The high osmotic pressure in a lens fiber as a driving force for the development of senile cortical cataract

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Abstract

In lens cataract, the clouding change in the lens leads to a decline of transparency of a part of the lens. There are three types of senile cataract: cortical cataract, nuclear cataract, and posterior/anterior sub-capsular cataract. The cataract that develops in most old people is cortical cataract. The clouding change in senile cortical cataract begins from the edge of the lens and develops progressively to lens centre. The pathology of a clouding change in cortical cataract is characterized by disruption of some lens fibers, swelling of some other fibers, and deposition of water between fibers. Based on the property of a lens fiber, we propose here a hypothesis on the mechanism of development of senile cortical cataract. I. Cortical cataract is triggered by the disruption of a cortical lens fiber as a result of an injury. The disrupted fiber will release water and crystallin proteins. II. The neighbor fibers can absorb this water due to the high intracellular osmotic pressure (IOP) and become swollen. Swelling makes a fiber be stiff and have increased risk to disrupt when it is curved during the accommodations of the lens. These fibers will release water again when they disrupt, and the water will make more local fibers swelling. In this way, the local fibers become swollen and then disrupt successively. III. The successive swellings and disruptions of local fibers result in the enlargement of a clouding change in lens. Since the fibers on the outer part of lens cortex have higher risk to be injured than that in the inner part, a clouding change starts from the edge of the lens. Conclusion: in our view, the progressive development of senile cortical cataract is a result of successive swellings and disruptions of local lens fibers, which is driven by the high IOP in lens fibers.

Keywords

Lens cataract, cortical cataract, nuclear cataract, non-living structure, lens fibers, crystallin proteins, intracellular osmotic pressure (IOP), swelling of lens fibers, disruption of lens fibers, Misrepair, and accumulation of Misrepairs

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Lens cataract is a disease of the lens that affects most of the old people. The clouding change in cataract leads to an irreversible decline of lens transparency. There are three types of senile cataract: nuclear cataract, cortical cataract, and posterior/anterior sub-capsular cataract, and among them the cortical cataract has the highest rate in old people. The clouding change in senile cortical cataract begins from the edge of lens cortex and develops progressively to the inner part of cortex, appearing as aging of the lens (Van den Brom, 1990). On interpreting aging, we proposed recently a novel theory, the Misrepair-accumulation theory (Wang et al., 2009). Interestingly, cortical cataract cannot be explained by this theory, because the body of lens cortex and lens centre is a non-living structure, and Misrepair mechanism applies only to living-structures. After analyzing the property of lens fibers, we found that the high intracellular osmotic pressure (IOP) in a lens fiber might play an important role in the progressive development of cortical cataract. On this basis, we propose in the present paper a hypothesis on the mechanism of development of cortical cataract. Our discussion tackles the following issues:

I. Development of cortical cataract as a result of progressive degeneration of lens cortex

II. Effect of the high intracellular osmotic pressure (IOP) in a lens fiber

III. A hypothesis on the development of cortical cataract

IV. The high IOP of a lens fiber as a driving force for the development of cortical cataract

I. Development of senile cortical cataract as a result of progressive degeneration of lens cortex

The lens is a transparent and curvable structure in the anterior part of the eye, and it is important in refracting and focusing light on retina. Curvature of the lens can be regulated by ciliary muscles for accommodation. A lens consists of two parts of structure: lens envelope and lens fibers. Lens capsule is the outer layer of lens envelope and it is made of basement membrane. Beneath the anterior capsule is a layer of lens epithelium. Lens epithelium is the unique living tissue in the lens. Lens cortex is the outer part of lens fibers, and lens center is the central part of lens fibers. Lens fiber cells are a type of epithelial cells. A new cell that is produced by lens epithelium needs to differentiate on the lens equator to become a lens fiber. New fibers distribute parallelly on the surface of the lens. Old fibers are being pushed by new fibers into lens centre, during which the fibers lose gradually their water and nuclei. The lens fibers in cortex contain water, but those in lens centre have lost water completely. It is the parallel arrangement of lens fibers that makes the lens transparent. Continuous production of new lens fibers is essential for the maintenance of the transparency of the lens.

An alteration of the arrangement of lens fibers will result in degeneration of a part of the lens, which appears as a clouding change. In senile cortical cataract, the degeneration of the lens is pathologically characterized by disruption of some fibers, swelling of some other fibers, and

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deposition of water between fibers. Interestingly, the degeneration of the lens begins from the edge of lens cortex, which appears as a radial-like or wheel-like clouding change. With time, the clouding change develops progressively to the inner part of lens cortex. One may ask, - What is the element that causes the disruption and the swelling of lens fibers in cortical cataract? - Why does the degeneration of the lens begin from the outer part of lens cortex? In our view, the property of a lens fiber, especially the high intracellular osmotic pressure (IOP) of a lens fiber plays an important role in the progress of the clouding change in senile cortical cataract.

