The Detection of both Global Motion and Global Form Is Disrupted in Glaucoma

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PURPOSE. It is well known that glaucoma results in performance impairments on tasks processed early in the visual pathways. Glaucoma should also impair cortical visual processing because of reduced input from retinal ganglion cells and also possibly because of abnormal cortical function. This study was undertaken to assess whether cortically processed global percepts are disrupted in glaucoma in areas of visual field classified as normal by standard automated perimetry (SAP). Performance on global tasks (motion and form) was compared to measures of presumed pre cortical magnocellular and parvocellular function in the same individuals.

METHODS. Fifteen control subjects and 12 patients with primary open-angle glaucoma participated. Testing was performed foveally and midperipherally (12.5°). Contrast-discrimination thresholds were measured by using the steady-pedestal (magnocellular) and pulsed-pedestal (parvocellular) contrast-discrimination tasks of Pokorny and Smith. Global motion coherence and global form coherence thresholds were measured at high and low contrast.

RESULTS. Patients with glaucoma demonstrated higher global motion and form-coherence thresholds than did control subjects for targets presented in the midperiphery (P < 0.05), but not foveally. Different individuals performed poorly on the motion and form tasks. The subjects with the greatest presumed magnocellular and parvocellular loss were those with the largest deficits on the global motion and form tasks, respectively.

CONCLUSIONS. Some subjects with glaucoma demonstrate profound impairments of global motion or global form integration in areas of visual field classified as normal by SAP. This finding implies that some people with glaucoma may have far greater difficulty with complex visual tasks (for example, navigation through the environment or face recognition) than is predicted by their visual field loss. (Invest Ophthalmol Vis Sci. 2005;46: 3693–3701) DOI:10.1167/iovs.04-1406

Numerous visual tasks designed to selectively assess specific subsets of retinal ganglion cells (RGCs) have been trialed in the assessment of early glaucomatous functional loss, with the purpose of improving on the performance of existing tests. Much of this research has concentrated on evaluating tasks that assess either the magnocellular (M) pathways (for example frequency-doubling technology [FDT] perimeter,1–3 motion perimetry4–6) or the koniocellular [K] pathways (for example, short wavelength automated perimeter [SWAP]).7,9 This research was initially motivated by reports that RGCs with large cell bodies and axons may be particularly susceptible to glaucomatous damage.10,11 More recent histologic studies suggest that neural loss in glaucoma is not as selective as initially thought.12–14 Psychophysical evidence also indicates that functional deficits may be measured using tasks designed to assess M, K, or parvocellular (P) function in early glaucoma (for example, see Refs. 7,15–17). Tasks designed to assess the patency of the M and K pathways may show larger deficits than those assessing P pathway performance because of reduced neural redundancy,18 yet current evidence suggests that all these processes are affected by the disease. Nevertheless, although all RGC subtypes appear susceptible to glaucoma, in a given individual, greater functional damage may manifest in one visual pathway than in the others, and the pathway demonstrating the greatest functional loss may vary between individuals.15

The study of visual performance in glaucoma is important, not only to detect early disease and its subsequent progression, but also to understand the behavioral aspects of impairment experienced by individuals with glaucoma. Most studies directed at the assessment of glaucomatous vision loss assess early aspects of visual processing (for example contrast sensitivity to either simple luminance increments such as in SWAP, or flickering gratings as in FDT), because glaucoma is considered primarily a disease of the RGCs. Glaucoma will also affect more complex aspects of visual processing, both due to a flow-on effect of early perceptual loss and also as a consequence of cortical neural abnormalities. Recent studies indicate changes in cortical cellular metabolism in primates with glaucoma,19,20 as well as cortical cell loss.14,21

Our current understanding of visual processing is based on a hierarchical system, wherein simple local stimulus attributes are combined into more complex global percepts at later stages of processing. A well-studied example is motion perception. In brief, the magnocellular RGCs preferentially respond to flickering or moving stimuli and relay this information through the M layers of the lateral geniculate nucleus (LGN) to the primary visual cortex (V1).22,23 Layers 4a, 4b, 4c, and 6 of V1 contain neurons that are directionally selective and hence have the capacity to signal local directions of motion.24 Many of these neurons project to cortical area V5, where neurons have large receptive fields and have the capacity to integrate local motion cues into more global motion percepts.25,26

