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Effects of prenatal alcohol exposure on social behavior in humans and other species

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Abstract

Alcohol exposure during development causes central nervous system alterations in both humans and animals. Although the most common behavioral manifestation of these alterations is a reduction in cognitive abilities, it is becoming increasingly apparent that deficits in social behavior may be very prevalent sequelae of developmental alcohol exposure. In infancy and early childhood, deficits in attachment behavior and state regulation are seen in both alcohol-exposed people and animals, suggesting that these changes are largely the result of the alcohol exposure rather than maternal behavior. In the periadolescent period, people exposed to alcohol during development show a variety of difficulties in the social domain as measured by checklists filled out by either a parent or teacher. Rats exposed to alcohol during development show changes in play and parenting behaviors. In adulthood, prenatal alcohol exposure is related to high rates of trouble with the law, inappropriate sexual behavior, depression, suicide, and failure to care for children. These high rates all suggest that there may be fundamental problems in the social domain. In other animals, perinatal alcohol exposure alters aggression, active social interactions, social communication and recognition, maternal behavior, and sexual behavior in adults. In conclusion, research suggests that people exposed to alcohol during development may exhibit striking changes in social behavior; the animal research suggests that these changes may be largely the result of the alcohol insult and not the environment.

Keywords

Fetal alcohol syndrome; Social behavior; Prenatal alcohol

1. Introduction

Fetal alcohol syndrome (FAS) has been defined by a constellation of characteristics including growth retardation, organ anomalies, and central nervous system (CNS) dysfunction [32]. CNS dysfunction has most commonly been manifested by a decrease in intellectual function [44, 65]. However, people with FAS appear to differ from the mentally retarded population because of additional problems in the social domain [11,65]. Deficits in social behaviors in children with FAS are more severe than those seen in children with similar verbal IQ but who were not exposed to alcohol [75]. Furthermore, social behavior deficits have been associated with prenatal alcohol exposure in adolescents and adults without the full FAS diagnosis [65,67] and

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at lower doses of alcohol than would be necessary to produce the full FAS [13]. In fact, problems in the social domain are reported almost as frequently as the most commonly noted problem, namely attention deficits, in people with FAS [60].

Social behavior is very complex. Indeed, the complexity of social interactions among primates has been postulated to be the evolutionary change that resulted in selection for greater intelligence [17]. The socialization of human beings begins very early and continues throughout the lifespan. Social behavior in an adult individual is the result of a complex interaction of genetics, brain development, early childhood experiences pertaining to socialization, and learning throughout the lifespan; these factors combine to affect social cognition and motivation. Clearly, the changes in social behavior observed in adults with FAS could be a function of many things including their genetic background, alcohol-induced alterations in brain structures involved in social behavior, abnormal childhood socialization processes, and abnormalities in social learning processes throughout the lifespan.

Rodent models of FAS can be used as means to examine the effect of alcohol exposure during development on social behavior in a simpler and more easily controlled system than that seen in the human condition. Nevertheless, even in rodents, social behavior is not that simple. Social behavior in rats has been shown to follow similar principles as in humans and is also a function of genetics, teratogenic influences, early maternal-infant interactions, and later social learning. In experimental rodent models of FAS, the alcohol can be administered in the prenatal or postnatal period, because the period in the rat equivalent to brain development in the third trimester in humans extends as far as postnatal day 15 [5]. In these models, the variable of an alcohol-abusing rearing mother can be removed by cross-fostering. The variable of different genetic backgrounds can be controlled by using control groups with the same genetic background and the variable of undernutrition can be assessed by pair feeding a control group. However, alterations in early maternal-infant interactions still may occur by means of behavioral abnormalities in the rodent pup altering the maternal reaction of the dams (e.g. [49]), which results in altered dynamics of the maternal-infant interaction. Nevertheless, findings of changes in behavior in alcohol-exposed rodents are a powerful indication that the changes are initiated by the alcohol insult rather than by an abnormal environment. The similarities of findings in the human and animal literatures in terms of dose-response effects on the central nervous system and growth in the study of FAS have been striking [20], but changes in social behavior have not been compared.