II. Effect of the high intracellular osmotic pressure in a lens fiber

A lens fiber is a fiber-like non-living “cell” with lipid membrane. In our view, some properties of a lens fiber are similar to that of a keratinocyte in the skin. Keratinocytes are the outer layers of epithelial cells in skin, but they have lost the functionality as cells. However, these non-living cells have great potential of absorbing of water from environment due to the high concentrated keratins inside of cells. The keratins produce a high intracellular osmotic pressure (IOP) for the keratinocytes. The IOP in a keratinocyte is similar to the colloid osmotic pressure in blood circulation, which is produced by the white proteins in blood. The potential of absorbing of water is important for the functionality of keratinocytes. Filled with water, these cells are “full” in shape and are able to adhere densely to each other. Several layers of keratinocytes build up a dense and thick non-living wall for preventing the loss of water and the invasion of external substances of the skin. When new keratinocytes are produced in deeper layers of epithelium, old keratinocytes are pushed up to skin surface. They lose gradually water and finally drop off from the skin.

Similarly, a lens fiber in lens cortex is a dead cell that contains water and crystallin proteins. In a lens fiber, there are three types of crystallin proteins: crystallin α, crystallin β, and crystallin γ. A regular organization of these crystallin proteins is the basis for the property of a lens fiber. The high concentrated crystallin proteins give a lens fiber not only transparency but also a high intracellular osmotic pressure (IOP). With a high IOP, a lens fiber can absorb water from environment. Filled with water, the fibers can be densely packed, which is important for the tight arrangement of lens fibers. When a new fiber cell is still alive, it has the potential to control the entrance of water. However, when the fiber is dead, it will lose this ability. A dead fiber can become swollen and stiff when it absorbs too much water by IOP.

III. A hypothesis on the development of cortical cataract

It is known that an injury on lens fibers may result in a clouding change of the lens. Except accidents, three factors may cause small but repeated injuries to lens fibers: UV-radiation, high temperature, and the accommodation of the lens. UV-radiation can damage directly lens fibers, and high temperature can make fibers dry and stiff. Repeated adjustments of lens fibers may cause disruption of some fibers occasionally. Stiffening of a fiber, which is caused by high temperature or UV-radiation, will increase the risk of disruption of the fiber when it is curved during lens accommodations. Among all of the lens fibers, those ones that are at the

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edge of cortex have the highest risk to be injured by UV-radiation and by heating and have the highest risk to disrupt during lens accommodations.

In our view, disruption of a fiber in lens cortex is a trigger, and it can promote a series of changes on local lens fibers and lead to progressive degeneration of lens cortex. When a cortical fiber disrupts, water and crystallin proteins will be released and depose between fibers. The released proteins will degenerate due to change of environment, and aggregate into globing bodies, the Morgagnian-globules. Due to the high IOP, neighbor fibers will absorb the water and become swollen gradually. Swelling makes a fiber stiff and difficult to curve, disruption of the fiber may take place during lens accommodations. Additionally, disruption of the fiber produces a “water gap” between fibers and this may increase as well the physical load to the neighbor fibers by the adjustments of the lens. The disrupted fibers will release water again, which will make more neighbor fibers swelling. In this way, swellings and disruptions take place to more and more local fibers successively (Figure 1A, 1B, and 1C). In lens nucleus, disruption of a central fiber cannot cause swelling of its neighbor fibers, since a nuclear fiber is too dry to release water.

Swelling or disruption of a fiber may appear as a tiny clouding change; and the subsequent swellings and disruptions of the neighbor fibers will result in the enlargement of the clouding change. Such a process can take place multiply in the same time in different areas of lens cortex, resulting in the development of a clouding change in multiple locations, which will have a radial-like or/and a wheel–like distribution (Early stage of cataract). Degeneration of lens fibers in cortical cataract starts from the edge of lens cortex by two reasons: A. the lens fibers in the outer part of lens cortex have higher risk to be injured than that in the inner part; and B. the disrupted fibers will be pushed gradually by new fibers to lens centre.

In early stage of cortical cataract, the procedure of swelling-disruption of a lens fiber is slow, because the released water from a broken fiber is very limited. However, driven by the high IOP, disruption of a lens fiber, release of water, and swelling of neighbor fibers compose a viscous circle, and this circle makes local fibers disrupt successively without stop (Figure 2). With time, the number of disrupted fibers increases and the amount of released water augments, thus the procedure of swelling-disruption of a lens fiber accelerates. As a result, the growth of a clouding change is slow in the beginning but becomes rapid with time. Finally, the lens fibers in deeper layers of cortex will be affected, and the swelling of a great number of fibers make the whole lens swollen and stiff (Swollen stage of cataract). After the disruption of many swollen fibers, the degree of the swelling of the lens is reduced and the cataract becomes mature (Mature stage of cataract) (Figure 1D). When most of the lens fibers disrupt, lens liquefaction can be observed (Hypermature stage of cataract). The liquefied lens is soft, and the lens capsule is fragile in this stage. If the capsule is broken, dissolution of the lens and release of crystallin proteins can provoke severe complications in the eye. It can take more than 20 years for a cataract to develop from a radial-like clouding to a complete clouding of the lens.

