Thalamic Visual Prosthesis

Hieu T. Nguyen, Siva M. Tangutooru, Corey M. Rountree, Andrew J. Kantzos, Faris Tarlochan, W. Jong Yoon, and John B. Troy*

***Abstract*—Glaucoma is a neurological disorder leading to blindness initially through the loss of retinal ganglion cells, followed by loss of neurons higher in the visual system. Some work has been undertaken to develop prostheses for glaucoma patients targeting tissues along the visual pathway, including the lateral geniculate nucleus (LGN) of the thalamus, but especially the visual cortex. This review makes the case for a visual prosthesis that targets the LGN. The compact nature and orderly structure of this nucleus make it a potentially better target to restore vision than the visual cortex. Existing research for the development of a thalamic visual prosthesis will be discussed along with the gaps that need to be addressed before such a technology could be applied clinically, as well as the challenge posed by the loss of LGN neurons as glaucoma progresses.**

***Index Terms*—Electrical stimulation, glaucoma, lateral geniculate nucleus (LGN), thalamic visual prosthesis, vision repair.**

I. Introduction

THE leading cause of incurable blindness in the world is glaucoma [1], a group of neurodegenerative disorders that affects 60 million people, resulting from retinal ganglion cell (RGC) degeneration. RGCs link the image capturing and early visual signal processing retina of the eye with the immediately subsequent visual processing centers of the brain that include the lateral geniculate nucleus (LGN), superior colliculus, pretectal nuclei, accessory optic nuclei, and others. Of these structures, the LGN is the primary target for processing RGC signals before the visual cortex.

Many groups are seeking to combat vision loss through prostheses (see Fig. 1) and two retinal prostheses are now approved clinical devices [2]. Because the stimulation device for retinal prostheses is implanted in the eye, RGCs must be functionally intact for them to work. This method has merit for patients with impaired vision from diseases where the RGCs are little affected like age-related macular degeneration and retinitis pigmentosa, but not for patients who face the prospect of blindness through glaucoma. Optic nerve stimulation is another technique that can evoke visual sensations [3], [4], but as with retinal prostheses, it requires functional RGCs and so offers no benefit for glaucoma patients.

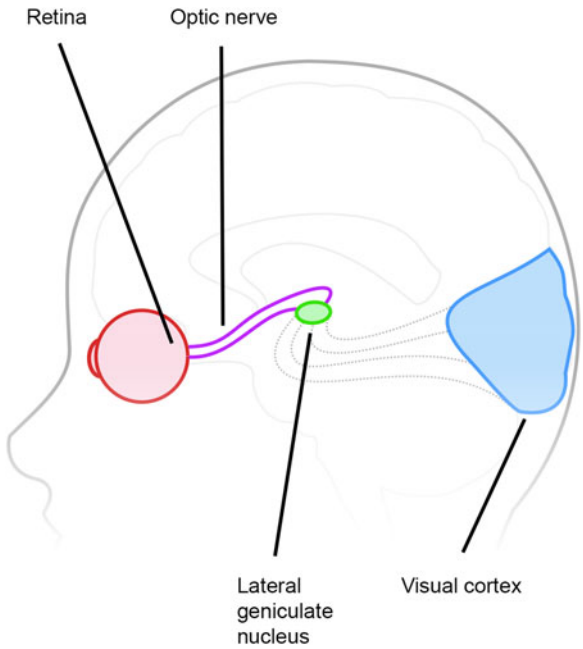

Fig. 1. Visual prostheses have been targeted to interface with the retina, optic nerve, LGN, and visual cortex.

We believe that the case for the LGN as the site for a visual prosthesis is strong. Studies with animal models, as summarized in Table I, and humans have shown that the stimulation of the LGN can produce visual sensation or evoke visual-like responses in the cortex [5]–[11]. The LGN is a compact nucleus and its layers create an anatomical segregation of functional cell-types [12]–[14], potentially permitting a cell-type specific pattern of stimulation [15]. Hence, even for diseases of photoreceptor degeneration where inner retinal neurons survive, stimulation of the LGN may have an advantage over a retinal prosthesis, where the differential stimulation of functional cell-types is challenging. The biggest drawback to a thalamic prosthesis is of course the fact that the LGN lies ∼8 cm below the brain surface making the placement of a stimulating electrode array daunting.

