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The Embryological Development of the Form of the Trabeculae Bridging the Subaracnoid Space

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Abstract

Introduction: Although it is commonly stated that the brain "floats" in the cerebrospinal fluid (CSF), the brain is actually suspended in the CSF-fluid-filled subarachnoid space by trabeculae. Subarachnoid trabaculae are sheets or columns of collagen-reinforced material that stretch between the arachnoid and pia membranes. They can be seen with light microscopes but they are too thin to be seen by ultrasound.

Study: A literature study of the physiology of the subarachnoid space was undertaken. There was a period of interest in trabecular structure in the 1970s, involving electron microscopy. Transmission electron microscopy enabled cell types, and collagen fibre layout, to be determined. The development of scanning electron microscopy techniques allowed the viewing of three dimensional form.

Early in mammalian embryo development, a layer of ground substance (gel filled-mesenchyme) advances from the future cervical region into the join between the ectoderm and the neuroepithelium of the telencephalon. It acts as a pia-arachnoid space holder.

Randomly spaced fluid-filled "holes" then appear in the gel. These enlarge into randomly spaced and sized, fluid filled, cavities. As the cavities enlarge the remaining mesenchyme elements between them get forced to congregate in the remaining tissue. It appears that when cavities meet, the mesenchyme material lining the two cavities resists further advance leaving, thin walls of mesenchyme which are the origin of trabeculae. The random nature of the original "holes" remains characteristic of trabecular structure thereafter.

Conclusions: The mature subarachnoid space is filled with an ultrasonically invisible "cobweb" of collagen reinforced sheets and cords linking the Arachnoid and Pia Maters. Trabeculae have no coherent structure, they are the result of random removal of tissue, not the generation of new structures.

Keywords: Subarachnoid space; Embryo development; Trabeculae

Introduction

In a modern textbook [1] one finds the comment "*Although it is commonly stated that the brain "floats" in the cerebrospinal fluid (CSF), the brain is suspended in the CSF-filled subarachnoid space by the trabeculae*". Subarachnoid trabaculae are sheets or columns of collagen reinforced material that stretch between the arachnoid and pia membranes. They can be seen with light microscopes but they are too thin to be displayed by ultrasound. The arachnoid membrane was discovered by Gerardus Blasius (1626-1692), who named it "arachnoid" (Gr. Spider) from the "cobweb" of fine fibres attached to its underside [2]. Thus the existence of trabeculae has been known to anatomists for a very long time. Trabeculae constrain relative movement between skull and brain such as postulated in the Shaken Baby Syndrome hypothesis [3].

The pattern of trabeculum structure is set in early embryonic development. This present paper is largely a based on the work of McLone and others in the 1970s.

Illustrations of trabeculae often show them as straight between arachnoid and pia membranes [1], but scanning electron microscopy shows a much more complex, and mechanically stronger honeycomb type of structure [4]. In Figure 1, (drawn from Figure 2 in that reference) elements appear to run in random directions, and be of random sizes. In such a structure there are no fault lines along which tears could run, and there are always some elements partially aligned with any imposed stress and hence able to resist stretch.

Subarachnoid *trabeculae* got the name trabeculae, "beams", from the fact that they appeared in sections as thin rods supporting the arachnoid above the pia. Scanning electron microscopy, (SEM), has revealed that many are actually sheets, or "curtains" that appear as rods when sectioned. Also, they are usually depicted as traversing straight across the cerebro-spinal fluid (CSF) filled subarachnoid space. Figure 1 is drawn from an electron microscope photograph of a section of a human optic nerve. Optic nerves are not actually nerves in the common use of that term. They are actually extensions of the forebrain (diencephalon) [5], carrying axons of retinal ganglion cells, shown in the yellow area. They are accompanied by extensions of the arachnoid and pial maters from the cerebrum surface, and enclosing a cerebro-spinal fluid (CSF) filled subarachnoid space. Their cross-section represents that of their brain. The trabeculae can be seen to have a random honey-comb like structure.

