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Effects of short-term IOP elevation on receptive field properties of cat LGN cells

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Abstract **To investigate the effects of short-term intraocular pressure (IOP) elevation on the receptive field properties of lateral geniculate nucleus (LGN) cells, responses of the LGN cells to annulus, disc and drifting gratings with high or low spatial frequencies have been recorded extracellularly in the cat with the retinal perfusion pressure kept stable (30 mmHg). Our results indicated that the responses of the X and Y type LGN cells were significantly weakened during IOP elevation. And the responses varied with the different mechanisms of receptive fields. Specifically, while using annulus and disc as stimuli, the responses of Y cells were more tolerant than X cells to IOP elevation. The surround area of the receptive field was more sensitive to IOP elevation than the center. The mean responses during IOP elevation decreased more than the peak responses did. IOP elevation has more influence on the responses of X cells than on the response of Y cells to the drifting gratings with high spatial frequency. These results may reflect different degrees of ischemia on corresponding retinal structures caused by IOP elevation.**

Keywords: intraocular pressure (IOP), lateral geniculate nucleus (LGN), retina, glaucoma, cat.

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Optic nerve atrophy and visual field defect are the typical symptoms of glaucoma, which can be induced by IOP elevation. Consequently, animals with IOP elevation have been the most popular model in experimental glaucoma research, even though IOP elevation does not take place in all kinds of glaucoma. Most previous studies on either acute or chronic IOP elevation[1,2] were focused on the anatomical and morphologic changes in the retina or optic nerves. However, few works have been done on the functional changes of single cell in different hierarchical level of the visual pathways. Our laboratory examined the receptive field properties of cat retinal ganglion cells during IOP elevation and demonstrated that Y cells were more resistant than X cells; off-center cells were more resistant than on-cells to IOP elevation[3,4]. Similar results were found in LGN cells during brief (<2 min) IOP elevation[5].

In the present study, we aimed to detail the receptive field properties of different LGN cells, the response changes in different mechanisms of receptive fields and the response characteristics of X and Y cells to drifting gratings with different spatial frequencies during short term IOP elevation, which, we think, will provide some insights into the mechanisms underlying glaucoma and LGN functions in abnormal physiological condition.

1 Materials and methods

(i) Animal preparation. Eighteen normal adult cats, weight 2.3—2.9 kg, were used in our experiment. Cats were anesthetized with ketamine (20 mg/kg) for surgery preparation. Intravenous and tracheal cannulae were inserted. Then, cats were placed in stereotaxic apparatus (Narishige, Japan). Animals were anesthetized with urethane (20 mg/kg per h) and paralyzed with gallamine triethiodide (10 mg/kg per h) during the experiment. Resuscitator was used. Femoral pressure testing and IOP elevation were performed as before[4,6,7]. The retinal perfusion pressure (PP) was defined as the difference between artery pressure and IOP.

(ii) Visual stimulation. The stimuli were generated by a computer-controlled visual stimulation system (Cambridge Electronic Design, UK) program, and displayed on a Tektronix 608 display (Beaverton, USA) driven by a Picasso image synthesizer (Cambridge, USA).

The stimuli can be generally classified into two groups: 1) Annulus and disc: Responses to annulus and disc were recorded before, during and after the IOP elevation. The diameter of central disc was 1°, while those for inner and outer diameters of a peripheral annulus were 3° and 8°, respectively. Each group of stimuli was performed for twenty trails. A one-minute interval was provided between each group. Four to five groups were performed before, during and after the short-term IOP elevation respectively. 2) Drifting gratings with high and low spatial frequencies: Spatial frequencies (high and low) were selected based on measured spatial frequency tuning curve of each cell. Temporal frequency was always 2.5 Hz. The grating moved along with its optimum direction. A group of stimuli consisted of five gratings with high frequency and five gratings with low frequency. Data from 3 groups were collected before, during and after IOP elevation, with an interval of 15—20 s between adjacent groups.

