

## ORIGINAL ARTICLE

# Neuropsychomotor development characteristics of the infants who born from women who used drugs during pregnancy



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## Abstract

**Introduction:** The use of street drugs during pregnancy, due to their deleterious effects on the health of the infant, may have clinical implications for neuropsychomotor development.

**Objective:** The aim of this study was to analyse the characteristics of the neuropsychomotor development of infants born from women who used street drugs during pregnancy.

**Methods:** A cross-sectional retrospective study was carried out. A total of 51 medical records of infants weighing less than 1.500 grams, who were born in the Hospital de Clínicas da Universidade Federal de Uberlândia (HC/UFU), Minas Gerais, Brazil, from January 2014 to December 2015 were analysed. Using the Development Screening test Denver II at 6 or 9 months of corrected age performed the neuropsychomotor development evaluation. Statistical analysis included quantitative variables that were described by means of average, medians and standard deviation. Groups were compared by the t test or Mann-Whitney test. The associations of the qualitative variables were evaluated by means of the likelihood ratio test.

**Results:** Of the 51 records analysed, 39.2% belong to the group of children of mothers who used street drugs and 60.8% belong to the group of children of nonuser mothers. The neuropsychomotor development was predominantly abnormal and with a significant difference in the general performance classification ( $p < 0.001$ ) and, specifically, in the coarse motor area ( $p = 0.003$ ) in the group of infants born to mothers who used street drugs.

**Conclusion:** Infants of mothers who used street drugs had a greater delay in neuropsychomotor development.

**Keywords:** street drugs, infants, child development, pregnant women.

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## ■ INTRODUCTION

Exposure to substances such as tobacco, alcohol or street drugs can compromise the development of the individual at all stages of life, since the intrauterine period<sup>1</sup>. The use of street drugs by women during the fertile period has been growing worldwide and has become a public health issue<sup>2</sup>.

In the United States, the prevalence of use of street drugs during pregnancy in women aged 15-44 years was 10.8% for alcohol, 3% for tobacco and 4.4% for street drugs, with a more frequent use among younger women<sup>3</sup>. In Brazil, there are few studies on the subject. However, an analysis carried out in the city of São Luis, MA, with 1447 pregnant women, concluded that the use of psychoactive substances during pregnancy was 22.3% with regard to alcohol use, 4.2% tobacco use and 1.4% of some type of illicit drug<sup>4</sup>.

The use of street drugs during pregnancy can be devastating, since in some cases it results

in irreversible consequences to the mother-fetus binomial<sup>5</sup>. This happens because the drug can overcome the placental and blood-brain barrier, without previous metabolism, acting mainly on the central nervous system of the fetus. Due to their deleterious effects on infant health, these drugs may still have clinical implications for neuropsychomotor development, as well as the social and economic impact on health<sup>6</sup>.

Thus, the use of maternal and neonatal screening techniques on children exposed to intrauterine street drugs is extremely important, with the aim of promoting, preventing and intervening early, avoiding postnatal complications of the child's development<sup>7</sup>.

Therefore, the objective is to analyse the characteristics of the neuropsychomotor development of infants born from mothers who used street drugs during pregnancy.

## ■ METHODS

This is a cross-sectional study with medical records of infants from the Hospital de Clínicas da Universidade Federal de Uberlândia (HC/UFU), Minas Gerais, Brazil, from January 1st, 2014 to December 31st, 2015.

We included 51 medical records of preterm new-borns weighing less than 1.500 grams at birth and at 6 and 9 months of corrected gestational age. The infants were divided into two groups: Group 1 - (20 infants) children of street drugs users; and Group 2 - (31 infants) children of non-users.

The maternal variables were gestational age, prenatal, maternal age, schooling, use of street and/or licit drugs, gestational diabetes mellitus, chronic hypertension, peri-natal haemorrhage, neonatal steroid use, chorioamnionitis and type of delivery.

Neonatal variables that were analysed: gender, length, weight and cephalic perimeter at birth, apgar score at 5 minutes of life, neonatal infection, congenital infection, surfactant use, oxygen therapy time, time of invasive mechanical ventilation, bronchopulmonary dysplasia, periventricular haemorrhage, leukomalacia, ductus arteriosus persistence, enterocolitis, SNAP-PE scale and length of hospital stay in the Neonatal Intensive Care Unit (NICU).

