those three trials. In the following pages this block will be referred to as the "dishabituation block." (See Appendix D for a sample-scoring sheet).

One further calculation was conducted prior to data analysis. Since the time the infant spent in a "positive state" (i.e., not sleeping or fretting) could influence his or her performance on the information processing procedure, it was important to determine if group differences existed on this variable. The amount of time spent in a positive state was calculated by adding up the time (in seconds) that the infant was fretting or sleeping during each trial and dividing this sum by the total sum of all trial lengths (i.e., the total time for the phase). The percentage of time spent in a positive state was then derived by subtracting the percentage of time spent in a negative state from 100%. This procedure was performed separately for each phase of the procedure.

Dependent Measures.

Three dependent measures were employed to assess information processing ability, and two control measures were used to ensure that the groups did not differ on head-turning ability and amount of time spent in a positive state. The three primary dependent measures were: 1) in each trial block and quartile and in the dishabituation block, the percentage of trials with head turns toward the sound source; 2) the number of trials required to reach the criterion for orientation in the familiarization, novelty, and dishabituation phases and habituation in the familiarization and novelty phases; and 3) a "difference score" calculated by subtracting the number of head turns away from the stimulus from the number of head turns toward, within the first and last quartile of each phase (a measure of preferential head turning toward or away from the stimulus). The two control variables were: 1) the overall percentage of head turns during the procedure (to ensure that both groups were equally capable of making head turns) and 2) the percentage of time the infant spent in a positive state.

Results

General Approach to the data analysis.

Three statistical techniques were used to analyze the data: multivariate and univariate analysis of variance, χ^2 tests, and t tests. Each of these techniques was used to analyze specific types of data.

MANOVAs were used to assess between group differences on the matching/demographic control variables, the information processing control variables (i.e., positive state and the overall percentage of trials with head turns), and changes in the percentage of head turning towards the stimulus across quartiles and trial blocks in the three phases of the information processing procedure. Following the rules and conventions of MANOVA, if the multivariate Wilk's lambda F was significant for the effect of Group or the Variable x Group interaction, then univariate F tests for the effect of Group were conducted to determine the source of the significance.

Group differences in the degree of orientation to the stimulus in each of the familiarization, novelty, and dishabituation phases were assessed by first using χ^2 tests to determine if the frequency of cases meeting the criterion for orientation differed among groups. Following the χ^2 tests, ANOVA was used to determine if the groups differed on the number of trials required to reach the criterion for orientation (infants who did not meet the criterion were excluded prior to analysis). The same process was used for the analyses of degree of habituation for the familiarization and novelty phases.

The difference score measure (number of head turns away subtracted from number of head turns toward) was used to determine whether the infants in each group differed in terms of preferential direction of head turns in the first and last quartiles of each phase. The difference scores were compared with a mean of zero using one-sample t-tests within each group. A score significantly greater than zero indicated that the infants turned toward the stimulus more often than they turned away. A score less than zero indicated that they turned away from the stimulus more often than toward, and a score not different from zero indicated random responding or a lack of head-turning. Therefore, difference scores greater than zero would be expected at the beginning of the phase (the first quartile, signifying orientation) and scores less than zero would be expected near the end of the phase (the last quartile, signifying habituation).

Reliability of Saliva Cotinine Analyses for Determining Tobacco Use During Pregnancy.

For the purpose of assessing the reliability of the presence of cotinine (the primary metabolite of nicotine) in maternal saliva as an indicator of cigarette use during pregnancy, the saliva samples from all mothers participating in the study were analyzed. As recommended by Jarvis et al. (1987) a cutoff concentration of 14.2 ng/ml was used to determine smoking status (i.e., mothers with saliva samples at this concentration or above were considered to have tested positive for cotinine). Saliva samples were collected from 106 mothers and were analyzed for the presence of cotinine. Three of the samples were not of a sufficient quantity to permit analysis, resulting in a total of 103 maternal saliva samples available for analyses.

The sensitivity (percent of smokers detected) and specificity (percent of nonsmokers correctly classified) was determined by comparing mothers' self-report of smoking status with the concentrations of cotinine detected in the saliva samples. Maternal self-report of smoking cigarettes was coded as a dummy variable with "no smoking" coded as 0 and "smoking" coded as 1. Seventy-nine of the mothers with valid saliva samples for analyses described themselves as nonsmokers, while 24 considered themselves to be smokers. Cotinine verification revealed that 76 of the self-reported nonsmokers tested negative for the presence of cotinine, with a mean concentration of 5.32 ng/ml, resulting in a specificity of 96.2% (3 tested positive for cotinine). Of the smokers only 16 tested positive for the presence of cotinine, with a mean concentration of 112.18 ng/ml, resulting in a sensitivity of 66.7%. However, it is not surprising that some of the smokers tested negative for the presence of cotinine, given that they had just spent the last 12 to 24 hours giving birth and as such had not had time to smoke a cigarette. Since it was assumed that mothers who did not smoke during pregnancy would not falsely report that they had smoked, for the purposes of the information processing component of this study, mothers who tested negative for the presence of cotinine, but who self-reported smoking were considered to be smokers. On the other hand, the three mothers who self-reported not smoking and who tested positive for the presence of cotinine were excluded from the pool of possible controls for the information processing procedure analyses. Chi-square analyses indicated that the cotinine analysis was significantly more specific than it was sensitive (i.e., nonsmokers were classified more accurately than smokers, χ^2 (1) = 48.36, $\underline{p}$ <.000).

In summary, the specificity of using cotinine analysis to verify self-report of smoking status during pregnancy was at a comparable level to that reported by Jarvis et al. (1987)

who found the specificity of saliva cotinine analysis to be 99%. However, the sensitivity was much lower. Where Jarvis et al. (1987) found sensitivities of 96 %, the present study had a sensitivity of only 66.7%. However, given the short half-life of cotinine and the fact that many of the smokers had not ingested nicotine within the past 24 hours, it is not surprising that verification was less accurate among pregnant women as compared to a general sample.

Four variables were used in further analyses of cotinine verification of smoking during pregnancy: a) as described above, maternal self-report of smoking cigarettes during pregnancy was coded as a dummy variable; b) the number of cigarettes smoked per day ,with non-smokers receiving a score of 0; c) the detection of cotinine in the saliva sample was coded as a dummy variable; and d) the fourth variable was the quantity of cotinine detected (nanograms/milliliter) in the saliva sample.

Pearson product-moment correlation coefficients were calculated for the relation between maternal self-report of smoking, number of cigarettes smoked per day, the detection of cotinine in the saliva sample, and the quantity of cotinine detected in the saliva sample for the 103 participants for which all information was available. As shown in Table 3 maternal self reports of smoking during pregnancy and the results of the saliva cotinine analysis were highly correlated, with r's ranging from .509 to .687, with $p < .01$. There was a significant positive relationship between mothers' self-report of smoking during pregnancy and saliva cotinine analysis as well as a significant positive correlation between the number of cigarettes smoked per day and the quantity of cotinine detected in the mothers' saliva.

Table 3

Correlation Coefficients for the Relation Between Maternal Tobacco Use During Pregnancy and Cotinine in Maternal Saliva

Variable	SMOKE-YN	CIG#
COT-YN (n= 45)	.685*	.687*
COT-QTY (n=45)	.509*	.635*

*$p < .01$

COT-YN = continine present – yes/no; COT-QTY = quantity of cotinine detected (ng/ml); SMOKE-YN = smoking reported by mother – yes/no; CIG# = average number of cigarettes smoked per day (based on self-report).

Effect of Reporting Channel on Accuracy of Maternal Self-Report of Smoking

The mothers in the tobacco-exposed and control groups were divided according to the method by which they reported their smoking status (i.e., face-to-face interview vs. self-administered questionnaire). The sensitivities and specificities of the cotinine analyses were compared between the mothers who participated in a face-to-face interview and those who completed a self-administered questionnaire, to investigate whether the reporting channel had an impact on the accuracy of mothers' self-report. Of the self-reported smokers, 62.5% (n=15) completed the self-administered questionnaire and 37.5 % (n=9) participated in a face-to-face interview. Of the self-reported non-smokers, 44.3% (n=35) completed the questionnaire, while 55.7 %(n=44) participated in the interview.

The sensitivity (percent of smokers detected) of the saliva cotinine analyses was 55.6% for the face-to-face interview and 73.3 % for the self-administered questionnaire. However, chi square analyses indicated that this difference in the sensitivity of the saliva cotinine analyses between the interview and questionnaire conditions was not significant, χ^2 (1) = .800, p = .371. However, the sensitivities of the cotinine analyses appears to be different between the two different reporting channels and it is possible that the finding was not significant because of a lack of power due to the small sample sizes in each cell.

The specificity (percent of nonsmokers correctly classified) of the saliva cotinine analyses was 93.2 % for the face-to-face interview and 100% for the self-administered questionnaire. The specificity of the saliva cotinine analyses was not influenced by reporting channel, χ^2 (1) = 2.48, p = .115.

In summary, reporting channel did not significantly influence the specificity and sensitivity of the saliva cotinine analyses.

Analyses of Matching/Demographic Control Variables. The three matching variables chosen, birthweight (BW), gestational age (GA), and test age (TA), were the infant characteristics on which it was predicted that potential group differences that could influence the information processing variables might exist. A MANOVA with Group as the independent variable and the three matching variables as the dependent measures indicated that the groups did not differ on these three matching variables, F,(3,44) = .456, p=.714.

The three demographic control variables income, maternal age and maternal education, were assessed to determine if group differences existed on these variables. Results of a MANOVA with Group as the independent variable and the three demographic control variables as the dependent measures revealed a multivariate effect of Group, F (3,43) = 7.79, p<.000. Univariate analysis indicated that compared to controls, tobacco-exposed infants were born to mothers with a lower income level, F (1, 45) = 13.6, p<.001, lower levels of education, F (1, 45) = 8.84 , p<.005, and had mothers who were younger, F (1, 45) = 17.39 , p<.000 (means and standard deviations of the three matching variables and three demographic control variables are shown in Table 4). To investigate if the Group differences on the demographic control variables influenced the outcome variables, a repeated measures MANOVA was run with the three demographic variables as the independent variables and the outcome measures on the information processing task as the dependent variables. No significant multivariate or univariate effects were found.

Control Measures for Information Processing Ability. To rule out the possibility that as a result of prenatal tobacco exposure, the tobacco-exposed newborns might be less

Table 4

Group Means and Standard Deviations for Tobacco-Exposed and Control Newborns on the Three Matching and Three Demographic Control Variables.

Variable	Tobacco (n =24)	Control (n=24)
Subject Matching Variables		
Birthweight (g)	3330 (403) [a]	3371 (395)
Test age (hours)	26.0 (15.0)	32.2 (20.9)
Gestational age (wks)	39.4 (1.4)	39.4 (1.3)
Demographic Control Variables		
Income (x $1,000 per year)	24.6* (11.4)	39.2* (16.4)
Mother's age (yrs)	22.7* (4.5)	26.6* (4.2)
Mothers education (yrs)	11.6* (1.5)	13.4* (1.4)

[a]Standard deviations are in brackets beside each group mean.

* $p<.005$

capable of making head turns than the control infants, the tobacco-exposed and control newbornswere compared on the overall percentage of trials with head turns in either direction. The percentage of trials that ended in a head turn was collapsed across the three phases of the procedure. Between-group differences were examined by a one-way ANOVA with Group as the independent variable and the percentage of trials ending in a head-turn as the dependent variable. No significant group differences in the overall percentage of head-turning were found, F (1, 46) =1.76, p=.191, indicating that tobacco-exposed and control newborns were equally capable of making head turns. Tobacco-exposed and control infants made head turns on an average of 76.8% and 83.5% of trials, respectively. The second information processing control variable was the amount of time spent in a positive state. Since group differences on this variable would represent a serious confounding variable, it was important to ensure that any group differences on the information processing variables could not be attributed to differences in positive state. The group means and standard deviations for the percentage of time spent in a positive state in the three phases are shown in Table 5. A 2 (Group) x 3 (Phase) repeated measures MANOVA with the percentage of time spent in a positive state in each phase as the dependent measure, revealed that collapsed across groups, a high level of positive state was achieved in all three phases of the procedure, F (3, 44) = .158, p= .924, with grand means for the familiarization, novelty, and dishabituation phases of 82.6%, 82.8%, and 81.3%, respectively. No between-group differences were found, F (1,46) = .015, p=.903. The Phase x Group interaction was also not significant, F(3,44) = .302, p = .824.

Table 5

Group Means and Standard Deviations for Percentage of Time Spent in a Positive State Across Phases, for Tobacco-exposed and Control Neonates

Group	Familiarization	Novelty	Dishabituation
Tobacco-exposed	84.1% (21.3)	82.2% (25.6)	81.7% (29.6)
Controls	81.1% (20.8)	83.5% (21.0)	80.9% (24.7)

Effects of Tobacco Exposure

Analyses of Information Processing Ability. Figure 1 illustrates the percentage of head turning toward the sound source across the three phases of the procedure for the tobacco exposed and control infants. The familiarization phase is broken down into four quartiles as shown in Panel a, the scores for the novelty phase trial blocks are shown in Panel b, and the dishabituation block is shown in Panel c.

Familiarization Phase. To assess whether the tobacco-exposed and control infants showed an initial high percentage of head turns toward the familiarization stimulus (orientation) that decreased across the phase (habituation), a 2 (Group) x 4 (Quartiles) repeated measures MANOVA was conducted with percentage of head-turns toward the stimulus in each of the four quartiles as the dependent variables. The multivariate effect of Quartiles was significant, F (3, 44) = 25.5, p<.000, indicating that collapsed across Group, the percentage of head-turns toward the stimulus decreased across quartiles; the percentage of head turns decreased in a linear fashion from 60.7% in the first quartile to 21.9% in the fourth quartile. However, a Group x Quartile interaction, F (3, 44) = 5.98, p<.002, revealed that the groups differed in the percentage of head turns toward the stimulus across the four quartiles. A multivariate effect of Group was obscured due to the interaction, F (1,46) = 2.38, p=.130. Univariate analyses indicated that the two groups performed differently in the last quartile, F (1, 46) = 18.72, p < .000. Inspection of the means revealed that the tobacco-exposed group maintained a high level of head turning toward the sound source compared to the control group, with means of 39.6% and 4.2 % of trials ending with a turn towards the sound, respectively.