Despite the complexity of social behavior, it is critical on a number of levels to explore systematically the factors involved in the production of social deficits in people with FAS. From a social cost point of view, it is becoming apparent that people with FAS have a high probability of delinquency and/or criminality (see below for more detailed discussion) and some of these problems may arise from difficulties with social behavior in general. Difficulties in social behavior are likely to impair work performance, resulting in a high likelihood of the necessity of dependent living even into adulthood [67]. In addition to the social cost, there are costs to the individual with FAS. There is a high rate of depression and suicide in people with FAS that is as yet unexplained [22,40,67]; however, lack of social support, which can result from awkward social behavior, has been shown to be a major contributor to depression [48]. Thus, understanding the factors involved with the changes in social behavior could lead to targeted interventions and perhaps ameliorate both the social cost and the cost to the individual.

This review examines social behavior as it relates to prenatal alcohol exposure in the hope that the knowledge acquired from both animal and human research literatures can be used to delineate some of the factors involved in observed social deficits. The review will take a developmental lifespan perspective and include findings that range from those on children born

to moderate social drinkers to children with FAS born to alcoholic women and those derived from animal models of FAS.

2. Infancy and early childhood

Research on the social development of infants has been influenced by Bowlby [9], who proposed that attachment behaviors in an infant were part of a social behavior system that operated to ensure that the primary caretaker was nearby to provide protection for the infant. Bowlby also argued that the temperament of the infant interacted with the environment, particularly the primary caregiver, and that this interaction could influence later adult relationships. Note that the interaction is both the result of the infant's attachment behaviors and the responses of the caretaker to those behaviors. More recent conceptualizations of social development of the child have also focused on the mother-infant dyad. The emphasis is on the process of mutual regulation [77], where the infant's temperament and ability to regulate its own state can interact with maternal ability to meet the infant's needs.

Attachment in infants has often been examined using the strange situation procedure in which the infant is exposed to increasing degrees of separation from the primary caretaker, and the reactions of both the caretaker and infant are assessed [1]. O'Connor and colleagues [50,51] investigated attachment, as assessed by the strange situation experiment, in infants born to middle-class women who were social drinkers. Children in this sample contained a high number of infants who displayed a disorganized style of attachment, characterized by conflicting and confused behavior. Mothers of the infants with disorganized attachment styles were the heaviest social drinkers during pregnancy. Results from a causal modeling procedure suggested that the primary variable was the direct effect of alcohol consumption during pregnancy on the infants' temperament [51]. Consistent with O'Connor's causal model, others have suggested that whereas maternal sensitivity is a predictor of a secure attachment style, a disorganized attachment is predicted largely by the newborn's behavior [59].

Infants with FAS or infants exposed to alcohol during pregnancy show high levels of irritability [16], a temperament variable shown to contribute to maladjustment in attachment [44] and a possible indicator of later difficult temperament and behavioral problems in the child [74]. In addition, alcohol-exposed infants have been shown to have disturbed sleep patterns [14,16, 58] and feeding difficulties [16]. Steinhausen, Nestler, and Spohr [61] described significantly higher levels of both eating and sleeping disturbance in children born to alcoholic mothers compared to matched controls. Stoffer, Scher, Richardson, Day, and Coble [63] demonstrated prenatal alcohol disruption of sleep-state cycling in neonates. Prenatal alcohol was significantly related to state disregulation one day postpartum and weak suck and longer latency to suck two days postpartum; the mothers of these children were well-nourished social drinking mothers who had all been in prenatal care by the fifth month of pregnancy [42,62,68].

Disruption in sleep and feeding rhythms could represent early problems in state regulation in the infants themselves and could possibly disrupt the attachment process [23] or other important aspects of maternal-infant dynamics [6]. It is likely that alterations of the maternal-infant interactions where the mother is a social drinker are primarily the result of the disruption to the infant. One study that coded mother-child interactions during 8- and 18-month Bayley assessments of the child found that maternal drinking in this well-educated population was not associated with inappropriate mothering styles [69]. Similarly, Ragozin, Landsman-Dwyer, and Streissguth [54] found that in a subset of this same population maternal social drinking was not related to home environments at 12 months as measured on the HOME scale. However, when the mother is an alcoholic, it is quite likely that there would be a maternal contribution to a disruption of maternal-infant dynamics, in addition to the contribution from the infant (see Freier [24] for an interesting discussion of this interaction). Indeed, given that maternal

alcoholism is associated with child abuse, the maternal contribution could be quite strong [41].