(iii) Data collection and analysis. Extracellular recording technique was used in this study. Cells' types (X or Y cells) and their receptive field properties (On or Off) were determined using the method as given in ref. [4]. All data were collected via VS system (CED, UK). Post-stimulus time histograms (PSTH) of each cell's responses were recorded for off-line and on-line data analysis. For annulus and disc, peak responses and mean responses

(count value) were used as indexes. Responses to drifting gratings with high and low frequencies were indexed by the amplitude of the fundamental Fourier component of PSTHs. The relative response (R-value) was defined as the ratio of the response during IOP elevation to the response before IOP elevation, which reflected the relative decay of the responses during IOP elevation. The R-values were adopted throughout the whole work to compare the effects of IOP elevation on cells of different types (X vs. Y), different mechanisms (center vs. surround) of receptive field and varied indexes (peak vs. mean). Sensitivities of the responses of different cell types (X vs. Y) to drifting gratings with different spatial frequencies during IOP elevation were compared by using R-values as well.

2 Results

Responses of thirty-six cells (17 X cells and 19 Y cells) to annulus and disc stimuli were recorded extracellularly. To drifting gratings, another 38 cells' (18 X cells and 20 Y cells) responses were recorded. The time course of responses of all LGN cells we recorded was largely universal. The firing rate decreased dramatically when the retinal PP was at 30 mmHg, and reached a plateau in 2 min. It recovered in less than 5 min after the IOP elevation was removed.

(i) Responses of X and Y cells to annulus and disc during IOP elevation. For the responses of the center, the average peak R value of 17 X cells was 62.6% when the PP reached 30 mmHg while 71.6% for 19 Y cells (Fig. 1(a)). The discrepancy was marked (t-test, $P < 0.005$).

As far as mean responses were concerned, the average R-value was 45% for X cells and 56% for Y cells (Fig. 1(b)). The difference in the effect between the two type cells was also pronounced (t-test, $P < 0.05$).

For the responses of the surround average R-value of peak and mean responses was 65.1% and 50% for Y cells, 51.9% and 37% for X cells respectively. The difference between X cells and Y cells was also significant (t-test, $P < 0.05$).

These results indicated that under the PP of 30 mmHg, Y cells were more tolerant to IOP elevation than X cells no matter which index was used among peak response, mean response, center response and surround response.

(ii) Responses of the center and surround mechanisms to annulus and disc. After the IOP was elevated, both responses of the center and the surround decreased, yet the degree of decay varied. Fig. 2(a) and 2(b) illustrate the distributions of relative decay ratios for 36 LGN cells, which were defined as the ratios of R-value of surround responses to R-value of center responses.

Specifically, if the peak responses were used as indexes (Fig. 2(a)), the mean of relative decay ratios (surround vs center) was 88% (t-test, $P < 0.001$). Among the