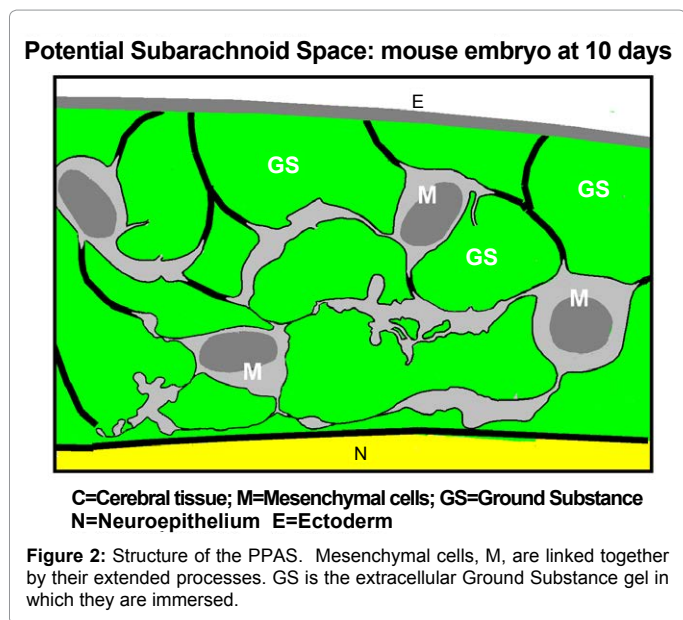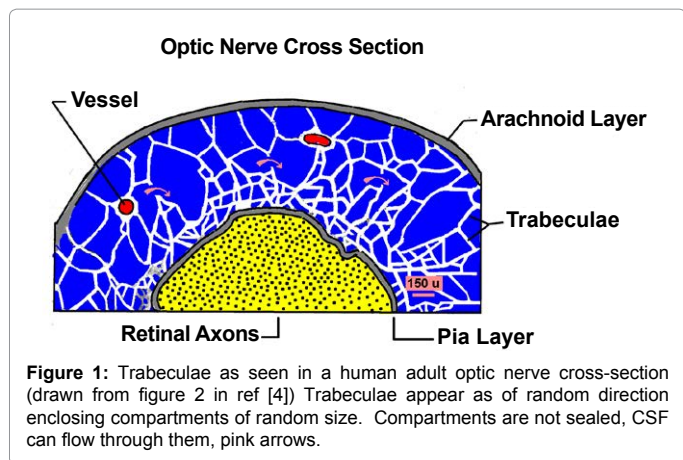## Early Development-the Potential Pia-Arachnoid Space (PPAS)

Much of the fundamental work on the initial development of the telencephalon was carried out by Weed, in 1917. In 1975 McLone [6,7]

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Figure 1: Trabeculae as seen in a human adult optic nerve cross-section (drawn from figure 2 in ref [4]) Trabeculae appear as of random direction enclosing compartments of random size. Compartments are not sealed, CSF can flow through them, pink arrows.

C=Cerebral tissue; M=Mesenchymal cells; GS=Ground Substance
N=Neuroepithelium E=Ectoderm

Figure 2: Structure of the PPAS. Mesenchymal cells, M, are linked together by their extended processes. GS is the extracellular Ground Substance gel in which they are immersed.

undertook a detailed electron microscopic study of this embryonic sequence in the mouse, and much of the following is based on his work.

The basic sequence of embryological development of the brain coverings (meninges) in mice and men is very similar. The significant differences relate to strengthening of the sub pia (neuroglia) in response to the greater brain weight [8].

The initial development of the subarachnoid space takes place in two phases during embryogenesis. The first phase is the development of a mesenchymal, space holding, layer. This comes forward from the future neck region and advances between the ectoderm and the neuroepithelium of the telencephalon [6]. It is composed of a gel-filled mesenchyme network, (ground substance) Figure 2. At this stage there are no arachnoid or pia membranes. The mesenchyme cells, are widely spaced, stellate cells, with long interconnecting cytoplasmid processes. The gel component is made up of chains of repeating disaccharides termed *glycosaminoglycans* [9]. Gases move through this gel by diffusion, there is no bulk movement. Osaka et al refer to this stage as meninx primitivea, or primitive subarachnoid space [10]. Initially there are no Pial or Arachnoid membranes in the PPAS.

