Physiological brainwashing

There is a barrier in the brain, known as the blood-brain barrier, which strictly regulates the exchange of substances between the blood and this organ. The blood-brain barrier restricts the passage of drugs into the brain and therefore, limits the available treatments for diseases such as Alzheimer's and Parkinson's. But this barrier not only restricts the entry of substances, but also their exit. So, how does the brain remove its waste products?

In recent studies, we show that the brain has its own waste collection system. Waste products are packaged in containers, the containers are expelled from the brain, and then, outside the brain, they are eliminated. As we will show, this will permit to obtain relevant information about the brain status. But let's not get ahead of ourselves and let’s describe how the garbage collection system works.

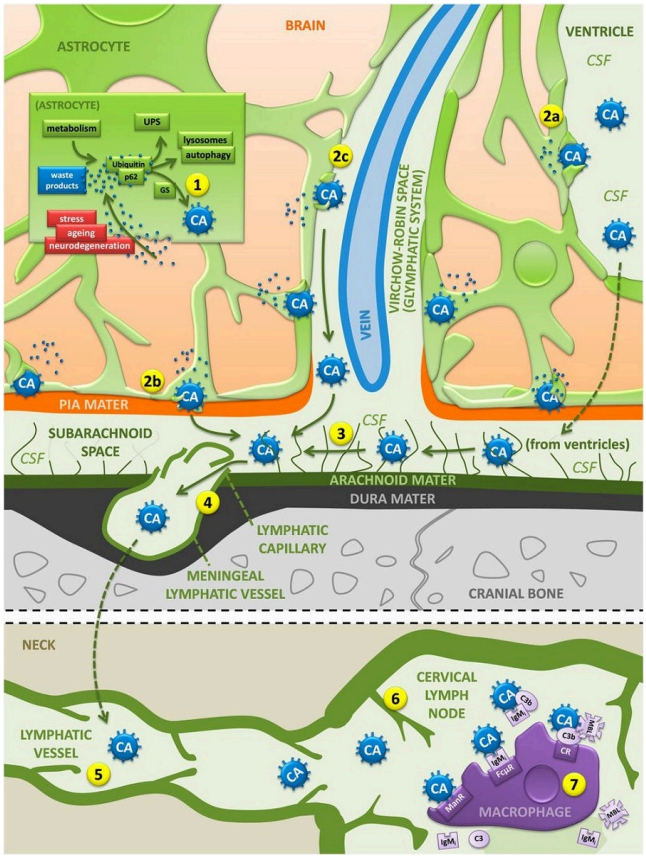

Fig. 1. Brain trash removal route. Author provided. (Marta Riba et al / PNAS 2019;116:51:26038-2604)

The containers of waste products, called *corpora amylacea*, are generated by astrocytes, star-

shaped brain cells with foot processes that expand around them. Astrocytes form the *corpora amylacea* and label them with particular markers called neo-epitopes, which specify their destination once they are expelled from the brain.

These *corpora amylacea* are spherical and relatively large structures. They can reach a diameter greater than 20 microns, exceeding the 10 microns of blood capillaries diameter. Although they are too large to be removed through blood, the brain has other resources to get rid of them.

Physically, the brain "floats" inside the skull suspended in an aqueous medium called cerebrospinal fluid. Well, some brain waste substances are poured directly into this fluid, and this is how *corpora amylacea* find their way out of the brain.

The cerebrospinal fluid, in turn, drains through the lymphatic system of the meninges. Meninges are membranes that separate cerebrospinal fluid from skull bones, as well as cerebrospinal fluid from the brain (the inflammation of these membranes, the meningitis, is a serious and sometimes fatal disease). In the meninges, there is the meningeal lymphatic system, recently rediscovered. The lymphatic capillaries of the meninges collect part of the cerebrospinal fluid and its products, and the lymphatic vessels of the meninges descend to the neck. In the neck, the lymphatic vessels encounter some lymph nodes. These lymph nodes filter the fluid and contain specialized cells called macrophages. Once macrophages read the target labels or the neo-epitopes present in the *corpora amylacea*, "eat" (phagocytose) them and proceed to their chemical degradation. In this way, residual brain substances that cannot be degraded in the brain and cannot exit through the blood find an escape route and are eliminated.

In summary, the result is a deep “brainwashing” that can be essential for brain’s correct working. Furthermore, these findings offer a new approach to diagnose brain diseases. The fact is that, in the same way that the analysis of garbage bag contents allows us to know the habits of the people who generated them, studying the waste products present in *corpora amylacea* of the cerebrospinal fluid can give us an idea of how the brain is working. Therefore, the analysis of the contents of the isolated *corpora amylacea* can be a useful diagnostic tool.

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