**Introduction**

Cocaine binds to and blocks the activity of monoamine transporters which results in a decreased monoamine re-uptake at the synapse and increased extracellular levels of these neurotransmitters. Cocaine can act both in CNS and in PNS, stimulating CNS and increasing sympathetic tone. It can cross the placenta barrier by simple diffusion so its mechanisms of action can exert significant teratogenic effects on the developing foetus. In addition, it can also act as an intrauterine stressor. Dopaminergic system develops early during gestational period so it can be affected by prenatal cocaine exposure (PCE). Specific areas of the human brain such as frontal lobe and limbic system are thought to be particularly vulnerable to the prenatal exposure to cocaine.

**Aims**

- Study the neurobiological and behavioural effects of prenatal cocaine exposure on children and adolescents.
- Clarify if there are significant differences in brain development, physical growth and behaviour between exposed and non-exposed subjects.

**Methodology**

Literature research on online databases, mainly PubMed and ScienceDirect. Consult basic textbooks of neuropathology and neurobiology of addiction.

**Brain abnormalities**

- Whole-brain volumetric study in children reported reduced cortical gray matter volume (GMV) and total parenchymal volumes in children prenatally exposed to cocaine (results lost statistical significance if exposure to other drugs was considered).
- Others reported significant reduced GMV in occipital and parietal lobes and white matter reductions in the corpus callosum, which were related to altered neurocognitive performance.
- A fMRI study reported 10% decrease in global cerebral blood flow in adolescents with prenatal cocaine exposure (PCE).

- In non-human primates early brain growth is compromised due to significant alterations in cortical cytoarchitecture including inappropriate positioning of many cortical neurons, loss of normal lamination, and reductions in the cortical volume, density and total number of cortical neurons.
- Studies with mouse show that the same conditions can be found in animals exposed to high doses.

**Behaviour regulation difficulties**

- Executive functioning: PCE leads to less optimal executive functioning including working memory, inhibitory control, problem solving, attention, planning and others. Important to study in children and adolescents because it can have implications for the decision making abilities.
- Attention and inhibitory control: PCE may increase the risk of attention and inhibitory control problems, especially in males. Go/no-go reversal task study showed that PCE had significant effects on attention errors in males and a trend of highly exposed males to make more inhibition errors. Similar results in a Stroop task study. The effects were dose related.
- Externalizing problems are those behaviours related towards other people, e.g. delinquency and aggressiveness. PCE is considered a risk factor for externalizing problems but there are many other risk factors such as exposure to other drugs of abuse and foster or adoptive care than can have an influence on it. PCE was correlated with aggressiveness in males (children and young rats) and male gender was considered a predictor for increased externalizing problems.

**Cognitive abilities**

- PCE alone does not lower general intelligence (IQ).
- PCE is associated with high need of individualized education plan and specialized support services.
- PCE has a direct negative impact on language skills, improvement with age.
- Higher quality home and caregiver settings can have some protective effects.
- Influence of other factors.

**Conclusions**

- PCE can have an influence on certain aspects of brain development, physical growth and behavioural regulation. However, there are many other risk factors that can have an impact on them and the results are not always consistent.
- Some of the possible limitations of the studies may be that in human experiments it is difficult to control for other variables such as the exact timing and dose of cocaine, use of other drugs, socioeconomic status and others, that most of the human studies are done in the United States and that the number of individuals studied may, in some cases, not be large enough to obtain statistically significant results. In animal studies some of these limitations can be avoided so it is risky to generalize the results of animals and consider them valid to humans.

**Effects on physical growth**

- At birth (children):
  - Preterm birth
  - Generalized growth retardation (reduced birth weight, length and head circumference)
- At 10 years of age (children):
  - Reduction in weight, length, head circumference, body mass index, probability to be obese
  - Specific data from Sale et al., 2013:
    - Weight: 4.54 kg less (41.73 vs. 46.27kg, p<0.05)
    - Length: 2.34 cm shorter (144.78 vs. 147.32 cm, p=0.04)
    - Head circumference: 0.6 mm smaller (540 vs. 546 mm, p=0.05)
    - BMI: a reduction of 1.6% in 21.4, p=0.05
  - Obesity - less likely to be obese (12 vs. 30% > 10% percentile, p<0.001)
- Other factors have to be considered that environment, life-style, infections, nutrition, genetics, and psychosocial status.

**Uncoupling of D1 dopamine receptor**

- It has been described that PCE in rabbit produces an specific uncoupling of the D1 dopamine receptor from its Gas protein in the caudate nucleus, frontal cortex and cingulated cortex (strongly innervated by dopaminergic fibers), possibly due to an adaptive reaction to the persistent increase in synaptic dopamine during development.
- Stimulation of Dopamine receptor suppression of asexual neurite outgrowth.
- Increased dopamine uncoupling of D1 dopamine receptor decreased suppression increased length and decreased bundling of layer III and V of pyramidal neuron dendrites and alterations in GABA neurotransmission which may increase extracellular dopamine levels.
- Structural abnormalities in the frontocingulated cortex may be associated with deficits in attentional and associative processes.

**BIBLIOGRAPHY**