During post conceptual days 10 to 13, liquid filled "holes" start to

appear in the gel, randomly distributed throughout the PPAS (coloured blue in Figure 3). They gradually increase in size, appearing to push the mesenchyme cells and fibres before them. At 13-16 days, loss of gel at the upper and lower surfaces of the PPAS allows compaction of the mesenchyme to form membranes. Mesenchyme cells are pluripotential, they can convert to connective tissue, blood cells and vessels. They reinforce these new membranes which become the Pia and Arachnoid membranes [8]. The collagen content of the cerebral pial layer increases with progression to high mammals (i.e. mouse, rat, monkey, man) [7], indicating its importance in stabilising the brain-skull positioning.

Concentrations of fibrous material also appear lining the expanding liquid filled lacunae. McLone and Bondareff comment "Bundles of microfibrils and collagen are commonly associated with lacunae in the outer pia-arachnoid layer and may serve as struts to maintain an open subarachnoid pathway." Actually these trabecular "struts" are under tension, "guy ropes" might be a better analogy.

Eventually, where the resulting lacunae approach each other closely, the remaining mesenchymal cells and fibres become pressed into "curtains" stretched across the subarachnoid space. These curtains have holes in them through which fluids can pass (Figure 4).
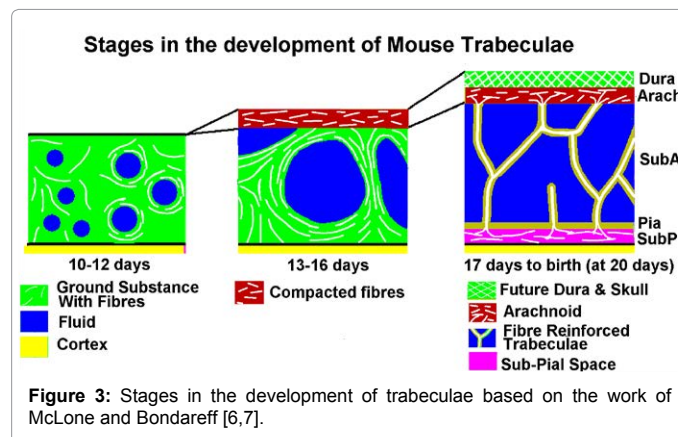
This establishes the possibility of cerebrospinal fluid flow. These remaining walls are the trabeculae. Osaka described the resultant fluid space as "essentially the 'cleared-out connective tissue space' which is formed in late embryonic life" [10].
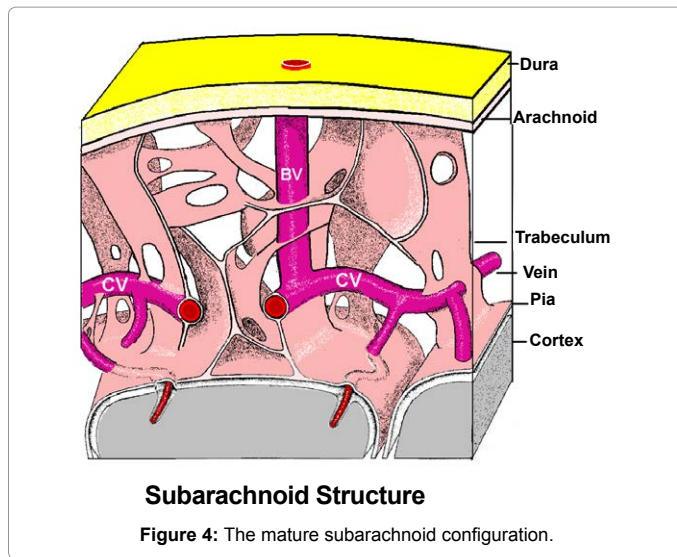
By the 17th day the framework of the subarachnoid space, consisting of the outer arachnoidal membrane, the trabeculae, and the inner pial layer has been established. It retains the random nature of the original liquid filled "holes" of early embryonic life.