The findings in the human population of a disruption of the maternal-infant dyad are strongly corroborated by the animal research. During the neonatal period, the rat pup must interact with its siblings and its dam. Alcohol exposure during development results in a longer latency to attach to a nipple and shorter periods spent attached to the nipple, regardless of whether testing is done with an anesthetized (and therefore nonlactating) dam [3,55] or nonanesthetized dam [73]. The suckling by prenatally exposed rat pups results in less milk intake, and these alterations in suckling behavior also result in a change in a foster dam's prolactin response to suckling by postnatal day 10 [73]. Another example of altered pup behavior resulting in altered dam response is that pups exposed to ethanol prenatally are unable to elicit retrieval from a dam as quickly as control pups [49]. Others have found that prenatal exposure to ethanol reduces isolation-induced ultrasonic vocalizations, which are vocalizations assumed to indicate distress [33]. Further, these vocalizations in prenatally exposed pups have altered responsiveness to opioids [33] and neurosteroids [81]. Again similar to the human literature, alcohol exposure during development disrupts the sleep [29,30,64] and feeding [73] rhythms and the development of the ability to regulate temperature [80,82] in rat pups, which would disrupt the process of psychobiological attunement that may underlie attachment [23]. The alcohol-induced changes in early pupdam interactions suggest the likelihood of cascade-like effects [49] such that deficits in pups could result in altered dam behavior, which in turn could result in even more aberrant behavior in the pups.

The interactions between the infant and primary caretaker are assumed to be fundamental to later social interactions, particularly interactions between two individuals. There is considerable evidence that the maternal-infant dyad in humans and the dam-pup interactions in rats are disrupted by alcohol exposure during development. In addition, infants exposed to alcohol during development also show deficits in modeling of others, an ability postulated to be extremely important for the development of social behavior [2,45]. In particular, Jacobson et al. [31] found that alcohol-exposed infants showed impaired ability to model play behavior exhibited by the experimenter. Given the possibility of a disruption in two fundamental processes to social behavior—the interaction between the mother and infant and modeling—it is not surprising that social problems occur in older children exposed to alcohol during development (see Table 1).

3. Periadolescence

Examination of social behaviors in children and adolescents exposed to alcohol during development has been largely based on standardized tests of adaptive behaviors and behavior checklists done by either the teacher or parent of the affected child. Both of these methods of assessing child behavior have their drawbacks, including being dependent on the perceptiveness of the observer and the influence of the observer's expectations.

Coles et al. [15] examined children (average age 6 years old) who had been moderately exposed to alcohol during development and found no deficits in adaptive behaviors after current maternal drinking had been controlled. Brown et al. [11] reported that there were no differences in children exposed to moderate amounts of alcohol during development in free play behaviors or aggression levels over a 5-min observation period. In the same population of children, teachers reported more aggression and other externalizing problems in children whose mothers drank alcohol throughout pregnancy compared to children whose mothers either stopped drinking in the third trimester of pregnancy or did not drink at all during pregnancy [11]. Steinhausen [60], using the Child Behavior Checklist, examined children of similar age but who had FAS and had been exposed to large amounts of alcohol during development. Both

the teachers' and parents' behavior ratings indicated severe deficits in the social domain; indeed the social problems were almost as prevalent as attention problems. Children exposed to alcohol but without FAS have been shown to do less well in school even after controlling for the current environment and the child's IQ score, suggesting difficulties in a behavioral domain [25]. Thomas et al. [75], using the Vineland Adaptive Behavior Scale, found that children with FAS had deficits in social skills of approximately three standard deviations below the mean for their age. In both the interpersonal skills and use of play and leisure time subdomains, the deficits were significantly greater than a control group matched on verbal IQ who were not exposed to alcohol.

Investigations of the effects of alcohol exposure during development on the periadolescent period in rats have examined two forms of affiliative behavior, namely play and parental behavior. Play is a primary reinforcer for animals during this period and also appears to be a need because it exhibits an increase in frequency when animals have been socially isolated [52,53]. Normally play behavior is more frequent in male rats than in female rats. However, prenatal alcohol exposure has been shown to reverse this difference such that alcohol-exposed male rats play less than male control rats and alcohol-exposed female rats play more than female control rats [46] (although there has been a failure to replicate this effect at least in males [7]). This effect of alcohol exposure suggests that some of the teratogenic effects of alcohol on social behavior may be mediated by alterations of normal developmental patterns of sex hormones. Parental behavior is another form of affiliation; male and female rats in the juvenile period exposed to rat pups will eventually retrieve and hover over the rat pups. Exposure to alcohol during the prenatal period [4] or postnatal period [78] results in an increase in the latency to retrieve rat pups in both male and female juvenile rats.

