

# Structure and Function of the Blood Brain Barrier

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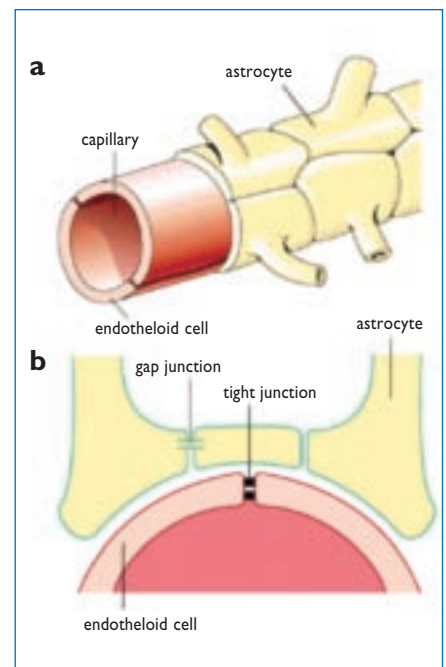
## Introduction

Every living creature on the earth is surrounded by natural and artificially produced electric, magnetic and electromagnetic fields of different frequency ranges and intensities. The use of modern technology and further developments in information and communication technology is constantly increasing and this in turn has caused an increase in the above-mentioned fields in our daily environment. Consequently there have been lively public discussions on the possible effects these fields may have on human, animal and plant life and moreover in many generally accessible publications, reports on the effects of these fields on humans are very superficial and very effective in terms of the media. Information obtained from magazines, whose content is not always scientifically confirmed, can cause the reader to become alarmed when reading that through the use of a mobile phone the blood brain barrier can be permeated and brain damage results. After talking to these alarmed and worried people, one comes to the conclusion that the ideas they have about the blood brain barrier are rather bizarre. Very often one hears that an organ opens up, the idea they have is similar to a train crossing gate, and then harmful substances can enter the brain and poison it.

## Barriers which exist between the blood and organs

Of course, the situation is not that simple, therefore, the anatomical situation has to be explained. Our body consists of individual organs and organ systems, which require different but constant conditions to function, such as nutrients, hormones and electrolytes. All of the body's organs are connected to each other by the circulatory system. Since the blood contains all of the components needed for providing the body with what it needs and for purification processes, filter systems have to ensure that the necessary substances pass through the organs and that some substances are partly held back. Some of the known blood barriers are as follows: the blood tissue barrier, also known as the blood parenchyma barrier, the blood liver barrier, the blood-cerebrospinal fluid barrier, the blood brain barrier, the cerebrospinal fluid brain barrier, the blood nerve barrier, the blood retina barrier, and the placental barrier. This filter mechanism functions with a so-called barrier effect, this means certain substances are permitted to permeate the barrier and others are restricted when the organ system does not need the components or only needs them in lower concentrations.

These "barriers" are not independent organs but are made up of many cells and space that exists between the cells allowing blood gases, nutrients, and certain chemicals permeate the barriers. They are made



Construction of the blood brain barrier

Schematic view

a) spatial

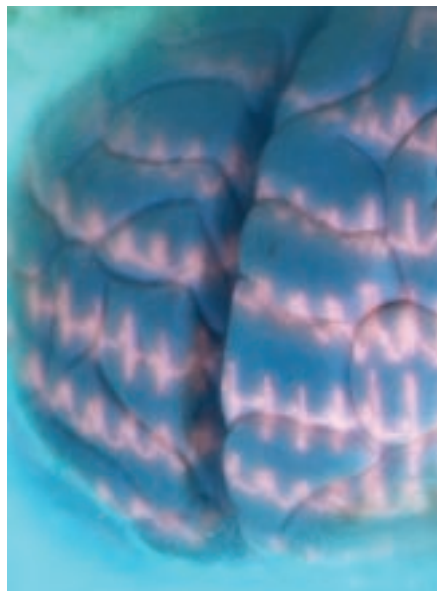
b) cross-section, source: Deetjen/Speckmann, *Physiology*

2<sup>nd</sup> printing, Urban & Schwarzenburg, 1994

up of endothelial pores which hold back macromolecules, or they could be lipid membranes located in vascular walls which have an inhibiting effect on the permeation of non lipid soluble substances or they have the selective effect of taking an active part in capillary transport processes. The brain and the nerve tissue are protected by two filter systems, the blood cerebrospinal fluid barrier and the blood brain barrier.

### The blood-cerebrospinal fluid barrier

This fluid is a brain and spinal cord fluid, which fills the inner and outer cerebrospinal fluid space in the cranial vault and in the vertebral canal. During cerebrospinal fluid production as well as when substances cross over from the blood into the fluid, filtration, diffusion and active transfer processes of carbon dioxide, glucose and amino acids take place. This exchange of substances is regulated by the blood-cerebrospinal fluid barrier, which is formed out of capillary endothelial cells and brain covering and can be found between blood vessels and the cerebrospinal fluid space. The different concentrations of glucose, protein and electrolytes in the blood and in the CSF is regulated by these filter functions in order to maintain optimal concentrations in the brain.



### The Blood Brain Barrier

The existence and the function of the so-called blood brain barrier has been known for more than 100 years and as early as 1885, Paul Ehrlich proved its existence in experiments.

