Although the cause of schizophrenia is not fully elucidated, there is increasing evidence that this severe psychiatric illness may result from a disturbance early in development. Evidence for this so called „neuro-developmental hypothesis“ comes from a variety of sources, including epidemiological, gynecological, psychological and pathological data.

Fetal and perinatal hypoxia-ischemia belongs to obstetric complications which can increase the risk of schizophrenia. These complications such as premature rupture of fetal membranes, low birth weight, newborn immaturity, forceps delivery and resuscitation at birth are frequently accompanied by hypoxic-ischemic brain damage during delivery. We assume that perinatal hypoxia together with genetic factors influence a susceptibility to schizophrenia and represent significant risk factors of this disease.

We used a heuristic model in our study to determine if brain hypoxic-ischemic episode can actually cause not only changes of biochemical markers but also behavioral changes resembling those seen in schizophrenia.

Neurodevelopmental processes in neonatal rats continue during the first three weeks of postnatal life and reach the level of those observed in human newborns at the end of the second postnatal week. Therefore, rat pups at postnatal day 12 (PND12) were used and subjected to one hour of continuous occlusion of both common carotid arteries. Under these conditions the neonatal brain suffered from oligemic hypoperfusion (stagnant hypoxia).

Hypoxic lesions were characterized biochemically using blood gas parameters (arterial pH, arterial partial pressures of CO_2 and O_2), activity membrane-bound gamma-glutamyl transpeptidase (GGT) in the brain and also activity soluble GGT in the blood. Expected hypofunction of the glutamatergic transmission observed in schizophrenics was the reason why we determined levels of second messengers in plasma and blood platelets. To determine whether the behavioural changes in the post-ischemic animals were already present early in life or emerged during the life we used battery of tests – social (play) behaviour (PND 22), reactivity in open field paradigm (PND 35 and 50) and the acoustic startle response and prepulse inhibition (PND 50).

Our results support this assumption and show that 1-h lasting continuous hypoperfusion of neonatal rat brains can induce biochemical and behavioural changes apparent in young adulthood that are in relation to schizophrenia. The present study supports the model of schizophrenia as a neurodevelopmental disorder. We believe that an early cerebral hypoxic/ischemic lesion is a risk factor of later neurodevelopment and consequently having a potency to alter CNS function. Thus, even though genetic vulnerability plays an important role in the development of schizophrenia, our findings suggest that obstetric complications also contribute as epigenetic factors-to the aetiology of schizophrenia.