

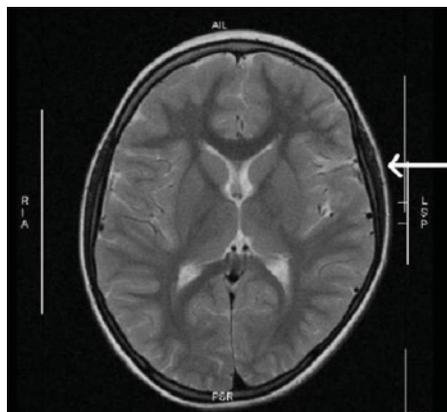
# STOP-CP in children!

Arne Jensen, CEO of BrainRepair UG and head of the Campus Clinic Gynaecology Bochum, Germany, outlines the motivation behind STOP-CP: **Stem cell Treatment Of Perinatal Cerebral Palsy** using cord blood



**B**rain damage is a prime risk factor for cerebral palsy, causing lifelong neurologic sequelae with severe consequences for young patients and their families. It is believed that brain damage is primarily a problem of the immature brain of preterm infants if, for example, cerebral haemorrhage or injury to the white matter in the periventricular regions occur where long fibre tracts from the cortex to the extremities pass.

However, a large cranial ultrasound screening study revealed that a substantial fraction of cases presenting cerebral haemorrhage and white matter damage (34-39%) is to be expected in infants born near term. While the aetiology of haemorrhagic injury and white matter damage in preterm infants is largely related to circulatory changes – for example systemic hypotension during and/or after lack of oxygen, and infection – the aetiology in term-born infants is less well understood. Though similar mechanisms may apply for preterm and term infants, there is growing evidence that, in large newborns, mechanical problems during delivery resulting in excessive moulding and depression of the skull may be involved and perhaps account for unexplained cases of developmental delay or



cerebral palsy, despite preserved vitality at birth, as recently observed.

### Infantile cerebral palsy

Infantile cerebral palsy as a result of brain damage in newborns is the most devastating and debilitating ailment in childhood, for which there exists no therapeutic option at present beyond active rehabilitation. Cerebral palsy leads to complex disabilities, including movement and posture disorder (all patients), chronic pain (three in four), mental retardation (one in two), inability to walk (one in three), and a life expectancy in severe cases of less than 18 years (one in two), to name only a few. The lifetime costs to society only for symptomatic treatment of affected infants amount to €800,000 in Europe according to conservative estimates. However, this figure only imperfectly reflects the true personal tragedy and family burden caused by this ailment, so there are urgent unmet needs to develop causative treatments for cerebral palsy.

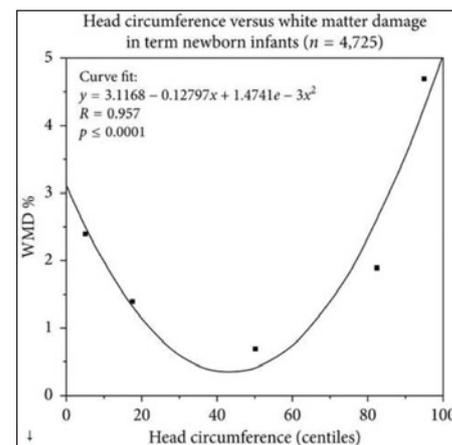
### First curative treatments

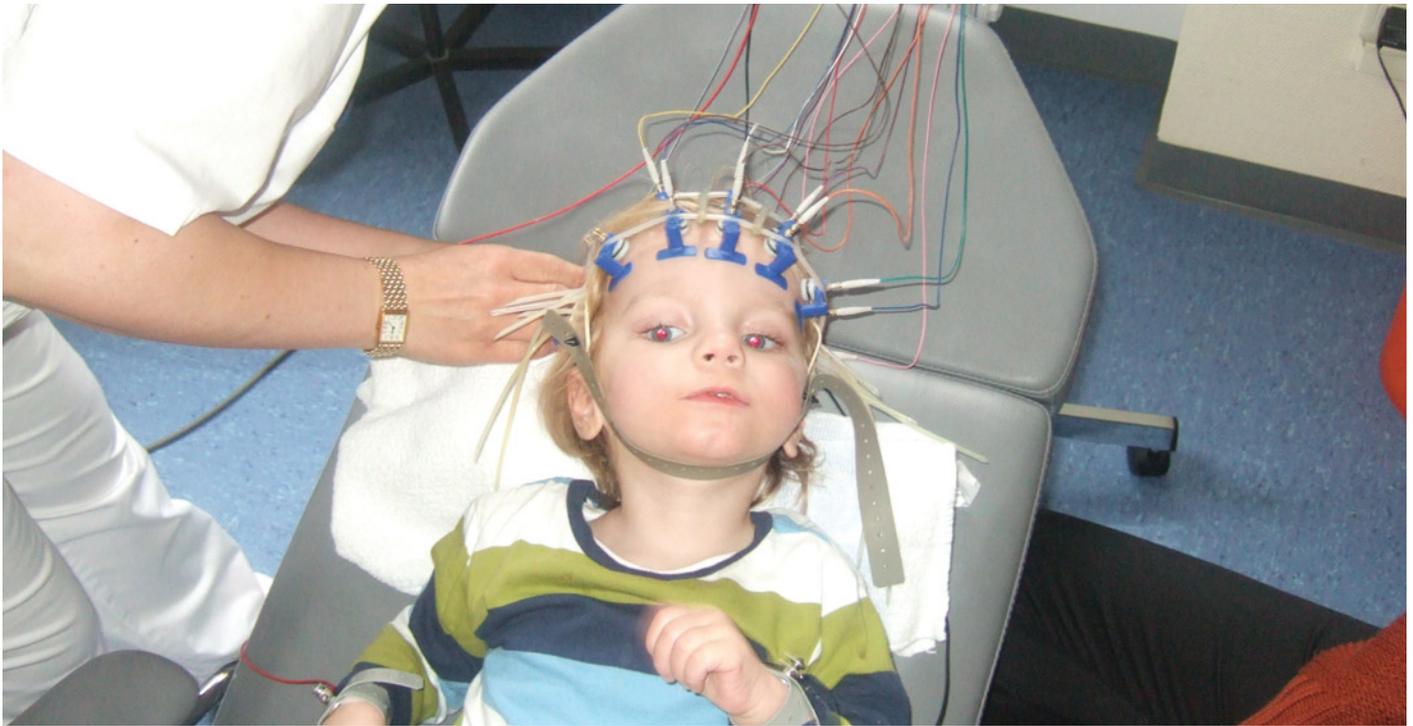
Only recently, preclinical studies were successfully completed and a medicinal product from cells derived from the patient's own (autologous) cord