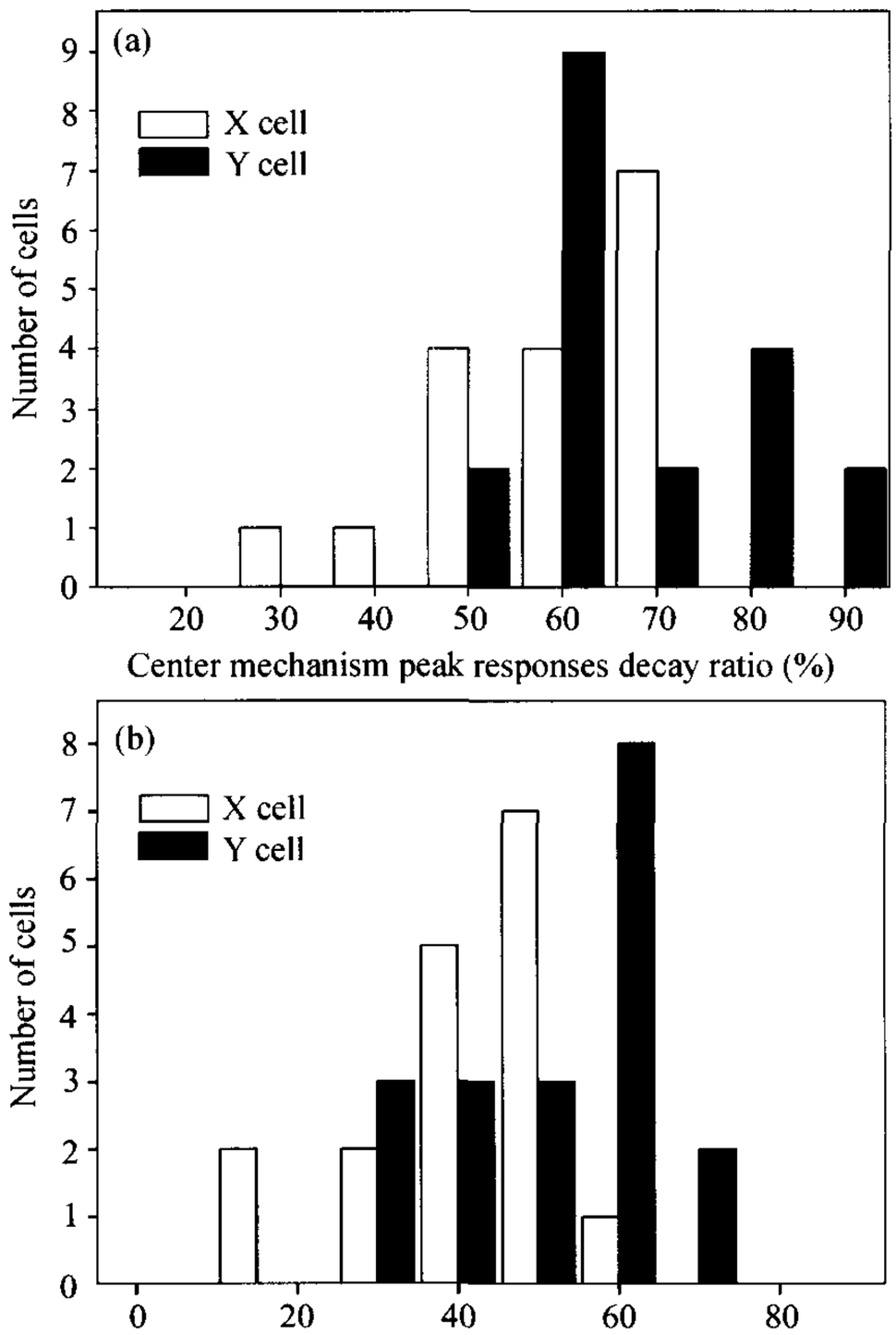

Fig. 1. Distribution of R-values (decay ratios), defined as the ratio of the response amplitudes during the later period of the response plateau after IOP elevation to that before IOP elevation, of X cells (white columns) and Y cells (black columns). (a) The peak responses of the center mechanism were used as the indexes; (b) the mean responses of the center mechanism were used as the indexes.

36 cells recorded, 86% of the cells' relative ratios were lower than 1 while only 14% were higher than 1. Similar effect could be observed if the responses were indexed by mean responses (Fig. 2(b)). Relative ratios of 84% cell's were lower than 1 while 16% were higher than 1, the average relative decay ratio being 86% (t-test, $P < 0.001$). To sum up, the results indicated that the center mechanism was more tolerant than the surround mechanism to short-term IOP elevation.

(iii) Comparison between peak and mean responses.

Similarly, different degrees of decay were observed, though both indexes decreased obviously when the PP reached 30 mmHg. We defined relative decay ratios as the ratios of R-value calculated by the mean responses to that derived from the peak responses. Fig. 3(a) and 3(b) show the relative decay ratios of the center mechanisms and the surround mechanisms, respectively.