Neuropsychomotor development of infants was evaluated by the Denver II Development Screening Test and compared the groups: Group 1 - children exposed to street drugs during pregnancy and Group 2 - children not exposed to street drugs during pregnancy. The test evaluates children's development from 0 to 6 years and consists of 125 items, which are divided into four areas: social-personal, fine-adaptive motor, language and large or gross motor. Each of the evaluated items is classified in: delay, caution or attention and passes. The 90th

percentile is the cut-off point used in the Denver II test to define the delay. When the child fails an item or test, and is totally in the left side of the age line, i.e. in addition to the p90; caution, or attention when the child fails a test that was intercepted by the age line between p75 and p90 and passes when the child successfully performs the test<sup>8-10</sup>.

The performance of each infant was classified according to the number of failures (delay and caution) and classified as: abnormal - when the infant had two or more delays independent of the area or sector; questionable - when the evaluated infant presented only one delay or two or more cautions; normal - when the infant presented no delay and at most a caution<sup>8,9</sup>.

The statistical analysis included quantitative variables, which were described, within each group, in averages, medians and standard deviations. The Shapiro-Wilk normality test was applied, and the Student's t-test was applied to the variables that presented normal distribution in the two groups, otherwise the Mann-Whitney test was applied. The associations of the qualitative variables were evaluated using the likelihood ratio test (G test). Univariate logistic regression was used to evaluate the risk factors for the occurrence of delayed neuropsychomotor development. For the elaboration of the database and statistical analysis the SPSS program, version 20.0 was used and the level of significance was adopted of 5%.

The study was approved by the Research Ethics Committee of the Federal University of Uberlândia (Protocol 1628014) and obeyed the norms for conducting research with humans, according to Resolution 466/12 of the National Health Council. Numbers identified patients in order to preserve your identity.

## RESULTS

We analysed 51 medical records, 20 (39.2%) belonging to Group 1 (children of street drugs user mothers) and 31 (60.8%) to Group 2 (children of nonuser mothers).

Maternal characteristics are presented in Table 1. The consumption of licit drugs (alcohol and tobacco)

was 27.5% and 11.8% of street drugs (marijuana, crack, cocaine) concomitant with licit drugs. With regard to schooling, 72.5% studied from 8 to 11 years and, in relation to prenatal care, 92.2% had medical appointments.

**Table 1:** Maternal characteristics of women who used drug during pregnancy

Variable	Total		Group n=20		Group 2 n=31		p value
Drug types							
Licit drugs	14	27,5	14	70,0	0	0,0	<0,001
Street drugs	0	0,0	0	0,0	0	0,0	
Licit and street drugs	6	11,8	6	30,0	0	0,0	
Non user	31	60,8	0	0,0	31	100,0	
Years of study							
1-3 years	1	2,0	1	5,0	0	0,0	0,014
4-7 years	5	9,8	2	10,0	3	9,7	
8-11 years	37	72,5	17	85,0	20	64,5	
12 years or more	8	15,7	0	0,0	8	25,8	
Prenatal care							
Yes	47	92,2	16	80,0	31	100,0	0,039
No	4	7,8	4	20,0	0	0,0	
Chronic arterial hypertension							
Yes	15	29,4	2	10,0	13	41,9	0,033
No	36	70,6	18	90,0	18	58,1	
Gestational diabetes							
Yes	1	2,0	0	0,0	1	3,2	0,315
No	50	98,0	20	100,0	30	96,8	
Chorioamnionitis							
Yes	10	19,6	5	25,0	5	16,1	0,440
No	41	80,4	15	75,0	26	83,9	
Antenatal Steroid							
Yes	32	62,7	10	50,0	22	71,0	0,131
No	19	37,3	10	50,0	9	29,0	
Periparturient haemorrhage							
Yes	4	7,8	2	10,0	2	6,5	0,649
No	47	92,2	18	90,0	29	6,5	
Birth type							
Caesarean	34	66,7	8	40,0	26	83,9	0,001
Vaginal	17	33,3	12	60,0	5	16,1	

When the groups were compared, it was observed that the neonatal population exposed to drugs in the gestational period (Table 2) presented significant data for neonatal infection ( $p < 0.001$ ) and bronchopulmonary dysplasia ( $p = 0.001$ ). Children exposed to intrauterine street drugs remained for a longer period hospitalized in the NICU when compared to children of non-users ( $p = 0.027$ ) (Table 3).