blood has been developed, which is intended to treat brain damage in both newborns and children, thus preventing cerebral palsy. This therapeutic breakthrough has been acknowledged by the European Medicinal Agency (EMA), and the European Commission has granted 'Orphan Medicinal Product Designation' for the treatment of brain damage in preterm (EC/3/16/1744) and term newborns (EC/3/16/1743).

### From bench to bedside

Human cord blood is collected at birth after clamping the umbilical cord. The collected blood volume is cooled and banked. The end product contains among other mononuclear cells, including haematopoietic and epithelial progenitor cells, monocytes and lymphocyte subpopulations. In case there is evidence for brain damage in the donor child, as assessed by imaging techniques and clinical examination, the medicinal product derived from the patient's own cord blood can be re-transfused and the therapeutic process will be initiated as demonstrated in preclinical studies from various groups worldwide.





Intriguingly, the stem cells contained in the product migrate actively (so-called 'homing') into the damaged brain region and induce a neuroregeneration by releasing various proteins, including anti-inflammatory cytokines, growth factors, and chemokines, thus reducing spastic (stiff) paresis, the key symptom of cerebral palsy, and improving gross and fine motor function of the patient.

Moreover, due to the fact that the product is autologous in nature, derived from the patient's own cord blood, there are no immunologic side effects. The treatment is safe. Worldwide approximately 400 infants have been treated so far and only 1.5% minor adverse effects have been observed. Thus, the benefit/risk ratio of the treatment of brain damage to prevent infantile cerebral palsy is extraordinary high.

### Who will profit?

The prevalence of brain damage in preterm infants is higher than in term-born infants; however, a substantial part of brain damage, such as haemorrhage and damage to the white brain matter, also happens in term-born infants, as recently observed. Given the subsequent occurrence of cognitive, behavioural, attentional, or socialisation deficits and of major motor deficits such as cerebral palsy, it is obvious that every child with suspected brain damage that has the opportunity to have its own cord blood stored and available will profit most. But also those seemingly 'healthy' large term-born infants that are clinically unremarkable as assessed by Apgar score, heart rate pattern, and acid-base balance presenting a head circumference beyond the 75th centile may profit significantly from stem cell treatment because up to 5% of these newborns contract white matter brain damage by depression of the skull and brain during prolonged or obstructed delivery.

A recent review of the prevalence of brain damage in EU member states has revealed that about 70,000 newborns and infants suffer from various forms of brain damage that are diagnosed after birth each year, not including the group of seemingly healthy large term-born infants with large head circumference, amounting to an estimated further 43,000 newborns. Thus, roughly 110,000 infants (2.2%) would profit from autologous stem cell treatment of brain damage in the European Union each year.

### Costs to society

From what is known about the estimated lifetime costs for children suffering from cerebral palsy (€800,000), it becomes obvious that society, and particularly the insurance companies, would profit most from a curative treatment of cerebral palsy, because lifetime costs for symptomatic care of €88bn will ensue from the untreated brain damage in children born in the European Union each year.

These costs can be cut by a factor of 20 when autologous stem cell treatment of brain damage in newborns is implemented. This view was shared by the reviewers of our recent Horizon 2020 proposal 'STOP-CP! Implementation of the first stem cell based treatment of infantile cerebral palsy in Europe', which has been awarded the 'Seal of Excellence' by the European Commission (805781-SMEINST-2-2016-2017).

### Conclusion

Combat infantile cerebral palsy by using autologous cord blood stem cells – the future of brain repair is now!



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