

# **Blur Representation in the Amblyopic Visual System**

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# Abstract

Amblyopia is diagnosed as a reduced acuity in an otherwise healthy eye, which indicates that the deficit is not happening in the eye per se, but in the brain. Amblyopia is caused by a disruption of binocular experience in the early stages of life. This disruption leads to both a shift in the proportion of neurons that are controlled by the amblyopic eye, as well as a reduced sensitivity of the cells that carry high spatial frequency information (Hess, Thompson & Baker, 2014; Sale, Vetencourt, Medini, Cenni et al., 2007). Those anatomical changes result in a loss in visual acuity and in contrast sensitivity, which should consequently affect the sensitivity of amblyopes to blur differences.

Many researches have disagreed on how to model the losses in amblyopia. One explanation lies in the increased amount of intrinsic blur in the amblyopic visual system compared to normal observers. This level of “internally produced blur” (as opposed to “external” blurring of the image before it reaches the retina) cannot be directly measured, but it can be estimated by using the “equivalent intrinsic blur” paradigm (Watt & Hess, 1987; Levi & Klein, 1990). That is, it can be estimated by measuring blur discrimination thresholds while systematically increasing the external blur in the physical stimulus (Skoczenski, Aslin, 1994). This blur perception is likely to differ between synthetic stimuli such as edges, and natural stimuli such as pictures. Since our visual system is presumably tuned to process natural stimuli, testing artificial stimuli only could result in performances that are non-representative (Sebastian, Burge & Geisler, 2015).

The aim of this study is to fill this gap in the literature and for the first time measure the perception of blur added to natural images in amblyopia. A second aim is to compare natural image blur discrimination and edge blur discrimination performance in both normal and amblyopic

groups. Specifically, we test two hypotheses: First, that vision through the amblyopic eye is affected by a higher level of intrinsic blur in the visual system as compared to the fellow-fixing eye or normal eyes. Second, that as a consequence of the statistical differences between natural and artificial stimuli, there will be a difference in blur discrimination between natural images and edge for both amblyopic and normal groups. We found evidence in support of the first hypothesis, but only when amblyopes were tested on natural images. This finding also supports our second hypothesis, that natural images and edges generate different blur perceptions. This study shows that assessing blur using artificial stimuli only could result in performances that are not ecologically valid. The results hint at the need for more generalizable stimuli and procedures in psychophysics.

## Résumé

L'amblyopie est caractérisée par une baisse d'acuité visuelle dans l'un des deux yeux qui ne peut être expliquée par un déficit dans l'œil en lui-même, mais par un problème qui se produit dans le cerveau. L'amblyopie est la conséquence d'une perturbation de la vision binoculaire lors des premières années de vie. Cette perturbation entraîne un changement dans la proportion de neurones contrôlés par l'œil amblyope, ainsi qu'une baisse de sensibilité des cellules spécialisées dans les hautes fréquences spatiales (Hess, Thompson & Baker, 2014 ; Sale, Vetencourt, Medini, Cenni & ci, 2007). Ces changements anatomiques mènent par la suite à une baisse de l'acuité visuelle ainsi qu'à une baisse de sensibilité au contraste, qui conséquemment affecte la sensibilité des amblyopes aux différences entre multiples niveaux de flou.

Les chercheurs sont en désaccord quant au type de modèle sur lequel se baser afin d'expliquer les déficits de l'amblyopie. Certains croient que cette maladie peut être expliquée par une augmentation du flou interne dans le système visuel des amblyopes comparativement à celui des participants ne souffrant pas d'amblyopie. Ce niveau de flou interne ne peut être mesuré directement, mais peut être estimé en employant le paradigme nommé « l'équivalence du flou interne » (Watt & Hess, 1987 ; Levi & Klein, 1990). C'est-à-dire, il peut être estimé en mesurant les seuils de discrimination de flou de chaque sujet tout en augmentant systématiquement le flou externe dans le stimulus testé (Skoczenski, Aslin, 1994). La perception du flou sera probablement différente entre des stimuli synthétiques, tels que des bordures noires et blanches, et des stimuli naturels, tels que des photos. Puisque notre système visuel est supposé adapté pour traiter des stimuli naturels, tester des stimuli artificiels uniquement pourrait entraîner des performances non-représentatives (Sebastian, Burge & Geisler, 2015).

Le but de cette étude est de mesurer la perception du flou avec des images naturelles chez les personnes souffrant d'amblyopie. Un second objectif de cette étude est de comparer la discrimination du flou entre les amblyopes et les sujets normaux lorsque testés avec des images naturelles ou bien, lorsque testés avec des bordures artificielles. Nous testons spécifiquement deux hypothèses : Premièrement, que la vision de l'œil amblyope est affectée par une plus grosse proportion de flou interne dans le système visuel comparativement à l'œil non affecté des mêmes sujets amblyopes, ou comparativement aux yeux des sujets normaux. Deuxièmement, que du aux différences statistiques entre les stimuli naturels et artificiels, il y aura une différence dans la discrimination du flou entre les images naturelles et les bordures artificielles, et ce dans les deux groupes (amblyopes et normaux). Les résultats confirment notre première hypothèse, mais seulement lorsque les amblyopes sont testés avec des images naturelles. Ces résultats supportent aussi notre deuxième hypothèse, que les images naturelles et les bordures génèrent différentes perceptions de flou. Cette étude montre qu'évaluer le flou à travers des stimuli artificiels pourraient mener à des performances qui ne sont écologiquement pas valides, et souligne l'importance d'utiliser des procédures et stimuli psychophysiques plus représentatifs de notre environnement.

## **Acknowledgements**

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# Background Information

## Early Animal Models

While the signals from the two eyes are anatomically and functionally separated in the lateral geniculate body (LGN), information from the two eyes is combined in the primary visual cortex (V1). This means that the cells found at the level of the LGN can be driven by one eye only (monocular cells), whereas those found in V1 can be stimulated by the two eyes (binocular cells). However, while some V1 cells will be influenced equally by both eyes, others will be dominated more strongly by one eye than the other (Hubel & Wiesel, 1964). The visual cortex is organized into ocular dominance columns, which represent stripes of neurons that respond preferentially more to one eye than the other (Hubel & Wiesel, 1962; Swisher, Gatenby, Gore et al., 2010). Early animal models were used by Hubel and Wiesel in 1964 to study the consequences of visual deprivation on those ocular dominance columns. Their main research question was whether “preventing vision in one eye of a kitten, by sewing the lids of one eye shut for the first three months of life, would produce blindness in that eye, and a defect in normal cortical physiology” (Hubel & Wiesel, 1964). They found that most of the cells in the visual cortex of these kittens were influenced by the normal eye (84 cells driven by the normal eye against one cell driven by the previously-sutured eye). Monocular deprivation therefore led to an ocular dominance shift, whereby a given cell would come to favor more one eye and lose all the connections with the sutured eye (Hubel & Wiesel, 1964). The researchers also recorded from single cells in the LGN and found that they were normally driven by the eye that was deprived, meaning that ocular dominance shift was restricted to the striate cortex itself. No cortical deficit was found in adult deprived cats compared to the young ones, meaning that the effect of deprivation also depends on

age. This study therefore demonstrates that a lack of interaction or cooperation between the two eyes at an early age is enough to disrupt the neural connections used for binocular interaction and can lead to a permanent reduction in the proportion of binocular neurons (Hubel & Wiesel, 1964).

## **Amblyopia**

Amblyopia is a visual deficit that happens when disruption in binocular visual experience occurs during a critical period in childhood. This period ranges from a few months to 7 or 8 years of age and can be defined as the time during which deprivation is effective (W. Daw, Nigel, 1998). This visual deprivation leads to an ocular dominance shift of the cortical neurons in favor of the normal eye (similar to what was found in the Hubel and Wiesel's study on cats mentioned earlier), which itself leads to a loss of visual acuity in the deprived eye, as well as a reduced sensitivity of the cells that carry high spatial frequency information (Hess, Thompson & Baker, 2014; Sale, Vetencourt, Medini, Cenni & ci, 2007). There are two types of amblyopia: anisometric amblyopia, which occurs when there is an unequal focus between the two eyes, and strabismic amblyopia, which occurs when the eyes do not properly align.

## **Visual Deficits of Amblyopes**

In a study measuring blur perception in amblyopia, it was shown that edge blur-discrimination was noisier than for normal observers, indicating a visual acuity impairment (Simmers, Bex, Hess, 2003). Several studies also showed that amblyopes had marked deficits in Vernier acuity that were highly correlated with their loss of Snellen acuity (Levi, Polat, 1996). Contrast sensitivity is another dimension of visual loss that has extensively been documented in

amblyopia. In a study measuring cortical fMRI deficits in amblyopia, it was found that the deficit was more pronounced at higher than at lower contrasts (Hess, Li, Lu, Thompson, Hansen, 2010). Another study using psychophysics measured and compared the contrast response of the eyes of amblyopic subjects at each spatial frequency. They found that subjects showed a loss of contrast sensitivity in the amblyopic eye for a limited band of high spatial frequencies (Hess, Campbell & Greenhalgh, 1978). In sum, several studies agree that amblyopia is characterized by a loss of contrast sensitivity at high spatial frequencies (Kiorpes et al., 1999; Levi & Klein, 2003; Hess & Howell, 1977; Gstalder & Green, 1971; Levi & Harwerth, 1977; Hess, Thompson, B., & Baker, 2014). Both deficits in visual acuity and contrast sensitivity should lead amblyopes to be less sensitive to differences in blur compared to normal observers.