It is this latter problem which has encouraged many investigators to focus on the development of a visual cortical prosthesis, specifically one that aims to stimulate the primary visual cortex (V1) [16]. Although V1 is organized retinotopically and functionally layered like the LGN (see Fig. 2), the representation of visual information in this region is complex, spread across orders of magnitude more neurons (see Fig. 3), and perhaps less well understood than for the LGN, so the production of stimulation

Manuscript received July 29, 2015; accepted April 28, 2016. Date of publication May 16, 2016; date of current version July 15, 2016. This work was supported in part by the NPRP under Grant # NPRP 5-457-2-181 from the Qatar National Research Fund (a member of Qatar Foundation). The statements made herein are solely the responsibility of the authors.*Asterisk indicates corresponding author.*

*J. B. Troy is with Northwestern University, Evanston, IL 60208 USA. (e-mail: j-troy@northwestern.edu).

H. T. Nguyen, C. M. Rountree, and A. J. Kantzos are with Northwestern University.

S. M. Tangutooru and F. Tarlochan are with Qatar University.

W. J. Yoon was with Qatar University. He is now with The University of Washington.

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Digital Object Identifier 10.1109/TBME.2016.2567300

TABLE I
PUBLICATIONS ON ELECTRICAL STIMULATION OF THE LGN

Publication	Animal model	LGN stimulus parameters	Observations
Pezaris and Reid [8]	Macaque	40μA or 2.5 V, 80–200 ms, 100–200 Hz, 10–40 pulses, sinusoid	Measured eye saccades responding to stimulus-generated percepts
Logothetis *et al.* [9]	Macaque	$10-250\mu$A, 0.2 ms, 200 Hz, biphasic	Measured BOLD fMRI in V1
Panetsos *et al.* [10]	Rat	$100-600\mu$A, 50–100 ms, 3–7 stimuli trains	Evoked potential activity in V1
Choi *et al.* [11]	Pig	0.5–5 mA, 0.3 ms, biphasic square	Evoked potential activity in V1

A number of studies has demonstrated the potential for thalamic prostheses to evoke visual percepts. BOLD fMRI = Blood oxygen level dependent (BOLD) contrast used in functional magnetic resonance imaging (fMRI)

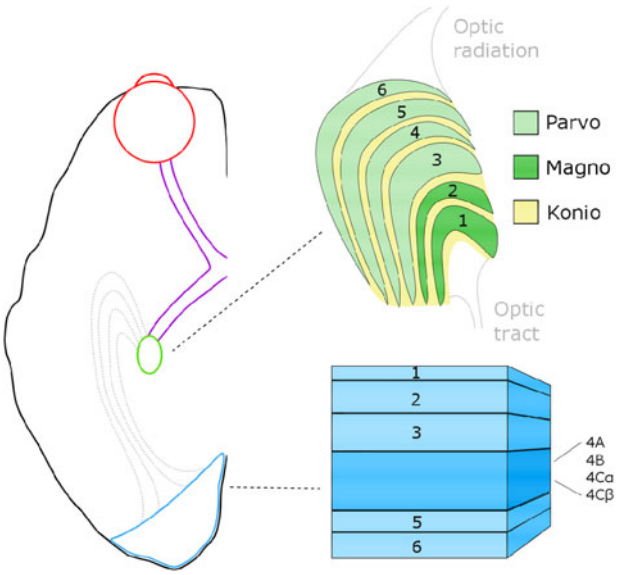

Fig. 2. Vision begins when optical images are captured and transformed into a neural image represented by the pattern of activity across the array of photoreceptors of the eye. Signal processing within the retina and along the visual pathway, which includes the LGN, primary visual cortex, V1, and higher cortical visual centers, leads to a pattern of neural activity in the brain that results in a visual percept. The design of all visual prostheses is underpinned by the assumption that, if one can stimulate the visual pathway artificially, at any point along its length, in a manner that mimics the pattern of stimulation that would be evoked naturally at that point when viewing a specific scene, the resulting percept would be as accurate a representation of that scene as occurs under natural viewing.