Trabecular Attachments

Trabeculae may be strong but they will only be as useful as the strength of their attachments. In the arachnoid mater collagen fibres from the trabeculae stitch into the arachnoid mater which has formed in the top surface of the PPAS (Primitive Pia Arachnoid Space). The arachnoid mater becomes strongly reinforced with collagen and so can withstand relatively powerful forces.

The Pia Mater itself is only one cell thick so its strength depends on the structures below it. With electron microscopy, trabecular collagen fibres can traced through the Pia Mater to fibres in the Sub Pial space. In turn, fibres in the subpial space are attached to a basement membrane beneath which are a bed of astrocytes and oligodendocytes [11]. These

Figure 3: Stages in the development of trabeculae based on the work of McLone and Bondareff [6,7].

Figure 4: The mature subarachnoid configuration.

are described as Glia (Gr. Glue) because they act to hold neurons and capillaries together, though not with glue! They may be thought of as micro-octopuses. Instead of suction cups they wrap the end of each tentacle several times round the nearest axon, blood capillary, etc., a different one with each tentacle. There will be many more astrocytes than neurons so the net effect is that they are all drawn together. There are many astrocytes holding on to the basement membrane with one tentacle while holding axons etc. with the others. The result is that if a trabeculum pulls on the basement membrane from above, the local neurones get stretched below. When a boxer is temporarily knocked out various axons will have been stretched. This may act directly on the axon, or the stretch may have been transmitted to a local arteriole and induced temporary vasoconstriction. If the jolt is much stronger, as in Ommaya's experiments [12], vessels may be overstretched and bleed, showing as contusions. (The damage is below the Pia, at the brain surface, not above the arachnoid mater in the dura, as presumed in the Shaken Baby Syndrome hypothesis.

This study has found that trabecular form and generation were well understood by anatomists in the 1970's and 1980's, but their significance for child protection was not recognised then, nor since. The subarachnoid space is not empty (Figure 4). It is full of fine fibres (trabeculae) which are too thin to show up on ultrasound machines. These trabeculae inherit their random direction, size, configuration etc. from the random positions of initiation of the substitution of fluid for ground substance gel in embryonic development. This is the explanation of the random appearance of the human optic nerve illustration in Figure 1.

Conclusions

Summarising the embryological findings in this study:-

1. Very early in embryonic life, shortly after closure of the neural tube [13] a mesenchymal layer moves forward from the developing spine to invade between the embryonic epithelium and the developing telencephalon epithelial surface. This formless layer acts as a placeholder for the future pia-arachnoid structures.

2. This layer is made up of mesenchymal cells linked to each other with long extended pseudopodia. There is considerable extracellular space filled with a glycosaminoglycans gel.

3. The trabecular structure originates from localised withdrawal of the gel. This occurs from randomly positioned centres, resulting in randomly spaced and sized, fluid filled, cavities. As the cavities enlarge the remaining mesenchyme elements get forced to congregate in the tissue remaining between cavities. It appears that when cavities meet, the mesenchyme material lining the two cavities resists further advance leaving thin walls of mesenchyme which are the origin of trabeculae. In the upper and lower surfaces of the placeholder mesenchymal cells start to specialise, becoming fibrocytes etc. These surfaces then become the arachnoid and pial structures to which the trabecular structure remains attached.

4. This leaves walls in random directions, in three dimensions, which produces in engineering terms, a "redundant structure". Redundant structures are resilient. They have no fault lines and can suffer the loss of a few elements without failure. Stress is redistributed among the remaining elements.

5. Relative movement between the skull and brain surface will be severely restricted by the collagen reinforced "Trabeculae" which bind together the Arachnoid Mater and Pia Mater across the fluid filled subarachnoid space. The implications are considered elsewhere [14,15].

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