## **Blur Perception**

Blur is a difficult concept to define. People usually consider an object blurry when it is unclear, cloudy, when it lacks sharp details or when it feels like there was some kind of degradation applied to the visual stimuli. Technically, blur is caused by a loss of the high spatial frequency content due to the reduction of luminance contrast in this specific frequency range (Crété-Roffet, Dolmiere, Ladret, Nicolas, 2007; Skoczenski & Aslin, 1994; Campbell, Howell & Johnstone, 1978). Performance on blur detection and discrimination tasks can be influenced by different sources of blur (Skoczenski & Aslin, 1994). One of them is physical blur which is blur that can be found in the stimulus itself and which constitutes an important measure of image quality. An image can be artificially blurred by convolving it with a filter that will average out rapid changes in intensity from one pixel to the next. More specifically, it will reduce the high-spatial frequency information while retaining the low spatial frequency information (Marziliano, Dufaux, Winkler

& Ebrahimi, 2002). An example of such a filter is the Gaussian filter and is widely used in blur perception studies (Aurich & Weule, 1995; Marziliano, Dufaux, Winkler & Ebrahimi, 2002). The width of the Gaussian governs the amount of blur in the stimulus. (Wang & Ciuffreda, 2005; Watson & Ahumada, 2011; O'Hare & Hibbard, 2013). Other organismic factors, such as accommodation (Kruger & Pola, 1989) aging (Polat, Schor, Tong, Zomet & Lev, 2012) disease (Marmor & Gawande, 1988) or motion of the observer or object (Hammet, Georgeson, Gorea, 1998) can also contribute to perceived blur. Assuming a sharp image has been formed on the retina, another source of blur that can influence performance on discrimination tasks is internal blur which represents the blur that is caused by neural factors (Valeshabad, Wanek, McAnany & Shahidi, 2015; Skoczenski & Aslin, 1994). This is termed “intrinsic blur”.

It was previously hypothesized that performance on tasks, such as the Vernier acuity task, was limited by an internal error in the visual system of amblyopes that was combined with a stimulus error. In other words, that performance was first determined by an internal error and then proportional to an external error, if any external error were present (Watt & Hess, 1987). One idea is that this error was acting like blur and, more specifically, that the deficits in amblyopia could be modeled by a higher level of intrinsic blur in the visual cortex (Watt & Hess, 1987; Levi & Klein, 1989). As this level of “internally produced blur” cannot be directly measured, multiple studies (Hess & Watt, 1990; Levi & Klein, 1990; Watt & Hess, 1987, Skoczenski & Aslin, 1994) have attempted to estimate it using the “equivalent intrinsic blur paradigm” (Watt & Hess, 1987; Levi & Klein, 1989). This paradigm is based on both Barlow's estimation of neural noise in the visual system (Barlow, 1956), and on Pelli's measurements of the equivalent intrinsic noise that limits contrast detection (Pelli, 1990; Levi & Klein, 1990; Skoczenski & Aslin, 1994). The equivalent intrinsic blur can be estimated by measuring blur discrimination thresholds while systematically

increasing the external blur in the physical stimulus (Skoczenski & Aslin, 1994; Hess & Watt, 1990; Levi & Klein, 1990a, b; Watt & Hess, 1987). Adding external blur to the stimuli allows us to infer the amount of internal blur: performance only decreases after a certain level of added blur, referred to as equivalent intrinsic blur.

## **Models of Amblyopia**

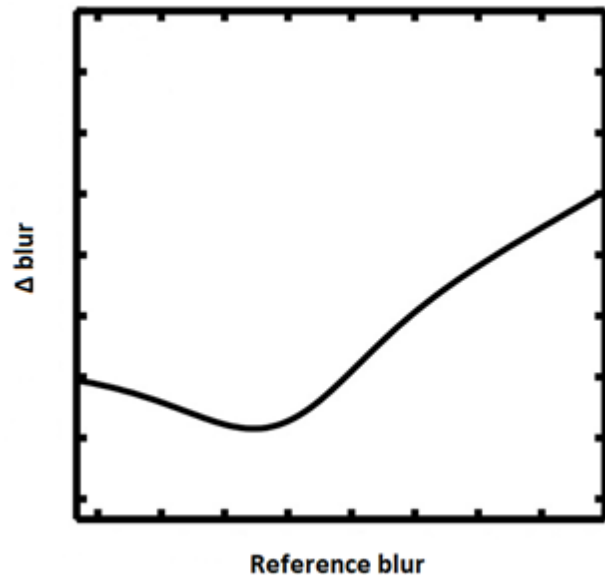
Levi and Klein (1989) believed that amblyopia could be explained by raised amounts of equivalent intrinsic blur in the brain of amblyopes, and that it could provide a valid measure of this internal error found in the amblyopic visual system. They tested anisometropic, strabismic and mixed amblyopes on a line detection and spatial interval discrimination task, where subjects had to discriminate between two sets of unblurred lines with different separations (a reference separation and a test separation both including one pair of lines) by using each eye separately (monocular testing). The goal of the study was to equate the performance of the fellow (good) eye with that of the amblyopic (bad) eye of the amblyopic subjects. To do so, they tested both 5x and 10x increases in contrast of the stimulus presented to the amblyopic eye, but both resulted in the failure of equating the fellow eye's performance. As another alternative, the researchers repeated the same discrimination task in the fellow eye, but this time used blurred lines as their testing stimuli (to compensate for blurred perception in the amblyopic eye). They found evidence showing that performance in the fellow eye in the blurred lines condition was equivalent to that of the amblyopic eye's in the unblurred lines condition: they observed a shift in the optimal threshold of the fellow eye towards the amblyopic eye. They concluded that the amblyopic eye could be mimicked by increased level of intrinsic blur and contrast (Levi & Klein, 1989).

Higher intrinsic blur in the amblyopic visual system constitutes only one of the hypotheses that have been proposed to model the losses in amblyopia. In contradiction to Levi and Klein (1990), Watt and Hess (1987) believed that this internal error was not due to blur but to local spatial scrambling. They used a version of the Vernier acuity task where subjects were asked to judge the offset of two Gaussian luminance profiles with either eye. The threshold in this experiment corresponded to the amount of separation observers needed in order to tell the two lines apart. Intrinsic blur was believed to represent the point at which the thresholds rose with external blur. As they did not find any difference between the level of intrinsic blur in the amblyopic eye compared to the fellow eye, as well as compared to the eyes of normal subjects, Watt and Hess (1987) concluded that amblyopia could not be explained by raised amount of intrinsic blur. In a separate experiment, they tested Vernier acuity with targets on which positional jitter was introduced and found that this jitter degraded the performance of the fellow eye, but not of the amblyopic eye (Levi & Klein, 1990). Watt and Hess (1987) therefore argued that this internal error in the amblyopic visual system was not due to higher levels of intrinsic blur, but to local spatial scrambling which implied an elevated degree of “relative positional uncertainty” in the visual system of anisometric amblyopes (Watt & Hess, 1987; Bedell & Flom, 1981; Bradley & Freeman, 1985; Pointer & Watt, 1987).

Simmers, Bex and Hess (2003) also disagreed on modeling amblyopia based on higher levels of intrinsic blur. They asked different types of amblyopic subjects (anisometric, strabismic and mixed) to perform an edge blur discrimination task and modeled blur discrimination with a dipper function, where the x axis represents the reference blur and the y axis represents the amount of additional blur needed in the test edge to distinguish it from the reference blurred edge (threshold). They took the level of intrinsic blur as the inflection point of the curve in the dipper

function. The inflection point represents the minimum on the y axis, that is, the point at which performance is the best (see schematic in Figure 1).

Simmers, Bex and Hess (2003) found that the value of the inflection point did not differ between the amblyopic eye and the fellow eye, as well as between the amblyopic eye and the eyes of control groups. If amblyopia was to be characterized by increased level of intrinsic blur, the point at which blur discrimination threshold is the lowest (the inflection point) would have been expected to shift to the right (i.e.



**Figure 1.** Schematic figure of a typical dipper function (logarithmic scale).

increased intrinsic blur) compared to the fellow eye or to the eyes of normal observers. Therefore, they concluded that amblyopes did not show increased level of intrinsic blur, but showed a reduction in sensitivity—that is, noisier discrimination thresholds (Simmer, Bex, Hess, 2003). Similar to Watt and Hess (1987), they believed that the losses in amblyopia could be explained by models based on spatial scrambling, that is, by more distorted and perturbed spatial representations in the cortex (Simmers, Bex, Hess, 2003; Watt & Hess, 1987; Hess, Campbell & Greenhalgh, 1978; Hess, 1982).

## **Blur Discrimination and Dipper Functions**

Blur discrimination is usually represented by a characteristic dipper function (see schematic in Figure 1), which occurs both in normal and in amblyopic populations. In other words,

as reference blur increases from zero, thresholds first decrease progressively until reaching the optimal threshold at medium reference blurs, and then increase again with higher reference blurs. Different theories on the shape of the dipper function have been developed based on contrast detection and discrimination. One of those theories is called channel uncertainty (Green, 1980; Tanner, 1961; Solomon, 2009) and is based on the idea that at low signal levels, when the stimulus is barely detectable, observers are “monitoring” many irrelevant channels, making detection harder (Solomon, 2009). However, as the stimulus gets stronger, the choice of channels gets more specific and leads to better performance (explains the dip). However, this theory is primarily relevant to contrast discrimination and does not readily translate to make predictions for blur discrimination.

Another theory that attempts to explain the shape of the dipper function in relation to blur discrimination is the concept of intrinsic blur introduced earlier. Blur can come from both the stimulus or from the visual system, and performance is limited by the greatest source of uncertainty (Simmers, Bex & Hess, 2003; Watt & Hess, 1987). This is exploited by the equivalent intrinsic blur paradigm where intrinsic blur is inferred from performance under various levels of stimulus blurs. When blur in the stimulus is small, performance is limited by intrinsic blur, whereas when the blur in the stimulus is large, performance is limited by the external blur in the stimulus and follows a power law (Simmer, Bex & Hess, 1987). You therefore need a certain amount of added external blur in the visual stimulus in order to surpass intrinsic blur and effectively impair performance. The dip of the dipper function is believed to represent the equivalent intrinsic blur of the visual system.