In the assessment of the neuropsychomotor development of infants (Table 4), a statistically significant difference was observed in the overall performance classification ( $p < 0.001$ ), with the gross motor area ( $p = 0.003$ ) being the most affected and with the highest

number of delays in the infants exposed to drugs of abuse during the gestational period.

Univariate logistic regression made it possible to compare the use of street drugs with other neonatal variables as risk factors that may increase the chances of delayed neuropsychomotor development (Table 5). It was possible to observe that the time of oxygen use (OR = 1.06, 95% CI 1.02-1.10), length of hospital stay (OR = 1.05, 95% CI 1.02-1.08) and, mainly the patent ductus arteriosus (OR = 7.00, 95% CI 1.86-26.36) were factors that also increased the risk for delayed neuropsychomotor development.

**Table 2:** Characteristics of new-born children of street drug users (G1) and children of non-users (G2), Uberlandia - MG, Brazil, 2018

Variable	total		Group 1 n=20		Group 2 n=31		p value
Sex							
Male	33	64,7	12	60,0	21	67,7	0,573
Female	18	35,3	8	40,0	10	32,3	
Use of surfactant							
Yes	28	54,9	12	60,0	15	48,4	0,556
No	23	45,1	8	40,0	16	51,6	
Bronchopulmonary dysplasia							
Yes	22	43,1	14	70,0	8	25,8	0,001
No	29	56,9	6	30,0	23	74,2	
Periventricular Leukomalacia							
Yes	1	2,0	0	0,0	1,0	3,2	0,315
No	50	98,0	20	100,0	30,0	96,8	
Persistence of the Arterial Canal							
Yes	26	51,0	11	55,0	15	48,4	0,644
No	25	49,0	9	45,0	16	51,6	
Necrotizing enterocolitis							
Yes	4	7,8	2	10,0	2	6,5	0,649
No	47	92,0	18	90,0	29	93,5	
Neonatal infection							
Yes	24	52,9	16	80,0	8	25,8	<0,001
No	27	47,1	4	20,0	23	74,2	
Congenital infection							
Yes	4	7,8	3	15,0	1	3,2	0,129
No	47	92,2	17	85,0	30	96,8	
Degree of Perinterventricular Haemorrhage							
No Haemorrhage	38	74,5	12	60,0	26	83,9	0,246
Degree 1	5	9,8	3	15,0	2	6,5	
Degree 2	4	7,8	3	15,0	1	3,2	
Degree 3	4	7,8	2	10,0	2	6,5	
Degree 4	0	0,0	0	0,0	0	0,0	

**Table 3:** Comparison of maternal and neonatal characteristics between the groups (Group 1 - users of street drugs and Group 2 - non-users), Uberlandia - MG, Brazil, 2018

Variable	Group 1 n=20		Group 2 n=31		p value
	Average	SD	Average	SD	
Gestational Age (weeks)	29,6	2,7	28,8	2,4	0,121
Maternal Age (years)	25,0	6,6	26,0	6,2	0,377
Birth Weight (grams)	1059,4	257,3	1089,2	254,5	0,941
Length of Birth (centimetre)	36,1	3,04	36,2	2,37	0,801
Cephalic perimeter to birth (centimetre)	24,7	2,1	25,4	2,2	0,378
5th Minute Apgar Score	8,0	1,1	7,8	1,2	0,835
Oxygen therapy (days)	39,6	31,8	22,9	33,8	0,088
Mechanical ventilation (days)	11,4	16,0	4,2	7,9	0,075
Length of stay (days)	80,3	28,4	59,9	32,7	0,027
SNAP-PE	29,7	21,9	32,4	17,4	0,621

**Table 4:** Comparison of neuropsychomotor development between the groups according to the Denver II test, Uberlandia - MG, Brazil, 2018

Denver II	Group 1 n=20	Group 2 n=31	Total n=51	p value
Personal – Social				
Normal	14	25	39	0,334
1 delay	3	3	6	
2 delays	3	1	4	
3 delays	0	1	1	
1 caution	0	1	1	
Language				
Normal	12	25	37	0,122
1 delay	7	4	11	
2 delays	0	1	1	
1 caution	1	0	1	
2 cautions	0	1	1	
Adaptive Fine Motor				
Normal	12	26	38	0,118
1 delay	2	1	3	
2 delays	3	1	4	
3 delays	2	0	2	
1 caution	1	2	3	
2 cautions	0	1	1	
Gross Motor				
Normal	5	17	22	0,003
1 delay	8	6	14	
2 delays	4	2	6	
3 delays	3	0	3	
1 caution	0	2	2	
2 cautions	0	4	4	
Performance Rating				
Abnormal	14	4	18	<0,001
Questionable	4	11	15	
Normal	2	16	18	