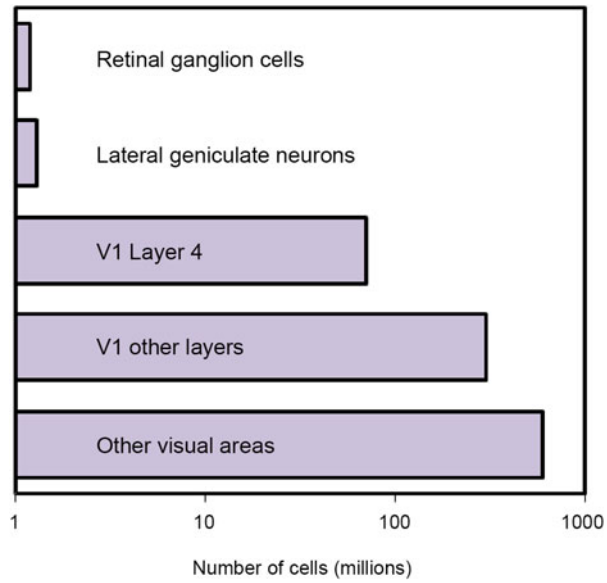

Fig. 3. Cells encoding a monocular image at different levels of the visual system (note the logarithmic scale).

patterns that target an array of neurons appropriately to recreate images of the world remains a formidable challenge.

Another disadvantage that LGN and visual cortical prostheses have in relation to a retinal prosthesis is that, because representation of the visual field is split between the two hemispheres, even recreation of monocular vision will require two implants rather than one, as is the case for a retinal prosthesis.

Retinal and visual cortical prostheses have been reviewed recently [2], [16]. It is timely therefore to consider the potential benefits of the alternative thalamic prosthesis.

II. ADVANTAGES ACCRUING FROM THE STRUCTURE OF THE LGN

The most successful sensory prosthesis to date has been the cochlear implant. It employs 20 or less electrodes to provide stimulation to an auditory nerve with approximately 35 000 axons [17]. The optic nerve has 35-fold more axons, so one might expect that, for a retinal prosthesis to be as therapeutically effective as the cochlear implant, it would need 700 electrodes. Carrying forward this reasoning to the LGN, a comparable number of electrodes would be required to engage its principal cells, since they exist in a similar number to the RGCs. However, the arithmetic is less favorable for a cortical prosthesis. To provide stimulation to just the cells of layer 4 of the primary visual cortex (the layer where the overwhelming majority of LGN axons project), applying the same ratio of electrodes to cells, requires an electrode array 70 times larger; i.e., 50 000 electrodes (density $\sim$10 mm^{-2}).

Models of auditory perception were used in the development of the cochlear implant [18], specifically with regard to the number of electrodes [19]. Simulations of prosthetic vision have likewise been employed as a tool during the design of visual prostheses [20]–[24], including the LGN prosthesis [25]–[27]. Central to the simulations are model phosphenes, a subject's visual percept resulting from stimulation of a single electrode. Simulated visual images that would result from stimulation of an array of electrodes are predicted through the superposition of a set of model phosphenes positioned according to electrode location. These simulated visual images can then be used in human psychophysical tests to predict expected performance for such visual tasks as face and object recognition, acuity, reading, and navigation. Most simulations are rigorous and thoughtful; e.g., using an array of jittered phosphene locations to more

realistically represent the imprecise placement of electrode tips [25]. But, the validity and thus utility of the simulations rests ultimately on how reliable the modeled phosphenes are, and all simulations to date have been perhaps too simplistic [18], taking insufficient consideration of perceptual variation in phosphene form.

Following stimulation of the visual cortex, phosphenes have been reported to appear as small flickering white lights in the central 10° of vision, to assume more elongated shape in the near visual periphery and to take the form of diffuse round clouds in the far visual periphery [28]. Unsurprisingly, this implies that, as one stimulates visual neurons encoding more peripheral parts of a scene, the phosphenes evoked become larger. This is expected. Receptive field size of visual neurons increases and their spatial frequency resolution decreases with eccentricity. Some simulations have incorporated this variation in phosphene form [20], but reports also suggest that variation in phosphene form evoked by a single stimulation pulse is more complex. Sometimes a single stimulation pulse can evoke many points of light spreading some distance across the visual field [28], presumably because multiple neuronal elements are activated, perhaps a soma and many axons. Increases in stimulation amplitude can also increase the number of neurons driven and phosphene persistence [28]. There have been reports of colored phosphenes (e.g., small polychromatic pinwheels) [29], [30]. Phosphenes evoked by retinal stimulation include large dots or rings [31], and phosphene size grows with stimulation amplitude [31], [32]. To our knowledge, no simulations to date have attempted to incorporate the full variation of phosphene forms, which, as has been noted [18], [19], would degrade the visual image perceived. Another failing in the use of phosphene simulations to predict visual prosthesis performance is the fact that no group has yet proven the validity of assuming superposition for groups of phosphenes. Accepting these limitations, the most thorough use of simulation of phosphenes in the design of an LGN prosthesis to date arrived at an estimate of 800 electrodes for a monocular prosthesis [25], a number close to the 700 electrode estimate arrived at through quite different reasoning above.

