

A small structure hidden in the brain that might play a big role in diseases like depression and autism

The choroid plexus is a hidden and often neglected, but important, structure in the brain. The choroid plexus hangs inside the brain ventricles which are filled with cerebrospinal fluid (CSF) (Fig. 1). Importantly, the choroid plexus is the main source of this CSF. More specifically, the choroid plexus epithelial (CPE) cells are the main cells responsible for CSF production. The CSF composition has an important impact on brain homeostasis and function. Consequently, when CSF secretion by the choroid plexus epithelial cells is altered, this has important consequences on brain functionality. Also, the CPE cells are essential as a barrier between the blood and the brain. Indeed, they form one of the central nervous system (CNS) barriers, called the blood-CSF barrier, and this barrier is essential to prevent leakage from blood components into the brain tissue, as this might disturb brain homeostasis and induce brain inflammation. Also when blood-CSF barrier integrity is impaired, this will have negative consequences on brain functionality. Clearly, the choroid plexus plays an crucial role in maintaining brain homeostasis, via both CSF secretion and barrier formation.

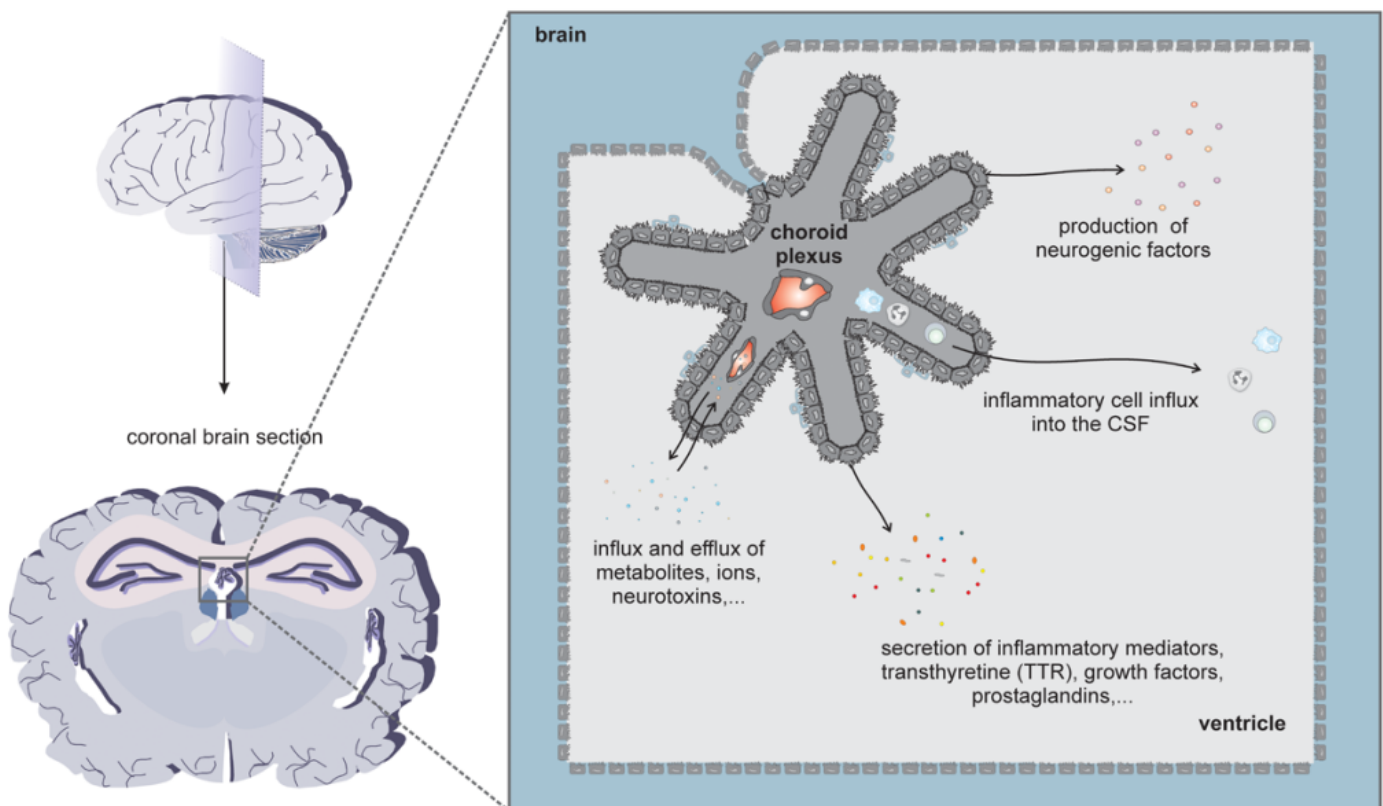


Fig. 1. The choroid plexus hangs inside the with cerebrospinal fluid (CSF) filled brain ventricles and plays an crucial role in maintaining brain homeostasis, via both CSF secretion and barrier formation.

More and more evidence points towards a role of the choroid plexus in neuroinflammatory diseases such as traumatic brain injury (TBI), multiple sclerosis (MS), Alzheimer's diseases (AD) but also neuropsychiatric diseases including schizophrenia, autism and depression. However, in case of neuropsychiatric diseases, there is mainly indirect evidence.

One reason to believe that the choroid plexus is important in the development of neuropsychiatric diseases is based on its location close to two important neurogenic regions in the brain: the subgranular and subventricular zone. The choroid plexus is known to release neurogenic factors into the CSF and changes in the secretory activity of the choroid plexus might consequently disturb the formation of new neurons, which is an important factor in neuropsychiatric disorders. Apart from neurogenic factors, also other molecules secreted by the choroid plexus might affect the brain, including inflammatory mediators, transthyretine (TTR), growth factors and prostaglandins. Moreover, the choroid plexus plays a central role in the influx and efflux of metabolites, ions, neurotoxins and other molecules which all directly or indirectly affect brain function and which might be dysregulated under specific (inflammatory) conditions. Additionally, the choroid plexus is considered to be the main gateway to the brain for inflammatory cells and several neuropsychiatric diseases are known to be associated with increased levels of inflammatory cells in the CSF. Additionally, inflammatory cell infiltration into the brain is often accompanied with loss of barrier integrity and *e.g.* depression and sleep disorders are correlated with physical disruption of CNS barriers, again indicative for a role of the choroid plexus in these disorders.

Importantly, further research is needed to unravel the mechanisms at the choroid plexus which might play a detrimental role in the development of neuropsychiatric diseases and this might open up new therapeutic avenues to treat these diseases.

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Publication

[Therapeutic implications of the choroid plexus-cerebrospinal fluid interface in neuropsychiatric disorders.](#)

Demeestere D, Libert C, Vandenbroucke RE
Brain Behav Immun. 2015 Nov