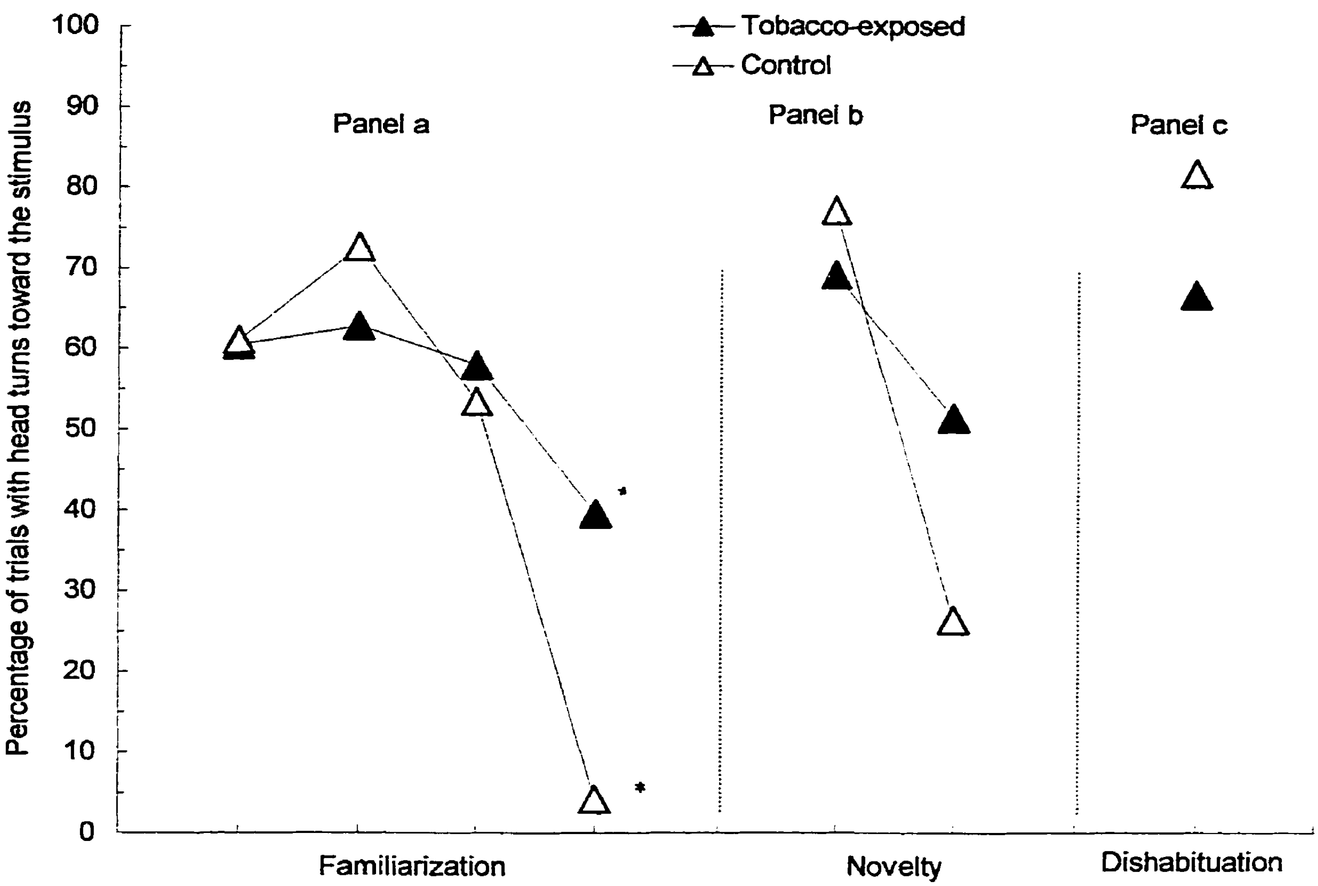

Figure 1. Mean percentage of head turns toward the sound source across the four quartiles in the familiarization phase (panel a), the two trial blocks of the novelty phase (panel b), and the dishabituation block (panel c) for the tobacco-exposed and control groups.

*$\underline{p}<.001$

To assess whether turns toward or away from the familiarization stimulus exceeded chance levels at the beginning and end of the familiarization phase, difference scores (turns toward minus turns away) were compared with a mean of zero in the first and last quartiles for each group. One-sample t tests were used to determine whether the mean difference for each group was significantly different from zero. Analyses revealed that both the nicotine-exposed group, t (23) = 6.09, p< .000, and the control group, t (23) = 4.38, p< .000, turned preferentially toward the stimulus in the first quartile of the familiarization phase. However, in the last quartile, the mean difference for the nicotine-exposed group was not significantly different from zero, t (23) = 1.96, p = .062, indicating that the direction for head turning was random. However, the control group turned preferentially away from the stimulus in the last quartile, t (23) = -6.41, p<.000.

To determine if the nicotine-exposed and control newborns exhibited similar levels of orientation and habituation to the stimulus, between group comparisons on the number of newborns reaching the criterion for orientation and habituation were carried out using χ^2 analyses. No group differences were found for the percentage of neonates who reached the criterion for orientation, χ^2 (1) = 2.00, p = .156, with 83 % of the tobacco-exposed and 96% of the control group reaching criterion. The infants who achieved the criterion for orientation were included in a one-way ANOVA to determine if there were group differences in the number of trials required to reach orientation. The results of this analysis indicated that there were no group differences in the number of trials required to reach criterion for orientation, F (1, 41) = 1.59, p = .215. As shown in figure 2 (panel a) of the infants who oriented, the tobacco-exposed infants oriented in an average of 5.6 trials, and the control infants oriented in an average of 4.6 trials.

Tobacco-exposed infants were less likely to reach the criterion for habituation, χ^2 (1) = 15.39, p<.000. Ninety-two percent of the control group reached criterion for habituation, while only 37.5% of the tobacco-exposed infants achieved this criterion. Of the infants who habituated there was no difference in the number of trials required to reach criterion, F (1, 29) = .764, p = .389. As shown in figure 2 (panel a), the tobacco-exposed infants required 10.6 trials to reach criterion, and control infants required 9.7 trials.

In summary, the results of the data analyses for the familiarization phase indicate that tobacco-exposed infants performed at the same level as matched controls on measures of orientation to the familiarization stimulus. However, the tobacco-exposed group was less likely than controls to reach the criterion for habituation. While both the control group and the tobacco-exposed group turned systematically toward the stimulus in the first part of the familiarization phase, indicating orientation, only the control group turned systematically away from the sound source in the last part of the phase, indicating habituation. The tobacco-exposed group turned randomly toward and away from the sound source in the last part of this phase, indicating a lack of habituation to the sound stimulus.

Novelty Phase. A 2(Group) x 4(Quartiles) repeated measures MANOVA with percentage of head-turns toward the stimulus as the dependent measure was used to compare the tobacco-exposed and control infants on the percentage of head turns toward the stimulus across the four quartiles of the novelty phase. The multivariate effect of quartiles was significant, F (3,44) = 17.75, p <.000, reflecting a decrease in the percentage of head-turns toward the stimulus across quartiles. Collapsed across groups, the percentage of head-turns decreased in a linear fashion from 71.4% in the first quartile

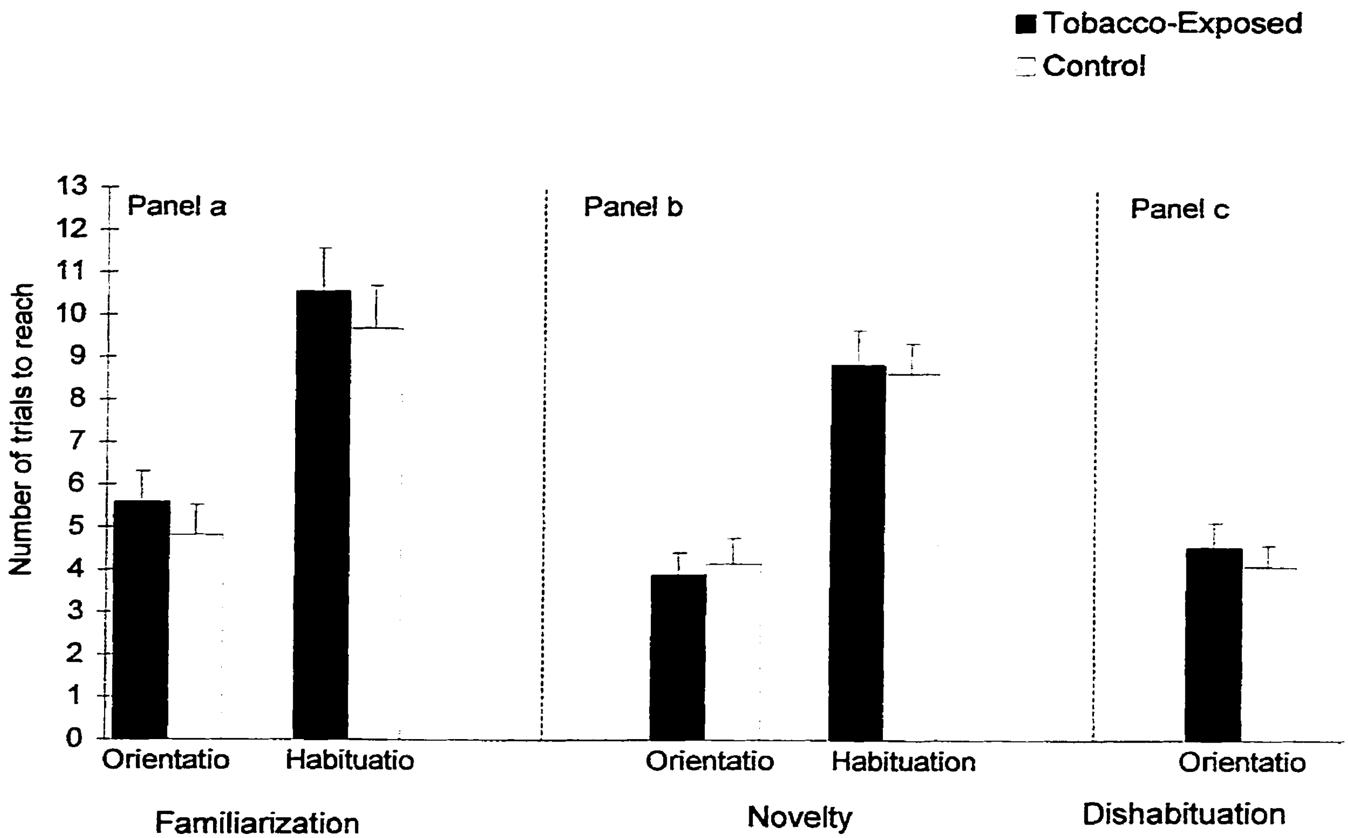

Figure 2. Number of trials required to reach criteria for orientation and habituation in the familiarization (panel a) and novelty (panel b) phases, and orientation in the dishabituation phase, for tobacco-exposed and control neonates.

to 28.5% in the last quartile. A main effect of Group was not found, F (1, 46) = 1.59, p = .213; however, a Group x Quartile interaction approached significance, F (3,44) = 2.32, p<.088. Due to the small sample size, univariate analyses were explored to investigate possible differences in the percentage of head turns toward the sound stimulus. A univariate effect was found in the last quartile of the novelty phase, F (1,46) = 7.78, p<.008. Inspection of means revealed that the tobacco-exposed group maintained a higher percentage of head-turns toward the stimulus in the last quartile of the novelty phase compared to the control group, with means of 41.7% (tobacco-exposed) and 15.2 % (control). The mean percentage of turns toward the stimulus for each group across the four quartiles is shown in Figure 3.

Since recovery to novelty following habituation to a familiarization stimulus has been demonstrated by previous research to be the best information processing measure for discriminating among infants at high, moderate, and low risk for developmental delay (Zelazo et al., 1989), analyses investigating recovery to a novel stimulus were of particular importance to this study. Recovery of head turning upon introduction of the novel stimulus was assessed by comparing the percentage of head turns toward the stimulus in the last trial block of the familiarization phase and first trial block of the novelty phase.

A 2 (Group) x 2 (Trial Block) repeated measures MANOVA, with percentage of head-turns toward the stimulus as the dependent variable, revealed a multivariate effect of trial block, F (1,46) = 71.6, p<.000, indicating that collapsed across Group, the overall percentage of turns toward the stimulus increased between the last trial block of the familiarization phase and the first trial block of the novelty phase, from 37.7% in the last block of the familiarization phase to 73.1% in the first block of the novelty phase. The

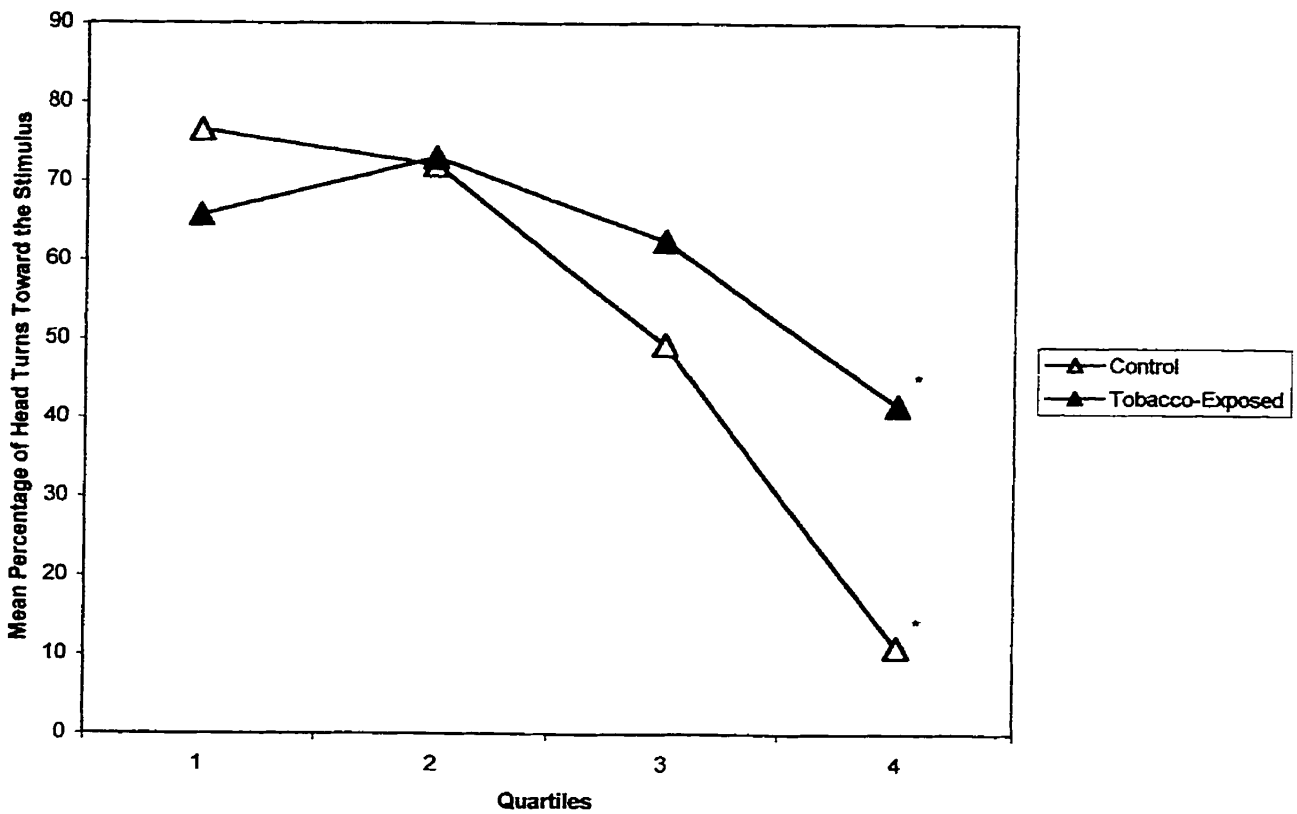

Figure 3. Mean percentages of head turns toward the stimulus during the four quartiles of the novelty phase, for tobacco-exposed and control neonates.