LGN and visual cortical prostheses have an advantage over retinal prostheses with respect to stimulation of the central visual field. At the fovea, RGCs and retinal bipolar cells are packed tightly, displaced laterally, and stacked. It is hard to envisage how current retinal prosthetic designs would be able to provide meaningful stimulation of this important region for human vision. One might argue, with the low electrode density estimated relative to RGC number, that high visual acuity would be precluded, negating a need for foveal stimulation. But, in normal viewing, we direct our gaze to center points of interest on the fovea. So, adaptation to a visual prosthesis should be easier if stimulation is arranged to evoke images in a fovea-centric manner. Neglecting foveal stimulation may come at a significant cost, such as requiring patients to adapt to unnatural viewing strategies like attending to images induced with a peripheral focus. In consequence, stimulation in a fovea centric manner seems desirable.

Because neural real estate in the central visual system is allotted proportionate to the number of RGCs, regions that represent retinal areas of high RGC density have more space per unit area of visual field. This is known as magnification which both the LGN and the visual cortex benefit from [33]. They provide more area for placement and spacing of electrodes to stimulate foveal and other central visual field areas. Indeed, since space is partitioned in relation to RGC units, the goal of stimulating the visual system at a level of granularity proportionate to RGC density is well supported by the structure of both the LGN and visual cortex.

The human LGN is a relatively small region of the thalamus with a volume of about 125–150 mm^3 in each hemisphere [34]–[36]. It is considered to have six layers, although this is not the case throughout its full extent and there is individual variation in lamination [37]. The deeper (ventral) layers 1 and 2 contain larger magnocellular (M) cells, while the upper (dorsal) layers 3–6 contain smaller parvocellular (P) cells. Between the layers lie interlaminar regions (the yellow strata in Fig. 2) that contain koniocellular (K) cells. It has been proposed, although not without controversy, that cells of the M-layers code primarily for movement, coarse spatial information, and high contrast whereas cells of the P-layers code for fine detail and red/green color discrimination [38], [39]. The K cells have more diverse functions although some have been implicated in blue/yellow color discrimination [14], [40]. Consequently, the ordering of LGN layers according to cellular function provides the ideal substrate for differential stimulation of the functionally distinct K-, M-, and P-cell pathways. This convenient arrangement supports the design of a visual prosthesis in which different components of the neural visual code could be engaged intelligently to enable a naturalistic visual percept.

Information from the two eyes is also organized systematically in the LGN. Each hemisphere receives input from the nasal retina of the contralateral eye in layers 1, 4, and 6 and from the temporal retina of the ipsilateral eye in layers 2, 3, and 5. Furthermore, among its parvocellular layers, the LGN has another interesting and, from the perspective of visual stimulation, structural advantage. LGN layers 3 and 4 are found to process signals of OFF-center cells primarily while 5 and 6 process signals of ON-center cells primarily [13]. Therefore, differential stimulation of the OFF and ON systems is also possible for P-cells at the level of the LGN. This is a particularly important advantage because OFF and ON signals are two halves of a differential message and, when engaged inappropriately (e.g., if stimulated simultaneously as is likely with electrical stimulation of the retina), their signals cancel.

A growing body of evidence indicates that the diversity of RGC types encode different aspects of the visual image and are used by the brain for distinctly different functions [41], [42]. Hence, the ability to engage the pathways that originate with these different RGC subtype arrays in a precise and rational fashion, as would be aided by LGN structure, should enable a more naturalistic pattern of neural activity than is possible when RGCs or inner retinal neurons are recruited haphazardly as is done through electrical stimulation with retinal prostheses. This is a major advantage for the LGN prosthesis.

We believe that this is likely to be of critical importance to the design of a prosthesis that activates the visual system

in a manner analogous to how the cochlear implant does the auditory system, with an equivalent therapeutic benefit. Because frequency is ordered spatially along the length of the cochlea, a linear array of electrodes few in number can successfully provide appropriate activation of the auditory nerve. The intended auditory signal can be decomposed into frequency bands and the stimulating electrodes enlisted through their spatial location to provide the higher levels of the auditory system with a naturalistic, albeit impoverished, message to process. One might expect that, by exploiting the LGN's ordering of visual information into layers and its magnified map of the visual field, noted earlier, an LGN prosthesis could engage the visual system in a naturalistic manner, drawing parallels to the cochlear implant. As a result, success more akin to that enjoyed by cochlear implants might at last be shared by a visual prosthesis.