The ability to perform global motion integration can be assessed by using global dot motion stimuli.27 The typical measure is termed motion coherence, which describes the minimum percentage of dots that must move in a common direction for the correct identification of that direction, within a field of dots moving in random directions. The stimuli are constructed to remove coherent local motion signals (provided

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that the coherence level is low) by choosing different dots to be signaled on each frame of the dot-motion movie sequence. Consequently, individual dots cannot be tracked to establish the direction of motion; rather, global integration must occur. Glaucoma affects the ability to perform such global motion tasks. In several previous studies, investigators have used random-dot motion stimuli to test visual function in glaucoma but have not removed the local motion component of the stimulus, and hence have not measured the ability to perform global motion integration. Intermediate global motion processing is considered a prerequisite for optimal processing of more complex visual motion information, such as is used for judging self-motion, assisting in the control of posture, and navigation through the environment.

Form perception is realized through hierarchical processing similar to that of motion processing. Input to the form processing pathways is largely from the parvocellular RGCs, which may show an orientation bias but are not strongly orientation selective. Simple and complex cells in the primary visual cortex are able to detect the orientation of local elements. This local information can then be integrated by cells in extra-striate cortical visual areas to produce a global form percept, which is a likely necessity for optimal object and face recognition. Cortical area V4 in the ventral visual pathway is considered critical to global form perception. Studies of whether glaucoma impairs global form perception have not been reported.

In this study, we assessed visual processing of the M and P pathways and then examined intermediate aspects of global form and motion processing in the same individuals. It is sensible to predict that RGC deficits will result in impairment of performance of global tasks. However, it is not clear whether, in early disease, the level of deficit in performance of the more complex tasks should be greater, less, or equivalent to that manifesting early in visual processing. In early stages of glaucoma, global processing may be relatively unaffected, as neurons in V4 and V5 have large receptive fields and pool information from large retinal areas, much of which may be unaffected by the disease process. Conversely, mild degrees of loss early in the system may compound when required to be integrated to form the global percept. We were interested in exploring functional loss in early disease and hence assessed patients in areas of their visual field that were classified as normal using standard automated perimeter (SAP). Patients were recruited from a cohort that had previously demonstrated contrast-discrimination deficits presumed to reflect both magnocellular and parvocellular RGC dysfunction. We were interested in determining whether these early functional losses would manifest as deficits in the processing of global motion and global form.

METHODS

Subjects

Subjects were recruited from those who participated in our previous study. They were experienced observers and provided an opportunity to collect retest data on the contrast-discrimination task. All subjects who participated in the previous study were invited to return within 4 months of their previous visits. Twelve subjects with primary open-angle glaucoma (POAG) and 15 control subjects participated. Two control subjects and five patients with glaucoma declined to participate due to ill health or having relocated residence. There was no significant difference ($t$-test: $t(25) = 1.07, P = 0.29$) in mean age between the groups (mean age ± SD of patients with glaucoma 69.8 ± 10.3 years and of control subjects 66.1 ± 7.7 years). All subjects had to have best corrected visual acuity of 20/25 or better. Full details of inclusion and exclusion criteria for participants appears elsewhere. All subjects with glaucoma had to have previously documented glaucomatous visual field loss but to have at least one visual field quadrant classified as normal (see Ref. 16). Visual field defects ranged from early to more advanced visual field loss (Humphrey Field Analyzer [HFA] 24-2; Carl Zeiss Meditec, Dublin, CA). The mean defect ranged from $-0.99$ to $-17.45$ dB (mean, $-8.60$) and pattern standard deviation from $2.06$ to $15.11$ dB (mean, 8.14). Before participation, all subjects provided written informed consent in accordance with a protocol approved by the University of Western Australia Human Research Ethics Committee and in accordance with the tenets of the Declaration of Helsinki.

Overview of Test Procedures

Computerized visual assessment was performed. Stimuli were generated using a video card (VSG 2/5; Cambridge Research Systems, Kent, UK) housed in a computer. Experiments were run using custom designed programs (Matlab, ver. 6.1; The MathWorks, Natick, MA). Stimuli were displayed on a γ-corrected high-intensity gray-scale monitor (frame rate 100 Hz, CIE1931 x: 0.25, y: 0.31; GD 402; Phillips, Eindhoven, The Netherlands), which was viewed at a distance of 75 cm (monitor subtended $28.5^\circ \times 21.5^\circ$). A chin and forehead rest was used. After each trial, the subject’s responses were signaled with a button box (model CB3; Cambridge Research Systems). All measures were made within a single test session of approximately 1 hour's duration.