*p<. 008 post hoc

multivariate effect of Group did not reach significance, F (1,46) = 1.52, p = .224; however, a Group x Trial Block interaction was significant, F (1,46) = 11.79, p<.001, reflecting group differences in the pattern of head-turning toward the stimulus in the two Trial Blocks. Univariate analyses indicated that this difference was accounted for solely by the difference in head turning in the last trial block of the familiarization phase, F (1, 46) = 10.06, p<.003. Inspection of means revealed that the tobacco-exposed group maintained a higher level of head turning toward the stimulus (M = 48.1%) relative to controls (M = 27.3%), in the last trial block of the familiarization phase. The groups did not differ on recovery to novelty, F (1,46) = 1.38, p =.247. However, a paired sample t – test comparing the last trial block of the familiarization phase with the first trial block of the novelty phase revealed that both the tobacco-exposed, t (23) = -3.46, p< .002, and the control, t (23) = -8.65 p< .000, groups did recover responding upon introduction of the novel stimulus. Examination of the means revealed an increase in the percentage of head turns toward the stimulus from the last trial block of the familiarization phase to the first trial block of the novelty phase, with means for the tobacco-exposed group of 48.1% and 69.2%, respectively, and the 27.3 % and 77.1%, respectively, for the controls, as shown in figure 4.

To assess the number of turns toward the stimulus relative to turns away at the beginning and end of the novelty phase, the difference scores for the first and last quartiles for each group in the novelty phase were compared with a mean of zero. Analyses indicated that both the tobacco-exposed, t (23) = 4.33, p<.000, and control groups, t (23) = 7.40, p<.000, turned preferentially toward the stimulus in the first quartile. However, in the last quartile, while the control group turned systematically away from the stimulus,

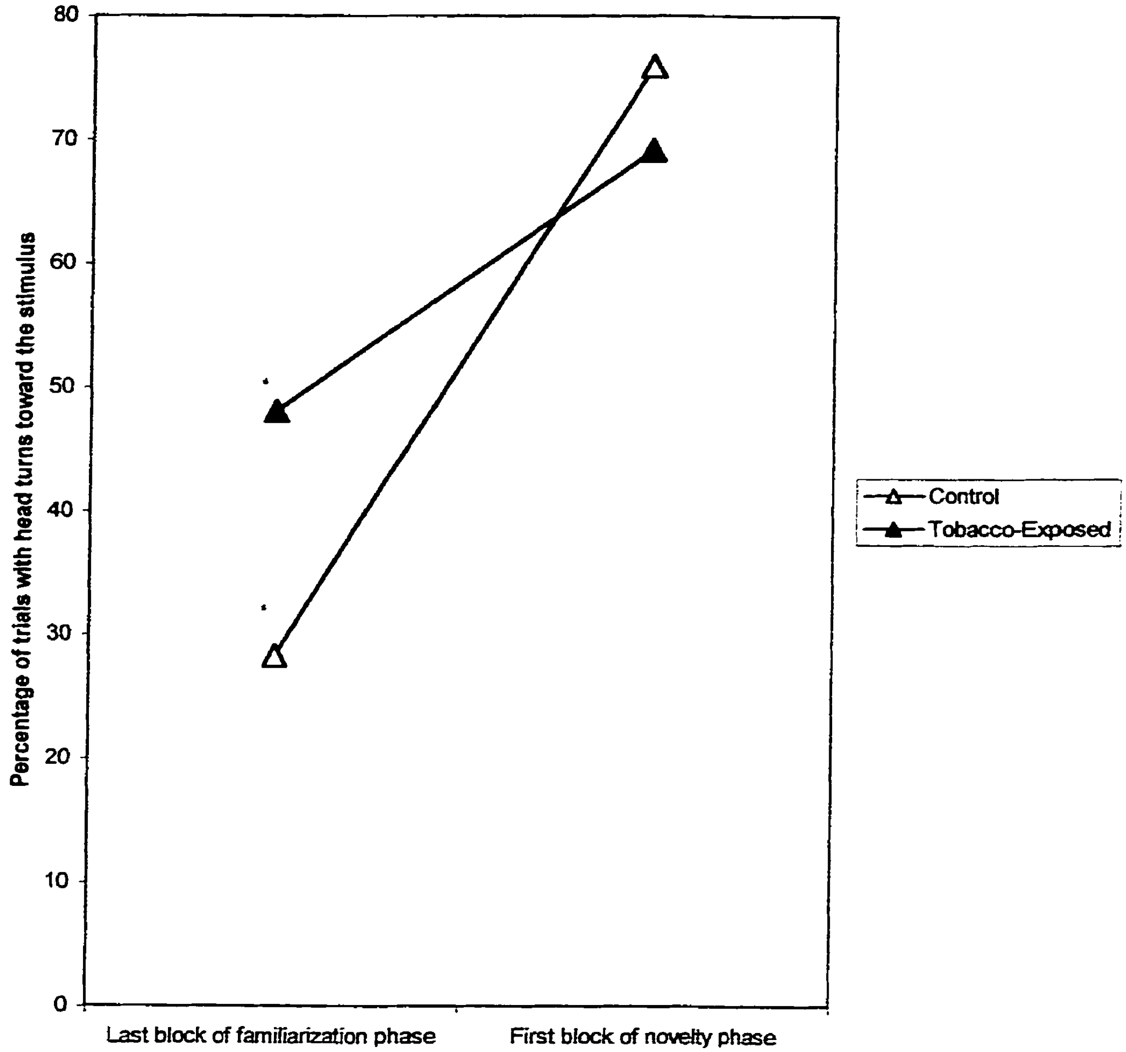

Figure 4. Response to novelty among tobacco-exposed and control neonates as determined by change in head turns toward the sound source between the last trial block of the familiarization phase and the first trial block of the novelty phase.

*$p<.003$

t (23) = -6.79, p<.000, the tobacco-exposed group turned randomly toward and away from the stimulus, t (23) = 1.06, p=.302.

The percentage of infants in each group who reached the criterion for orientation and habituation to the novel stimulus were compared using χ^2 analyses. No group differences were found on orientation to the novel stimulus, χ^2 (1) = 2.40, p = .121. Ninety-two percent of control infants and 75 % of tobacco-exposed infants reached criterion for orientation. However, tobacco-exposed infants were less likely than controls to reach criterion for habituation, χ^2 (1) = 14.11, p <.000, with 79% of controls and only 25% of tobacco-exposed infants reaching criterion. As illustrated in figure 2(Panel b) there was no difference in the number of trials required to reach the criteria for orientation, F (1, 38) = .001, p =.971, or habituation, F, (1, 23) = .343, p=.564.

Together, the results of these analyses for the novelty phase indicate that the information processing ability of the tobacco-exposed infants is compromised relative to controls. Specifically, exploration of univariate analyses revealed a that the tobacco-exposed group maintained a higher percentage of head turns toward the stimulus in the last quartile of the novelty phase relative to controls. While both groups oriented to the novelty stimulus, the tobacco-exposed infants were less likely to habituate to the novelty stimulus as compared to the control group. Moreover, the tobacco-exposed infants turned randomly toward and away from the novelty stimulus in the last quartile whereas the control group turned systematically away. However, both the tobacco-exposed and control groups exhibited similar responses in recovery of responding to the novel stimulus.

Dishabituation Phase. In the dishabituation phase the original stimulus in the familiarization phase was reintroduced. To determine if the introduction of the dishabituation stimulus would elicit recovery of head turning, the percentage of head turns toward the stimulus during the second block of the novelty phase was compared with the percentage of head turns toward the stimulus in the dishabituation block. A 2 (Group) x 2 (Block) repeated measures MANOVA with percentage of head turns toward the stimulus as the dependent measure, revealed a multivariate effect of Block, $\underline{F}$ (1,46) = 69.9, $\underline{p}$<.000, indicating that collapsed across Group, the percentage of head turns toward the stimulus increased across the two trial blocks, from 38.9% in the last trial block of the novelty phase to 74.2% in the dishabituation block. There was no main effect of Group, $\underline{F}$ (1,46) = .674, $\underline{p}$=.416, however, a significant Group x Block interaction, $\underline{F}$ (1, 46) = 25.6, $\underline{p}$<.000, revealed differences in the pattern of head-turning between groups. As shown in figure 5, univariate analyses indicated that this effect was due to differences in head turning responses in the last block of the novelty phase, $\underline{F}$ (1,46) = 13.35, $\underline{p}$<.001. Inspection of the group means revealed that the tobacco-exposed group responded with a greater percentage of head turns toward the stimulus in the last block of the novelty phase ($\underline{M}$ = 51.45%) as compared to the control group ($\underline{M}$ = 26.39%). Paired sample $\underline{t}$ – tests comparing the last trial block of the novelty phase with the dishabituation block indicated that both the tobacco-exposed, $\underline{t}$ (23) = -2.26, $\underline{p}$<.033, and control groups, $\underline{t}$ (23) = -10.87, $\underline{p}$<.000, recovered responding to the dishabituation stimulus with means of 66.7% and 81.74%, respectively. A one-way, between-groups ANOVA with the percentage of head-turns toward the stimulus in the dishabituation trial block as the dependent measure approached significance, $\underline{F}$ (1, 46) = 3.60, $\underline{p}$ = .064. Comparison of the relative number of turns toward versus turns away from the dishabituation stimulus with a mean of zero, indicated that both the control group, $\underline{t}$ (23) = 19.22, $\underline{p}$<.000, and the tobacco-exposed

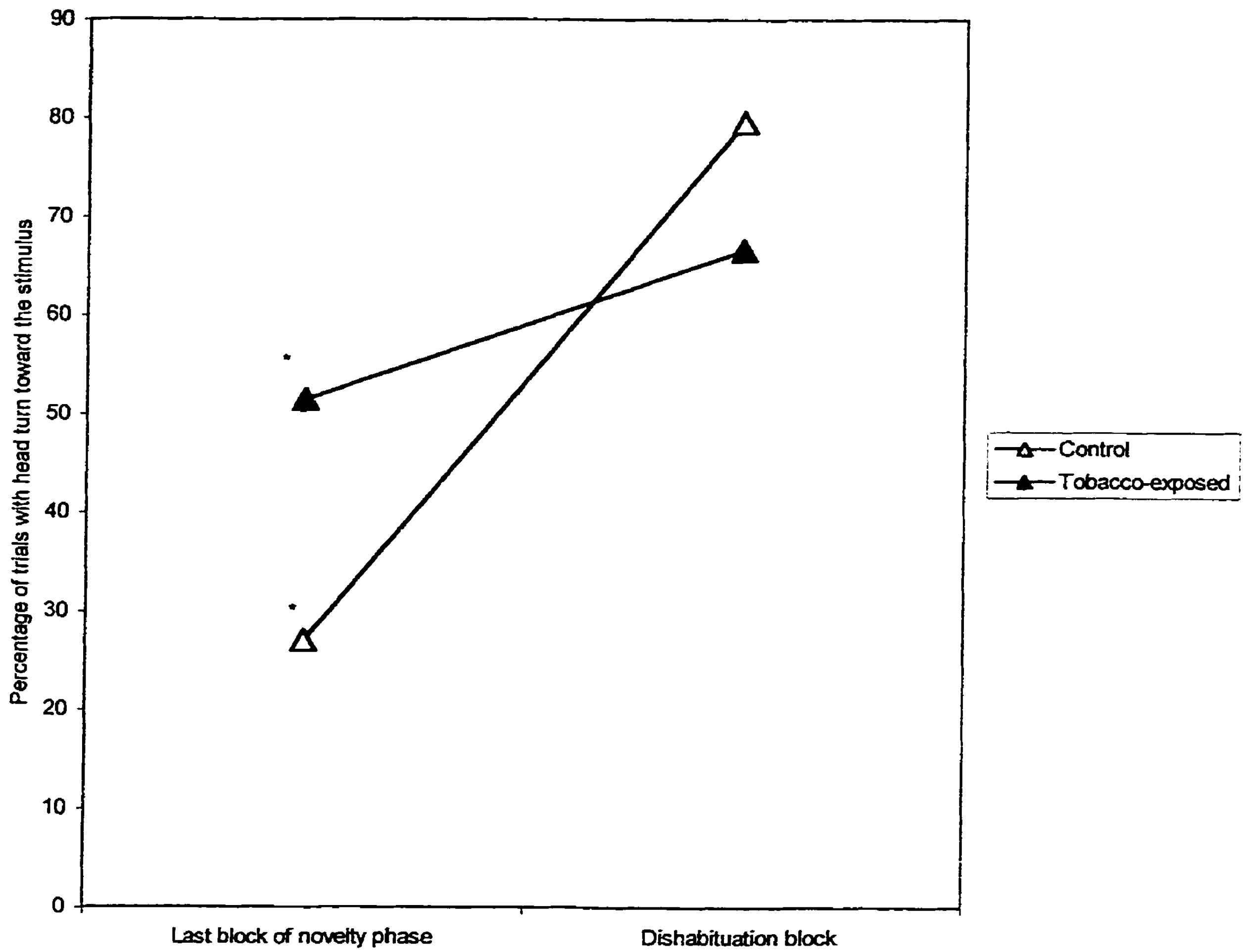

Figure 5. Recovery of responding to the familiarization phase among the tobacco-exposed and control infants determined by change in head turns toward the stimulus between the last block of the novelty phase and the first block of the dishabituation phase.

*$p<.001$

group, t (23) = 7.65, p<.000, turned systematically toward the dishabituation stimulus. However, χ^2 analyses revealed that the two groups differed in the percentage of infants in each group who reached the criterion for orientation, χ^2 (1) = 5.58, p< .018. Whereas, 100% of the control group reached criterion for orientation, only 79% of the tobacco-exposed infants oriented. However, of the infants who oriented in each group, there was no difference in the number of trials required to reach the criterion for orientation, F, (1, 41) = 1.17, p = .285, with mean number of trials for the control group of 4.00 and for the tobacco-exposed group of 4.53, as shown in figure 2 (panel c).

Together, the results of the dishabituation analyses indicate that upon introduction of the dishabituation stimulus, both groups recovered responding to the stimulus and turned preferentially toward the stimulus. Moreover, both groups required a similar number of trials to reach criterion for orientation, although the tobacco-exposed infants were less likely to orient to the dishabituation stimulus than controls.

Summary

Compared to controls, infants born to mothers who smoked tobacco during pregnancy had mothers who were younger, had less education, and were at a lower income level. There were no differences in the ability of the infants in either group to make head turns toward or away from the sound source, and there were no differences in the degree of positive state achieved in each phase of the procedure. However, the tobacco-exposed and control groups differed on numerous information processing measures. In both the familiarization and novelty phases, the tobacco-exposed and control infants oriented to the sound source in a similar number of trials. However, the tobacco-exposed infants were less likely to habituate than the controls. Further, while both the control group and the tobacco-exposed group turned preferentially toward the sound source in the first part of the phase (implying orientation) only the control group turned systematically away from the sound source (implying habituation) during the second part of the phase while the tobacco-exposed group turned randomly toward and away from the sound source. In the novelty phase, both groups recovered responding to the novel stimulus although the tobacco-exposed infants did not habituate as well as controls. In the dishabituation phase, both groups recovered responding to the stimulus and turned preferentially toward the dishabituation stimulus, implying orientation. However, control infants were more likely to orient to the dishabituation stimulus relative to the tobacco-exposed infants.

Effects of Tobacco-Exposure: Three-Week Follow-Up

One objective of this study involved retesting the infants at three weeks of age in order to assess if any differences found at birth would remain after a period of time. The main reason for this retest was to remove the influences of nicotine withdrawal on the infants' performance on the information processing procedure.