Within the central nervous system the space between the neurons is almost completely filled with glia cells and their end feet/expansions. The entire nerve cell metabolism takes place via these glia cells- or endothelial cells, whose purpose is to install nerve cells and -fibres, and to nourish and isolate them. A type of glia cells are astrocytes. One type of astrocytes has numerous expansions of end feet which adhere to capillary walls and another type encloses the capillaries on all sides with a nearly leak-proof lining of endothelial cells. These endothelial cells are joined together by connective elements, or tight junctions (see diagram) and are equipped with a selective substance permeability which allows only particles with a diameter of less than 20nm to cross over. In this way the entire metabolism of nerve cells takes place via this endothelial network, so that when necessary any substances present in the blood are immediately passed through a biological filter. However, any substances which may harm brain function are kept away from the nervous system.

### Blood brain barrier function

This endothelial network and the endothelial cells which cover the capillaries as a basal membrane, is designated as the blood brain barrier. Unhindered oxygen, carbon dioxide, D-glucose, D-Hexose, some L-amino acids and lipid soluble substances permeate the BBB, which are all necessary for proper brain function. In this way breakdown products are also passed on into the blood.

The feet end and extensions of astrocytes represent a certain barrier for specific hormones, non soluble lipids, water soluble and numerous other chemical substances, and this ensures that a constant

environment is maintained for neurons and the nervous system.

### Blood brain barrier malfunctions

The cell structure of astrocytes is so constructed that it is able to build an effective shield against higher molecular substances and organisms. However, under normal conditions it is not completely sealed, so some particles are able to permeate the barrier. In cases of infection, trauma, inflammation, poisoning, hypoxia-dose, fever and in cases of tumours, the tight junctions between the endothelial cells become stretched out due to astrocyte swelling and this in turn makes the BBB more permeable for other substances. Changes in the width of the openings are due to the swelling and the de-swelling of endothelial cells. Even the capillary basal membrane is not a sealed layer. Whether or not there are pores in the membrane, which play an active part in the exchange of substances, depends on the density of the fibre network. The vascular systems of pathological tumours do not develop any blood brain barriers. Since this has been known, it has been used in diagnostic procedures. A contrast medium is administered into the vascular system to check if the contrast medium stays in the vascular system or passes over into the tumour.

Long before the use of antibiotics, physicians increased the permeability of the blood brain barrier by inducing an artificial fever, similar to what occurs during an infectious illness. This type of treatment was used to treat syphilis of the central nervous system and for shock therapy in the field of psychiatry, with this type of treatment medication could be administered directly to the brain. When the conditions that produced the blood brain barrier's temporary increase in permeability are stopped it returns to its original state.

### Conclusions

When considering this article in its entirety it would make more sense to consider

the blood brain barrier as a selective filter rather than a barrier. Investigations have shown that permeability increases when there is an increase in the body's temperature and when there is an increase in function. An increase in the brain's temperature while using a mobile phone hardly ever occurs. Concerning this, after the test person had been using the telephone for a quarter of an hour at maximum power, the temperature under the cranial calotte was increased by 0.1°K. During a warm bath, hard physical labour or being exposed to the sun for a longer period of time all lead to an greater increase in temperature. How the blood brain barrier reacts in these situations or how the body tolerates such changes is yet to be investigated.

Since the extent of permeability returns to its original state after an increase in temperature, experiments should be done investigating these effects shortly after the influential factors produce an effect. If changes are discovered weeks after exposure, as described in the Salford (5) study, it can not be ruled out that in the duration there were other effects which could have affected the test animals and gave rise to changes affecting the filter function of the blood brain barrier.

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## Developments in research concerning this subject

# Is the blood brain barrier effected by mobile radio fields?

**Roland Glaser**

**Again and again the public is alarmed by reports stating that telephoning with a mobile phone will cause the blood brain barrier BBB to open and nerve damage will result or even brain tumours may develop. How serious are these warnings and how protected are we by the current limit values?**

Firstly, it must be established that the blood brain barrier is not an anatomically localized organ but is a special feature of the blood capillaries located in most areas of the brain. In order to protect the brain, which is the most sensitive organ in the human body, from toxic substances the capillary endothelial cells are joined by tight junctions, a sealing mechanism that makes it difficult or impossible for certain substances to permeate the BBB. Only soluble gases required for cell respiration, oxygen and carbon dioxide, as well as nutrients such as D-glucose, D-hexose, L-amino acids and lipid soluble molecules are able to permeate this barrier. In stress situations, cranial trauma and with various illnesses a malfunction of the barrier

can occur, these malfunctions are usually quickly repaired. (Blasberg et al. 79).

Quite early on one thought that high frequency fields could cause an increase in temperature and quasi induce an artificial fever and this in turn would lead to the BBB being affected. This unwanted side-effect had been observed in conjunction with the so-called short-wave therapy. However on the other hand, it was used to administer medication directly to the brain (Lin et al. 98). Therefore, this effect has been investigated for more than three decades.

The first animal experiments in connection with possible harmful effects to the BBB caused by radio and radar fields were done in the 1970s by Frey et al., at first they thought that this would also promote cancerostatica in the brain (Frey et al. 75, Frey 79). Sutton and Carroll (79) have pointed out that when the temperature of rats' brains is increased to 45° C induced by a 2450 MHz-field there is an increase in protein absorption.

Oscar and Hawkins (77) examined in rats the absorption of <sup>14</sup>C marked sugar molecules of various molecular weights, while they were being exposed to different power densities of continuous and pulsing fields of 1.3 GHz. While dextrin with a molecular weight (MG) of 60.000-75.000 was not absorbed at all, they discovered that mannitol (MG = 182.2) and inulin (MG = 5.000-5.500) had an absorption intensity as a function of the applied power flow density, which showed the maximum to be at about 10 W/m<sup>2</sup>. Pulses of the same average power flow density but of differ-