Another related interpretation has to do with the contrast sensitivity function. Blurring an edge effectively reduces the high spatial frequencies information, while sharpening an edge reduces low spatial frequencies. The fact that our performance is better when there is some amount



of blur in the stimulus (where the dip is located) compared to when it is sharp or very blurry can be explained by our greater sensitivity to medium spatial frequencies, as well as our lower sensitivity to high spatial frequencies and low spatial frequencies (Watson & Ahumada, 2011).

Finally, another idea of the dipper shaped function is proposed by Sebastian, Burge and Geisler (2015) who believed that the dip was the result of accommodation, that is, the adjustment of the eyes to keep object in focus. They measured human sensitivity to defocus blur (blur imposed on images presented at different distances) on 21 natural image patches, and the data was successfully modeled with a dipper shaped function. However, when accommodation was disabled by the administration of cyclopentolate on the eye, the “dip” in the dipper function disappeared. They therefore concluded that the shape of the dipper function was a consequence of accommodative fluctuations (Sebastian, Burge, Geisler, 2015).

## **Natural vs. Synthetic Stimuli for Blur Discrimination Studies**

There are different types of stimuli that we can use in a blur discrimination experiment. Edges have been widely used as test stimuli. They represent a border where a surface terminates or a change in material (V. Torre & T. Poggio, 1984). Technically, edges can be defined as local and abrupt changes in intensity (Senthilkumaran & Rajesh, 2009). All spatial frequencies’ phases converge and align at the border of an edge. They represent object boundaries and are necessary for scene understanding (Zhang & Bergholm, 1996). Other types of stimuli that we can also use are natural images which represent sparse collections of changes in intensity (Olshausen & Field, 1996). There are major differences between edges and natural images. Firstly, they possess different statistics. A natural image contains oriented, localized and bandpass structures which are

characterized by their phase spectrum (Farivar, Thompson, Mansouri & Hess, 2011; Olshausen & Field, 1996). There are also multiple distances between the edges that make up a natural image, whereas a single edge only represents one localized event in an image. The power spectrum of each stimuli is also different. Natural images can be recognized by their characteristic  $1/f$  power spectrum shape and those statistical regularities only represent a set of all the possible patterns that can be created. Secondly, edges and natural images are likely processed differently in the brain, namely that natural images represent more complex stimuli that engage a larger portion of the cortex, including regions in the ventral visual pathway (Kobatake & Tanaka, 1994; Kravitz, Saleem, Baker, Ungerleider & Mishkin, 2013) whereas edges are poor at driving responses beyond early visual areas. Another important thing to note is that edges are monochromatic whereas natural images usually contain chromatic information. Finally, measurements made with natural images are more likely to be ecologically valid than synthetic edges, as the visual system is thought to be tuned to natural images.

In summary, natural images are more complex and varied than single edges in terms of statistics, processing and basic characteristics. It is largely believed that, due to the spatial organization of neurons' receptive fields in the early parts of the visual cortex, as well as to the tuning characteristics of individual channels, the visual system is optimized for processing information in the natural environment (Sutherland, 1982; Barlow, 1961; Laughlin, 1983). This proposition is based on the fact that the "statistics of spatial features of natural images" seem to match the spatial organization of the receptive fields found in the cortex (Hancock, Baddeley & Smith, 1992; Olshausen & Field, 1997; Srinivasan, Laughlin, & Dubs, 1982).

## Rationale

While a number of researchers have assessed blur discrimination using synthetic edge stimuli in both normal and amblyopic populations (Hamerly & Dvorak, 1981; Watt & Morgan, 1983; Hess, Pointer & Watt, 1989; Paakkonen & Morgan, 1994; Wuerger, Owens & Westland, 2001; Mather & Smith, 2002; Chen, Chen, Tseng, Kuo & Wu, 2009; Westheimer, Brincat & Wehrhahn, 1999; Simmers, Bex & Hess, 2003), very few have assessed blur discrimination with natural images (Sebastian, Burge & Geisler, 2015; de Ridder, 2001; Field & Brady, 1997; Parraga et al., 2005), and no one has used natural images to measure blur discrimination in amblyopia. As noted before, edges and natural images represent different type of stimuli with differences that are non-negligible. Testing only artificial stimuli could result in performance that are not ecologically valid due to the way our visual system is tuned (Sebastian, Burge & Geisler, 2015; Parraga et al., 2005). The first aim of this experiment is to fill this gap and measure, for the first time, natural image blur perception in amblyopia to reconcile the divergent theories of the visual deficits in amblyopia. A second aim is to compare natural image blur discrimination and edge blur discrimination performance in both normal and amblyopic groups.

Specifically, we test two hypotheses: First, that vision through the amblyopic eye is affected by a higher level of intrinsic blur in the visual system compared to the fellow-fixing eye or normal eyes. Second, that because of the statistical differences between natural and artificial stimuli, there will be a difference in the blur discrimination performance between natural images and edge for both amblyopic and normal groups.

# Methods and materials

## Observers

A test group of 14 amblyopes, six with strabismus only, one with anisometropia only, and six with both strabismus and anisometropia (mean age = 36.4 years old; SD = 11.93) were recruited for the study (see Table 1). A control group of 14 observers (mean age = 37.3 years old; SD = 14.9; nine females and five males) with normal binocular vision and visual acuity were also recruited for the study. All amblyopic subjects were optically corrected for this experiment to ensure that the effects seen are due to amblyopia only. As seen in Table 1, the

**Table 1.** Clinical Characteristics of Amblyopic Subjects

Subject	Age/Sex	VA difference	Type
AH	32/M	0.7	mixed
CD	35/M	0.1	strabismic
CF	54/F	0.15	strabismic
CT	65/F	1	strabismic
DO	57/M	1	mixed
DT	38/M	0.4	strabismic
DV	28/M	0.1	animesotropic
GH	55/M	0.4	mixed
JL	23/M	0.5	mixed
JZ	22/M	0.54	strabismic
KS	27/M	0.7	anisometropic
KW	23/F	0.16	strabismic
MPG	27/M	0.6	mixed
SM	24/M	0.14	mixed

amblyopic group includes subjects from the three subdiagnostics of amblyopia (strabismic, anisometropic, mixed amblyopia). All research participants were provided with consent forms to make an informed and voluntary decision about whether or not to participate in this research study.

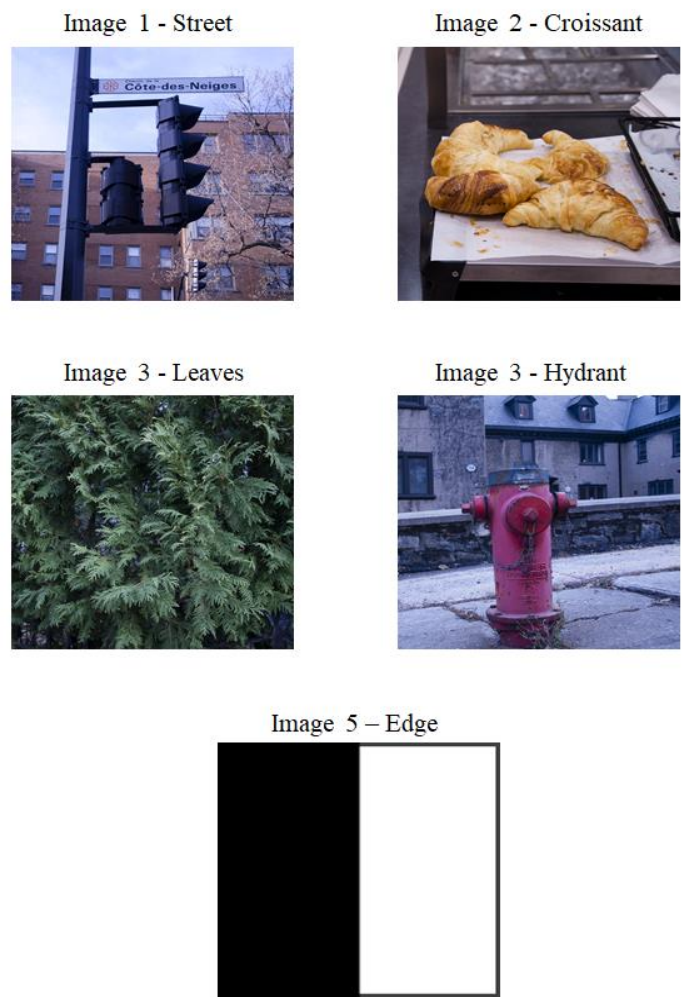
## Image Blur Discrimination Experiment

Monocular image blur discrimination thresholds were measured in the fellow and amblyopic eye of the amblyopic group and in the dominant and non-dominant eye of the control group. This was achieved by using an opaque eye patch on one eye at a time.

### Apparatus and Natural-Image Stimuli

Four natural colored images and one black and white edge were used as our testing stimuli (see Figure 2). The natural images were taken outside with a Nikon D90 camera, using the automatic mode and with RAW capture (12-bit colour, uncompressed). The captured images were color corrected by using reference color patches during the photo shooting that included standard 24 sRGB color space plus additional color targets for more precision and accuracy using the SpyderCHECKR

standard system. The images were then analyzed using the SpyderCHECKR calibration software



**Figure 2.** Test stimuli used for the blur discrimination experiment.

and processed in Adobe Photoshop CS5.1 (64 bit) and Adobe Lightroom CC. The final images were cropped and stored as 16-bit TIFF files without compression, to maintain their fidelity.