Participants

Nine tobacco-exposed infants were tested on the information processing procedure at three-week follow-up. Thirty-four participants from the control group were tested at three-week follow-up. From this sample, nine controls were matched on the three matching variables (BW, GA, and TA) using the same matching procedure as the initial testing sample. The raw data for each tobacco-exposed infant and their matched control is in Table 5. As in the previous sample, infants prenatally exposed to tobacco had mothers who were younger, had less education and were from a lower income level compared to the matched control group. The means and standard deviations for the matching and demographic control variables for the tobacco-exposed and control groups are shown in Table 6.

Procedure

Mothers who had agreed to be contacted were telephoned and asked to come into the Valley Regional Hospital to participate in the three-week follow-up test. The information processing procedure was identical to that used in the testing at birth.

Analyses of Information Processing Ability

Unfortunately, the small sample size (n=18) at three-week follow-up precluded the use of quantitative analyses; therefore, the results of this part of the study will be discussed qualitatively. As in the first part of this study, figure 6 illustrates the percentage of head turning toward the sound source across the three phases of the procedure for the tobacco exposed and control infants. The familiarization phase is broken down into four quartiles as shown in Panel a, the scores for the novelty phase trial blocks are shown in Panel b, and the dishabituation block is shown in Panel c.

Information Processing Control Variables. Two information processing control variables were explored in this part of the study, 1) positive state, and 2) overall percentage of turns. Both the tobacco exposed and control groups maintained a high level of positive state throughout the information processing procedure with grand means of 89.9% for the tobacco-exposed and 87.1% for the control group. Both the tobacco-exposed group and the control group made similar percentages of head-turns toward the stimulus with means of 73.7% and 71.5%, respectively. Observation of this data would suggest that the groups did not differ on these control measures.

Table 6.

Raw data on Subject Matching for Tobacco-Exposed Infants and their Matched Controls at Three-Week Follow-Up

Birthweight (g)		Gestational Age (weeks)		Test Age (hours)	
Smoker	Control	Smoker	Control	Smoker	Control
4342	4115	40	40	31	33
2881	2953	39	38	21	24
3141	3062	41.5	40	21	23
2923	2890	37.5	38.5	22	21
3200	3596	42.5	39	29	22
3046	3511	39	39	20	22
3881	3451	41.5	41.5	29	26
3119	3489	38	40	23	23
2990	3683*	40	41	22	21

*matched control is outside of the matching criteria for that particular variable.

Table 7

Group Means and Standard Deviations for Tobacco-Exposed and Control Newborns on the Three Matching and Three Demographic Control Variables at Three-Week Follow-Up.

Variable	Tobacco (n =9)	Control (n=9)
Subject Matching Variables		
Birthweight (g)	3280 (495)[a]	3496 (391)
Test age (days)	24.4 (3.7)	24.2 (4.2)
Gestational age (wks)	39.9 (1.7)	39.7 (1.1)
Demographic Control Variables		
Income (x $1,000 per year)	24.6 (11.4)	39.2 (16.4)
Mother's age (yrs)	23.8 (4.9)	31.0 (2.8)
Mothers education (yrs)	10.4 (1.2)	13.6 (1.3)

[a]Standard deviations are listed in brackets beside each group mean.

Familiarization Phase. Observation of the data for this phase indicates that a similar pattern of results was found at three-week follow-up as at initial testing. Figure 6 (panel a) illustrates that the infants made a similar percentage of head turns toward the sound source in the first three quartiles of the familiarization phase (indicating orientation), while it would appear that the tobacco-exposed group maintained a higher percentage of head turning in the last quartile compared to controls, with mean percentage of head-turns toward the sound source of 41.7 % for the tobacco-exposed group and 13.9% for the control group.

As shown in figure 7 (panel a), there appears to be no difference in the percentage of infants who oriented in the familiarization phase, with 77.8% of the control group and 88.9% of the tobacco-exposed group reaching the criterion for orientation. However, the percentage of infants who reached the criterion for habituation appears to be higher for the control group, with 77.8% reaching criterion, compared to the tobacco- exposed group, of whom 44.4% reached the criterion for habituation. Of the infants who reached the criteria for orientation and habituation there appears to be no difference in the number of trials required to reach the criteria, as shown in Figure 8 (panel a).

Novelty Phase. In this phase of the procedure the data seem to indicate that, as in the familiarization phase, both groups of infants had similar percentages of head turns toward the sound source in the first three quartiles; however, the tobacco-exposed group had a higher percentage of head turns in the last quartile relative to controls, as illustrated in Figure 9. The mean percentage of head turns toward the stimulus in the last quartile of the novelty phase was 52.0 % for the tobacco-exposed group and 25.9% for the control group.

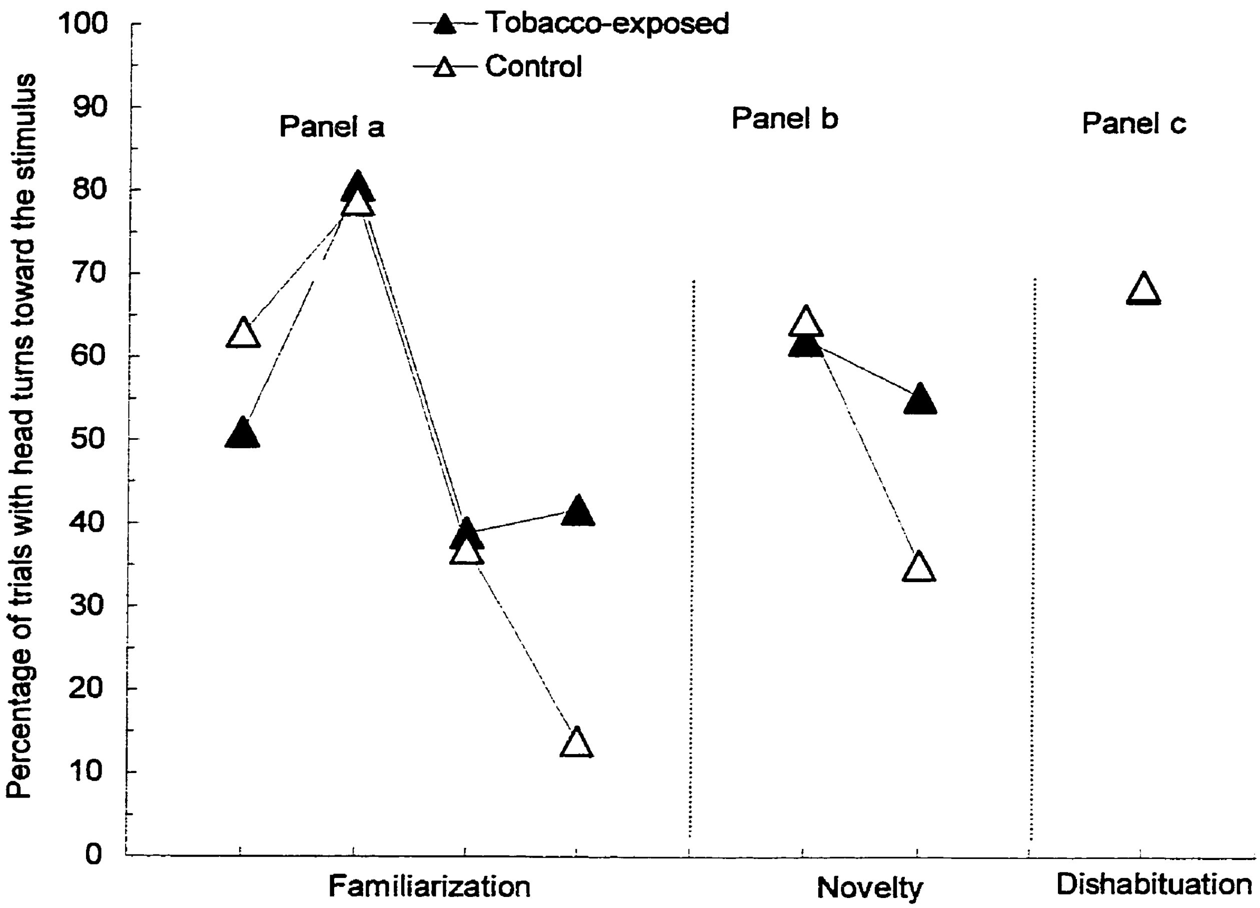

Figure 6. Mean percentage of head-turning toward the sound source for the tobacco-exposed and control infants during: familiarization phase quartiles (panel a); novelty phase trial blocks (panel b); and the dishabituation phase block (panel c) at three-week follow-up.

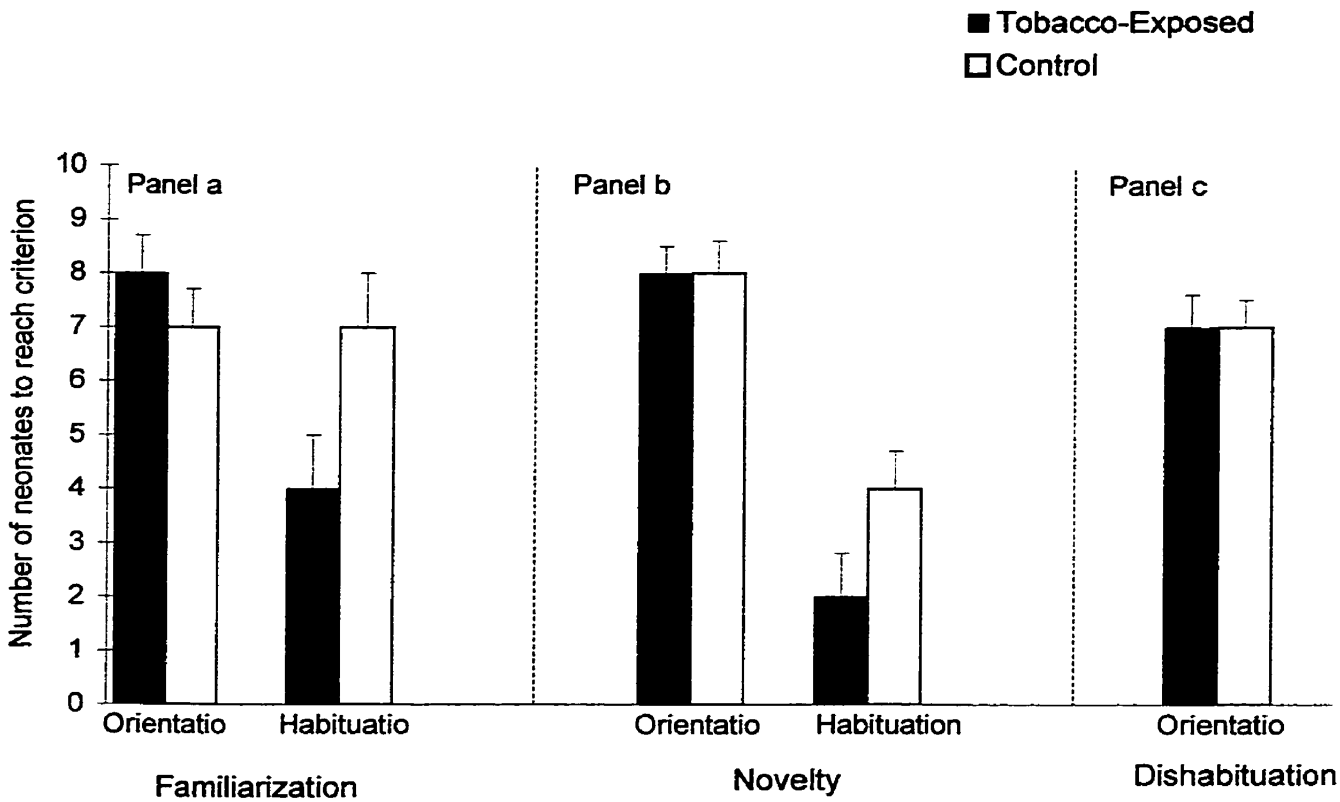

Figure 7. Number of neonates who reached criteria for orientation and habituation in the familiarization (panel a) and novelty (panel b) phases, and orientation in the dishabituation phase, for tobacco-exposed and control neonates, at three-week follow-up.

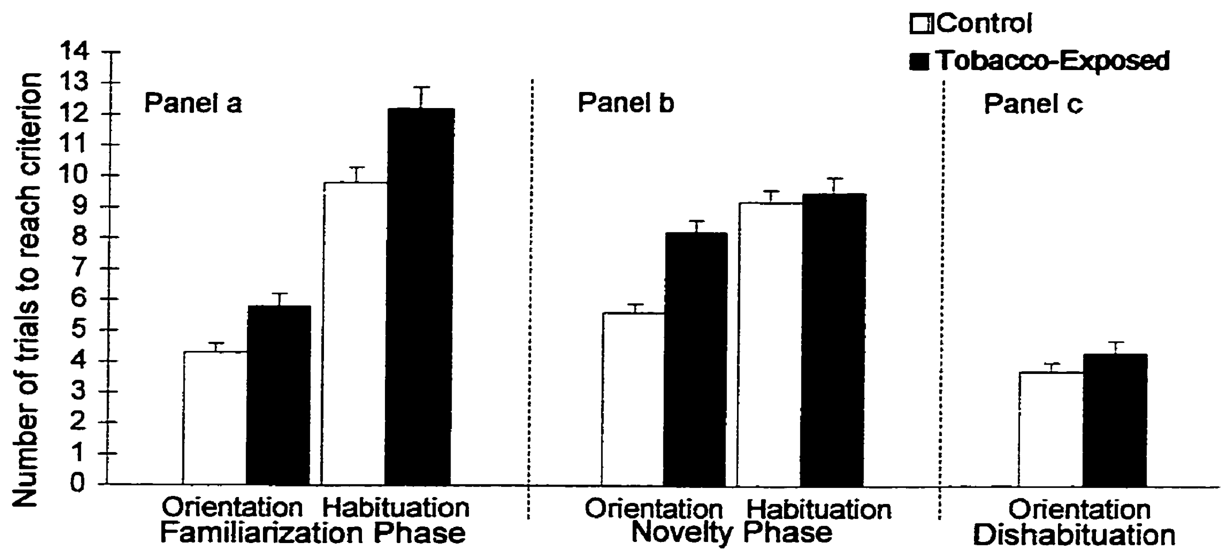

Figure 8. Number of trials required to reach criterion for orientation and habituation in the familiarization (panel a) and novelty phases (panel b), and orientation in the dishabituation phase (panel c), for tobacco-exposed and control infants, at three-week follow-up.