III. Design of a Thalamic Prosthesis

All visual prostheses require the following set of system components: 1) a device to capture images, 2) electronic circuitry to process the images and create stimulation patterns that would mimic the firing of natural neurons, and 3) an array of miniature electrodes, each of which can stimulate a small number of visual neurons. Consideration must be made for implant and stimulation evoked damage, power consumption, and heat generation, hermetic sealing of electronic packaging, and a number of other factors. These latter issues are encountered commonly in the neuromodulation field and have been discussed extensively elsewhere [16], [43]–[46]. Here, we will focus on challenges that are specific to visual prostheses and, in particular, one interfacing with the LGN.

One major problem that is faced by most visual prosthesis is the fact that the image cast on the retina is moving due to body, head, and eye movements. When these movements are controlled by the brain or are registered by it as sensory (e.g., vestibular) signals, circuitry within the brain can correct for the motion and create a stable visual percept. Unless the spatiotemporal pattern of stimulation provided by the prosthesis reflects the image as it would be presented onto the retina and subject to the movements controlled or sensed by the brain, there will be a mismatch of registration resulting in at best distorted and at worst meaningless and potentially disturbing visual images. So most visual prostheses also require a system to track and compensate stimulation appropriately for body, head, and eye movements. The alpha IMS system of Retinal Implant AG does not face this problem because its images are captured by an array of photodiodes implanted under the neural retina. Image displacement through body, head, and eye movements is therefore naturalistic. A recent imaginative solution to overcome the problem of image mismatch for all visual prostheses is the idea of capturing images with an intraocular camera [47]. This would seem therefore to be a good design feature for any LGN prosthesis (but see [48]).

Based on the comparison above with respect to the cochlear implant, a target of 700 electrodes for an LGN prosthesis—350 in each hemisphere—would seem like a good starting point. Pezaris and Reid working toward an LGN prosthesis suggest an array with 800 electrode tips (stimulation sites) for the LGN of each hemisphere [15]. Since their proposal considers a prosthesis that would substitute for two optic nerves, permitting binocular drive, their ratio of electrodes to nerve fibers also closely matches that of the cochlear implant. However, we would argue that engaging just those LGN layers fed from the same eye in both hemispheres, sacrificing binocular stimulation, is preferable. It requires a twofold lower electrode count, reducing power and heat. Also, any patient considered for an LGN prosthesis would be blind from both eyes, so restoration of monocular vision would alone be a worthy goal. Moreover, the challenge of providing appropriate binocular stimulation using a massively depleted density compared to what occurs naturally is formidable. The possibility of generating diplopia or other disturbing visual imagery seems high.

Assuming that the full visual field is engaged with electrode tips evenly spaced, that every tip remains functional long-term and provides independent and perfect stimulation of its targeted neuronal population, the 700 monocular electrode prosthesis we propose could create a visual percept on the order of 1/2000th the pixel density of that provided by natural vision (acuity 20/700; i.e., the letters a normal individual can read from an eye chart at 700 feet, this individual could read with the eye chart at 20 feet). The more realistic outcome though is likely worse. The standard for legal blindness in the U.S. is a visual acuity of 20/200 in the best eye. It is inconceivable; therefore, that the vision of patients receiving a 700 electrode prosthesis would be improved sufficiently to pass the threshold of legal blindness. Nevertheless, meaningful visual sensations are likely and patients would embrace that. Parenthetically, the visual acuity of the mouse sits above 20/200 and yet it uses its visual system satisfactorily.

Beside acuity, there is a second criterion for legal blindness that being a visual field smaller than 20° in the best eye. This reflects the fact that we use vision both for detailed study (e.g., reading) and for navigation in the world. The ideal visual prosthesis might therefore space electrodes more sparsely across the peripheral visual field in exchange for a higher electrode density centrally. Such an approach might permit reasonable peripheral vision for navigation with satisfactory acuity for central vision. The LGN allots neural space according to RGC density automatically, so even spacing of electrodes would appear to be a good first step. Based on the analysis of Pezaris and Reid an electrode spacing of 0.6 mm would result in an 800 electrode prosthesis.

