

Oral presentation

## CSF circulation and cerebral cortex development

Jaleel Miyan

Address: The Faculty of Life Sciences, The University of Manchester, AV Hill Building, Oxford Road, Manchester M34 2RJ, UK

Email: Jaleel Miyan - J.Miyan@manchester.ac.uk

from 53rd Annual Meeting of the Society for Research into Hydrocephalus and Spina Bifida  
Belfast, UK. 24-27 June 2009

Published: 27 November 2009

*Cerebrospinal Fluid Research* 2009, **6**(Suppl 2):S13 doi:10.1186/1743-8454-6-S2-S13

This abstract is available from: <http://www.cerebrospinalfluidresearch.com/content/6/S2/S13>

© 2009 Miyan; licensee BioMed Central Ltd.

Over the past decade, studies of a number of CSF conditions, in particular the H-Tx rat and curly tail mouse, have demonstrated a critical role for CSF in the development of the cerebral cortex and, more specifically, in the developmental defect associated with fetal-onset hydrocephalus and neural tube defects. This paper is an attempt to present a CSF hypothesis for CNS and brain development.

CNS development proceeds around a fluid-filled neural tube. The source of fluid within the developing central nervous system changes from an active blood-CSF barrier in the mesencephalon transporting specific proteins and water into the growing fluid cavity and maintaining the osmotic potential of the fluid [1-3], to a high volume fluid and protein secreting choroid plexus [4]. The fluid volume output changes coincident with a change in fluid pathway from simply filling a sealed tube to bulk flow, reaching a production of 0.3 ml/min in adult brain, forcing fluid through the ventricles and out into and around the subarachnoid space [5]. Moreover the composition changes driving and supporting development of the brain stem and spinal cord and, later, through CSF output, the cerebral cortex [6]. Evidence from *in vitro* experiments demonstrates that CSF is sufficient to support the viability, proliferation and differentiation of neural stem/progenitor in age dependent manner [7]. Evidence from the curly tail mouse as well as from brain slice experiments demonstrate that CSF passage through the subarachnoid space is required for correct migration and lamination of the cortex with neurons generated in the ventricular zone. Evidence from the hydrocephalic H-Tx rat shows that CSF composition alone can arrest development through a blockade of cell division. This blockade involves abnor-

mal folate handling and has recently been shown to be amenable to treatment through maternal folate supplementation, but not folic acid [8].

Further understanding of the role of CSF in CNS and brain development will help expose many of the missing elements in our understanding of how the CNS develops and how this can go wrong. The future may thus provide treatments to prevent and/or treat conditions of poor development.

### References

1. Cottingham K: **The complex composition of embryonic CSF.** *J Proteome Res* 2007, **6**:3537-3548.
2. Parvas M, Parada C, Bueno D: **A blood-CSF barrier function controls embryonic CSF protein composition and homeostasis during early CNS development.** *Dev Biol* 2008, **321**:51-63.
3. Gato A, Desmond ME: **Why the embryo still matters: CSF and the neuroepithelium as interdependent regulators of embryonic brain growth, morphogenesis and histogenesis.** *Dev Biol* 2009, **327**:263-272.
4. Johanson CE, Duncan JA, Stopa EG, Baird A: **Enhanced prospects for drug delivery and brain targeting by the choroid plexus-CSF route.** *Pharm Res* 2005, **22**:1011-1037.
5. Pourghasem M, Mashayekhi F, Bannister CM, Miyan J: **Changes in the CSF fluid pathways in the developing rat fetus with early onset hydrocephalus.** *Eur J Pediatr Surg* 2001, **11**(Suppl 1):S10-S13.
6. Miyan JA, Nabiyouni M, Zendah M: **Development of the brain: a vital role for cerebrospinal fluid.** *Can J Physiol Pharmacol* 2003, **81**:317-328.
7. Miyan JA, Zendah M, Mashayekhi F, Owen-Lynch PJ: **Cerebrospinal fluid supports viability and proliferation of cortical cells in vitro, mirroring in vivo development.** *Cerebrospinal Fluid Res* 2006, **3**:2.
8. Cains S, Shepherd A, Nabiuni M, Owen-Lynch PJ, Miyan J: **Addressing a folate imbalance in fetal cerebrospinal fluid can decrease the incidence of congenital hydrocephalus.** *J Neuropathol Exp Neurol* 2009, **68**:404-416.