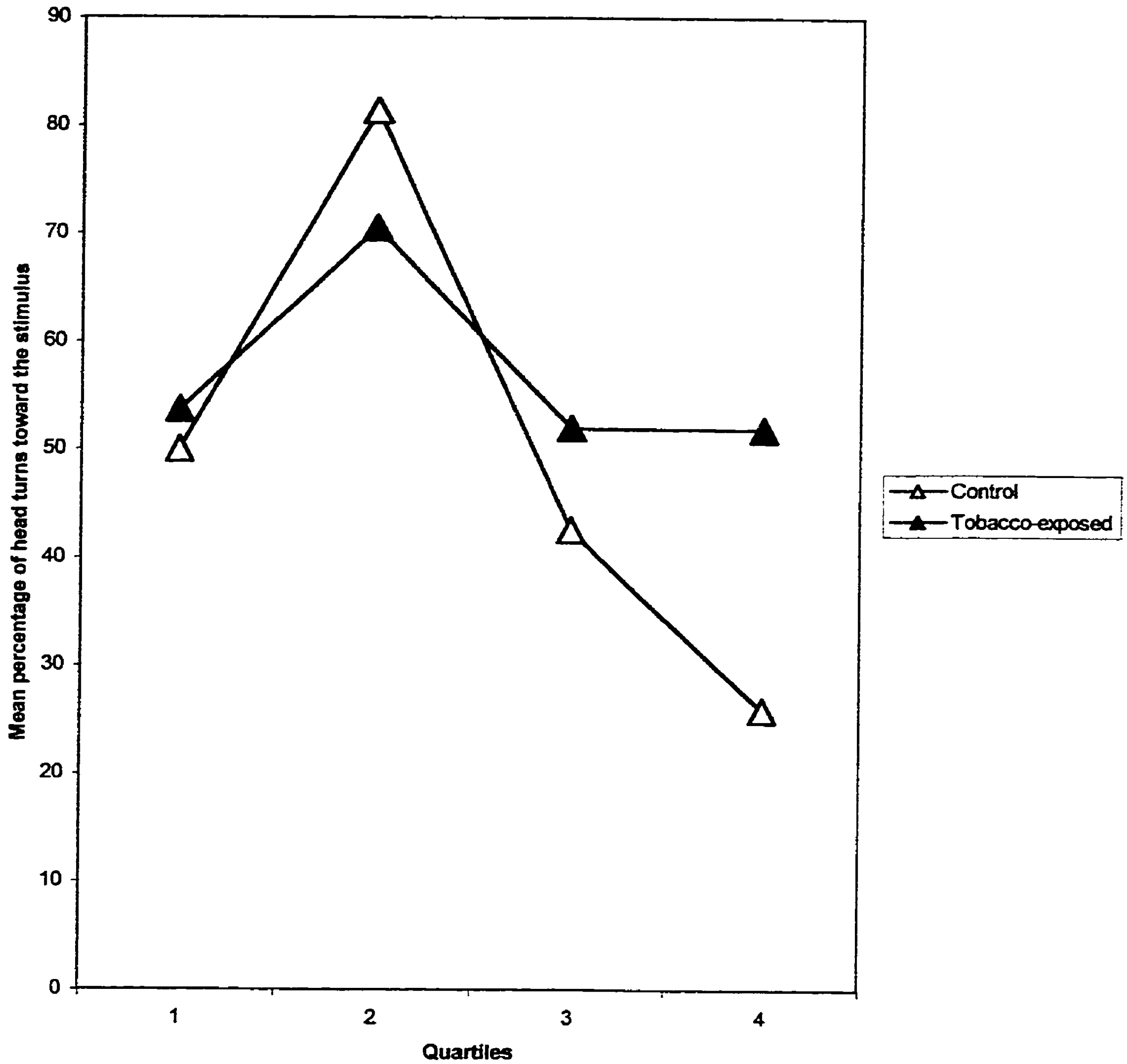

Figure 9. Mean percentage of head turns toward the sound source across the four quartiles of the novelty phase for the tobacco-exposed and control groups at three-week follow-up.

The percentage of head turns toward the stimulus increased between the last block of the familiarization phase and the first block of the novelty phase for both the tobacco-exposed and control groups implying recovery to the novel stimulus. The control group turned toward the stimulus on only 22.0% of trials during the last block of the familiarization phase and 64.6% of trials during the first block of the novelty phase, whereas the same means were 40.1% and 62.1%, respectively, for the tobacco-exposed group.

For both the tobacco-exposed and control groups, 88.9% of the infants reached the criterion for orientation and required a similar number of trials to achieve this, with 5.6 trials for the control group and 6.2 trials for the tobacco-exposed. However, the data indicate that the control group may have been more likely to habituate to the novel stimulus than the tobacco-exposed group, with 44.4% of control infants reaching the criterion compared to only 28.6% of the tobacco exposed infants (see Figure 7, panel b). Of those who habituated in each group, they did so within a similar number of trials, 9.2 for the control group and 9.5 for the tobacco-exposed. Figure 8 (panel b) illustrates the number of trials required to reach the criteria for orientation and habituation for the tobacco-exposed and control infants in the novelty phase.

Dishabituation Phase. With respect to recovery of responding to the dishabituation stimulus, the data suggest that the control group recovered responding to the stimulus with 35.1% of head turns toward the stimulus in the last trial block of the novelty phase and 68.7% for the dishabituation block. The tobacco-exposed group also seemed to recover responding, but to a lesser degree with mean head turns toward the stimulus of 55.2% and 68.5%, respectively.

There appears to be no difference between the groups in the percentage of head turns toward the dishabituation stimulus, with means of 68.7 % for the control group and 68.5% for the tobacco exposed group. There was no difference in the number of infants who reached the criterion for orientation with 77.8 % of the control and tobacco-exposed infants reaching this criterion and both groups required a similar number of trials to reach the criteria, 3.7 and 4.3, respectively.

Summary

In summary, the descriptive data from this part of the study seem to indicate that the infants exhibited a similar pattern of responding at three-week follow-up as they displayed at birth. The tobacco-exposed group maintained a greater percentage of head turns toward the sound source in the last quartile of the familiarization and novelty phases compared to the control infants. Both the control and tobacco-exposed groups recovered responding upon introduction of the novelty and dishabituation stimuli. Both groups oriented to the sound source in all three phases of the procedure, but the control group appeared to be more likely to reach the criterion for habituation.

Discussion

Information Processing

Summary of Findings. As hypothesized, differences in information processing ability were found in each phase of the information processing procedure among the tobacco-exposed infants, at birth, and the data suggest that the information processing impairments remain at 3 weeks of age. The results indicate that prenatal exposure to tobacco adversely affects performance on the newborn information processing procedure. Maternal smoking was associated with impairments in habituation to the auditory familiarization and novelty stimuli and recovery of responding to the dishabituation stimulus. Orientation to the familiarization stimulus and recovery of head-turning to the novelty stimulus were not affected. Both groups systematically turned toward the stimulus at the beginning of the familiarization phase indicating orientation. However, during the last quartiles of the familiarization phase, the control group turned systematically away from the stimulus indicating habituation, whereas the nicotine-exposed infants turned randomly toward and away from the stimulus. Turning away from the stimulus is a robust finding that has been demonstrated repeatedly with normal, healthy infants during habituation and implies active processing of the stimulus (e.g., Brody et al., 1984; Swain et al., 1991; Tarquinio et al., 1990; Tarquinio et al., 1991; Zelazo et al., 1984). Failure to turn away from the stimulus during the last quartile of the phases implies a disruption in the expected processing response (i.e., turning away from the now redundant stimulus). This interpretation is supported by the fact that nicotine-exposed infants were also less likely to reach the criterion for habituation in the familiarization phase.

Following repeated presentations of the familiarization stimulus, the novel stimulus was introduced and both the control and tobacco-exposed groups displayed a high level of head turning toward the sound source, turning systematically towards the sound source, implying recovery of responding. Thus, the control infants switched from turning away to turning toward the sound source upon introduction of the novel stimulus, while the tobacco-exposed group switched from the random head-turning response at the end of the familiarization phase to systematic turns toward the novel stimulus.

After repeated presentations of the novel stimulus, the control infants habituated, and during the last few trials of the novelty phase, they turned systematically away from the stimulus as predicted. The tobacco-exposed group exhibited the same pattern of responding to the novel stimulus as they did to the familiarization stimulus. Following systematic turning toward the stimulus in the beginning of the phase, they began turning randomly toward and away from the novel stimulus at the end of the phase. The tobacco-exposed infants were also less likely to habituate to the novel stimulus relative to controls.

Upon presentation of the dishabituation stimulus both the tobacco-exposed and control groups recovered responding to the previously familiarized stimulus. However, there was a trend for the tobacco-exposed group to show deficits in recovery of responding relative to controls, although both the tobacco-exposed and control groups turned systematically toward the sound source during the initial trials of the dishabituation phase. However, in contrast to their performance in the previous two phases, the tobacco-exposed group was less likely to reach the criterion for orientation to the dishabituation stimulus.

Fetal tobacco-exposure was associated with impairments in habituation to the familiarization and novelty stimuli, but recovery to novelty did not discriminate among the groups. Both the tobacco-exposed and control infants recovered responding to the novelty and dishabituation stimuli; however, the tobacco-exposed infants were less likely to reach the criterion for orientation in the dishabituation phase. The small sample size at follow-up testing significantly reduced the power of any statistical analyses and it must be cautioned that the findings are based on qualitative data analyses and it is possible that an increase in sample size may obscure any trends noted in this part of the study. A similar pattern of results was observed at three weeks of age, with impairments in habituation to the familiarization and novelty stimuli for the tobacco-exposed infants. The differences in orientation found in the dishabituation phase at initial testing were not evident at three-week follow-up. Since the effects of nicotine withdrawal would have dissipated by the three-week follow-up testing, the data suggest that the effects observed at birth may not be solely attributable to the effects of nicotine withdrawal. In fact, the trends observed at three weeks of age provide support for longer-term effects, at least beyond the perinatal period, of prenatal nicotine exposure.

The differences between the tobacco-exposed and control infants cannot be attributed to differences in positive state or ability to make head turns. There were no differences among the groups in terms of percentage of time spent in a positive state or in the overall percentage of trials with head turns. In addition, the fact that group differences were not observed on measures of orientation to the familiarization and novelty stimuli implies that both groups were equally capable of localizing the sound and organizing the appropriate head turning responses. The group differences appear to reflect differences in information processing ability. The fact that the infants were matched on important control variables increases the probability that the observed differences in performance are attributable to maternal prenatal tobacco smoking. All infants at initial testing, and all but one at three-week follow-up, were matched on birthweight. The majority of infants were also matched on test age and gestational age. The fact that clear differences exist despite control of birthweight, possibly the most severe confounding variable, increases the likelihood that the observed effects are due to fetal tobacco exposure. The tobacco-exposed and control groups differed on maternal age, SES, and education, but analyses with both the control and tobacco-exposed group showed that infant performance on the information processing procedure was not related to these variables. Lower maternal age, SES, and education are part of the constellation of factors that go along with maternal smoking during pregnancy and as such were treated as intervening variables, rather than confounding variables in the present study (Kiely, 1991). Unlike previous studies assessing the effects of prenatal exposure to tobacco on newborn outcome using the NBAS (Brazelton, 1984), this study employed the most valid measure of auditory information processing currently available. The procedure, developed by Zelazo and colleagues, has been extensively researched and shown to consistently elicit a reliable response pattern from normal healthy infants (e.g., Brody et al., 1984; Swain et al., 1991; Tarquinio et al., 1990; Tarquinio et al., 1991; Zelazo et al., 1984), and has been found to reliably discriminate among infants prenatally exposed to tobacco (Potter, 1996) and cocaine (Potter et al., 2000). Deviation from the expected response pattern in an infant who is in an alert, testable state implies deficits in the processing of the auditory stimuli.

Interpretation of Findings. Numerous studies conducted by Zelazo and colleagues using the auditory information processing procedure have demonstrated that normal, healthy neonates orient and habituate to a familiarization stimulus, recover responding and subsequently habituate to a novel stimulus, and dishabituate to the return of the familiarization stimulus (e.g., Brody et al., 1984; Swain et al., 1991; Tarquinio et al., 1990; Tarquinio et al., 1991; Zelazo et al., 1984; Zelazo et al., 1987, Zelazo et al., 1989). In addition, habituation is not only determined by a lack of head turning toward the stimulus, but by systematic turning away from the stimulus. This robust finding implies that newborns actively process auditory stimuli and habituation is not simply a result of selective receptor adaptation (Zelazo et al., 1991). Failure to turn preferentially toward the stimulus during the initial trials of a given phase or to turn away from the stimulus in the last trials of a phase implies a lack of processing of the stimulus.

Orientation, habituation, and recovery to a novel stimulus are separate behavioral responses which all rely on one common cognitive process, the creation of mental representations (Bornstein, 1989; Bornstein & Sigman, 1986; Weiss et al., 1988; Zelazo, 1988; Zelazo et al., 1991). The initial orientation observed upon presentation of the familiarization stimulus has been described as primarily reflexive behavior (Muir & Clifton, 1985; Zelazo et al., 1991), although the response may take several stimulus presentations to develop. With repeated exposure to the stimulus, the infant creates a mental representation of the stimulus. Each stimulus presentation is actively compared with the mental representation and, depending upon the strength of the memory trace and the parameters of the stimulus, the infant may respond by turning toward the stimulus, away from the stimulus, or by not turning at all (Zelazo et al., 1991). Turning away from the stimulus after repeated presentations implies that a mental representation was created and that the stimulus is recognized as familiar. The consistency of the finding that newborns turn away from a redundant stimulus suggests that an affective component is elicited that results in the infants' attempt to actively avoid the redundant sound (Zelazo et al., 1991). Failure to habituate implies a deficit in the ability to create an accurate representation of the stimulus, while failure to turn systematically away from the stimulus may indicate a lack of processing of the stimulus.

Recovery of responding to a novel stimulus involves the recognition that the stimulus is different from the one previously presented. It is hypothesized that an active comparatory process takes place, in which the novel stimulus is compared with the mental representation. If a mismatch results, recovery of responding occurs. In the high-risk sample assessed by Zelazo et al. (1991) in which infants who had previously habituated to a familiarized stimulus failed to recover responding to the novel stimulus, a breakdown in the comparatory process was inferred. That is, habituation to the stimulus was evidence of the creation of a mental representation of the previous stimulus, however, the novel stimulus was not processed as a mismatch and recognized as different from the previous stimulus.

In the present study, the tobacco-exposed infants decreased their responding to the familiarization and novelty stimuli, but failed to habituate to the same degree as controls. This decrement in responding implies that only a partial representation of the stimulus was created, whereas the control group habituated, indicating that a strong mental representation was created. Further, the tobacco-exposed group failed to turn systematically away from the familiarization and novelty stimuli, indicating lack of processing of the stimulus. However, it is clear that the tobacco-exposed group did create some mental representation as evidenced by their ability to recover responding to novelty.

While the tobacco-exposed group failed to create an accurate representation of the familiarization and novelty stimuli, as evidenced by the lack of habituation to these stimuli, and did not process the stimuli to the same degree as the control group, as evidenced by the failure to turn systematically away from the stimuli, they did form some mental representation of the stimuli, as evidenced by their ability to recover responding to the novel and dishabituation stimuli. The ability of the infants to recover responding to the novel and dishabituation stimuli implies that the comparatory process is intact. However, the evidence for deficits in habituation implies that the creation of this mental representation was not well formed. These findings indicate that there is a breakdown in the infants' ability to actively process the auditory information.