It is difficult to draw parallels between the animal and human literature in the periadolescent period at this time, largely because the measures of social behavior are obviously very different. Direct observation of play behavior has not been conducted in children with FAS and observations of general social behavior have not been done in juvenile rats exposed to alcohol. Striking gender differences have not been found in the human syndrome. However, it should be noted that in rat models of FAS, the behaviors that show sexually dimorphic effects of alcohol exposure are sexually dimorphic in control postpubertal rats; none of the measures used in the human population have been ones that are normally sexually dimorphic, and so the lack of gender differences in FAS might be a function of the type of measures used and the age of the children evaluated.

Although there have not been many studies directly examining social behavior in this age group, there are a number of studies reporting certain temperament characteristics, that are important in social behavior, occurring at a high frequency in individuals with FAS. In particular, there have been frequent reports of impulsivity and distractability in children with FAS [66] and in children born to mothers who were social drinkers [12,57,70-72]. In the literature on delinquency, impulsivity, in particular, is considered to be one of the best predictors of early onset of delinquency, at least in boys [76]. In fact, 60% of young adolescents with FAS have had problems with the law, with one in three individuals having committed their first crime between the ages of 9 and 14 years [66]. The most predominant crimes are crimes against persons, including theft, burglary, assault, and murder [66].

4. Late adolescence and adulthood

Adolescents and adults with FAS or fetal alcohol effects (FAE; mean age 17 years) show unresponsiveness to social cues, lack of reciprocal friendships, lack of tact, and difficulty in cooperating with peers, as measured by the Vineland Adaptive Behavioral Scale [39,65]. Indeed, adults with FAS who have normal IQ scores still exhibit problems in the social domain

[65]. Women with either FAS or FAE often have difficulty in caring for their children. In one study, 36% of children born to 30 women with FAS or FAE had been taken from their mothers by children's protective services agencies [26,66].

Although there are very few studies directly examining social behavior in adults exposed to alcohol during development, there are findings that are suggestive of difficulties with social behavior in individuals with FAS or FAE. In adults with FAS or FAE who are 21 years of age or older, 58% have had trouble with the law, suggesting possible difficulties in integrating with society [66]. In this same group of individuals, over 40% have had a history of inappropriate sexual behavior, perhaps indicating a failure to appreciate social norms [66]. Also, individuals with FAS or FAE have very high rates of depression and of suicide and parasuicide behaviors [22,40,60,66], possibly indicating failure of social support of these individuals or a failure to utilize existing supports due to cognitive and temperamental characteristics [48].

Animal models of FAS have been used to examine social behaviors in adult rats exposed to alcohol during development. In normal rats, active social interactions between adult males are greater than those seen in adult females. This pattern is reversed by alcohol exposure during the early postnatal period [36]. There is some evidence that aggression and social investigation are increased in male mice by exposure to alcohol during development [10,21,38,79]; however, pair-fed control mice were not used in these studies and care should be taken in their interpretation. In adult rats, exposure to alcohol during the prenatal period increases offensive aggression compared to pair-fed controls [56]. Social recognition is impaired in alcohol-exposed rats of both sexes [37] and social communication appears to be altered at least in female rats by exposure to alcohol during development [37]. Prenatal alcohol exposure also feminizes adult male sexual behavior [19,28] and delays the onset of vaginal opening and behavioral estrus in female rats [8,18,43,47].

Two studies have now demonstrated that female rats prenatally exposed to alcohol at levels not high enough to produce malformations show marked disruption of maternal behaviors [4, 27]. Compared with control rats who retrieved their pups in rapid succession, licked them, and crouched over them protectively, the prenatally exposed dams built nests of inferior quality and took, on average, twice as long to retrieve the first pup back to the nest. By 30 min half the fetal-alcohol-exposed dams had not retrieved their litters. Although the rat pups were themselves normal in calling to their dams, the retrieval behavior of the alcohol-exposed dams appeared to be disoriented, unmotivated, and disorganized. They sometimes carried a pup halfway to the nest, and then dropped it to pick up another pup, or they spent much time grooming themselves and eating and drinking while ignoring the pups [27].