**Table 5:** Odds ratio values and respective 95% confidence intervals for risk factors to which new-borns were exposed and that could influence neuropsychomotor development, Uberlandia - MG, Brazil, 2018

Variable	OR*	CI* 95%	p value
Oxygen Time	1,0	1,02-1,10	0,005
Mechanical Ventilation Time	1,2	0,98-1,58	0,073
Length of stay	1,0	1,02-1,08	0,004
Canal Arterial Patent	7,0	1,86-26,36	0,004

\*OR, Odds Ratio; CI, Confidence Interval.

## DISCUSSION

In this study, infants whose mothers used street drugs during pregnancy had a greater delay in neuropsychomotor development when compared to infants born to non-users.

In the findings of Miller-Loncar *et al.*<sup>11</sup>, when evaluating the motor development pattern during the first 18 months of children's life with utero exposure to street

drugs, they observed that infants with cocaine exposure had low motor skills with 1 month old, but have had a significant increase in these abilities over time. In addition, the authors reported that both the highest and lowest levels of tobacco use were related to the poorest motor performance on average.

Belcher *et al.*<sup>12</sup> also observed a higher prevalence in the delay of the gross motor development of infants exposed to street drugs in intrauterine life when compared to the unexposed infants. The acquisition of motor milestones, such as rolling and walking, were delayed and presented abnormal tonus patterns.

In the United Kingdom, in a longitudinal study evaluating infants, children of women using recreational drugs (ecstasy) during pregnancy, from birth to 4, 12, 18 and 24 months of age, it was shown that exposure (greater use of tablets per week) resulted in worse motor development, but without affecting mental development. These infants with more intense exposure were twice as likely to demonstrate poorer quality of motor performance than the non-exposed ones<sup>13</sup>.

Prenatal exposure to cocaine and crack has been associated with a broad spectrum of structural abnormalities in the infant brain. A retrospective study of children who were pregnant with crack and cocaine during the first days of life showed abnormalities in 34.9% of the study population<sup>14</sup>. The changes detected were subependymal cysts in 24 children (18.6%), lenticular vascular disease in 18 children (14%), subependymal haemorrhage in 9 children (7%) and choroid plexus cysts in 9 children (7%)<sup>13</sup>. Dixon and Bejar<sup>15</sup>, in a study of full-term new-borns exposed to cocaine and methamphetamine and evaluated by cranial ultrasonography, also identified lesions such as intraventricular haemorrhage, necrosis and cavitory lesions in the basal ganglia, frontal lobes, and posterior fossa. We emphasize that focused behavioural tests and psychophysiological measures can help to identify specific areas affected by prenatal exposure to drugs, which is essential to aid intervention measures<sup>16,17</sup>.

When analysing the index of street drugs, a greater number of licit drugs were observed (Table 1). As well as the survey carried out in the city of Maringá, Paraná, Brazil, in 2012, with 394 pregnant women assisted in basic health units, which identified the highest rate of use of licit drugs in this region, being 6.09% for alcohol use, 9.14% for cigarettes and 1.02% for street drugs<sup>18</sup>.

All pregnant women in this study who used street drugs during pregnancy used concomitant licit drugs. Licit drugs, such as alcohol or nicotine, may be equally or more detrimental to the developing fetus than illicit drugs<sup>19</sup>. In addition, most pregnant women who use illegal substances during pregnancy also use legal drugs. The multicentre study of 10,000 pregnant women conducted by Bauer *et al.*<sup>20</sup> found that 93% of all women who used cocaine or opiates during pregnancy also used alcohol and tobacco.

Exposure of the pregnant woman to alcohol and cigarette smoking has deleterious effects on fetal development in the pre and postnatal period. These include increased stillbirth rates, dysfunction of the nervous system, abortion cases, congenital abnormalities<sup>21</sup>, fetal alcohol syndrome, and developmental delay<sup>22</sup>, fetal growth disorders, low birth weight, and sudden death syndrome<sup>23</sup>.

## CONCLUSION

Thus, it was concluded that infants born to mothers who used drugs of abuse had a greater delay in neuropsychomotor development.