For center mechanisms (Fig. 3(a)), the relative decay ratios of 80.6% cells were lower than 1 while 19.4% were higher than 1 (t-test, $P < 0.001$). Averaged over all cells

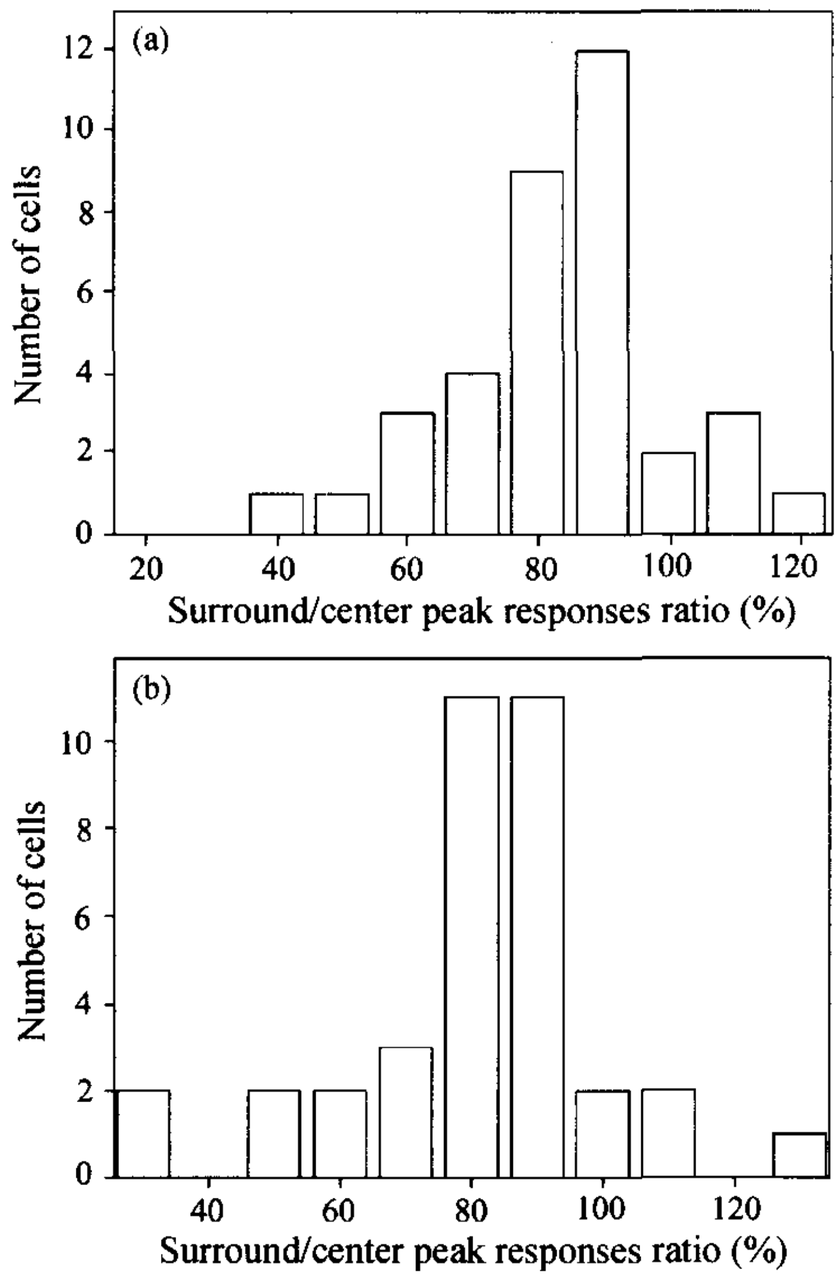

Fig. 2. During the later period of the response plateau after IOP elevation, the distribution of relative decay ratios, which were defined as a ratio of the *R*-values of the surround mechanism to that of the center mechanism. (a) The peak responses were used as the index; (b) the mean responses were used as the index.