The following visual thresholds were measured: (1) steady- and pulsed-pedestal contrast-discrimination thresholds for a pedestal of 24 cd/m$^2$, (2) global motion-detection thresholds, and (3) local form-detection thresholds. Because our previous study demonstrated that our glaucoma group had reduced contrast sensitivity relative to control subjects in the tested area, the global tasks were performed at high contrast, and at lower contrast, matched for salience across all observers (10 times the subject’s own contrast threshold for detection of the presence of the dot pattern). Although it is well established that global motion performance is not enhanced by increasing contrast above approximately 20% in normal observers, the effect of contrast on global form performance in individuals with glaucoma is unknown. We wanted to ensure that any group differences were a result of difficulty with the global tasks rather than reduced relative visibility of the targets in the glaucoma group.

Each of the tasks was performed foveally and at a single peripheral location centered on 12.5°. Subjects were tested in the same quadrant as assessed in our previous study. The rationale for the choice of test quadrant is described in detail elsewhere. In brief, glaucoma participants were tested in a quadrant classified as normal on their most recent HFA 24-2 or 30-2 test (Carl Zeiss Meditec). Control subjects were tested in quadrants matched to those of the participants with glaucoma.

Steady-Pedestal and Pulsed-Pedestal Contrast Discrimination

The steady-pedestal and pulsed-pedestal contrast-discrimination tasks were based on those described by Pokorny and Smith and our methodology, as described elsewhere. These tasks are thought to enable separate assessment of the M (steady-pedestal) and P (pulsed-pedestal) visual pathways. In our prior study, we assessed performance of our subjects using seven different pedestal luminances. In the present study, we used a pedestal luminance of 24 cd/m$^2$, as this pedestal resulted in the greatest difference in performance between control and glaucoma groups in our previous study. The stimuli are illustrated schematically in Figure 1. The subject’s task (identification of the brightest square during the test interval) was the same in both
a) Steady Pedestal condition

![Steady Pedestal condition](image1)

b) Pulsed Pedestal condition

![Pulsed Pedestal condition](image2)

c) Placement of peripheral stimuli

![Placement of peripheral stimuli](image3)

steady and pulsed conditions. It was only the adaptation phase that differed.

The stimulus squares were 1° for the foveal task and 1.75° for the peripheral task. Figure 1c shows the placement of stimuli for peripheral testing, using the upper visual field as an example. Stimuli were presented on the diagonal meridians, with squares placed so that the nearest corner to fixation was at 10° and the center of the stimulus was at 12.5° from fixation. A two-alternate, forced-choice procedure was used, in which the two possible test squares were those on the diagonals indicated by the crosses in Figure 1c. Luminance increment thresholds for detection of the brightest square were determined using a staircase procedure. Three correct responses resulted in a decrease of the test square’s luminance of 20%, whereas one incorrect response resulted in an increase of the test square’s luminance of 20%, which resulted in the staircase’s converging on the 79% correct response level. The staircase terminated after six reversals, with the mean of the last four reversals being taken as the threshold.

Global Motion Detection

The global motion stimulus was generated with an eight-frame motion sequence in which each frame was shown for 50 ms. A total of 100 dots (dot diameter, 8.6 minutes of arc) were shown within a 10° circular patch. The dots were white (Fig. 2) and were presented on a black background (0.5 cd/m²). Signal dots were randomly chosen for each frame transition and were displaced spatially by 8.6 minutes arc (producing an effective velocity of 2.80 deg/sec) in the signal direction (randomly chosen on each presentation to be either left or right). Randomly assigning signal dots on each frame minimizes the utility of local motion cues being extracted by tracking individual dots from frame to frame. Consequently, global processing is necessary to determine the coherent motion direction at normal threshold levels. Noise dots were placed on the same distance but in random directions, excluding directions within 10° of the signal direction so that no noise dots were moving in exactly the same direction as the signal dots. If the displacement moved the dots outside of the 10° aperture they were randomly replotted within the aperture for the next frame. Dots were not permitted to be chosen as signal dots if the necessary displacement would move them outside the borders of the aperture.

