

## Increase in perivascular innervation of the human umbilical cord of newborns prenatally exposed to cocaine: impact on clinical variables

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**Introduction:** Substance use during pregnancy represents a critical public health concern, linked with several harmful maternal and fetal consequences. Women are at their highest risk of developing a substance use disorder throughout their reproductive years. Particularly, cocaine use represents a worldwide problem. Given that vasoconstriction is modulated by sympathetic innervation, and cocaine is a sympathomimetic drug, we hypothesized that modifications in this type of innervation around umbilical vessels could compromise maternal-filial blood flow, however, the impact of these changes remains to be evaluated.

**Objectives:** Study the perivascular sympathetic innervation in newborns' umbilical cord (UC) from cocaine pregnant users and seek for correlations between UC innervation and clinical manifestations. The impact of tobacco consumption was also addressed to identify possible deleterious exposure combinations.

**Methods:** Perinatal clinical histories (SIP; by PAHO) of UC donors were evaluated (informed consent: INDT version-N°6/30-10-18). Analyses were conducted in: **Control-group** (clinically normal pregnancies; no pre-gestational/gestational pathologies); **cocaine-group** (self-reported history of cocaine use during pregnancy); **tobacco-group** (self-reported history of tobacco smoking without other drug consumption during pregnancy). Influence of poly-consumption, gestational age and mother's nutritional status were considered. **Immunofluorescence:** UC cryosections were co-labelled with anti-human PGP 9.5 (Abcam-rabbit), a general nerve fiber marker; and anti-TH (Tyrosine Hydroxylase; Millipore-mouse), a specific marker for sympathetic fibers.

**Results:** We found a subpopulation of newborns' UC from cocaine users that had increased perivascular sympathetic innervation compared to healthy peers. Additionally, there was a negative correlation between the immunoreactive area occupied by nerve fibers in the umbilical arteries and the body weight, size and cephalic perimeter percentiles of newborns. No difference in age, size, weight and BMI (body mass index) of mothers from different groups was found. Also, we confirmed that 66% of UC from newborns of tobacco-group were not innervated.

**Conclusions:** The subpopulation of newborns prenatally exposed to cocaine that had altered innervation in their umbilical arteries were those who presented the lowest size and weight. This supports our hypothesis and reveals a potential mechanism underlying the relationship between developmental disorders and prenatal drug exposure. Our results from the tobacco-group will allow us to assess the effect of poly-substance use during pregnancies.

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