Relation to Previous Research. The hypotheses that tobacco exposure would be associated with deficits in performance in all three phases of the information processing procedure was based upon inconsistent findings from previous research investigating various risk factors for developmental delay. Zelazo et al. (1989) demonstrated the discriminant validity of the information processing procedure with infants at different levels of risk for developmental delay. High-risk infants failed to recover responding to the novel stimulus following orientation and habituation to the familiarization stimulus. The results of Potter et al. (2000) corroborated these findings; recovery to novelty discriminated among infants prenatally exposed to cocaine and non-exposed infants. Further, Potter (1996) found that tobacco-exposed infants showed deficits in recovery to novelty, only in the dishabituation phase. Contrary to Zelazo et al. (1989), these two studies (Potter et al., 2000; Potter, 1996) found that orientation and habituation measures also discriminated among the infants in different exposure groups in the familiarization phase. Specifically, the cocaine-exposed group was less likely to reach the criterion for habituation in the familiarization phase, the criteria for orientation and habituation in the novelty phase; and orientation in the dishabituation phase (Potter et al., 2000); nicotine exposed infants were less likely to reach the criterion for orientation and habituation in the familiarization phase and orientation in the dishabituation phase, group differences were not found for the novelty phase (Potter, 1996).

However, the analyses of the familiarization phase data revealed dose-response effects of maternal smoking on newborn responses to the familiarization stimulus. The infants born to mothers who smoked more than 10 cigarettes per day (HS) exhibited a lower percentage of head turns toward the stimulus during the first half of the familiarization phase and a greater percentage of head turns toward the stimulus during the second half of the familiarization phase than either the infants born to mothers who smoked less than 10 cigarettes per day (LS) or controls. Additionally, the HS infants required more trials to reach criterion for orientation to the familiarization stimulus compared with the controls, and the LS infants fell between the two groups. These results suggest that smoking during pregnancy has adverse effects on newborn information processing as assessed by the familiarization phase measures, and that the decrement in performance is related to the number of cigarettes smoked per day. Planned between group comparisons on the mean percentage of head turns toward the stimulus during the dishabituation phase indicated that the HS infants made a lower percentage of head turns toward the stimulus relative to the control infants (p <.05). The other group comparisons were non-significant. In the present study only the habituation measures reliably discriminated among the tobacco-exposed and non-exposed groups. Specifically, similar to the findings of Potter (1996), particularly the infants born to heavy smokers, the tobacco-exposed infants in the present study were less likely to habituate in the familiarization and novelty phases, and were less likely to orient in the dishabituation phase. Both studies found that recovery to novelty was not affected by prenatal tobacco exposure. However, in contrast to Potter (1996), in the familiarization phase of the present study, the tobacco-exposed group and control group were equally likely to orient to the stimulus.

There are two findings in the present study which seem to contradict previous research. First, in the present study, the tobacco-exposed and control groups did not exhibit any differences in recovery to novelty, whereas in previous studies, recovery to novelty was found to discriminate among groups at varying levels of risk (Zelazo et al., 1989; Potter et al., 2000; Potter, 1996). Second, as in the studies by Potter, habituation measures in the familiarization phase discriminated among groups in the present study, but not in the study conducted by Zelazo et al. (1989). There are, however, two possible explanations for these findings.

First, with respect to recovery to novelty in the present study, Potter (1996) did not find that recovery to novelty discriminated among groups and that finding was replicated in the present study. However, Potter (1996) did find differences between the tobacco-exposed group and the non-exposed group on recovery to the dishabituation stimulus. While there were no statistically significant differences between the tobacco-exposed and control groups in the present study, there was a trend evident that the tobacco-exposed group did not recover responding to the same degree as the control group. This difference was marginally significant (p=.062) and it is possible that with increased sample size this difference would become more evident. The fact that the present study partially replicated the results of Potter (1996) indicates that tobacco-exposure may selectively affect the infants' information processing ability with a different mechanism than that in infants born with high risk conditions (e.g., asphyxiation requiring ventilation, hydrocephalus, and low grade intracranial hemorrhages), and those who were prenatally exposed to cocaine. It is possible prenatal exposure to nicotine does not have as adverse an effect on fetal brain development as the more serious CNS insults associated with various high risk conditions and prenatal cocaine exposure. Second, with respect to differences on the orientation and habituation measures, in Zelazo's et al. (1989) sample, 14 of the original 167 infants tested on the procedure were excluded prior to data analyses due to failure to reach the criterion for orientation in the familiarization phase. Unlike the present study, exclusion of infants who failed to orient in the study by Zelazo et al. was justified by the fact that these infants had suffered a number of serious perinatal complications that placed them at a greater risk for auditory impairments. Zelazo's et al. (1989) exclusion of the infants who failed to orient would have resulted in a reduction in the variability in performance on the information processing measures and diminished the likelihood of finding any differences on the orientation and habituation measures in the three phases of the procedure. In the studies conducted by Potter and colleagues (Potter et al., 2000; Potter, 1996), and in the current study, infants who failed to orient in the familiarization phase were not excluded prior to data analyses which allowed for variability on the orientation and recovery measures and subsequently the habituation measures in the familiarization and novelty phases, and thus differences were detected.

The impairments associated with tobacco exposure on the information processing procedure are strikingly consistent with the findings of Potter (1996) with the exception of differences in orientation to the familiarization stimulus. Examination of the data from the two studies indicates that the tobacco-exposed group performed approximately the same in both the present study and the study by Potter. It was the superior performance of the control infants in Potter's study relative to control infants in the present study which accounts for the discrepant findings. The reason for the difference in performance between the control infants in the present study and those in Potter's study is not clear given that the procedures were identical. Potter (1996) was the first to investigate auditory information processing in newborns prenatally exposed to tobacco and the findings of the present study support the notion that prenatal tobacco-exposure selectively impairs auditory information processing ability.

Similar findings have been found in previous studies employing the NBAS to investigate tobacco-associated impairments in orientation and habituation (Fried & Makin, 1987; Picone et al., 1982; Richardson, et al., 1989; Saxton, 1978). In these studies infants whose mothers smoked during pregnancy exhibited deficits on the auditory orientation and habituation measures of the NBAS. It has been suggested that such deficits may be secondary to an increased auditory threshold among tobacco-exposed infants (Fried & Makin, 1978; Picone et al., 1982; Saxton, 1978). Although this is only one possible interpretation of the results, the possibility that disturbances in auditory threshold were responsible for the impaired performance of the tobacco-exposed neonates in the present study is an important one.

Auditory Threshold Disturbance Versus Information Processing Disturbance

Results of studies comparing tobacco-exposed infants with non-exposed controls on the NBAS have raised the possibility that tobacco-exposure may have a detrimental effect on hearing ability, possibly by raising the auditory threshold (Fried & Makin, 1987; Picone et al., 1982; Saxton, 1978). However, there is little evidence in the literature that children whose mothers smoked cigarettes during pregnancy are at a higher risk for deafness. For example, Trammer, Aust, Koster, and Obladen (1992) examined the auditory evoked potentials of non-drug-exposed infants and infants exposed to either tobacco only or to tobacco and narcotics. The results indicated that tobacco-exposure alone did not affect the integrity of the neonatal auditory system, although impairments were observed among infants prenatally exposed to both tobacco and narcotics. Since the previous studies assessing prenatal tobacco-exposure using the NBAS did not assess prental use of narcotics, it is possible that the use of such drugs may have confounded their results.

Anderssen, Nicolaisen, and Gabrielsen (1993) found that both tobacco-exposed and non-exposed infants responded autonomically and behaviorally to a sudden 80 decibel noise; although, the tobacco-exposed newborns were more likely to respond with apnea than non-exposed infants. Finally, Kallail, Rainbott, and Bruntzel (1987), in a survey of the parents of school children who failed the schools' hearing test indicated that children with hearing impairments were no more likely to have mothers who smoked during pregnancy than those without hearing impairments.

In the present study, two findings imply that group performances on the information processing measures represent problems other than hearing impairments. First, an examination of the turns toward the stimulus as compared to turns away at the beginning of the phases, indicated that both the tobacco-exposed and control infants turned systematically toward the stimuli in all phases. Second, when the novel stimulus was introduced following the familiarization stimulus, the tobacco-exposed and control groups recovered responding, i.e., both groups changed their response pattern from the familiarization stimulus to the novel stimulus. Specifically, the tobacco-exposed group changed their response from turning randomly toward and away from the familiarization stimulus, to a systematic turning toward the novel stimulus; a similar pattern of responding was evident in the change from the novel to the dishabituation stimulus. If the tobacco-exposed infants could not hear the stimuli these response patterns would not be expected.

Although the data from prior studies and the present study appear to indicate that prenatal tobacco-exposure does not have adverse effects on auditory threshold, the possibility cannot be ruled out on the basis of such a small number of studies.

Implications

Recovery to novelty has been demonstrated to be a sensitive measure for discriminating among infants at different risk levels for developmental delay (Zelazo et al., 1989), prenatal cocaine exposure (Potter et al., 2000), and prenatal tobacco-exposure (Potter, 1996). However, orientation, habituation, and recovery to novelty all depend upon intact information processing ability. Thus, while recovery to novelty discriminated among the high-risk infants in Zelazo's et al. (1989) study and among infants prenatally exposed to cocaine in Potter's et al. (2000) study, it is possible that information processing deficits among infants parentally exposed to tobacco may manifest in a different response pattern. While Potter (1996) found that recovery to the dishabituation stimulus was impaired and this difference was marginally significant in the present study, in both the present study and Potter's study, recovery to the first novel stimulus (i.e., the novelty phase stimulus) was not influenced by tobacco exposure. It could be argued that recovery to the novelty phase stimulus is a more reliable measure than recovery to the dishabituation stimulus because most studies employing the information processing procedure show a significant decline in positive state by the dishabituation phase. That is, relative to the novelty phase stimulus, failure to recover responding to the dishabituation stimulus is more likely to be due to fatigue and fretfulness.

In the clinical sample of high, moderate, and low risk infants tested with the information processing procedure, deficits in performance were evident from the point where the novel stimulus was introduced following habituation to the familiarization stimulus (Zelazo et al., 1989). Further, the effects appeared to be cumulative in that the infants who failed to recover responding to the novelty stimulus also were less likely to habituate and recover responding to the dishabituation stimulus. A similar cumulative response pattern was demonstrated among cocaine-exposed infants by Potter et al. (2000). However, the effects observed for tobacco-exposed infants in Potter (1996) as well as the present study were not cumulative, rather the performance of the tobacco-exposed infants was inconsistent across the phases. In the present study, although the tobacco-exposed infants did not habituate to the familiarization and novelty stimuli to the same degree as controls, they recovered responding to the novel stimulus and to a lesser degree the dishabituation stimulus. Therefore, information processing does not appear to be consistently impaired in the tobacco-exposed neonates, but is limited to one or two parts of each phase.

Potter (1996) suggested that inconsistency in performance might not imply information processing deficits primarily, but rather indicates deficits in the ability of the tobacco-exposed infants to regulate arousal and attention. In order to create an accurate mental representation of the stimulus, the infant must be at an appropriate level of arousal and attend to the stimulus long enough to process the information (Lécuyer, 1989; Racine & Kairiss, 1987).

A number of investigators have emphasized the importance of arousal level in mediating responsiveness to stimulation on information processing measures, specifically habituation/novelty paradigms (Gardner & Karmel, 1984; Gardner & Turkewitz, 1982; Kaplan, Werner, & Rudy, 1990). Kaplan and Werner (1991) argue that deficits in habituation and recovery to novelty do not simply reflect breakdowns in the creation of mental representations, the depth of the processing of the stimuli, or the comparatory process between the familiar and novel, but rather they are influenced by the infants' present level of *sensitization*, which they define as a function of the infants' arousal. The theory of Kaplan and colleagues is based upon the dual-process theory, which posits that two neural pathways interact to determine the behavioral response of the infant during repeated encounters with a stimulus. Each stimulus presentation has two effects. First, it generates activity in a specific stimulus-response (S-R) pathway in the nervous system and this pathway ultimately determines the level of responding to the stimulus. Second, it influences the state of the infant, where state refers to the general level of arousal, excitation, or tendency to respond (Kaplan & Werner, 1991). The state system feeds back onto the S-R pathway and modifies its activity, with an eventual effect on the behavioral response. Two effects are said to occur with the repeated presentation of a stimulus. First, there is a build-up of an inhibitory response tendency (habituation) resulting in a smaller and smaller output of the S-R pathway. Second, there is a change in the excitatory response tendency (sensitization), which first grows in strength and then dissipates over time. Sensitization develops over the course of the initial trials of a stimulus presentation and results in a gradual increase in the level of responding, similar to that observed among the control infants in Figure 1. These two processes, habituation and sensitization, interact in each trial to determine the level of responding. Therefore, in normal infants, after repeated exposure to the stimulus, sensitization diminishes and habituation remains, which results in a decrease in the level of responding (Kaplan & Werner, 1991).

It is possible that among the tobacco-exposed infants, the sensitization process takes longer to dissipate, therefore causing delayed habituation to the familiarization and novelty stimuli. Kaplan and colleagues propose that the novel stimulus, in addition to exciting a different neural network than that excited by the previously habituated stimulus, also generates sensitization (Kaplan & Werner, 1991). Thus, increased responding to novelty is not simply a result of central processing, but a result of the interaction between central processing and sensitization. An integral part of the dual process theory is dishabituation as defined by Thompson and Spencer (1966; as cited in Kaplan & Werner, 1991). Thompson-Spencer dishabituation refers to the renewed response to the original stimulus upon its retest during or after the introduction of the novel stimulus. Moreover, increased responding to the dishabituation stimulus occurs over and above that observed upon presentation of the stimulus in the familiarization phase. According to the dual-process theory, Thompson-Spencer dishabituation does not reflect a disruption in the habituation process, but rather is indicative of superimposed sensitization. In the present study, the tobacco-exposed infants' response to the dishabituation stimulus was greater than that observed in the familiarization phase, providing evidence for the sensitization process. The sensitization process may also provide an explanation for the inconsistent response of the tobacco-exposed infants throughout the information-processing procedure. Specifically, the tobacco-exposed infants showed deficits in their ability to habituate to the stimuli presented, but were then able to recover responding to the novel and dishabituation stimuli. It is possible that once the sensitization process dissipated, the tobacco-exposed infants were then free to recover responding to the novelty stimulus. However, the repeated presentations of the novelty stimulus created a new sensitization process that may have taken longer to dissipate in the tobacco-exposed group, thereby inhibiting their ability to habituate to the novelty stimulus. However, by the time the dishabituation stimulus was presented the sensitization process would have dissipated enough to allow for normal processing and thus recovery of responding to the dishabituation stimulus.

Further, it is possible that the sensitization processes initiated by the presentation of the familiarization and novelty stimuli interfered with the tobacco-exposed infants' ability to orient to the dishabituation stimulus. It is possible that the repeated presentation of the first two stimuli caused a state of over arousal among the tobacco-exposed group and therefore prevented them from fully attending to the dishabituation stimulus.

Kaplan and Werner (1991) suggest that interpretive problems arise in the comparison of healthy, full term infants to infants at risk for developmental delay. Special populations frequently respond with slower response decrements than do healthy, full-term infants. Kaplan and colleagues suggest that a slow response decrement may be due either to a slow buildup of the habituation process (i.e., a breakdown in the creation of a mental representation) or to strong action in the sensitization process, or to some combination of the two (Kaplan et al., 1990). Therefore, the inconsistent performance of the tobacco-exposed infants in the slow rate of response decrement (habituation) could reflect a slow rate of underlying encoding, or it could indicate fast encoding with strong sensitization (Kaplan & Werner, 1991). However, the evidence from the present study seems to be in support of the latter. If the performance of the tobacco-exposed group was due to a slow rate of underlying encoding or deficits in the creation of a mental representation, then the strong recovery response to the novel stimulus would not be expected. However, the tobacco-exposed infants did recover responding to novelty, indicating that while the sensitization process to the familiarization stimulus may not have dissipated entirely as evidenced by the failure to habituate, the infants were able to make a distinction between the familiar and the novel and recover responding. This recovery to novelty suggests that an appropriate mental representation was made. Therefore, it remains likely that the sensitization process is in some way responsible for the inconsistency in performance of the tobacco-exposed infants.