Global motion-detection thresholds were measured using both high- and low-contrast stimuli. For the high-contrast condition the luminance of the white dots was 170 cd/m². The luminance of the low-contrast stimuli varied between participants as it was set to be 10 times the subjects’ own contrast threshold for detection of the dot pattern. This resulted in the salience of the patterns being matched across all participants at low contrast. Individual contrast thresholds for detection of the presence of the global-motion stimulus were determined for each subject, by using a yes/no staircase procedure. Subjects were required to view a central fixation marker while global motion stimuli were presented at an eccentricity of 12.5° in the test quadrant. They were asked to press a button on the response box if they were aware of the presence of the stimulus. These stimuli had a signal coherence of 50%; however, for this task, the subject was simply responding to the presence of the stimuli. Three sequential “seen” responses resulted in a decrease in the contrast of the stimulus of 20%. The contrast of the stimulus was increased by 20% after every “not-seen” response. Two staircases were interleaved within the test run, and each terminated after six reversals. The mean of the last four reversals of each staircase was determined, and the average of the two staircases was used as the contrast threshold estimate for the detection of the global motion stimulus.

After the determination of contrast thresholds for the global motion stimulus, global motion coherence thresholds were determined for both the high- and low-contrast stimuli. A single-interval, forced-choice procedure was used. Subjects were required to indicate whether the coherent motion appeared leftward or rightward for each trial. Three correct responses resulted in a decrease in the number of dots moving in the signal direction, whereas one incorrect response resulted in an increase. Initially, 80% dots moved in the signal direction. As this coherence level was substantially suprathreshold for most subjects, if the subject responded correctly to the first presentation, the coherence level was reduced by 8% after each correct response (rather than after three correct responses) until the first incorrect response. Staircase step size commenced at 8% dots initially, which was halved at the first two reversals, resulting in a final step size of 2% dots. Two staircases were interleaved. Each terminated after six reversals, with the threshold being taken as the mean of the last four reversals. The results of the two interleaved staircases were averaged to determine the motion-coherence threshold.
Global Form Task

Global form perception was assessed by using Glass patterns. To create the pattern, pairs of dots (separated by 6.5 minutes of arc) were placed at random within a 10° circular aperture. The orientation of the pairs was either directly away from the center of the image (creating a "radial" pattern; Fig. 3b), or perpendicular to the center of the image (creating a "concentric" pattern; Fig. 3a). To enable measurement of coherence thresholds for the detection of global structure, the patterns were degraded by replacing a percentage of the signal pairs with two randomly placed noise dots. This type of Glass pattern construction has been used to explore global form perception. The coherence of the stimulus was measured as the percentage of signal pairs required to create the percept of the global pattern (either radial or concentric).

The duration of each glass pattern presentation was 400 ms, and patterns were selected at random to have either radial or concentric structure. It has been reported that coherence thresholds for the detection of concentric glass patterns are lower than for radial patterns when viewed foveally; however, this difference is minimal with...
luminance, 170 cd/m²) and at 10 times the subject’s own contrast thresholds were then determined for the high-contrast stimulus (dot determined by using a procedure identical with that described for the assessing global form thresholds in a clinical setting.

To explore whether there are differences in sensitivity to the radial and concentric patterns used in this study, we pilot tested a group of six subjects with normal vision (aged 24–45 years). Coherence thresholds were measured for both concentric and radial stimuli separately using a two-interval, forced-choice procedure (structured glass pattern presented in the test interval, random pattern presented in the control interval). Thresholds were determined using a three-down, one-up staircase design that terminated after six reversals. Using this procedure, we found no significant difference between radial and concentric thresholds collected at either eccentricity (paired t-test, fovea: t(5) = 1.78, P = 0.14; periphery: t(5) = −0.45, P = 0.67). To more thoroughly explore for differences in sensitivity peripherally, we conducted further pilot testing on three control subjects with normal vision (aged 24–33 years) for patterns presented at 15°. This testing did not reveal any threshold asymmetry in the midperipheral visual field between radial and concentric patterns (Fig. 4). As we found no evidence of differential sensitivity to the radial and concentric patterns, we interleaved these configurations within our test procedure for assessing global form thresholds in a clinical setting.