Although it is tempting to point to the parallels between the animal findings and human findings on maternal and sexual behavior, it should be kept in mind that the relationship between these behaviors in rats and humans is distant, particularly with respect to the extent of hormonal influences. Perhaps more compelling are the findings that simple interaction frequencies and processing of social cues is altered in rats exposed to alcohol during development. Given the apparent breadth of problems in social behavior seen in people with FAS or FAE, it may that there is a fundamental difficulty in some subprocess underlying social behavior, whether it be in perception of social cues, social motivation, or selection of the appropriate social response.

5. Conclusions

It is apparent that there are changes in social behavior induced by alcohol exposure during development both in rats and in adults. Some of the changes are apparent very early in life, suggesting that some of the basic building blocks of social behavior in infancy are abnormal, heralding difficulty with social behavior later in life. The extent and impact of the changes in

social behaviors appear to increase in adulthood such that in humans, very gross indicators of social maladjustment, such as suicide and arrest rates, detect these difficulties.

At this point, there is enough evidence to indicate that in addition to cognitive deficits, another very common and important indicator of CNS dysfunction in FAS is problems in the social domain. Questions abound about the extent and nature of these difficulties, demanding observational and laboratory studies specifically aimed at social behavior in people with FAS. Future studies examining early attachment and other social behaviors in infants with FAS still with their alcoholic parent or in stable adoption environments would greatly increase our understanding about the relative contributions of altered infant behaviors versus altered maternal behaviors to attachment difficulties. The natural environment in which children with FAS are raised has recently been documented in one large study [66], but others are needed, as are laboratory studies examining environmental conditions exacerbating and ameliorating problems with socialization. The possible interaction of the availability or lack of social support services for affected adults and their lack of social skills should also be examined. Finally, studies in children and adults with FAS should focus on the nature of the subprocesses in social behavior that may be altered.

Animal models of FAS could and should be used to aid the research process. The use of models can facilitate the examination of simple social processes and can establish more clearly the degree to which the changes in social behaviors are the direct result of alcohol-induced brain changes. These data can then be used to guide and design longitudinal studies to be conducted in humans. Animal models of FAS can also be used to establish the underlying neural bases of the changes in social behavior. Whereas structures critically involved in social behaviors, such as the hypothalalmus [34], amygdala [36], septal region [35], and hippocampus [35], have been shown to be altered by exposure to alcohol during development, strong causal links between specific behavioral alterations and neural changes have yet to be drawn. Animal models are ideal for this difficult task and this type of research may suggest possible pharmacological treatments for FAS.

In summary, both animal and human studies strongly suggest that alcohol exposure during development alters social behaviors and both types of studies have specific contributions to make to further explore these alterations. The FAS research field has a long history of collaboration and communication between basic and applied researchers and the domain of social behavior is one in which the contributions from both types of research are necessary and should yield much needed and important insights for behavioral interventions.

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Table 1

Changes in social behavior observed in alcohol-exposed people and animal models of FAS

	Other species	Humans
Infancy and early childhood	Behavioral alterations in maternal-infant dyad [3,55,73]	Disorganized attachment of the infant [50,51]
	Disruption of sleep and feeding rhythms and temperature regulation [29, 30,64,73,80,82]	Disruption of sleep and feeding rhythms [14,16,42,58,61,62,63,68]
	?	Deficits in modeling [31]
Periadolescence	Sexually dimorphic changes in play [7,46]	?
	Delays in induction of maternal behavior [4,78]	?
	?	Social deficits as measured by behavior checklists [11,60,25,75]
	?	Impulsivity and irritable temperament [58,66,70]
Late adolescence and adulthood	Changes in active social interactions [36]	Social deficits as measured by behavior checklists [39,65]
	Disruption of maternal behavior in females [4,27]	Difficulties in caring for children by mothers [26,66]
	Alterations in sexual behavior [8,18,19,25,43,27]	Inappropriate sexual behavior [66]
	Increased aggression in males [10,21,38,56,79]	?