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Spotlight on vision

Retinal prostheses: Clinical results and future challenges

Les prothèses rétiniennes : résultats cliniques et défis futurs

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ABSTRACT

Retinal prostheses aim at restoring visual perception in blind patients affected by retinal diseases leading to the loss of photoreceptors, such as age-related macular degeneration or retinitis pigmentosa. Recent clinical trials have demonstrated the feasibility of this approach for restoring useful vision. Despite a limited number of electrodes (60), and therefore of pixels, some patients were able to read words and to recognize high-contrast objects. Face recognition and independent locomotion in unknown urban environments imply technological breakthroughs to increase the number and density of electrodes. This review presents recent clinical results and discusses future solutions to answer the major technological challenges.

RÉSUMÉ

Les prothèses rétiniennes ont pour objet de restaurer la perception visuelle de patients devenus aveugles dans des pathologies reposant sur la perte des photorécepteurs, comme la dégénérescence maculaire liée à l'âge ou la rétinopathie pigmentaire. Les essais cliniques récents ont démontré la faisabilité de cette approche pour redonner une certaine vision. Malgré un nombre limité d'électrodes (60) et donc a fortiori de pixels, certains patients étaient en mesure de lire des mots ou de reconnaître des objets très contrastés. Le retour à l'autonomie pour la locomotion en milieu urbain inconnu ou la reconnaissance des visages impose des sauts technologiques pour augmenter le nombre et la densité des électrodes. Cette revue expose les résultats récents des essais cliniques et discute les solutions d'avenir envisagées pour résoudre les défis technologiques posés.

1. Introduction

Although blindness is one of the most feared handicaps, 39 million people worldwide are blind (WHO, 2012: http://www.who.int/blindness/en/). The first cause of blindness (51%), cataract, can be efficiently treated to recover vision. Other major causes of blindness are due to ocular diseases leading to loss of retinal cells: photoreceptors in age-related macular degeneration (ARMD) and retinitis pigmentosa (RP) or retinal ganglion cells in glaucoma. Photoreceptors are transforming luminance changes into an electrical activity while retinal ganglion cells are the output retinal neurons extracting and

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compressing visual information to be sent to the brain via the optic nerve. For some of the considered diseases, there is currently no effective treatment to prevent vision impairment leading to blindness or treatments are only efficient for a limited number of patients. For patients who became blind, visual prostheses aim at restoring some visual perception. Although the idea of restoring vision in blind patients by electrical stimulations was originally proposed by Charles Leroy in 1755, its re-examination was recently highly motivated by the success of cochlear implants to restore audition or the success of deep brain stimulation to treat Parkinson disease. Depending on the pathology and therefore the degenerated cells, it is possible to intervene at different levels in the visual system. When it comes to loss of photoreceptors, retinal prostheses are designed to stimulate the residual retina, while, in diseases with optic nerve atrophy, devices have to activate the visual cortex. For such cortical implants, clinical tests conducted in the 70s and 80s showed functional visual recovery, often transient, with prostheses comprising 100 electrodes [1,2]. The lack of persistence of vision restoration resulted in the cessation of clinical trials, in the expectation of a stable solution.

For diseases affecting the photoreceptors (PR in Fig. 1), retinal prostheses have been introduced at different ocular levels. Indeed, the loss of photoreceptors leaves two neuronal layers in the retina:

- the inner nuclear layer containing cell bodies of the bipolar cells (BC in Fig. 1), the neurones postsynaptic to photoreceptors;
- the ganglion cell layer where all retinal ganglion cells (RGC in Fig. 1) are generating visual information sent to the brain by their axons via the optic nerve (NO).

In the normal operation of the retina, these two layers process neuronal information for converting the analogue visual information of photoreceptors (their membrane potential is a linear function of the light intensity) into a digital code at retinal ganglion cells (information is coded as spike frequencies). Different positions were assessed for stimulating the residual retina after the photoreceptor loss:

- into the subretinal space where photoreceptors were originally located (subretinal implant);
- on the vitreal side of the retina close to the ganglion cell layer (epiretinal implant);
- around the optic nerve as an optic nerve cuff (Fig. 1).

If all of these implants induced the perception of phosphenes, optic nerve cuffs were not able to generate coherent images because phosphenes are scattered throughout the visual field [3,4]. A trans-choroid approach that prevents the introduction of the implants into the eye was also recently proposed [5]. This review will focus on the recent clinical trials of subretinal and epiretinal implants with their future challenges to increase electrode resolution and the resulting visual performances.

2. Clinical trials

At the early phase of the retinal prosthesis development, investigators started by asking whether activating the residual tissue following photoreceptor degeneration could elicit visual perception. This question was not trivial because neurons in the residual tissue undergo a secondary degeneration [6]. Histological examination of postmortem tissue indicated that patients in advanced stages of retinitis pigmentosa retain only a third to a quarter of their retinal ganglion cells [7]. Remodelling of retinal tissue and loss of ganglion cells have also been reported in animal models of the disease [8–12]. Different causes of this degeneration have been proposed in the literature, from axonal compression to taurine deficiency [8,13]. It was unclear if such cells in a degenerative state would still transmit visual information to the brain, which could then be interpreted as visual perception. The first clinical trials thus consisted in acute stimulations of the degenerated retina. An electrode or an electrode array was introduced on the vitreal side of the retina and patients were asked if they perceived electrically elicited phosphenes. In these clinical trials, patients reported the perception of phosphenes taking different forms depending on the stimulation protocols [14–18]. These results demonstrated that residual neurones in blind patients could elicit visual perception when electrically activated.

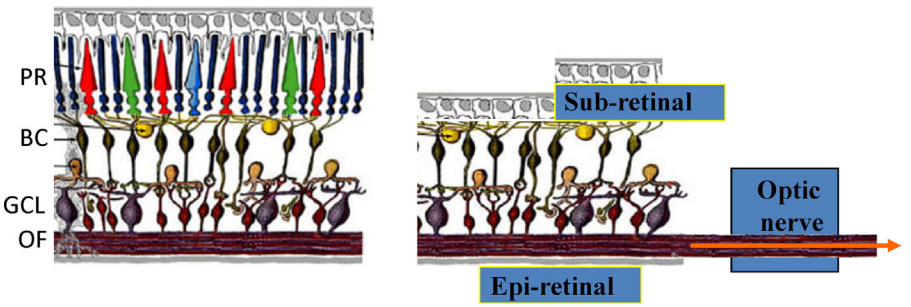

Fig. 1. (Colour online.) Concept of retinal prostheses. A. Schematic of a retina with different neuronal layers: the photoreceptor layer (PR), the inner nuclear layer containing bipolar cells (BC), the ganglion cell layer (GCL) and optic fibres or axons (OF) pointing to the optic nerve (NO). B. Diagram showing the position of subretinal implants between residual retinal pigment epithelium, epiretinal implants on the retina at the vitreous side, and finally the cuff of electrodes around the optic nerve.
Adapted from Webvision.