If an infant is not at an appropriate level of arousal during the information processing procedure, attention to and central processing of the stimulus followed by accurate responding would not be expected (Gardner & Karmel, 1984; Karmel & Gardner, 1996). Gardner and Karmel (1984) have demonstrated variations in stimulus preference across different levels of arousal in healthy infants. Karmel et al. (1991) demonstrated that infants who are swaddled and tested immediately after feeding (low arousal condition) prefer high intensity visual stimuli to low intensity stimuli. On the other hand, infants who are tested unswaddled immediately prior to feeding (high arousal condition) prefer low intensity stimuli. Additionally, these effects are not as evident among infants with CNS injury as they are among normal infants (Karmel et al., 1991), Therefore, disturbances in arousal modulation may reflect CNS injury (Karmel et al., 1991; Karmel & Gardner, 1996). The inconsistent performance of the tobacco-exposed infants may be a function of changes in arousal level throughout the procedure. Therefore, it is possible that prenatal tobacco-exposure may negatively affect the development of brain structures that are related to arousal modulation.

Neurodevelopmental Effects of Prenatal Nicotine Exposure

Animal studies have shown that nicotine is a neuroteratogenic agent and disrupts the development of several neural networks involved in the regulation of attention and arousal levels. Prenatal exposure to nicotine increases the number of nicotinic cholinergic receptors in several regions of the brain, including the hypothalamus, hippocampus, and various other subcortical structures (Slotkin et al., 1987) and the inner layers of the neocortex (Lichtensteiger et al., 1988; Slotkin et al., 1987). Nicotinic receptors provide input to catecholaminergic neural pathways both during fetal development, where they act in the modulation and organization of neural development (Lauder, 1983; 1988; as cited in Potter, 1996), and postnatally where they are involved in neurobehavioral functioning through their role in autonomic nervous system impulse transmission (Slotkin et al., 1987). Therefore, normal brain development may be compromised early in fetal development, with the developmental changes at these early stages affecting the course and pattern of future neuronal development.

One possible mechanism of nicotine's interference in normal CNS development is fetal hypoxia (Naeye, 1992; Cole et al., 1972). CNS damage produced primarily by hypoxia often occurs to subcortical structures (Fawer et al., 1983, as cited in Karmel et al., 1991). These structures are in close proximity to areas or pathways that are involved in the processes of attention and arousal (such as the ascending and descending pathways of the reticular formation). Additionally, behaviors that are thought to involve state organization and attention at or shortly following birth are thought to be linked to such subcortical structures (Karmel et al., 1991). Karmel et al. (1991) proposed that behavioral problems associated with lack of state organization provide evidence for lowered functional integrity of the CNS.

Karmel et al. (1991) suggest that prior to two months of age, visual attention is predominately controlled by subcortical mechanisms rather than sensory-specific visual system receptors at the cortical level. Due to the continued development throughout the neonatal period of the cortical structures, they propose that an explanation of visual attention through subcortical structures is more parsimonious. Gardner and Karmel (1984) speculated that the CNS mechanisms mediating the arousal x stimulus effects would specifically involve at least the actions of the reticular formation on other subcortical regions controlling the young infants' visual behavior. It is possible that subcortical structures could be adversely affected by prenatal exposure to tobacco through the effects of fetal hypoxia or by the direct effects of nicotine on the nicotinic receptors. As a result, it is possible that the increased arousal levels observed in the performance of the tobacco-exposed infants are due to damage to specific fetal CNS structures during development, caused by prenatal tobacco-exposure.

Several studies have documented small, but measurable decrements in intelligence and achievement test scores among children whose mothers smoked cigarettes during pregnancy (Butler & Goldstein, 1973; Fried et al., 1992; Fried & Watkinson, 1990; Hardy & Mellits, 1972; Naeye & Peters, 1984). However, despite these findings, it is extremely difficult, if not impossible, to isolate the direct effects of prenatal tobacco exposure from the postnatal environment when studying older children. The neonatal period provides a rare opportunity for the investigation of the impact of suspected teratogenic agents, before any prenatal effects become intertwined with the postnatal environment. Therefore, it is possible that the small, but measurable deficits in intelligence and achievement test scores may be evident in deficits in auditory information processing ability in the neonatal period. In support of these findings, many studies have found that verbal ability is more adversely affected in tobacco-exposed children than nonverbal ability (Fried & Watkinson, 1990; Naeye & Peters, 1984, Sexton et al., 1990). This suggests that if deficits in verbal ability are related to prenatal tobacco-exposure, then tobacco may selectively impair the auditory system. It is possible that using the auditory information processing procedure in the neonatal period may allow for the assessment of the functions of neural structures involved in the development of verbal skills. While it is impossible to know the exact influence of fetal tobacco-exposure on the developing fetal brain, this study partially replicates the findings of Potter (1996) who suggested that prenatal tobacco-exposure selectively impairs the development of the newborns' auditory system.

Study Design Issues

Confounding and Intervening Variables. At initial testing and three-week follow-up testing, the infants of smokers were compared with those of nonsmokers on the information processing measures, and a number of potential confounding infant and maternal variables were examined. The two groups were found to be similar in terms of infant gestational age, age at time of testing, and birthweight. Maternal alcohol consumption was a control variable and a similar pattern of drinking was found for both the control and tobacco-exposed groups with about one-third of mothers in each group reporting any alcohol use during pregnancy. However, the tobacco-exposed infants had mothers who were younger, had less education and were from lower-income households.

To rule out the possibility that variations between groups on the information processing measures are a result of factors other than maternal smoking, statistical control of covariates is often regarded as necessary. However, a number of researchers have warned against 'over-control' of covariates based solely on statistical differences between groups in studies assessing risks associated with maternal smoking (Baghurst et al., 1992; Kiely, 1991; Tong & Michael, 1992). It is known that women who smoke give birth to babies with lower birthweights (Ahlborg & Bodin, 1991), have less education, come from a lower SES (Naeye, 1992), and are younger than women who do not smoke (Stewart &

Streiner, 1996). Kiely (1991) recommends that researchers take care to distinguish between "intervening variables" and "confounding variables"; for example, he states that in the "study of the effect of maternal cigarette smoking on perinatal mortality, birthweight is an intervening variable and it makes no sense to control for it" (p. 247). Statistical adjustment for group differences on these intervening variables (variables that are associated with smoking), such as birthweight, SES, maternal age, and education, in studies investigating the influence of prenatal exposure to tobacco on infant development, would result in partial control of the smoking variable itself (Baghurst, Tong, Woodward, & McMichael, 1992; Tong & McMichael, 1992). On the basis of these arguments and since SES, maternal age, and maternal education were not associated with the outcome measures, group differences on these measures were not statistically controlled in the data analyses.

A generally superior alternative to statistical control procedures is matched pair designs (Briere & Elliot, 1993). Subject matching procedures provide control over the matching variable itself as well as other factors associated with the chosen variable. For example, choosing birthweight as a matching variable allowed for control of some of the potential physical effects associated with lower birthweights that were not measured in the present study.

Despite subject matching on birthweight, gestational age, and age at time of testing, it is possible that there were other covariates that were not assessed. For example, some researchers have reported that in follow-up studies of children whose mothers smoked during pregnancy, maternal intelligence was related to child outcome (e.g., Baghurst et al., 1992; Olds, Henderson, & Tatelbaum, 1994a, 1994b). Maternal intelligence could conceivably affect performance on the information processing measures through genetic influences. However, there is no evidence to suggest that maternal smoking is associated with lower intelligence (Baghurst et al., 1992), and as such it is unlikely that this variable selectively affected the tobacco-exposed infants. Even so, maternal intelligence was not assessed in the present study and the possibility that the mothers who smoked were of lower intelligence than control mothers and that this influenced infant performance, cannot be ruled out.

One possible confound in the present study is the influence of other drug use during pregnancy on the performance of the infants on the information processing procedure in either the control or the tobacco-exposed groups. Illicit drug use was not assessed in the present study due to ethical constraints imposed by the Ethics Boards involved in the study preventing questions regarding illicit drug use to be asked due to difficulties maintaining confidentiality if a mother reported illegal drug use. However, the use of illicit substances was believed to be low in this population. In the investigation of the effects of prenatal cocaine and nicotine exposure on newborn auditory information processing, Potter (1996) reported that of a sample of 120 control subjects recruited from an urban setting, only 2 reported any marijuana/hashish use and none of the mothers reported any heroin/cocaine use Although, it could be assumed that drug use was low in the rural setting of the present study, information concerning illicit drug use was not collected and the possibility of including mothers who had used illicit drugs during pregnancy in either the control or tobacco-exposed group cannot be ruled out.

One other potential confounding variable not assessed in the present study was maternal caffeine consumption. Jacobson and colleagues (1984) found that maternal consumption of caffeine prior to pregnancy was associated with reduced scores among newborns assessed with the NBAS, and caffeine intake during pregnancy was associated with poor neuromuscular development and reflex functioning. Additionally, while prenatal tobacco exposure was related to reduced orientation scores, this effect disappeared once caffeine intake prior to pregnancy and SES were statistically controlled. Naeye (1992) reported that women who smoke reportedly drink more coffee than those who do not smoke, raising the possibility that the mothers who smoked also consumed more caffeinated beverages than the nonsmokers. As a result of these findings, there is the possibility that maternal caffeine consumption prior to pregnancy could confound the information processing results.

In summary, a number of variables were controlled in this study through subject matching procedures, the most important variable being birthweight. In an extension of the recommendation by Kiely (1991) to treat birthweight as an intervening variable and since SES, maternal age, and education were not related to the information processing measures, these three variables were treated as intervening variables and were not statistically controlled in the data analyses. Although attempts were made to control for various potential confounds, illicit drug use during pregnancy, maternal intelligence, and caffeine consumption were not assessed and it is possible that they, or some other unidentified factors, influenced the results.

Identification of Maternal Smokers. Maternal smoking was assessed initially through self-report and verified through maternal saliva cotinine analyses. The specificity (percent of nonsmokers correctly classified) of cotinine analysis used to verify self-report of smoking status during pregnancy was at a comparable level to that reported by Jarvis et al.

(1987) who found the specificity of saliva cotinine analysis to be 99%. However, the sensitivity (percent of smokers detected) was much lower. Whereas Jarvis et al. (1987) found sensitivities of 96 %, the results of the present study yielded a sensitivity of only 66.7%. However, given the short half-life of cotinine and the fact that many of the smokers had most likely not ingested nicotine within the past 24 hours or more, it is not surprising that verification was less accurate among parturient women compared to the general sample used by Jarvis et al. (1987). However, given this deficiency of the cotinine analyses to correctly classify smokers in the present study, it is possible that some of the self-reported nonsmokers may have been misclassified and, therefore, the reliability of saliva cotinine verification of smoking status is questionable for use with parturient women or more specifically in samples where participants had not smoked recently.

In the present study, while mothers were asked specifically about their smoking status throughout pregnancy, such as number of cigarettes smoked per day and brand of cigarettes smoked, one important question, the time since the last cigarette smoked or exposure to cigarette smoke, was inadvertently omitted. In the sample used by Jarvis et al. (1987), 97% of the self-reported smokers reported smoking on the test day with a mean of 1.5 hours since last cigarette. Lack of exposure to nicotine during the past day or two may have resulted in the discrepant results found in the present study with regard to the sensitivity of the saliva cotinine analyses. This information would aid in discovering if the cotinine analysis was perhaps only accurate for classifying recent smokers. However, two control subjects who reported exposure to second hand smoke two to six times per week tested positive for the presence of cotinine. One could assume that these two mothers had not been exposed within the past 24 hours, however, this information was not collected.

Certainly, the time frame of smoking and exposure to second hand smoke should be considered in future research.

Reliability of Self-Administered Questionnaire versus Face-to-Face Interview. While no statistical differences were found with regard to reporting channel, indicating that mothers were as honest in both the face-to-face interview and questionnaire conditions, given the small sample size for the tobacco-exposed group in the questionnaire condition (n=9) firm conclusions cannot be drawn. However, there was a trend evident that runs contrary to previous research (Patrick et al., 1994); the mothers who self-reported smoking during pregnancy were more accurate in the questionnaire condition than in the face-to-face interview. Additionally, one hundred percent of the nonsmokers were correctly classified in the questionnaire condition with a slightly smaller amount classified correctly in the face-to-face interview condition (93%). Patrick et al. (1994) suggested that the interview condition would be more accurate given the behavioral cues related to smoking, such as stained fingers and the odor of smoke evident in an interview condition. However, given the strong social sanctions with regard to smoking during pregnancy, mothers may have felt more comfortable reporting smoking during pregnancy in a confidential questionnaire than admitting such use in a face-to-face interview. Furthermore, in the sample of pregnant women interviewed, many had not had the opportunity to smoke since the birth of their child, so the observable cues of smoking behavior may not have been as obvious and, therefore, would not have the expected influence. Future research investigating the influence of reporting channel with pregnant women would clarify this issue.

Limitations of the Present Study.

Although the data clearly indicate that prenatal tobacco-exposure has an adverse effect on information processing ability, this study is not without limitations that must be considered in evaluating the implications of the findings. First, although attempts were made to control for experimenter bias during the procedure by having the holder and coder wear headphones so they could not hear the stimulus being played or the direction of the sound source, the experimenters were often aware of group membership. This was due to the interview component of the study design and the often spontaneous admission of smoking status by the mothers at initial presentation of the study. Therefore, it is possible that knowledge of the infants' group membership may have influenced the results through some means other than awareness of the stimulus and direction of the sound source. One possible way this could happen is if head turns were coded more or less often among the tobacco-exposed group. However, given that the percentage of head turns was the same for both groups across the procedure, this is unlikely.

Second, while the saliva cotinine analyses were specific to nonsmokers, the decreased sensitivity (ability to detect smokers) is of concern. While this would not be an issue in the identification of smokers, since it is believed that due to the strong social sanctions against smoking during pregnancy, if a mother reported smoking during pregnancy then it was unlikely that she was misreporting such use. However, the decreased sensitivity allows for the possibility that some smokers who reported that they were nonsmokers may have been included in the control group. However, given that the control group performed in the pattern expected for normal, healthy infants on the information processing procedure and that the infants who were exposed to second hand smoke on a regular basis were excluded from the analyses, it is unlikely that some, if any, of the nonsmokers were incorrectly classified.

Despite these limitations, it is unlikely that any one of them could completely account for the observed differences in performance between the tobacco-exposed and control infants on the information processing procedure. Moreover, it is doubtful that the limitations outweigh the improvements made over prior studies, including, a) the use of the current auditory procedure over the NBAS for assessing information processing ability; b) the use of saliva cotinine analyses in addition to self-report for determining smoking status; c) controlling for a number of potential confounding variables through subject matching techniques; and d) taking care to ensure that each infant was in an alert, inactive state prior to beginning the testing procedure. Thus, despite its limitations, a number of techniques were employed to increase the likelihood that the observed effects were related to prenatal tobacco-exposure.