The biggest hurdle facing the LGN prosthesis is the need to drive a microelectrode array deep into the brain. The surface of the human LGN sits $\sim$8 cm below the brain surface, with its dorsal to ventral extent about 5–6 mm [37], [49]. Pezaris and Eskandar discuss the challenge of driving an electrode array into the LGN and argue convincingly that the technological barrier is not as significant as perhaps it might first appear [15]. The implantation of electrodes to deep structures in human brain is a well-established surgical procedure [50], [51], and once implanted, electrode location is generally stable [15]. So perhaps the major barrier to clinical implementation is regulatory approval of an electrode implant. Current millimeter-sized deep brain stimulation electrodes have insufficient tip density to drive

a meaningful visual percept and, if one is to exploit the structural advantage of the LGN discussed above, electrode arrays customized to interface with the LGN layers would be needed [52].

Alignment of electrode tips with respect to LGN layers will be imprecise, so an electrode array must have built in redundancy. If we assume that just half of the electrodes align with their neural targets, we would need arrays with 700 electrodes for the LGN of each hemisphere. We envisage an array of shafts with an average of 40 electrodes along the shaft length. Since the thickness of the LGN varies with brain coordinates, the number of electrodes along the shaft for particular locations must vary in accordance with geniculate topology. That means that some shafts would have 60 stimulation sites, while others have 20. There would be $\sim$20 shafts and these need to be directed into $\sim$30 mm^2 of LGN; i.e., 1.5 mm^2 per electrode shaft. The current standard in the neuroprosthetic field is that electrodes should occupy no more than 3% of the volume of their targeted neural structures, which requires the electrode shafts to have diameters of 0.24 mm. To build shafts as small as this with sufficient mechanical rigidity and strength to pass through brain tissue to the depth of the human LGN is clearly a major engineering challenge.

Obviously, not every electrode of an array can be positioned to create useful phosphenes. But, the retinotopic order and cell specific lamination of the LGN should permit one to enable only those electrodes that do. In addition to a patient's report of phosphenes, evoked potentials recorded from the patient's occipital lobe following electrical stimulation could be used to verify retinotopy.

IV. Surgical Approach

The shortest route (~ 4.5 cm) to guide electrodes to the LGN would be from the side but there may be an advantage to the vertical approach [15]. Currently, rather little consideration has been given to choosing an entry route that minimizes damage to critical brain structures or that facilitates layer specific stimulation. Surgical planning therefore remains an area in need of much more work before an LGN prosthesis can be contemplated for human subjects.

V. Electrical Stimulation of LGN Neurons

The neuronal circuitry of the LGN has been studied for many decades and this work, together with an equally extensive literature on the functional and biophysical properties of LGN neurons, should be exploited to arrive at an intelligent design for the stimulation protocol of an LGN prosthesis. It has been well established that the firing of thalamocortical (TC) neurons in response to retinal drive can adopt two distinct modes, the so-called tonic and burst modes. More controversial is whether these two modes reflect sleep states or attention swings [53], [54]. The retinal input to the LGN is modulated by a number of other neural inputs [55] and thought needs to be given to how to drive LGN neural circuits electrically in a manner that could engage these other inputs appropriately. Fig. 4 illustrates schematically the major inputs and outputs of the LGN. RGCs provide strong excitatory drive to TC relay cells through

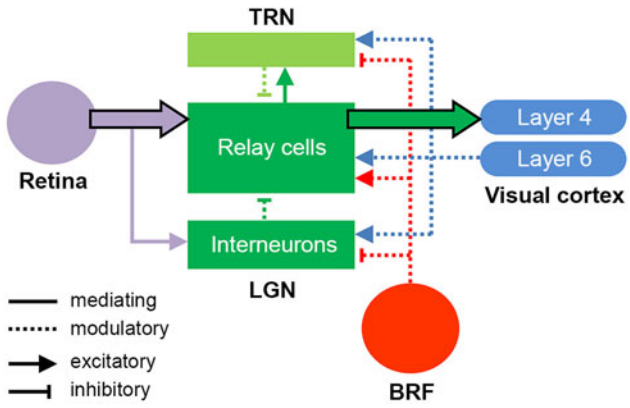

Fig. 4. Schematic of the LGN neural circuit. TC relay cells receive strong excitatory drive from RGCs, which also provide input to intrageniculate interneurons. These interneurons provide inhibitory input to the relay cells. The relay cell output goes primarily to layer 4 of the visual cortex, although axon collaterals also feed the thalamic reticular nucleus (TRN). There is feedback from cells of layer 6 of the visual cortex onto relay cells, intrageniculate interneurons and cells of the TRN. Input is also provided to these three targets from cells of the brainstem reticular formation. The size of the arrows is intended to signify the strength of the drive. The key at the lower left indicates the nature of the synaptic connections.

