PROGRAMMING THE BRAIN

Towards intervention strategies

Sanne Claessens

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Towards intervention strategies
Sanne Claessens
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PREFACE

Synthetic glucocorticoids such as dexamethasone are frequently used to enhance pulmonary development in preterm ventilator-dependent infants. In contrast to the short-term benefit on survival and lung maturation, early glucocorticoid exposure has been shown to adversely affect neurodevelopmental processes. Both human and animals studies have reported acute and long-lasting impairment in response to neonatal dexamethasone treatment. In rodent studies, this treatment is even reported to result in shortening of the lifespan. These findings have led to the question whether the benefits of this treatment outweigh its costs.

Therefore, the objective of the studies described in this thesis is to investigate using an animal model: 1) the short- and long-term consequences of neonatal synthetic glucocorticoid treatment and 2) the possibility to prevent these effects using pharmacological and behavioural intervention strategies.

We report that systemic glucocorticoid treatment acutely affects brain development by suppressing cell proliferation and glial activity. These acute effects on the brain can be partially prevented by central glucocorticoid receptor antagonist pre-treatment. Accordingly, central administration of the antagonist might serve as a protective strategy against the adverse neurodevelopmental effects of dexamethasone treatment.

Although glucocorticoid exposure clearly affects the developmental trajectory, the long-lasting consequences of this treatment were not as detrimental as previously reported. We suggest that daily handling of the neonate, which was an inevitable component of our experimental design and leads to enhanced levels of maternal care towards the offspring, may compensate for the adverse effects of glucocorticoid exposure.

We conclude that the impact of neonatal glucocorticoid exposure highly depends on interactions with other components of the early environment and is therefore susceptible to pharmacological and behavioural intervention strategies.