Conclusion

Infants born to mothers who smoked cigarettes during pregnancy demonstrated deficits in performance on an auditory information processing task relative to infants born to mothers who did not smoke during pregnancy. These deficits were in evidence on a three-week follow-up test, suggesting that the adverse effects of prenatal nicotine exposure last beyond the nicotine withdrawal period. The response pattern observed on this task partially replicated previous research (Potter, 1996). Specifically, infants prenatally exposed to nicotine exhibited poorer habituation to the familiarization stimulus, recovered responding to the novelty stimulus and demonstrated poorer responding to the dishabituation stimulus.

The control over important potentially confounding factors, the use of cotinine analyses to identify infants born to mothers who smoked during pregnancy, and the addition of the three-week follow-up test, increased the likelihood that the observed deficits were a direct result of prenatal tobacco exposure rather than other factors. It is hypothesized that prenatal exposure to nicotine disrupts the normal development of the CNS structures involved in the modulation of arousal and attentional processes and possibly those involved in the processing of auditory stimulation. Deficits in arousal and attention would have adverse effects on learning ability, and may eventually result in reduced scores on standardized tests later in childhood. Whatever the mechanism may be, it is possible that the impairments in auditory information processing observed in the tobacco-exposed neonates are related to the subsequent decrements in cognitive ability and achievement test scores observed by a number of researchers later in childhood.

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Appendix A

Statement of Informed Consent

Study Title: Newborn Information Processing

Investigators:

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INTRODUCTION & PURPOSE OF STUDY: The purpose of this study is to gain an understanding of how newborn babies respond to sounds. Babies whose mothers smoked cigarettes during pregnancy and/or were exposed to second hand smoke and babies born to mothers who did not smoke during pregnancy will be studied in order to determine if exposure to tobacco affects the way babies respond to sounds.

WHO CAN PARTICIPATE IN THIS STUDY: You can participate in this study if you experienced a healthy pregnancy and birth and are able to recall approximately how much you smoked during pregnancy, if you smoked at all.

STUDY PROCEDURES: If you agree to participate in this study, a researcher will ask you to respond to a series of questions following the birth of your baby at the Valley Regional Hospital. These questions will include general background information questions such as your age and level of education. These will be followed by questions concerning smoking during pregnancy, such as how many cigarettes per day you usually smoked, whether you quit or cut down, and whether you were exposed to second hand smoke. We will also be asking questions concerning your present newborn and pregnancy, medications received during labour and delivery, and alcohol consumption during this pregnancy. A researcher would, with your permission, access your hospital chart to get information about any medications you received during labour and delivery. You will then be asked to provide a saliva sample to test for the amount of nicotine exposure you experienced during the past few days.

Babies will be tested for information processing ability at the Valley Regional Hospital in a room on the postpartum ward, prior to discharge. To ensure an alert and inactive state for testing, some of your baby's natural reflexes will be elicited first. The baby will be held by a researcher and will listen to words played through speakers at a normal speaking volume. Your baby's head turning in response to the sound will be noted. This procedure will take approximately 15 minutes.

It is possible that the effects of withdrawal from nicotine can explain the way newborn infants who have been exposed to tobacco respond to sounds. To determine if nicotine withdrawal affects babies' head-turning responses, we will retest your baby at approximately three weeks of age. This test will be identical to the one conducted at the hospital. With your permission, a researcher will contact you shortly after you return home from the hospital and arrange a time for your baby to be tested. If you prefer, the researcher will bring the testing apparatus to your home and test your baby there. This test will also take approximately 15 minutes.

RISKS AND DISCOMFORTS: There is a potential for discomfort as some of the questions concern sensitive material regarding substance use during pregnancy.

POSSIBLE BENEFITS: Participating in this study will not benefit you or your baby directly, but your participation may provide information that will help researchers, in the future, identify gestational smokers and learn about the effects of smoking during pregnancy on the baby.

PARTICIPANTS RIGHTS: You are under no obligation to participate in this study, and whether or not you agree to participate will in no way affect your care. If you do choose to participate, you may, at any time, end you participation in this study. You have the right, at any time, to refuse to answer any question.

COMPENSATION: There will be no costs or compensation to you for participating in this study.

CONFIDENTIALITY: Neither you nor your infant will be identified as a study participant in any reports or publications of this research. Neither your name nor your infant's name will appear on any interview information forms or saliva samples. These will be identified by code number only. Your records will be kept in a locked file cabinet. Only the staff involved in the research will see them. All information you provide will be held in confidence.

QUESTIONS OR PROBLEMS: You have the right to ask questions about this study at any time. If you have any questions about the study, please contact:

Dr. Susan Potter (902) 585 - 1220

Debbie Johnson (902) 423 - 8050

Leanne Campbell (902) 678 - 7381 ext. 3055

You may also contact the Acadia University Research and Graduate Studies office at (902) 585 - 1498 for information about participating in this study from an outside source.

I have read and understood this informed consent. I agree to participate and give permission for my baby to participate in this research study. I give my permission for my saliva sample to be analyzed for exposure to nicotine and for the researcher to access my hospital chart for information concerning medications I received during labour and delivery. I am willing to be contacted by telephone after I leave the hospital so arrangements can be made for the second testing. I have been given the opportunity to ask questions and all of my questions have been answered. I acknowledge that a copy of this consent form has been given to me.

______________________	______________________	______________________
Signature of participant	Printed name of participant	Date of Signature

____

Phone number of participant

______________________	______________________	______________________
Signature of person obtaining consent	Printed name of person obtaining consent	Date of signature

Would you like to receive a copy of the results of this research? Yes ____ No

Address:____

____

Appendix B

Debriefing Procedure

Debriefing Procedure

Following administration of the questionnaire and collection of the saliva sample the researcher will speak with the participant and explain that one of the factors that may increase the accuracy of mothers' reports is the way the report is given. The researcher will explain that there is some research that says that a face-to-face interview will provide more accurate reports than a self-administered questionnaire. The participant will be informed that they were randomly selected to be in either the face-to-face interview condition or the self-administered questionnaire condition. The researcher will explain the need to keep this hypothesis from the participant so as not to influence their responses.

Appendix C

Questionnaire

Newborn Information Processing
A Research Study Conducted at the Valley Regional Hospital
in Association with Acadia University
Study #____________
Date____________

General Information Demographics

1) How old are you?

2) Marital Status:

3) Occupation:

4) Occupation of baby's Father:

5) Last year of education completed:

6) Last year of education completed by baby's Father:

7) Income Scale (circle one that best describes the total income of the household):

a) less than $10,000	e) $40,001 - $50,000
b) $10,000 - $20,000	f) $50,001 - $60, 000c
c) $20,001 - $30,000	g) $60,001 - $70, 000
d) $30,001 - $40,000	h) Over $70, 000

The following questions concern your present newborn and pregnancy:

8) Sex of Infant:

9) Date of birth of infant:

10) Time of birth:

11) Number of hours in labour:

12) Type of Delivery:
- a) spontaneous vaginal
- b) forceps
- c) Caesarean section
- d) Induced labour

13) If caesarean section or induced labour, what was the reason?

14) What pain medications, if any, did you receive during labour?

15) How much weight did you gain during your pregnancy?

16) Were you examined by a doctor during your pregnancy?

17) If yes, how often did you see a doctor?

18) Did you suffer any illnesses during your pregnancy?

19) If yes, please describe.

20) What was the estimated date of delivery:
Calculated from the first day of your last menstrual period?
Calculated by ultrasound?

The following questions concern smoking during your pregnancy as well as exposure to second hand smoke.

21) Have you ever smoked cigarettes?
(If no, go to question #30)

22) Just before you found out you were pregnant were you smoking cigarettes?

23) If yes, how many cigarettes did you smoke each day?

24) During this pregnancy have you smoked?_____ (If no, go to question #30)

25) During the first trimester, about how many cigarettes per day did you smoke?

26) During the second trimester, about how many cigarettes per day did you smoke?

27) How many cigarettes per day are you smoking now?

28) What brand of cigarettes do you usually smoke?
(Brand name, light, king size, etc.)

29) Did you change the brand you smoke during this pregnancy?

If yes, when did you change?
What change did you make?

30) Were you exposed to second-hand smoke during your pregnancy?

If yes, how often?
Every Day
2 - 6 times per week
Once a week
Once a month

The following questions concern alcohol consumption during pregnancy.

31) During this pregnancy, when was the last time you drank alcoholic beverages?
Within the last week
1 week to 1 month ago
1 month to 3 months ago
More than 3 months ago

a) What did you drink on that occasion?
Beer
Wine
Hard liquor
Liqueurs

b) How much did you drink on that occasion?
One drink
2 to 4 drinks
5 or more drinks

32) During this pregnancy, what is the most you drank at one time?
One drink
2 to 4 drinks
5 or more drinks

33) If you drank alcohol during this pregnancy, please describe how much and how often you drank during:

a) the first 3 months

b) the second 3 months

c) the last 3 months

Thank you for your participation.

Appendix D

Sample Scoring Sheet

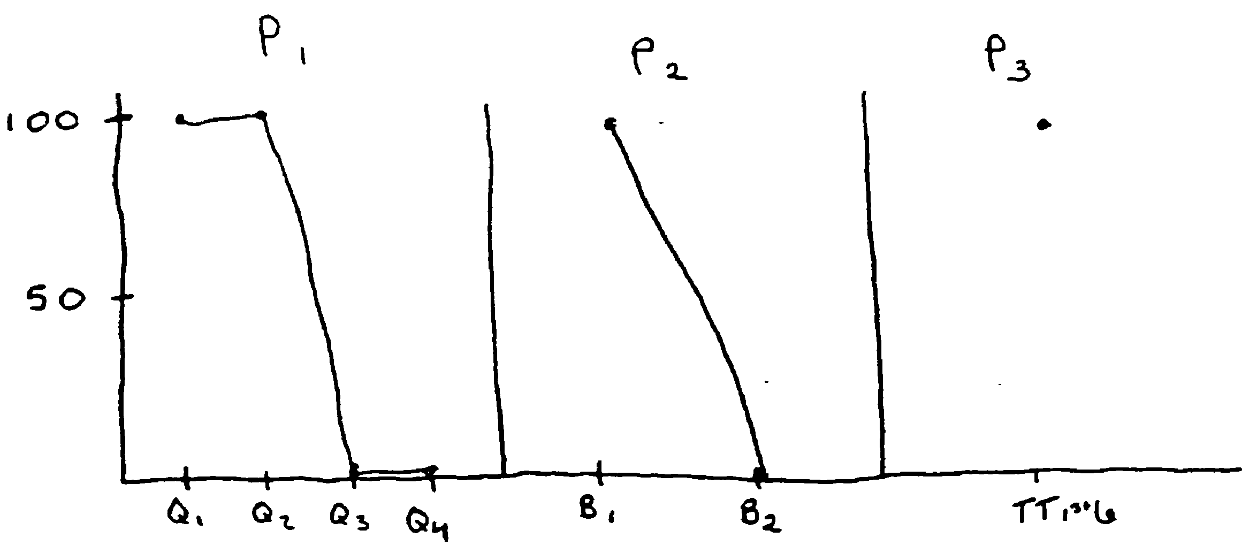
SAMPLE

P_1 # OR = 3
P_1 # H = 7
$P_1 Q_1$ (T-A) = 2
$P_1 Q_4$ (T-A) = -2
P_1 OR? = Y
P_1 H? = Y
Pos state (P_1) = 99.7
$P_1 B_1$ = 100%
$P_1 B_2$ = 0 %
$P_1 Q_1$ = 100%
$P_1 Q_2$ = 100%
$P_1 Q_3$ = 0 %
$P_1 Q_4$ = 0 %

P_2 # OR = 3
P_2 # H = 7
$P_2 Q_1$ (T-A) = 2
$P_2 Q_4$ (T-A) = -1
P_2 OR? = Y
P_2 H? = Y
Pos state (P_2) = 100%
$P_2 B_1$ = 100%
$P_2 B_2$ = 0 %
$P_2 Q_1$ = 100%
$P_2 Q_2$ = 100%
$P_2 Q_3$ = 0 %
$P_2 Q_4$ = 0 %

P_3 # OR = 3
P_3 (T-A) 1st 6 = 3
P_3 OR? = Y
Pos state (P_3) = 100%
P_3 Turns Towards (1st 6) = 100

Overall % turns (T-A) = 86.2
Overall # trials = 17
Overall time = 262.35
Overall Pos state = 99.9%



Code # : Sample
Date of Birth : ____________
Birth Wt. : ____________ - g
Gender : ____________
Age :

Test Date : Jul 17, 2000 10:57

Holder : ____________
Coder : ____________

Familiarization

Times are in seconds

Trial #	Response	Sound	Direction	Towards	Away	Fret	Sleep	Total	# Twds	# Away	Or.?	Hab.?	Comments
1	Towards	c:\my documents\babytest\b.wav	L	4.07	-	-	-	8.62	2	0	No	No	
2	Towards	c:\my documents\babytest\b.wav	R	3.00	-	0.29	-	10.16	1	0	No	No	
3	Towards	c:\my documents\babytest\b.wav	R	3.00	-	-	-	5.83	1	0	Yes	No	
4	Towards	c:\my documents\babytest\b.wav	L	3.00	-	-	-	19.27	1	0	Yes	No	
5	Away	c:\my documents\babytest\b.wav	L	-	3.00	-	-	19.70	0	1	Yes	No	
6	Away	c:\my documents\babytest\b.wav	R	-	3.00	-	-	15.31	0	1	Yes	No	
7	Away	c:\my documents\babytest\b.wav	R	-	3.00	-	-	13.69	0	1	Yes	Yes	
				13.07	9.00	0.29	-	92.58					

Novelty

Trial #	Response	Sound	Direction	Towards	Away	Fret	Sleep	Total	# Twds	# Away	Or.?	Hab.?	Comments
1	Towards	c:\my documents\babytest\t.wav	L	3.00	-	-	-	10.69	1	0	No	No	
2	Towards	c:\my documents\babytest\t.wav	L	3.00	-	-	-	20.76	1	0	No	No	
3	Towards	c:\my documents\babytest\t.wav	R	3.00	-	-	-	7.88	1	0	Yes	No	
4	Towards	c:\my documents\babytest\t.wav	R	3.00	-	-	-	16.56	1	0	Yes	No	
5	None	c:\my documents\babytest\t.wav	L	-	-	-	-	30.00	0	0	Yes	No	
6	None	c:\my documents\babytest\t.wav	L	-	-	-	-	30.00	0	0	Yes	No	
7	Away	c:\my documents\babytest\t.wav	R	-	3.00	-	-	19.47	0	1	Yes	Yes	
				12.00	3.00	-	-	135.36					

Dis-Habituation

Trial #	Response	Sound	Direction	Towards	Away	Fret	Sleep	Total	# Twds	# Away	Or.?	Hab.?	Comments
1	Towards	c:\my documents\babytest\b.wav	R	3.00	-	-	-	20.81	1	0	No	No	
2	Towards	c:\my documents\babytest\b.wav	L	3.00	-	-	-	7.86	1	0	No	No	
3	Towards	c:\my documents\babytest\b.wav	L	3.00	-	-	-	5.75	1	0	Yes	No	
				9.00	-	-	-	34.41					