Contrast detection thresholds for the global form stimuli were determined by using a procedure identical with that described for the contrast detection of the global motion stimulus. Global form detection thresholds were then determined for the high-contrast stimulus (dot luminance, 170 cd/m²) and at 10 times the subject’s own contrast threshold. A two-alternative, forced-choice staircase procedure was used in which, in any given trial, the subject was required to choose whether the stimulus was “radial” or “concentric.” The staircase procedure was identical with that used for the global motion task.

RESULTS

Steady-Pedestal and Pulsed-Pedestal Contrast-Discrimination Thresholds

Glaucoma and control subjects were retested on the steady-pedestal and pulsed-pedestal contrast-discrimination task, and results were compared to those reported previously.32,43 These previous findings may not be directly applicable to our study, as our glass patterns differ in size and dot density. It is also unknown from previous studies whether differences in sensitivity to radial and concentric patterns exist in the midperipheral visual field.

To more thoroughly explore for differences in sensitivity to the radial and concentric patterns used in this study, we pilot tested a group of six subjects with normal vision (aged 24–45 years). Coherence thresholds were measured for both concentric and radial stimuli separately using a two-interval, forced-choice procedure (structured glass pattern presented in the test interval, random pattern presented in the control interval). Thresholds were determined using a three-down, one-up staircase design that terminated after six reversals. Using this procedure, we found no significant difference between radial and concentric thresholds collected at either eccentricity (paired t-test, fovea: t(5) = 1.78, P = 0.14; periphery: t(5) = −0.45, P = 0.67). To more thoroughly explore for differences in sensitivity peripherally, we conducted further pilot testing on three control subjects with normal vision (aged 24–33 years) for patterns presented at 15°. This testing did not reveal any threshold asymmetry in the midperipheral visual field between radial and concentric patterns (Fig. 4). As we found no evidence of differential sensitivity to the radial and concentric patterns, we interleaved these configurations within our test procedure for assessing global form thresholds in a clinical setting.

Global Motion and Global Form Detection Viewed Foveally

Figure 6 shows individual subject performance at both high and low contrast measured with central fixation. As the group data were not normally distributed, a log₁₀ transform of the raw data was conducted before analysis. There was no significant difference between groups at either high contrast (two-way repeated-measures ANOVA: F₂₅,₁ = 0.46, P = 0.50) or at matched lower contrast (two-way repeated-measures ANOVA: F₂₅,₁ = 2.5, P = 0.12). In general, performance on the high-contrast task predicted performance on the low-contrast task (Pearson product moment correlations for all subjects pooled: global motion: r² = 0.75, P < 0.01; global form: r² = 0.53, P < 0.01). Although there were no significant group differences in performance on these tasks there were several glaucoma subjects who had particular difficulty with these tasks. The two subjects with particularly high motion-coherence thresholds were different individuals than the two subjects with high form coherence.
thresholds. Note that the data points in Figure 6 represent the average of two interleaved staircases. To obtain such high thresholds, both staircases must return similar high thresholds. Such abnormal results cannot be due to an early mistake in one of the staircases.

Global Motion and Global Form Tasks Viewed Midperipherally

Figure 7 shows individual performance on the global tasks measured with high- and low-contrast stimuli in the midperiph-

![Graphs showing performance on global motion and form tasks](image-url)
Glaucoma group performance was poorer than that of control subjects both at high contrast (two-way repeated-measures ANOVA; \( F_{25,1} = 9.47, P < 0.01 \)) and low contrast (two-way repeated-measures ANOVA: \( F_{25,1} = 13.29, P < 0.01 \)). There were no significant interactions (\( P > 0.05 \)) between group and global task for either contrast condition.

Figure 8 plots individual data for the low-contrast condition and compares performance on the global motion and global form tasks in the midperiphery. The salience of the targets should be approximately equivalent for all observers for this condition (it is possible that 10 times contrast threshold may not be quite perceptually equivalent between groups).\(^{16}\) It can be seen that the most poorly performing subjects on the global form task are not the same individuals as the most poorly performing subjects on the global motion task. Possible explanations for this finding include either that glaucoma affects individuals in different ways early in the disease (as suggested by Sample et al.\(^{15}\)), or that these individuals are highly variable observers and possibly lost concentration on one task (as has been suggested by Roach et al.\(^{44}\) to explain clinical data with extensive tails). If these deficits represent a genuine deficit of global processing that stems from reduced M or P RGC inputs, then those subjects who were poor performers on the global motion and global form tasks should also be poor performers on the steady-pedestal and pulsed-pedestal tasks, respectively.