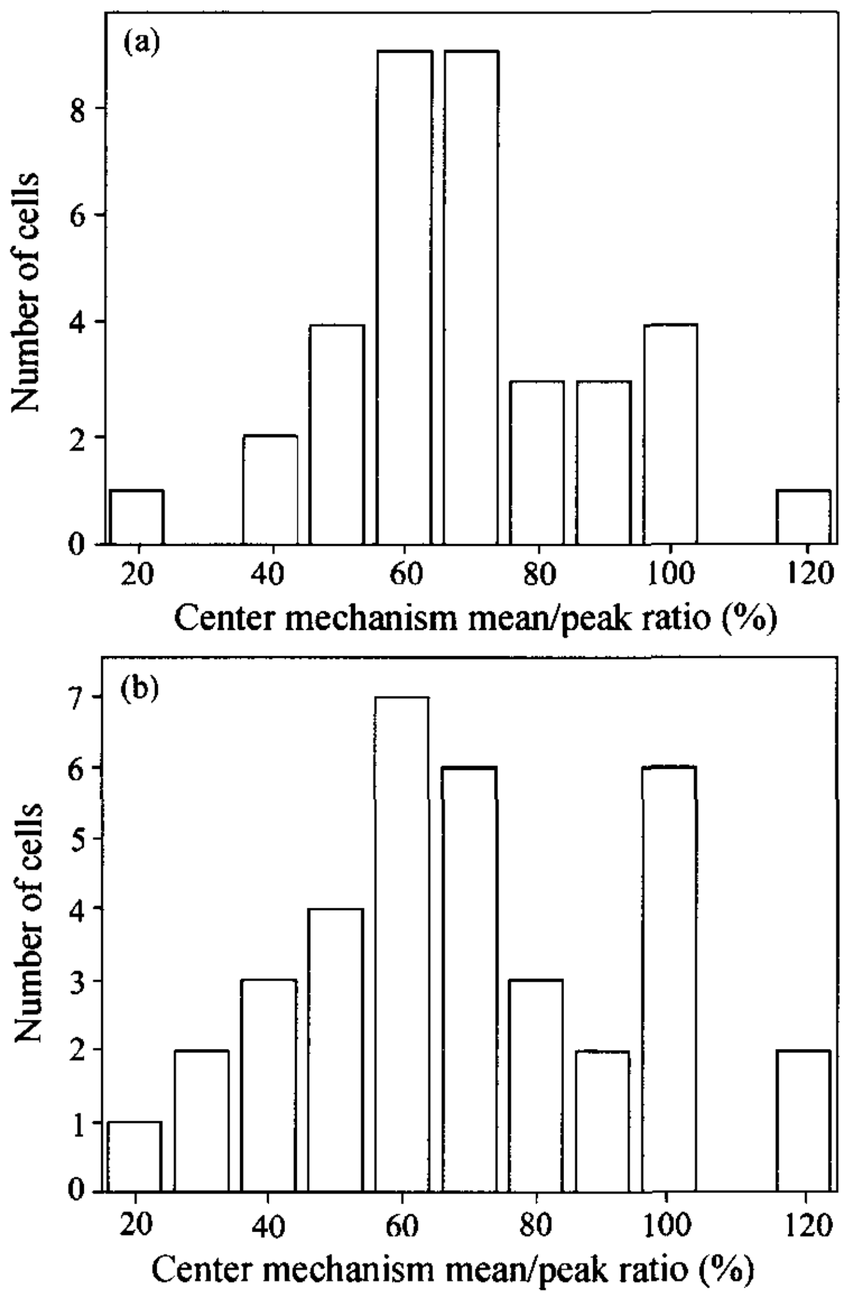

Fig. 3. During the later period of the response plateau after IOP elevation, the distribution of the relative decay ratios (defined by the *R*-values indexed by the mean responses to that indexed by peak responses) of the center mechanism (a) and the surround mechanism (b).

studied, the mean was 77%, suggesting that mean responses were more sensitive than peak responses in center mechanisms to IOP elevation.

Significant difference in similar manner between the *R*-values calculated from peak and mean responses for surround mechanisms was also observed (*t*-test, $P < 0.001$, Fig. 3(b)). Specifically, 83.4% cells' relative decay ratios were below 1 while only 16.6% were above 1, with a mean ratio of 75% for overall cells. The results indicated that for either center or surround mechanisms, the peak responses were more resistant than the mean responses during IOP elevation.

(iv) Responses of X and Y cells to drifting sinusoid gratings. The results have been summarized in Table 1. Responses of X and Y cells to gratings of either high or low spatial frequencies decreased dissimilarly.

Table 1 Responses of X and Y cells to drifting gratings of high and low spatial frequencies during short-term IOP elevation

	Mean *R*	*SD*	*N*
X cell, low frequency	0.744	0.178	18
X cell, high frequency	0.597	0.195	18
Y cell, low frequency	0.666	0.202	20
Y cell, high frequency	0.748	0.226	20

R, Ratio of the responses during IOP elevation to that before IOP elevation; *SD*, standard deviation; *N*, cell number.