The use of drugs of abuse is an important public health problem that requires epidemiological studies in Brazil and it is not easy to observe the occurrence of this outcome in pregnant women who are in prenatal care due to low adherence to care<sup>24</sup>. In this study, it was possible to observe a lower adherence to the prenatal consultations of mothers using abusive drugs when compared to the group of non-users, perhaps because of this also the highest number of vaginal deliveries. Corroborating this result, Oliveira *et al.*<sup>25</sup>, when analysing 166 women (83 users and 83 non-users), found that half of the group of users also did not have any prenatal visits.

In general, street drugs act on the maternal cardiovascular system, causing adrenergic hyperstimulation and vasoconstriction. There is an increase in heart rate and maternal blood pressure with consequent decrease in blood flow to the uterus and risk of restriction of fetal growth<sup>26</sup>. However, in the findings of this study, a higher prevalence of arterial hypertension was observed in nonuser mothers. High blood pressure in pregnancy is associated with unfavourable perinatal outcomes<sup>27</sup>.

According to Carvalho *et al.*<sup>28</sup>, arterial hypertension presents a significantly increased risk for preterm birth, intrauterine growth restriction, and NICU admission. Since the population of the present study was composed of preterm newborns, all had characteristics similar to those described above.

The newborns of both groups (Group 1 - children of street drugs users and Group 2 - children of non-users) had similar clinical conditions at birth. However, among the variables related to the neonatal complications observed in the current study, we highlight bronchopulmonary dysplasia, infection and length of stay in the NICU, with a statistically significant difference between groups. We note, however, that the possible clinical complications during the neuropsychomotor development presented by children exposed in the intrauterine life to drugs, licit or illicit, is dependent on the type of drug, the time of exposure and the amount used<sup>29</sup>.

It was also observed that neonatal infection was more prevalent in the children of mothers using drugs of abuse. Similar results were identified in studies involving infants diagnosed with neonatal sepsis. According to the authors, neonatal sepsis is a risk factor for motor development<sup>30,31</sup>, but not necessarily for cognitive<sup>30</sup>.

In addition to the use of licit and/or street drugs, other variables presented a higher risk for delayed neuropsychomotor development, such as the length of hospital stay and the use of oxygen therapy, and especially the patent ductus arteriosus. It is known that clinical conditions at birth and hospitalization, social, psychosocial and behavioral risks may also interfere in the development of these infants<sup>32</sup>.

It is necessary to emphasize some limitations of this study as the non-evaluation of the gestational period in which the drug in question was used, since this period could also affect neuropsychomotor development.

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## Resumo

**Introdução:** O uso de drogas de abuso durante a gestação, em decorrência dos seus efeitos deletérios à saúde do lactante, pode acarretar implicações clínicas para o desenvolvimento neuropsicomotor.

**Objetivo:** Analisar as características do desenvolvimento neuropsicomotor de lactentes filhos de mães usuárias de drogas de abuso na gestação.

**Método:** Estudo retrospectivo transversal, que analisou 51 prontuários de lactentes nascidos com peso inferior a 1500 gramas, no Hospital de Clínicas da Universidade Federal de Uberlândia (HC/UFU), entre janeiro de 2014 a dezembro de 2015. A avaliação do desenvolvimento neuropsicomotor foi realizada por meio do teste de Triagem do Desenvolvimento Denver II aos 6 ou 9 meses de idade corrigida. A análise estatística incluiu variáveis quantitativas que foram descritas por meio de médias, medianas e desvios-padrão e grupos comparados pelo teste t ou Mann-Whitney. As associações das variáveis qualitativas foram avaliadas por meio do teste de razão de verossimilhança.

**Resultados:** Dos 51 prontuários analisados, 39,2% pertenciam ao grupo de filhos de mães usuárias de drogas de abuso e 60,8% ao grupo de filhos de mães não usuárias. O desenvolvimento neuropsicomotor foi predominantemente anormal e com diferença significativa na classificação geral de desempenho ( $p < 0,001$ ) e, especificamente, na área motor grosseira ( $p = 0,003$ ) do grupo de lactentes filhos de mães usuárias de drogas de abuso.

**Conclusão:** Lactentes filhos de mães usuárias de drogas de abuso apresentaram maior atraso no desenvolvimento neuropsicomotor

**Palavras-chave:** drogas ilícitas, lactentes, desenvolvimento infantil, gestantes.

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