Stimuli were blurred to different levels by convoluting them with Gaussian kernel of various widths, using the Image Processing Toolbox in MATLAB (R2016b, <https://www.mathworks.com/> developed by Cleve Moler and Edward B. Magrab). The size of the static blurred natural images and edge was  $5.7^\circ \times 6.7^\circ$ . All the images were presented on a CRT monitor (LG Electronics Flatron 915 FT Plus) that was gamma corrected to ensure the linearity of the monitor luminance profile. Using a professional Nvidia Graphic Card (Quadro 2000), images were shown with 10 bits of depth (1024 levels in each colour channel) on the analog monitor. Background of the screen was  $30.75 \text{ cd/m}^2$  and the resolution was set to  $1280 \times 1024$  with a refresh rate of 75 Hz. The viewing distance was fixed to 60 cm from the screen.

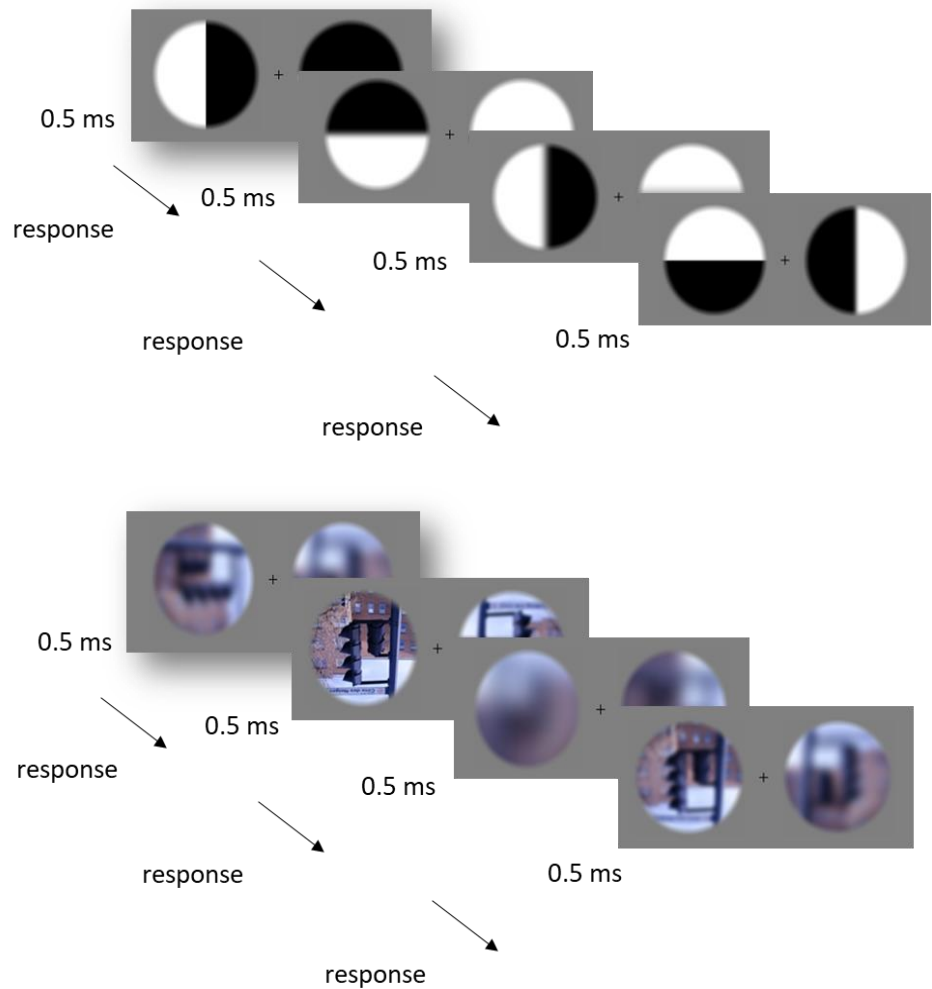
## **Procedure**

Participants were tested on a two-alternative forced choice procedure. For the first session, one of the two eyes was patched randomly so that monocular blur discrimination thresholds could be measured using a staircase approach. The stimuli were presented on each side of a fixation cross with an eccentricity of  $1.9^\circ$ . The reference blur levels were expressed as standard deviation of a Gaussian and were fixed at 0, 0.23, 0.46, 0.94, 1.88, 3.75, 7.5, 15 or 30 arcmin. The standard deviation of the comparison blurred image was set to be always greater than that of the reference image by  $\Delta$  blur. To prevent any strategy from the observer to use local contrast as a cue, we rotated the images either at  $90^\circ$ ,  $180^\circ$ ,  $270^\circ$  or  $360^\circ$  randomly from trial to trial (see Figure 3). We also prevented participants from using cues based on the pictures' external contour by using a gaussian aperture that was set around the image (see schematic Figure 3).

The subject was seated in a dark room and instructed to fixate on a centrally-presented cross. The participant then had to identify which of the two images (left or right) was the blurriest. Auditory feedback was given after each response (right or wrong, designated by a high or low tone). The first

session consisted of four blocks, each testing one natural image per block and a fifth block testing the edge stimulus. Each block contained 40 randomly interleaved trials for each of the six levels of blur. Once the first session was finished, the participants were asked to remove the patch and wait for 1h15min before

doing the second session. This time was fixed to ensure the removal of any effects of the patch on the eye (Zhou, Clavagnier & Hess, R, 2013). For the second session, the same procedure was repeated but this time with the eye that had been previously patched. The same stimuli and the



**Figure 3.** Schematic description of two testing blocks. Each block contains one type of stimuli tested across several trials.

same number of blocks were used. The image order presentation was randomized across the blocks and the sessions.

## **Analysis**

### Data Collection and Pre-Processing

Stimulus blur difference for each trial was determined using a 3-down-1-up staircase. The subject's responses to each staircase step was used to estimate the threshold by fitting the responses with a Gumbel function using a maximum-likelihood routine implemented in Palamedes toolbox (Prins & Kingdom, 2018). For fitting the psychometric Gumbel function, we allowed threshold and slope to vary and fixed the guessing rate at 0.5 and the lapse rate at 0.02. In cases where subjects performed inconsistently, we were unable to estimate a threshold for that image-eye session and these were excluded from the subsequent analysis, resulting in variable number of subjects in each image-eye session and corresponding degrees of freedom (see below).

### Model Fitting

Blur discrimination performance follows a typical “dipper” function. That is, the discrimination thresholds first decrease with smaller reference blurs and then increase at larger reference blurs. The finding that subjects are generally most sensitive to incremental blur when it is added to slightly blurred images, but not to very sharp images has been extensively reported in other experiments (Hess et al., 1989; Wuerger et al., 2001; Chen et al., 2009; Westheimer et al.; Watt & Mprgan, 1984; Watt, 1988; Paakkonen & Morgan, 1994; Simmers, Bex & Hess, 2003). We therefore fitted the data for each image and each eye with the Weber model, which has been

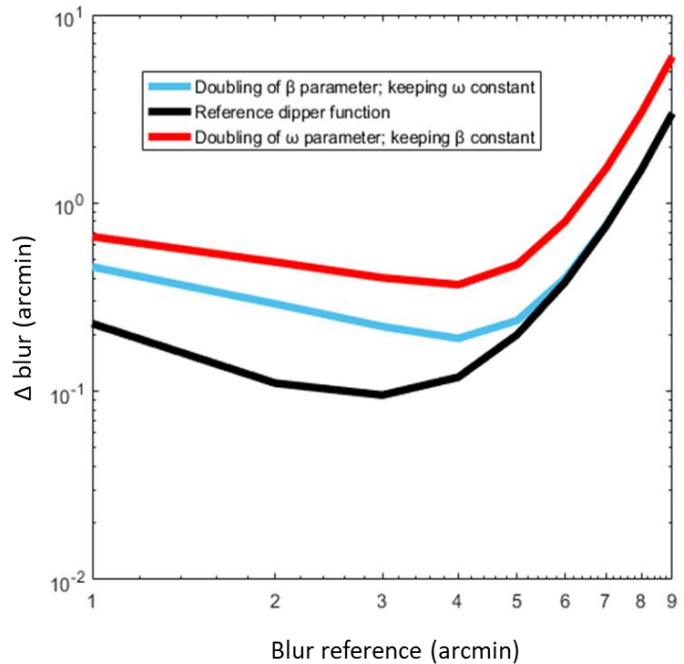


widely used in other studies (Mather & Smith, 2002; Paakkonen & Morgan, 1994; Morgan, 1994; Watt, 1988; Wuerger et al., 2001).

We fitted a  $\beta$  and a  $\omega$  parameter to the data for each eye and each image in both groups by using the following function (Wuerger, Owens & Westland, 2001):

$$a = -r + \sqrt{r^2 + (\omega^2 + 2\omega)(r^2 + \beta^2)}$$

The  $\beta$  parameter represents the level of intrinsic blur in the visual system and the Weber ratio ( $\omega$ ) represents the sensitivity to blur differences. These parameters each have different effects on the dipper function: increasing the  $\beta$  parameter shifts the early part of the curve vertically and the dip horizontally, whereas increasing the  $\omega$  parameter shifts the entire curve vertically (see Figure 4) (Watson & Ahumada, 2011).



**Figure 4.** Predictions of the Weber model.

The data was fitted to the model by using Matlab and by using the fmincon function to obtain estimates of  $\beta$  and  $\omega$  for each image-eye session for each subject.

## Inferential Statistics

We conducted a 2x2 mixed-design analysis of variance (ANOVA) using SPSS (IBM Corp.) with Eye (dominant/fellow vs. non-dominant/amblyopic) as the within-subject factors, and patient group (Normal or Amblyopic) as the between-group factor. The analysis was carried out separately for the  $\beta$  and  $\omega$  parameters, and also separately for the edge stimuli and the parameters averaged over the five natural images. Greenhouse-Geisser correction was used to correct for variance non-uniformity.