For X cells, responses to gratings with high spatial frequency declined more than that of gratings with low spatial frequency (*t*-test, $P < 0.05$). However, for Y cells, the case is somewhat different. The mean of *R*-values derived from high frequency was higher than that from low frequency, but with no statistical significance (*t*-test, $P > 0.05$).

No pronounced difference was found between *R* values of X and Y cells under the condition of low spatial frequency stimulation (*t*-test, $P > 0.05$), while significantly higher *R* values were observed in Y cells instead of X cells (*t*-test, $P < 0.05$) when it came to stimuli with high spatial frequency, which clearly demonstrated that spatial frequency might play an important role in the tolerance discrepancy between X and Y cells.

3 Discussions

Glaucoma is a common disease of the eye that will result in vision loss and blindness. The knowledge about its exact etiopathogenesis and clinical time courses was limited. The idea that glaucoma may be a kind of degenerative disease in the whole visual system may help us have a deep-going knowledge about its damage mechanism[8,9].

The LGN is the relay-center of visual information between the retina and visual cortex. Investigation of characteristic alterations of LGN cells during IOP elevation will be undoubtedly beneficial for us to learn more about functional changes of visual subcortical pathway

under pathological conditions, such as acute closure-angle glaucoma. In the present study, we compared the receptive field properties of X and Y cells, central mechanisms and surround mechanisms, as well as the peak and mean firing rates of the cells during IOP elevation. These observations were consistent with previous work in our laboratory. The findings also support the idea that the retinal ischemia induced by short-term IOP elevation, which leads to a decrease of retinal perfusion pressure, results in a reduction in ganglion cell responses.

Shou et al. reported that Y cells in the LGN were more tolerant than X cells during IOP brief elevation[5]. Our result was in accord with theirs, although different stimulations (flashing versus annulus, disc and gratings in this work) and criterions (half decay IOP versus response amplitude at constant IOP or PP) were used. When the IOP was elevated briefly (<2 min), similar phenomenon was observed, suggesting that both effects (short-term and brief IOP elevation) might originate from similar mechanism. There were several lines of evidence that Y cells might have more intracellular reverses of adenosine triphosphate, oxygen, and potassium than X cells[10,11], which presumably formed the logic why Y cells demonstrated more tolerance during short-term IOP elevation. Morphologically, in chronic ischemia, large optic nerve fibers of retinal are often affected at first[12,13]. A comparison of the behavior of X and Y cells during chronic IOP elevation is in progress.

The reason of the sensitive difference between the center and surround mechanisms during short-term IOP elevation possibly goes as follows. The center mechanisms of ganglion cells mainly represent the input from bipolar cells while the surround exhibits the interaction between photoreceptor and horizontal cells through more synapses. The retinal ischemia caused by IOP elevation may have stronger influence on the horizontal cells and longer neuronal paths, thus in the recording from LGN, center responses may have more tolerance than those of the surround. The peak response reflects the fast mechanism of the input, whereas the response of the mean firing rate demonstrates the overall mechanisms of inputs, including both the fast and slow mechanisms. The reason why response of the mean firing rate is more sensitive may be related to the insufficiency of energy supply.

Recently, by using the intrinsic signal method, Chen et al.[14] demonstrated that a selective loss of orientation maps elicited by relatively high-spatial-frequency gratings occurred in the visual cortex of the cat during short-term IOP elevation. This change may due to a remarkable function decline in subcortical X pathway. Our results suggest that during the short term IOP elevation, responses to low-spatial-frequency grating stimuli of X and Y cells in LGN do not show significant difference, while response decay ratio of X cells is less than that of the Y cells to stimuli with high spatial frequency, which can be regarded as the "subcortical build-block" of their observations.

Degeneration of visual functions elicited by glaucoma is complicated. The present work provides some new information about the effects on receptive field properties of LGN cells initiated by short-term IOP elevation and it is our hope that it can be conductive to the diagnosis, investigation and treatment of acute glaucoma.

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