A mechanobiologically grounded treatment of traumatic brain injury-induced psychosis, applying innovative osmotherapy and risperidone. Case report, follow-up and physical model

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Objectives and background

Objectives: To test and control the instant and long term effect of osmotherapy, on the antipsychotic treatment response rate, robustness and duration, on a patient with mild to severe TBI induced psychosis (1° objective) and cognitive decline (2° objective).

Normal Cortical Gyrification pattern

- Cortical density determines tissue elastic properties and convolution pattern, on a broad genetic protomap
- Tissue material instabilities remain localized and allow new gyral/ sulcal patterns.
- Cortical Stiffness > White matter Stiffness
- Mechanically stable system

Normal Cortical Function

- Gyrification allows great surface area for network embedment
- Great surface area allows optimal (minimal) average path length between neuronal network nodes (cortical areas).
- Network density energetically favorable at global system level.
- Information flow regulated genetically / neurochemically
- Systemic stability – Instabilities under system constraints

TBI & Edema – Structural impact

- Convolution pattern loss. Gyral flattening / sulcal narrowing
- Rapid strain leads to axonal disconnection or injury
- Swelling leads to slow, structurally tolerable axonal elongation in the white matter.
- Cortical and white matter areas compressed or stretched
- Stiffness inhomogeneity due to excess fluid presence.

TBI & Edema – Functional impact

- Axonal Electrophysiological alterations.
- Axonal elongation under pressure leads to ↑ average path length value in neuronal networks of deformed areas.
- Probable pyramidal cell synapse loss (intracortical circuits).
- Genetic alterations in pyramidal cells.
- Information flow instability in multiple areas/ multiparametric.

Background: Mathematical modelling, comparing a spheroid with cortical morphology, has linked cortical gyrification patterns, to optimal cortical information rate. Deformation of cortical convolution patterns, is a physical result of edema and hematoma, after Traumatic Brain Injury (TBI). Psychosis and Cognitive decline, are related to deformation level, duration and functional impact.

Response to antipsychotics, has been linked to close to normal gyrification patterns, in first-episode psychosis. This highlights the possibility that the neurochemical parameters regulated with antipsychotics can have a positive effect only if optimal topological restrictions (average path length, connectivity clustering and topological density) are present. Osmolytic therapy may be used for partial depressurization of axons/ glia, effectively facilitating return to normal axonal length/ regeneration and to toxicity reduction.

Materials & methods - Results

11.10.2018

06.10.2018

17.09.2018

Symptom Resolution

Materials and Methods : A TBI patient (CT 17.09.2018) with subtle pathological personality traits, completed first line osmotherapy in a neurosurgical department (3CT-scans), showed persisting disorientation and memory gaps during the 10-day rehabilitation period (1CT-scan) and was transferred at the psychiatric department after acute onset psychosis (CT 06.10.2018). Two new osmotherapy cycles were applied, with mannitol (cycle 1) and acetazolamide (cycle 2), (day D1- ~ D8 +D9-D11), plus low dose risperidone (D1- present). Vitamin supplementation was added at D15. New CT-scan was performed at D6 and MRI at month M4. Neurocognitive assessment was performed at M4 and M10. **Results:** Comparative cortical deformation reduction (CT-scans). Symptoms resolved rapidly (Left Image Above). MRI and Neuropsychological testing confirmed the results and ~total cognitive restoration at months M3 and M4, M10 respectively.

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