specialized structures known as glomeruli [56]. At these glomeruli, RGC axon terminals contact dendrites of TC neurons and interact with the geniculate neural circuit, specifically intrageniculate interneurons. These interneurons provide feedforward inhibition of TC neurons that can sculpt the LGN output in both spatial and temporal domains [57], [58]. TC neurons provide the LGN's output, feeding information to layer 4 of the primary visual cortex. Axon collaterals of TC cells also feed neurons of the thalamic reticular formation, which provides recurrent inhibitory drive [59]. In terms of synapse number, there is a substantial excitatory modulatory feedback input from layer 6 of the visual cortex to TC neurons [60]. The geniculate neural circuit is also modulated through inputs from the brainstem reticular formation (BRF) [60]. How the nonRGC inputs affect the flow of information through the LGN remains poorly understood and perhaps the reason why the nucleus retains its probably mistaken status as a relay. So, although there exists a large body of work, which could potentially be used to help craft stimulation protocols to mimic the natural firing of LGN neurons, little effort has been spent so far on doing this. An obvious and simple adjustment that has to be made for electrical stimulation is compensation for the temporal difference in electrical and visually evoked responses, the latter being significantly delayed relative to the former [11].

As far as we are aware, there has been no modeling of how LGN neural circuits would respond to electrical stimulation. There has been however some modeling of the effects of electrical stimulation on single TC neurons, using a biophysical model of an LGN principal cell [61], [62]. Nevertheless, there remains a significant need for further modeling of the effect of electrical stimulation both for individual LGN neurons, groups of LGN neurons, and the LGN neural circuits. Obviously, validation of models with experimental data is also needed.

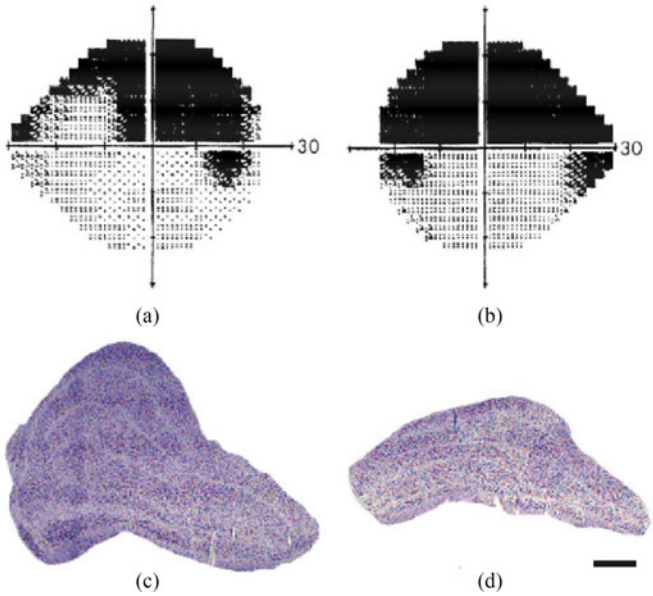

Fig. 5. LGN shrinks significantly in advanced glaucoma. Panels A and B show right and left Humphrey visual fields of a glaucoma patient while panel D shows a cross-section of the patient's LGN compared to that of an age-matched control (panel C). The scale bar is 1 mm. From Gupta *et al*. [63].

VI. How Glaucoma Affects the LGN

Although glaucoma is considered a disease of RGC degeneration, much research demonstrates that its impact touches the entirety of the visual system [63], [64]. In glaucomatous humans and nonhuman primates, functional magnetic resonance imaging(fMRI), positron emission tomography(PET), and postmortem anatomical studies have revealed changes in visual cortical activity [65], [66], microglial activation in the LGN [67], and reduced LGN size [36], [49], [63], [67]–[70]. When quantified by standard ophthalmological measures, the severity of glaucoma correlates negatively with LGN size. Changes in cup-to-disc ratio, thickness of the retinal nerve fiber layer, thickness of the RGC, and inner plexiform retinal layers, and visual field function measured by computerized perimetry provide a guide to loss of LGN volume in patients [68],[69], [71], [72] and, by inference, a basis upon which to select candidates for an LGN prosthesis.