We carried out planned comparisons using paired and independent sample t-tests, as well as exploratory post-hoc analysis, corrected for false discovery rate using Benjamini-Hochberg correction for multiple comparisons. Finally, we performed Spearman correlation between inter-ocular logMAR acuity difference and the magnitude of dipper function parameter differences, to determine whether the differences were related to amblyopia or not.

## Results

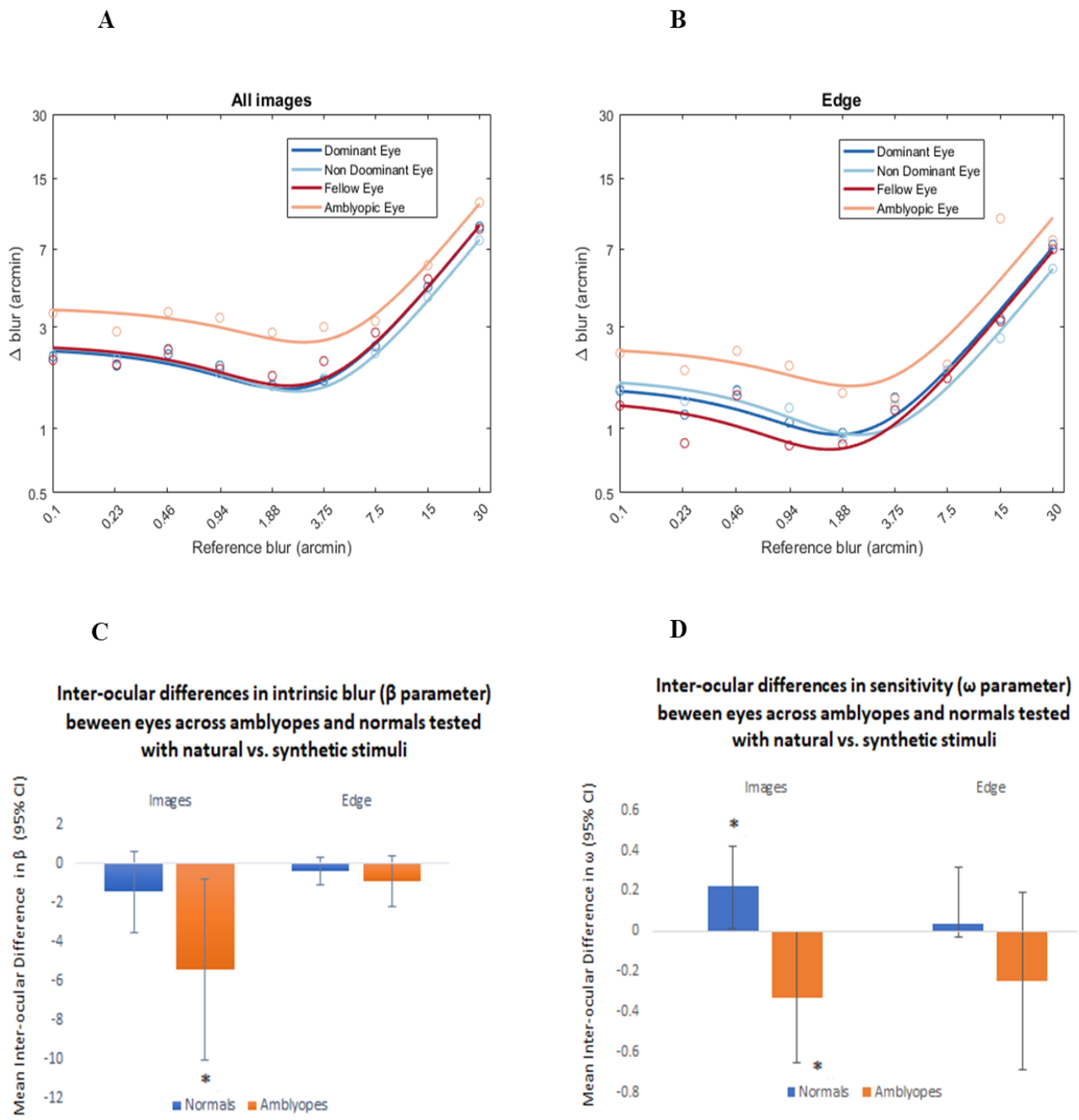
### **Inter-Ocular Differences in Intrinsic Blur and Sensitivity in the Amblyopic and Normal Groups using Natural Images**

We will first report the comparisons made between the fellow eye and the amblyopic eye of the amblyopic subjects on the fit of the Weber model to the averaged thresholds across images (Figure 5A). There was a significant difference in  $\beta$  parameter (reflecting intrinsic blur) between the fellow eye and the amblyopic eye,  $t(10) = -2.632, p < 0.05$ , with the amblyopic eye exhibiting higher intrinsic blur (Figure 5C). There was also a significant difference in  $\omega$  parameter (reflecting sensitivity to blur differences) between the fellow and the amblyopic eye,  $t(10) = -2.205, p < 0.05$ ,

meaning the amblyopic eye was less sensitive to blur differences in general across different levels of reference blur (Figure 5D). This same difference in sensitivity was found in the normal group whereby the non-dominant eye was surprisingly more sensitive than the dominant eye,  $t(8) = 2.464, p < 0.05$  (Figure 5D). However, no significant difference in the  $\beta$  parameter was found in the normal group (Figure 5C). This means that even if performance was generally better in the non-dominant eye compared to the dominant eye when tested on natural images, the level of intrinsic blur in both eyes was equivalent in the normal population. A significant difference in the  $\beta$  parameter was also found between the amblyopic eye and the dominant eye of the normal group,  $t(23) = -2.386, p < 0.05$ , as well as a difference in the  $\omega$  parameter,  $t(23) = -1.9, p < 0.05$ . The amblyopic and non-dominant eye of the normals were also significantly different from each other both in terms of intrinsic blur,  $t(20) = -1.703, p = 0.05$ , and sensitivity,  $t(20) = -2.298, p < 0.05$ . The amblyopic eye therefore exhibited higher levels of intrinsic blur than the fellow eye, and both eyes of the normal group. This lends support to our first hypothesis, namely that intrinsic blur is elevated in the visual system representing vision from the amblyopic eye, compared to the fellow eye and the eyes of normal subjects.

### **Inter-Ocular Differences in Intrinsic Blur and Sensitivity in the Amblyopic and Normal Groups using a Synthetic Edge**

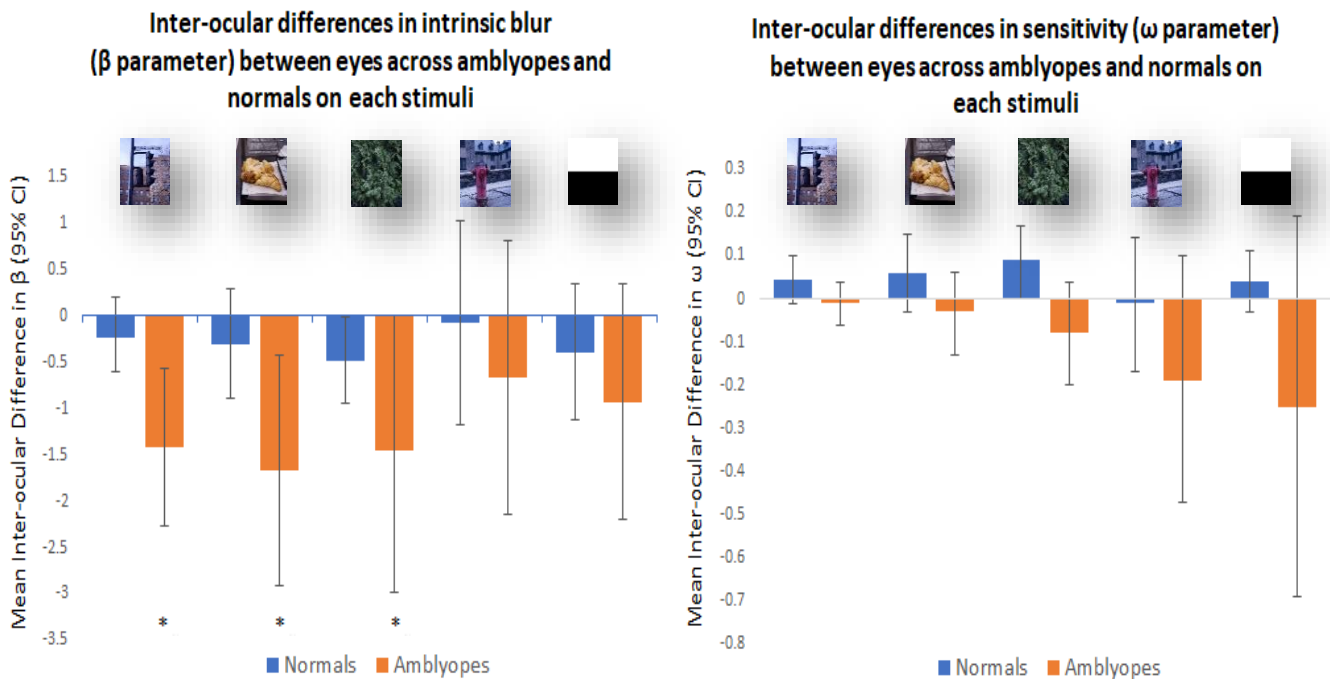
The edge stimulus resulted in patterns of blur discrimination that were comparable across eyes in both groups (Figure 5B) —we did not observe a significant effect of eye difference in  $\beta$  (Figure 5C) and  $\omega$  parameter (Figure 5D) in either group. This absence of an eye-specific effect lends support to our second hypothesis, namely that blur in natural images is perceived differently than synthetic stimuli.



