Conclusion

Our findings demonstrated that hypoxia during the neonatal period caused significant impact in the central nervous system both functionally and behaviourally. The evaluation of these damages at molecular level is very important, especially in a critical brain function to reduce the effects of damage during later developmental stages. Even though the body weight or blood glucose level is not altered after seven days of hypoxic insult, it caused alterations in the brain DA and metabolite contents. Brain requires continuous supply of oxygen for energy utilization and efficient functioning. Hypoxia leads to disruption of this energy utilization, resulting in neuronal functional failure, cerebral palsy and neuro-developmental delay. Structural and functional integrity of brain depends on regular glucose and oxygen supply. The receptor binding studies show alterations in the DA, DA D₁ and DA D₂ receptors in the cerebral cortex, brainstem and cerebellum. The NMDA receptors showed a decrease in cerebral cortex while it was significantly increased in brainstem and cerebellum during hypoxia. Real-Time PCR confirmed receptor data. The second messenger study confirmed that the changes in the receptor levels did percolate through alterations in IP3, cAMP and cGMP levels. The Ca²⁺ release studies showed a decrease in extracellular Ca²⁺ levels during hypoxia. The behavioural studies by rotarod test showed a decrease in motor activity. These studies suggest that DA D₁, DA D₂ receptor potentiates NMDA mediated overactivity leading to increased IP3
dependent Ca\(^{2+}\) release which triggers release of Cytochrome C thereby initiating the apoptotic process. This causes cell damage during hypoxic stress in the neonatal rats—hypoxic; hypoxic rats treated with oxygen; epinephrine and oxygen and a combination of glucose, epinephrine and oxygen. The glucose supplementation to hypoxic rats and along with oxygen is able to reverse this damage.

We conclude that glucose act as a neuroprotective agent in reversing the decreased DA content, DA D\(_1\) and DA D\(_2\) receptor function due to hypoxia. Altered DA through DA D\(_1\) and DA D\(_2\) receptor subtypes in hypoxic rats and those supplemented with oxygen and epinephrine suggest the occurrence of dopaminergic functional regulation in the brain of hypoxic rats. This impaired dopaminergic function will cause damage to the brain leading to behavioural changes during later developmental life. The efficient and timely supplementation of glucose reversed DA functional changes through DA D\(_1\) and DA D\(_2\) receptors observed in hypoxia, oxygen and epinephrine supplementation. Our results showed that hypoxia causes a significant modulation in dopaminergic function which is corrected by prior supplementation of glucose to oxygen in the resuscitation sequence. Thus it is suggested that immediate glucose administration during neonatal hypoxia with oxygenated air in the resuscitation programme will reduce the hypoxic damage to the brain cells. This has immense clinical significance in the management of hypoxia in neonatal care which will have role in intellectual and behavioural efficiency at later stages of life of an individual.