Changes at the cellular level indicate that shrinkage of LGN volume (see Fig. 5) is at least partly due to cell loss [73], [74]. The change in cell size results from both cell shrinkage and by a proportionately larger loss of large relative to small cells. There is some disagreement in the literature concerning changes in cell density in glaucoma from animal and human studies [73]–[77]. The discrepancy may result from sampling at different times during a dynamic process. Nonetheless, the picture that emerges is of cell shrinkage occurring first, leading to an increase in cell density, followed by cell death with a return to normal density but with fewer neurons.

While LGN damage starts in the layers corresponding to the affected eye, atrophy spreads to layers of the other eye [73]. The mechanism for degeneration is poorly understood, but there is evidence for astrogliosis [68], [78], microglial activation [67], [68], and endoplasmic reticulum stress [79].

Given that the LGN is vulnerable in glaucoma and would likely be compromised in late stages of the disease poses a challenge for the clinical application of a thalamic prosthesis. Because early models of the prosthesis would likely have a low electrode density and offer limited visual capacity, patients would need to be in a very advanced stage of glaucoma before they could benefit. The prosthesis would need to promise improvement and that would only be the case for blind patients. At that stage, the patient's LGN would likely have suffered significant cell loss and its capacity to generate visual percepts through electrical stimulation be questionable. Therefore, if an LGN prosthesis is to become a clinical reality, a few steps beyond refining the technology should be considered. More work is needed to understand the mechanisms driving LGN degeneration so that neuroprotective treatments might be applied to maintain LGN health even while RGC loss proceeds. Second, the initial patient target population should not be glaucoma patients. The best candidates would be patients who have suffered bilateral eye loss through injury. Such patients if recruited early would have minimal damage to their LGN and, since they have no vision whatsoever, even rudimentary recovery provided by an early model LGN prosthesis would be a valuable treatment.

VII. Brain Plasticity

It is now accepted that the success of neural implants rests to a high degree upon the brain's ability to adapt to a changed input. While plasticity is substantial early in life, there is abundant evidence that, even in adulthood, the brain tissue maintains significant capacity to remodel itself to accommodate functional losses. Numerous studies have shown there is residual vision and functional recovery following injury to the visual system in various animal and human studies [80]–[85]. Recovery of LGN function in patients visually impaired through optic neuritis has been demonstrated [84]. Visual rehabilitation training [82]–[84] is certainly of value in restoring function and it is most likely that recipients of an LGN prosthesis would benefit greatly from a well-structured rehabilitation regimen. While it is unknown exactly what cellular mechanisms are at play during functional recovery, the recruitment of local dormant neurons and their neural circuits has been demonstrated [86], [87]. In this context, a monocular LGN prosthesis provides an interesting cortical substrate that might seem to favor its rehabilitative potential. Since the organization of V1 involves an array of adjacent left and right eye ocular dominance columns [88], leaving one set unused provides extra local cortical real estate to potentially be invaded and used for recovery.

VIII. Conclusion

The field of visual prostheses has advanced substantially over the last decade. It has been shown that external stimulation with retinal prostheses can produce rudimentary vision in blind patients. But for individuals who have lost vision from glaucoma and other blinding disorders resulting from RGC loss, we make the case for a thalamic visual prosthesis. The LGN is retinotopically organized, has a layered structure that favors stimulation of different visual information streams separately, and a magnified

representation of central visual field. While the LGN is subject to degeneration following the loss of RGCs, if the mechanisms that drive cell loss become better understood, neuroprotective therapies could be applied to retard or stop the degeneration. At this stage, the initial most probable candidates for an LGN prosthesis would be patients blinded through the loss of both eyes. In this regard, the development of an LGN prosthesis would follow the development of the retinal prostheses in first targeting a smaller patient population. In the latter case, patients suffering photoreceptor loss through retinitis pigmentosa were the initial beneficiaries. It was only recently in July 2015 that the first patient with age-related macular degeneration was fitted with a retinal prosthesis. Since degeneration of the visual cortex occurs more slowly than for the LGN and since deep brain stimulation would not be required, one might think that a V1 prosthesis would be preferable to an LGN prosthesis. However, the full representation of the visual field is not exposed on the brain surface in V1, so electrode placement would be challenging. Even more damning is the large number of electrodes (50 000) that would be needed to engage V1 layer 4 neurons with the same granularity that 700 electrodes could drive LGN neurons. We believe therefore that an LGN prosthesis is worth considering seriously as an alternative to a visual cortical prosthesis.

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