**Figure 5.** (A) Blur discrimination thresholds were averaged across all images and across subjects for each eye condition. This figure shows the fit that was done on those averages. The x axis corresponds to the blur reference in arc minutes and the y axis corresponds to the discrimination threshold, that is, the amount of additional blur needed in the test image in order to distinguish it from the reference image. (B) Blur discrimination thresholds were averaged across subjects for each eye condition when tested on the edge only. (C) Mean inter-ocular differences in  $\beta$  (intrinsic blur) across groups for all images and for the edge. More negative values reflect worse intrinsic blur in the amblyopic or non-dominant eye. Error bars reflect 95% confidence intervals. (D) Mean inter-ocular differences in  $\omega$  (sensitivity) across groups for all images and for the edge. More negative values reflect lower sensitivity in the amblyopic or non-dominant eye. Error bars reflect 95% confidence intervals.

## Further Analysis

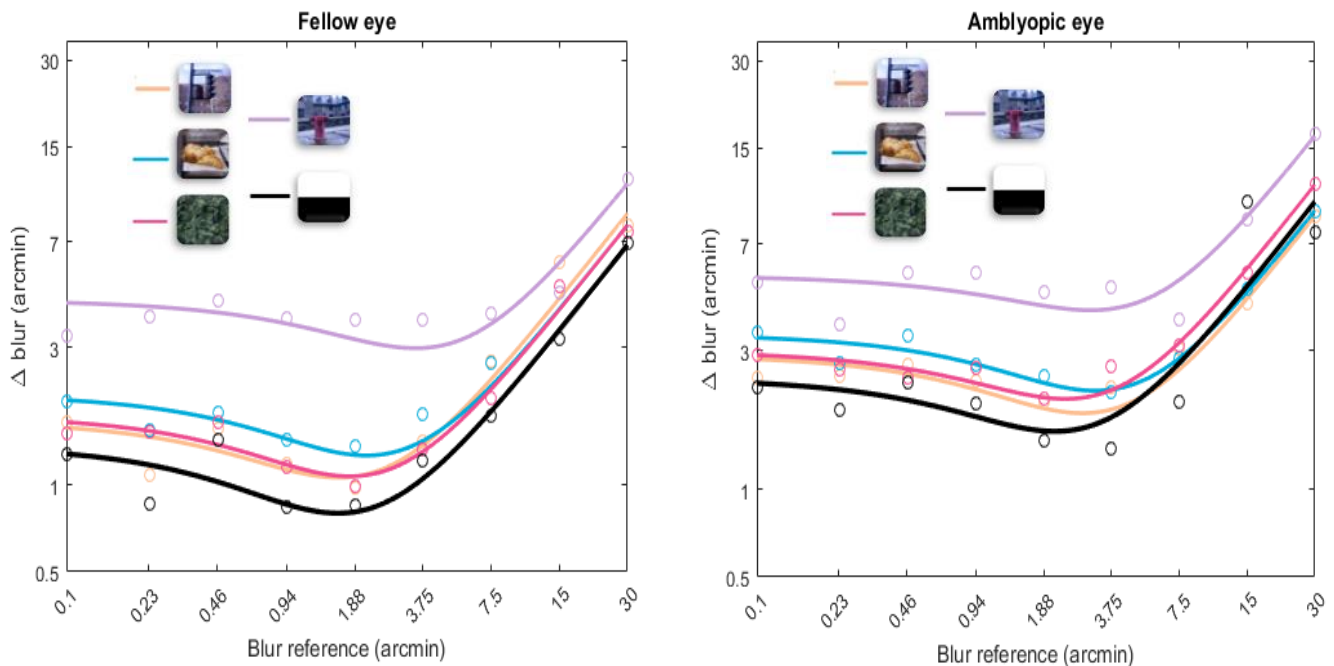
In this section we explore stimulus-specific differences further, using Benjamini-Hochberg correction for multiple comparisons (Benjamini & Yekutieli, 2001). There was a significant difference in  $\beta$  parameter (intrinsic blur) between the fellow eye and the amblyopic eye when tested on the street image,  $t(11) = -3.661$ ,  $p_{adjusted} < 0.008$ , the croissant image,  $t(13) = -2.882$ ,  $p_{adjusted} < 0.013$  and the tree image,  $t(13) = -2.067$ ,  $p_{adjusted} < 0.039$ , with the amblyopic eye exhibiting higher intrinsic blur (Figure 6A). However, no significant differences in the  $\beta$  parameter were found between the eyes when tested on the hydrant image and the edge (Figure 6A). There was no significant difference in the sensitivity parameter  $\omega$  between the fellow eye and the amblyopic eye for any of the five stimuli tested (Figure 6B). This means that even if intrinsic blur



**Figure 6.** (A) Mean inter-ocular differences in  $\beta$  (intrinsic blur) across groups for each stimulus. (B) Mean inter-ocular differences in  $\omega$  (sensitivity) across groups for each stimulus. Error bars reflect 95% confidence interval of the inter-ocular difference.

was heightened when the amblyopic eye was being tested on the street, croissant and tree image, sensitivity to blur differences was not affected.

From those previous analysis we can conclude that there was a higher level of intrinsic blur when the amblyopic eye was being tested on all-natural images expect for the hydrant image. However, the lack of difference between the amblyopic and fellow eye when tested on the hydrant image does not mean that there was no increase in intrinsic blur in the brain when the amblyopic eye was being tested. We can see on Figure 7 below that there is a tendency for the hydrant image to be worse than the other stimuli in both eyes. We could therefore infer that the hydrant image created as much intrinsic blur in the brain when the fellow eye was being tested than when the amblyopic eye was being tested, resulting in no significance between both eyes.



**Figure 7.** Blur discrimination thresholds averaged across subjects for each eye condition and for each stimulus. This figure shows the fit that was done on those averages. The x axis corresponds to the blur reference in arc minutes and the y axis corresponds to the discrimination threshold, that is, the amount of additional blur needed in the test image in order to distinguish it from the reference image.

## Correlation between $\beta$ , $\omega$ and Severity of Deficits

A Spearman's rank-order correlation test was run to determine the relationship between the amblyopic subject's visual acuity deficit (measured in terms of their visual acuity difference between the amblyopic and the fellow-fixing eye, in logMAR units) and their mean  $\beta$  parameter difference (difference in intrinsic blur between both eyes) estimated from the dipper function fits to the thresholds aggregated across all natural images. There was a significant negative correlation between the visual acuity deficit and intrinsic blur ( $r_s = -0.638$ ,  $p = 0.035$ ). The same test was conducted to look at the relationship between the amblyopic subject's visual acuity deficit and their mean  $\omega$  parameter difference (difference in sensitivity to blur between the two eyes). Again, a significant negative correlation was also found between visual acuity deficit and sensitivity, which was statistically significant ( $r_s = -0.619$ ,  $p = 0.042$ ). The difference in visual acuity between the amblyopic eye and the fellow eye is therefore correlated with the differences in intrinsic blur and sensitivity, such that as the severity in amblyopia increased, the difference in intrinsic blur and in sensitivity also increased between the eyes. This analysis lends support to our hypothesis that the blur discrimination differences are related to the amblyopic deficit, because they appear to be modulated by the intensity of the deficit.

## Discussion

### Intrinsic Blur in Amblyopia

We found that as a consequence of the neural deficit in amblyopia, the visual system will exhibit an increased level of intrinsic blur when the amblyopic eye is stimulated, compared to

when the fellow eye, or the eyes of healthy control subjects are stimulated. These results therefore support models of amblyopia based on intrinsic blur over models based on spatial scrambling. This higher level of intrinsic blur in the brain, as indicated by a higher  $\beta$  parameter, occurred when the amblyopic eye was being tested on almost all the natural images. The only exception was the hydrant image (see Figure 1 – image 4), for which no significant difference in the level of intrinsic blur was found between the two eyes of the amblyopic group. However, this lack of difference between the two eyes does not mean a lower level of intrinsic blur in the brain when the amblyopic eye was being tested on this image. The hydrant image created as much intrinsic blur in the brain when the fellow eye was tested than when the amblyopic eye was tested, as these comparable estimates between the two eyes were significantly higher compared to the edge (data not shown). In the case of the edge stimulus, when looking separately at the means (of the  $\beta$  parameter), both eyes showed low levels of intrinsic blur compared to the hydrant image.

While it is possible that the lack of difference in response to the edge is due to the amount of data (i.e., the data from four images were combined, but there was only one edge stimulus), this is an unlikely explanation—even in post-hoc comparisons, we found the amblyopic eye to exhibit greater intrinsic blur for three of four images individually. Thus, it is more likely that natural images are more effective at revealing intrinsic blur than synthetic edges.

We also found that the estimated parameters were related to the amblyopic deficit, as manifested by significant correlations between the logMAR acuity difference and the magnitude of the eye effects on the dipper function parameters. These results suggest that not only is blur perception for natural images affected in amblyopia, but it is modulated by the magnitude of the deficit.



## **Comparisons to Other Blur Discrimination Studies**

Watson & Ahumada (2011) reviewed several studies on blur perception that used the Weber model to fit their data. Paakkonen & Morgan (1994) tested normal subjects and found a level of intrinsic blur (dip value) at about 0.5-0.7 arcmin. Wuerger et al. (2001) also tested normal subjects and found a level of intrinsic blur at about 1.2 arcmin. Simmers, Bex & Hess (2003) tested each eye of both normal and amblyopic subjects and found a similar level of intrinsic blur of about 3-4 arcmin in both groups. As in Simmers, Bex & Hess (2003), we tested each eye of both amblyopic and normal groups. We found a level of intrinsic blur of about 1.57 arcmin for the fellow eye and of 2.11 arcmin for the amblyopic eye of the amblyopic group, and a level of intrinsic blur of 1.78 arcmin for the dominant eye and of 2.28 arcmin for the non-dominant eye of the normal group, when tested on the edge stimuli. However, those differences did not reach significance, and as also found by Simmers, Bex & Hess (2003), we concluded that there was no difference in intrinsic blur between each eye of both normal and amblyopic groups for the edge stimulus.