To compare the level of performance abnormality of individual subjects across the precortical and cortical tasks, the performance of each task by the patients with glaucoma was converted to a \( z \)-score relative to the control group performance. Figure 9a compares the \( z \)-scores for the low-contrast global motion task with those for the steady-pedestal task. Individual subjects with glaucoma are denoted by unique symbols. It is clear that the three subjects with the most abnormal performance on the global motion task (\( x \)-axis) also had the most abnormal performance on the steady-pedestal task (\( y \)-axis). The global motion thresholds were obtained with target saliency approximately matched across all observers and so should represent the subject's ability to make the global judgment. Figure 9b shows that the relationship between form coherence and pulsed pedestal thresholds is not as clear; however, the subjects with abnormal form coherence thresholds were among those with the highest pulsed-pedestal thresholds. Different individuals had difficulty with tasks presumed to be processed by either the dorsal or ventral visual pathways, consistent with previous observations that individuals appear affected differently at early stages of glaucoma.\(^{15}\)

**DISCUSSION**

In this study, we assessed both precortical and cortical visual processing in individuals with glaucoma in areas of their visual field classified as normal by SAP. To assess precortical function, we used a contrast-discrimination task and found deficits in both presumed M and P processing. We assessed cortical processing of motion and form in the same individuals and found that our glaucoma group performed significantly worse than control subjects in the midperiphery but not in the fovea. Different subjects performed poorly on the global motion and global form tasks.

Our glaucoma group demonstrated poor contrast-discrimination performance both foveally and midperipherally, yet
demonstrated global task abnormalities only in the midperiphery. The cortical neurons presumed to play a central role in the integration of global form (V4) and motion (V5) have large receptive fields and hence pool information from large retinal areas. In the fovea, it is possible that integration occurred across larger areas that were unaffected by the disease process relative to the midperiphery. Alternately, greater neural redundancy in the fovea may result in functionally normal performance on these tasks. Our previous study demonstrated that, relative to control subjects, the glaucomatous observers had greater abnormalities of contrast processing in the periphery than the fovea.

Within our glaucoma group we identified different individuals with markedly elevated thresholds for one of the global tasks (either form or motion) but with much reduced deficits on the other global task. This finding is consistent with previous observations that glaucoma affects different functional processes in different individuals, particularly early in the disease process. Histologic studies of primate models of glaucoma indicate that both magnocellular and parvocellular RGCs are damaged in the disease process. As the number of RGCs differs markedly between normal eyes and as normal aging results in a decrease in neuronal density, it is not unreasonable to assume that these processes, in combination with glaucoma, would result in an uneven reductions of neural redundancy within the visual pathways in a given individual.

It is important to understand the functional deficits arising from glaucoma not only to detect disease and its progression, but also to enable adequate management of the behavioral consequences of glaucomatous visual impairment. This study demonstrates that relatively early glaucomatous deficits of presumed M and P function are sufficient to manifest in abnormalities on intermediate perceptual tasks. It is obvious that having a reduced visual field will affect the ability to perform more complex visual tasks, but our study implies functional difficulty before standard classifications of visual field loss. Normal global motion perception is a likely necessity for normal processing of optic flow, which is thought important for judging self-motion, maintaining posture, and navigating through the environment. Likewise, intermediate form processing may be necessary for optimal object and face recognition. Within our subject group, several individuals demonstrated pronounced difficulty on these global tasks, in areas classified as normal with standard automated perimetry. Although not assessed directly, those subjects who performed poorly on the global motion task may be predicted to have difficulty in judging speed and direction of moving objects—for example, while driving, to a greater extent than reflected by their visual field loss. Other individuals with similar visual fields and difficulties on the global form task may have no difficulty with driving, yet may have impaired face recognition, which may hamper their confidence in daily social interaction. Further study is needed to understand the impact of glaucoma on complex visual processing.

References


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