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Figure 1. Schematic representation of the successive swellings and disruptions of fibers in cortical cataract

Development of senile cortical cataract is triggered by the disruption of a lens fiber in lens cortex. The disrupted fiber will release water and crystallin proteins, and the crystalline proteins will degenerate and aggregate into globing bodies (Morgagnian-globules) (A-B). Due to the high intracellular osmotic pressure (IOP), neighbor fibers will absorb the water and become swollen (B). Swelling will make a fiber be stiff and have
increased risk to disrupt when it is curved during lens accommodations. The swollen fibers will release water again when they disrupt (B-C). In this way, more and more local fibers become swollen successively and then disrupt (C-D). When most of the cortical fibers disrupt, lens cortex is liquefied (D).

**Figure 2. A vicious circle between the disruption of a lens fiber and the swelling of neighbor fibers in the enlargement of cortical cataract**

Development of cortical cataract is promoted by an injury of a cortical fiber from external damage. An injured fiber may disrupt when it is curved. Disruption of a fiber and release of water can cause the swelling of the neighbor fibers, which have high intracellular osmotic pressure (IOP). Due to the high IOP of a lens fiber, a viscous circle is built up between the disruption of a lens fiber and the swelling of the neighbor fibers. This viscous circle results in the successive swellings and disruptions of local fibers without stop. The high IOP of a lens fiber is thus a driving force for the enlargement of a clouding change in cortical cataract.

Senile nuclear cataract is rare, and it develops mainly on the individuals who have had prolonged exposure to UV light and the individuals who have had problem of high myopia. Differently from cortical cataract, in which the clouding change is grey, the lens change in nuclear cataract is brown. One reason for this difference is that the fibers in lens nucleus are dry and the disrupted fibers cannot release water and cause the swelling of neighbor fibers. The clouding change in nuclear cataract starts from lens centre and can develop gradually to lens cortex; however the process is rather slow. In our view, the development of nuclear cataract is simply a result of accumulation of disruptions of the fibers in lens nucleus. Since the disruption of a nuclear fiber does not affect its neighbor fibers by an IOP, the rate of accumulation of injuries of fibers is slow. Such deep injuries of the lens may be caused by severe UV light-exposure or over-adjustments of the lens in high myopia.

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In traumatic cortical cataract, a clouding change may “grow” with time in some but not in all of the patients. In our view, three factors are important in determining the consequence of a contusion-caused cataract: the location of the injury, the degree of the injury, and the age of the patient. Contusion of the lens may cause disruption of a lens fiber and the subsequent swelling of its neighbor fibers. However, when an injury is small and when it is in a deep part of cortex, the degeneration of lens cortex can be localized. Firstly, the amount of water that is released from a disrupted fiber in deep cortex is very limited, thus the degree of swelling of its neighbor fibers can be very low. Secondly, the fibers in deep cortex may have little load from the accommodations of the lens, thus the swollen fibers do not necessarily have high risk to disrupt. In another word, a traumatic cataract that occurs to the outer layers of lens cortex will have higher risk to “grow” with time. The age of the patient may also affect the procession of a cataract. With age, accumulation of injuries makes lens fibers have increased fragility. A traumatic cataract that has occurred in an old person may “grow” with time, but a similar cataract in a young person may stay unchanged for a long time.

IV. The high IOP of a lens fiber as a driving force for development of cortical cataract

The phenomenon of progressing of a clouding change in cortical cataract is similar to that one in aging changes, including age spots and atherosclerotic plaques. However, the mechanism for the development of cortical cataract is different from that for development of aging changes. In our view, aging of a living organism is a process of accumulation of Misrepairs of its structure (Wang-Michelitsch, 2015). In that paper, the concept of Misrepair is defined as incorrect reconstruction of an injured living structure. Misrepair is a strategy of repair for maintaining the structural integrity for increasing the surviving chance of an organism in situations of severe injuries. Without Misrepairs, an individual could not survive to the age of reproduction; thus Misrepair mechanism is essential for the survival of a species. However, a Misrepair results in an irreversible alteration of a living structure, thus the accumulation of Misrepairs disorganizes gradually the structure of a molecule, a cell, or a tissue, which appears as aging of the structure. A Misrepair in a tissue leads to increased damage-sensitivity and reduced repair-efficiency of part of the tissue. As a consequence, Misrepairs have a tendency to accumulate to a local area of the tissue, thus the accumulation of Misrepairs is focalized. The focal accumulation of Misrepairs results in an enlargement of an aging change rather than a homogenous development of aging changes in part of a tissue. Thus, the driving force for the “growing” of an aging change is the Misrepair itself.

Strictly speaking, development of cortical cataract is not a process of aging of the lens like that in other tissues, since the body of lens cortex and lens nucleus is a non-living structure. However, in lens cortex, the injuries and the disruptions of lens fibers do not take place randomly. Due to the high IOP of a lens fiber, the disruption of a fiber and the swelling of its neighbor fibers compose a viscous circle, which results in progressive degeneration of local lens cortex. Therefore, the high IOP of a lens fiber is the driving force for the development of cortical cataract.

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