It is difficult to compare our data on image blur discrimination to previous studies, as no such experiment was done in the amblyopic population. Sebastian, Burge & Geisler (2015) used natural optics to test defocus blur discrimination in natural images however, they only tested in the normal population and used defocus blur, which can lead to different results than on-screen blur.

## **Model Comparison and Clinical Types of Amblyopia**

It is important to mention that this blur discrimination experiment was conducted among different types of amblyopes. Because it is still unclear whether the performance discrepancies found in the types of amblyopia are due to developmental or mechanistic differences (Levi &

Klein, 1990, McKee, Levi & Movshon, 2003, Birch & Swanson, 2000), there is no consensus in the literature as how to approach this clinical population. As discussed in the introduction, Watt & Hess (1987) conducted their study on anisometric amblyopes, Levi & Klein (1990) on anisometric, strabismic and mixed amblyopes, but analyzed data from each category separately, and Simmers, Bex & Hess (2003) based their analysis across all different types of amblyopes. It is therefore hard to compare the conclusions from each study as they used different types of amblyopic subjects and grouped them in different ways. As mentioned in the introduction, several theories about how to model the internal error in amblyopia were developed with the goal of having a deeper understanding of its mechanisms. Most of the theories can fit into two main models: intrinsic blur and local spatial scrambling.

Watt & Hess (1987) believed that this internal error could be explained, not by raised amounts of intrinsic blur, but by increased spatial scrambling (distorted spatial representations in the visual space) which would imply an elevated degree of relative positional uncertainty in the visual system of anisometric amblyopes.

Simmers, Bex & Hess (2003) failed to find any difference in intrinsic blur between the amblyopic and the fellow eye, as well as between the amblyopic eye and the eyes of control subjects. They also found that amblyopes were able to match edges with spatial frequencies that were beyond their resolution limit. As Watt & Hess (1987), they therefore favored the local spatial scrambling hypothesis, because according to them, a scrambled edge should retain more information and global statistics than an undersampled one (Simmer, Bex & Hess, 2003). However, as opposed to Watt & Hess (1987) and Levi & Klein (1990) they tested subjects from the three subdiagnostics of amblyopia (strabismic, anisometric and mixed) and did not differentiate between the different types of amblyopes when they analyzed their data.

Levi & Klein (1990) believed that while anisometric and strabismic amblyopes could be modeled based on increased levels of intrinsic blur, the former could be explained by reduced contrast sensitivity of the high spatial frequency filters, while the latter could be explained by undersampling (Levi & Klein, 1990). Levi & Klein (1990) also believed that positional uncertainty in amblyopes could be explained not by spatial scrambling, but by heightened levels of intrinsic blur due to undersampling. As opposed to the previous authors, Levi & Klein (1990) tested both strabismic and anisometric amblyopes but conducted their analysis on each category separately.

Following Simmers, Bex & Hess (2003), we also conducted our analysis on the three subtypes of amblyopia (strabismic, anisometric and mixed) without differentiating each category, making it hard to compare our results to Levi & Klein (1990) or to Watt & Hess (1987). However, having more strabismic amblyopes than anisometric amblyopes, and having shown that there is an increase in intrinsic blur in the amblyopic visual system, my results would still be more comparable to Levi & Klein (1989)'s results about heightened levels of intrinsic blur in strabismic amblyopes. It is possible that intrinsic blur would be a more adequate model for a particular subtype of amblyopia such as strabismic. That being said, my results show that this increased level in intrinsic blur is only found when amblyopes are tested on natural images, not on synthetic edges, which could explain why Watt and Hess (1987) didn't find heightened levels of intrinsic blur if natural images are more effective at revealing intrinsic blur differences. In light of the previous literature, it seems that both the population sampling and the stimuli choice have a consequence on the type of model that fits the deficits of amblyopia.

## **Parvocellular Pathway Impaired in Amblyopia**

As mentioned in the introduction, edges and natural images differ in their characteristics. It is therefore not surprising that they yield different results. The increase in intrinsic blur in the visual system when the amblyopic eye is being tested on natural images, but not on the edge may be explained by the study of Hendrickson, Movshon & al (1987). They induced blur by depriving young macaque monkeys of vision in one eye and studied its effect on their visual system. More specifically, they assessed the consequences on the eye dominance of cortical neurons, on the spatial characteristics of the neuron's receptive fields, as well as on the functions of the visual pathways (Hendrickson, Movshon & al., 1987). Anatomically, they found that the cortical cells that were dominated by the deprived eye had a reduction in spatial resolution and in contrast sensitivity, compared to the non-deprived eye that had higher optimal spatial frequencies (Hendrickson, Movshon & al., 1987). They also observed a change in parvocellular cell size and parvocellular cells' distribution, which suggested that the parvocellular pathway was being more affected by the deprivation than the magnocellular pathway (Hendrickson, Movshon & al, 1987). This finding is consistent with other studies that claimed that the magnocellular pathway was relatively spared in amblyopia (Mullen, Sankeralli, Hess, 1996; Kubova, Kuba, Blakemore, 1996; Hess, Anderson, 1993; Demirci, Gezer, Sezen, Ovali & al., 2002).

Parvocellular neurons relay information about fine spatial details and chromatic content to the cortex (Merigan, 1989; Atkinson, 1992; Derington & Lennie, 1984; Kaplan, 2004), whereas magnocellular neurons relay information about lower spatial frequencies, temporal content, achromatic content and contrast detection, and are used to detect changes in luminance, as well as edges (Cheng, Eysel, Vidyasagar TR, 2004; Wolf, Arden, 1996; Kubova, Kuba, Blakemore, 1996). The finding that an increase in intrinsic blur is seen in response to amblyopic-eye stimulation when

subjects are tested on natural images—but not on edges—is consistent with the anatomical changes observed in macaque monkeys seen in Hendrickson, Movshon & al (1987) study. Intrinsic blur is believed to be due to the malfunction of the high spatial frequency filters (Levi & Klein, 1990) in the brain which are found in the parvocellular pathway. Those cells also convey information about chromaticity. It therefore makes sense that there is more intrinsic blur in the brain when the amblyopic eye is being tested on natural, color images, as they contain more high spatial frequency and chromatic information compared to synthetic black-and-white edges, and as the parvocellular pathway which processes this type of information is impaired in amblyopia.

### **Natural Images vs. Synthetic Edge in the Normal Group**

In a separate analysis we also looked at whether this difference in intrinsic blur between stimulus type would hold when looking at the normal group (See Figure 8 in Appendix). As for amblyopes, we found that intrinsic blur was higher when tested on natural images compared to when tested on the edge. This finding is quite surprising as it is believed that the normal visual system should be optimized to process natural images, since the spatial organization of the neuron's receptive fields, as well as the tuning characteristics of its individual channels, seem to match the spatial features of the stimuli that are found in the natural environment (Sutherland, 1982; Barlow, 1961; Laughlin, 1983; Hancock, Baddeley & Smith, 1992; Olshausen & Field, 1997; Srinivasan, Laughlin, & Dubs, 1982). One possible explanation for this latter finding might be that as images contain more high spatial frequencies—that is, finer and more numerous details scattered throughout the image than in a single synthetic edge—the process of blurring the natural images could render the perception noisier than when looking at a single edge. This more dramatic

alteration of the proportions of the power spectrum than in the case of the simple edge, would therefore explain higher levels of intrinsic blur in the normal group.

## **Justification for the Choice of Model**

We chose the Weber model as it has been widely replicated in previous blur discrimination experiments (Mather & Smith, 2002; Paakkonen & Morgan, 1994; Watt, 1988 and Wuerger et al., 2001), as well as because the roots of this model are based on the concept of intrinsic blur. According to this model, perceived blur results from an intrinsic blur and an external image blur (Watson & Ahumada, 2011). Intrinsic blur is given by the  $\beta$  parameter, which allows us to directly compare the amount of intrinsic blur between groups when performing statistical analysis on this parameter. One criticism of this model is that contrast has not been considered when looking at the variations in blur discrimination thresholds (Watson & Ahumada, 2011).

Other models have been used to explain blur discrimination data with the advantage of being based on existing models of contrast discrimination, such as the visible contrast energy (ViCE) model. In the ViCE model, two blurred edges will be discriminated when “the contrast energy of the difference between those two edges, after filtering by the contrast sensitivity function, will be equal to a criterion value” (Watson & Ahumada, 2011). This model basically sees the dipper function as a direct consequence of the contrast sensitivity function, whereby blur discrimination thresholds are elevated (lower performance) at both ends of the range of reference blurs due to our lower contrast sensitivity for very high and low spatial frequencies. Following the same logic, the low blur discrimination thresholds (higher performance) forming the dip result from our higher contrast sensitivity to medium spatial frequencies (Watson & Ahumada, 2011;

Barten, 1999). Advocates of this model believe that there is no need to use concepts such as intrinsic blur to explain the shape of the dipper and the blur discrimination behavior (Watson & Ahumada, 2005).

The MIRAGE model is another model that was developed based on computational models that tried to reproduce human blur discrimination performance with noise. They believed that edge blur discrimination resembled a spatial interval discrimination task in which “the cue is the spatial separation between stationary points in the second spatial derivative of the blurred edge” (Morgan, 2017). It was therefore thought that the positional uncertainty of those second derivatives was the result of increased noise in the visual system, probably due to undersampling (Morgan, 2017).

As we have seen, different blur discrimination models are based on different theories about the underlying factors behind the dipper function. The Weber model believes that it can be explained by raised amount of intrinsic blur. The ViCE model believes that the dipper shape is a direct consequence of the contrast sensitivity function. And the MIRAGE model believes that it has to do with increased internal noise. However, it is important to point out that all these models are not necessarily distinct from each other, as increased noise could result in both heightened amount of intrinsic blur in the visual system, as well as contrast sensitivity losses.

## **Contrast as the Critical Feature?**

As the Weber model does not consider contrast sensitivity across spatial frequencies when looking at the variations in blur discrimination thresholds and as we did not randomize the level of contrast when testing the images, it could be argued that amblyopes were using contrast as a

cue, making this task a contrast perception task, not a blur discrimination task. The reason why we chose to not randomly alter the level of contrast in our images is because doing so would alter the perception of blur—low contrast alone results in a wash-out effect on images, which makes them appear “hazy”, which is also confused with “blur”—and that it would therefore influence performance on the blur discrimination task. Even if contrast and blur are technically two different things (contrast has to do with the range of brightness in an image, whereas blur has to do with the width of transition from one shade to another) we found that the resulting perception of blur after manipulating the contrast on the images was impeded such that for example, if the contrast was lowered, it was perceived as an increase in blur. Therefore, instead of randomizing contrast level, we rotated the image pairs such that local edges could not be readily matched between the pairs, effectively preventing subjects from using local contrast as a cue. This meant that on a given trial, the image shown on the right would be rotated to one orientation (e.g. 45°), while the image on the left would be rotated to a different orientation (e.g. 90°), and on another trial the rotations would be randomly different (see Figure 3). This would therefore force subjects to look at the image as a whole and to prevent them from comparing the same image location in the two images to match local contrast.

If the task was based on contrast, the expected effect would be a decreased performance selectively in the low reference blur range, given the deficit of amblyopes for high spatial frequency. Our pattern of results does not support that, as the decreased performance are found across all reference blurs (as shown by a significant difference in  $\omega$  parameter). Purely contrast-related effects are therefore unlikely to explain our results.

When looking at the normal and amblyopic group data but this time for the edge only (Figure 5C and 5D), the statistical analysis indicates that there are no significant differences



between the amblyopic eye and the fellow eye, as well as between the dominant and non-dominant eye. Again, it is unlikely that contrast was used as a cue, as this putative “cue” would have been present in all the stimuli—the fact that the differences are unique to the natural images would suggest that use of contrast cues could not explain the pattern of results. Furthermore, we found that the effect size was different for different images (i.e., even absent in the case of the hydrant image), and these variations could not be explained by putative contrast differences being used as a cue. Said another way, if contrast was used as a cue, then we should have observed a comparable effect across all stimuli because the “contrast hypothesis” does not consider image structure or chromaticity. The fact that we observed a modulation of the dipper functions across the different images suggest that subjects performed the task utilizing blur, which had a differential effect in the different natural images because of their content and structure.

## **Clinical Implications for Amblyopia**

### **Suppression and Problems with Patching Therapy**

It has been thought that suppression is a consequence of the poor reliability of the amblyopic eye signals. Since the entire retina of the amblyopic eye is a poor source of input, its signals were thought to be completely attenuated or suppressed (Leonards, U., & Sireteanu, R., 1993; Baker, D. H., Meese, T. S., & Hess, R. F., 2008; Levi, D. M., & Harwerth, R. S., 1977; Hess, R. F., & Thompson, B., 2015; Levi & Klein, 2003; Hess, R. F., Thompson, B., & Baker, D. H., 2014; Li, J., Thompson, et al., 2011). This “attenuation hypothesis” constitutes the rationale behind patching therapy. This therapy is one of the most common treatment and consists of patching the fellow eye to force the amblyopic eye to improve (Ciuffreda, Levi & Selenow, 1991). However, this procedure has seen mixed results, with an improvement of monocular vision for amblyopic

children aged less than 12 years, but with no results in improved binocular function (Epelbaum, Buisseret & Dufier, 1993; Dixon-Woods, Awan & Gottlob, 2006). The “attenuation hypothesis” is challenged, not only due to the poor outcome of the patching therapy, but also because while the perception of fine details (i.e. high spatial frequencies) is affected in amblyopia (Hess, Pointer, Simmers & Bex, 2003; Simmers, Bex & Hess, 2003), perception of low spatial frequencies remains normal, and our results mimic this difference (no significant difference in  $\omega$  parameter for each stimuli tested). Amblyopic patients can even paradoxically perceive the sharpness of edges presented in the amblyopic eye despite its poor visual acuity (Simmers, Bex & Hess, 2003). It therefore seems that the amblyopic signals are not being suppressed by the fellow eye, but that its corrupt signals are being compensated for in some way.

### Efficient Coding and Adaptive Strategies

Demirci et al. (2002) believed that information treated by the parvocellular pathway should result in increased erroneous information through the amblyopic eye, and that they might therefore need to develop a technique to interpret what they see despite this degraded and unreliable information. One possibility is based on the concept of efficient coding, which is a mechanism that the brain uses by learning the correlations of natural scene features to be more efficient when processing visual information (Dan, Atick & Reid, 1996; Olshausen & Field, 1996). In other words, this system creates a code which allows you to represent visual signals more easily and reliably.

Farivar et al (2017) assessed the relationship between the joint representation of spatial frequency and phase information—phase information is directly related to the structure of the image. They found that the early visual cortex was more sensitive to phase-alignment, particularly

for high spatial frequencies, and they believe that this bias may represent a preference for representation of edges and contours. Based on the concept of efficient coding, it is inferred that a code could be used to predict high spatial frequencies simply from the phase-alignment of other adjacent high spatial frequency components.

We speculate that the amblyopic eye could predict high spatial frequencies based on the fellow eye's unaffected experience by learning the correlated features of a scene and using this information to either supplement missing information in the percept, or to overcome noisy components in a scene (i.e. high spatial frequencies). Amblyopia affects 1 to 4% (Levi, Knill & Bavelier, 2015) of the population and its treatment has lacked a principled approach. This adaptive compensator explanation could further our understanding of the neurophysiological mechanisms of amblyopia and could bring us closer to successful treatment.

## **Limitations of the Study**

While four stimuli were used to make up the natural image category, only one stimulus was used for the edge category. As the data from the four images were combined, having more edge stimuli would have allowed us to compare averages and increase statistical power.

As mentioned earlier, mixing all three subtypes of amblyopia (strabismic, anisometric, mixed) and conducting our analysis without differentiating each category is another limitation of this study. In future experiments, it would be interesting to separate each subtype to see whether it would yield different pattern of results that are specific to each category.

It could have been argued that the large age range between amblyopic subjects (22-65 years old) could have influenced the results of this study. However, there is no relationship between age

and the severity of amblyopia after a certain age (about 12 years old) (Donahue, 2006). There is a relationship between age and the magnitude of treatment response with subjects being more responsive to treatment before 7 years old (Holmes et al., 2011; Williams, et al., 2002). Therefore, whether those subjects have received treatment during this critical period could have more impact on the results of this study than the actual age range between subjects.

## **Conclusion**

The aim of this study was to measure the perception of blur added to natural images in amblyopia and to compare it to edge blur discrimination performance in both normal and amblyopic groups. We have found that vision through the amblyopic eye is affected by a higher level of intrinsic blur in the visual system compared to the fellow-fixing eye or to normal eyes. The fact that this effect was only seen in natural images, but not in edges, hints at the need for more generalizable stimuli and procedures in psychophysics in general and shows that blur perception differs between synthetic and natural stimuli in amblyopia. This could result from the bigger impact that the disruption in binocular vision has on the parvocellular pathway than on the magnocellular pathway. Amblyopes might be using adaptive strategies to overcome noisy information processed in the parvocellular pathway. However, more research will be needed to draw any solid mechanistic conclusions. For future directions, it would be good to test isochromatic edges as well as black and white images to see if those results can be generalized to the impairment of the parvocellular pathway in amblyopia.

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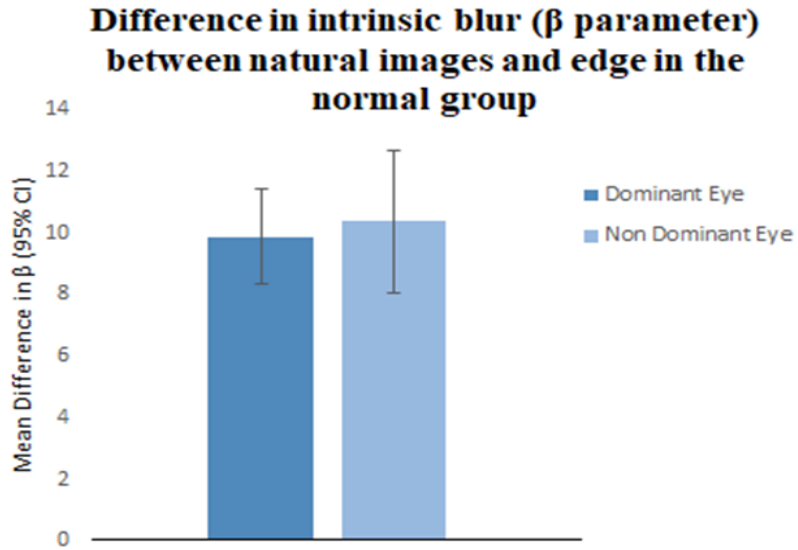
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# APPENDIX



**Figure 8.** Mean differences in intrinsic blur ( $\beta$  parameter) between natural images (average of the four natural images) and the edge when tested with the dominant and the non-dominant eye of the control group. More positive values reflect higher levels of intrinsic blur when tested on natural images. Error bars reflect 95% confidence intervals.