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How Visual Cortical Organization Is Altered by Ophthalmologic and Neurologic Disorders

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Abstract

Receptive fields are a core property of cortical organization. Modern neuroimaging allows routine access to visual population receptive fields (pRFs), enabling investigations of clinical disorders. Yet how the underlying neural circuitry operates is controversial. The controversy surrounds observations that measurements of pRFs can change in healthy adults as well as in patients with a range of ophthalmological and neurological disorders. The debate relates to the balance between plasticity and stability of the underlying neural circuitry. We propose that to move the debate forward, the field needs to define the implied mechanism. First, we review the pRF changes in both healthy subjects and those with clinical disorders. Then, we propose a computational model that describes how pRFs can change in healthy humans. We assert that we can correctly interpret the pRF changes in clinical disorders only if we establish the capabilities and limitations of pRF dynamics in healthy humans with mechanistic models that provide quantitative predictions.

INTRODUCTION

The visual cortex is organized at different spatial scales, ranging from the few micrometers of an individual neuron (microscopic scale), to cortical columns and layers at the millimeter scale (mesoscopic scale), and to the several centimeters covered by visual field maps, large-scale regions of functional specialization, and white matter tracts (macroscopic scale).

Ophthalmological and neurological disorders can alter cortical organization at any of these spatial scales. Moreover, these changes are not necessarily independent. For example, visual pathway disorders, such as achiasma, affect the connection between the eye and brain and lead to different columnar and visual field map organization (Hoffmann et al. 2012, Olman et al. 2016, Victor et al. 2000). In another example, polymicrogyria can alter the organization of cortical layering (Dumoulin et al. 2007). Surprisingly, in both achiasma and polymicrogyria, daily visual functioning is normal, suggesting that these different organizations do not necessarily impact function. This suggests a dissociation between alterations in cortical organization and their consequences for visual perception.

Here, we focus on a fundamental feature of sensory neural organization shared at all spatial scales [i.e., the notion of the receptive field (RF)]. The RF refers to the pattern of inputs in the sensory organ that a given neuron processes. In the visual system, this pattern is most commonly defined as the region of visual space but can also be defined in terms of other visual dimensions, such as orientation or color. Furthermore, the RF also exists in other sensory modalities—for example, in terms of auditory frequency or somatotopic location. Extending this notion of the neuronal receptive field, the population receptive field (pRF) then refers to the aggregate RF properties of a group of neurons.

The pRF concept is derived from invasive animal neurophysiological recordings (Jancke et al. 2004, Victor et al. 1994) but has been ported to human neuroimaging techniques (Dumoulin & Wandell 2008). The most widely used human neuroimaging technique is functional magnetic resonance imaging (fMRI), and consequently, the pRF has also been referred to as voxel RF, where a voxel refers to the volume element or basic unit of the MRI reconstruction. However, human pRF measurements are not limited to fMRI, as pRF properties have also been visualized with human intracranial electrodes (Harvey et al. 2013b, Winawer & Parvizi 2016, Winawer et al. 2013, Yoshor et al. 2007) and magnetoencephalography (MEG) (Nasiotis et al. 2017).

The ability to measure pRFs using human neuroimaging techniques has opened the window to study pRF properties in a wide range of ophthalmologic and neurologic diseases, which, as we discuss below, show changes in pRF properties. However, as many factors can lead to a change in the pRF properties, these changes are not always trivial to interpret.

Using different stimuli and tasks can also yield different pRF properties in healthy adults. That is, pRF properties can vary in both health and disease. Importantly, the different pRF properties are not due to instability of the pRF method, as they have proven stable, robust, and reproducible under identical conditions (Senden et al. 2014, van Dijk et al. 2016). On one hand, the notion that pRF properties can change even in healthy adults is surprising, because it appears to suggest that the connections between the eye and brain can change. It is further surprising because changing pRF properties break labeled-line coding; in other words, downstream brain areas can no longer be certain what region of the visual scene the information comes from. This is akin to changing the carpet that all else stands upon. On the other hand, our world is dynamic and change is constant. Information varies from environment to environment, and task demands change which information is relevant moment to moment. Thus, a dynamic world requires a dynamic brain—and therefore, dynamic pRFs too.

We assert that we can correctly interpret the pRF changes in clinical disorders only if we establish the capabilities and limitations of pRF dynamics in healthy humans with mechanistic models that provide quantitative predictions (Wandell & Winawer 2015). We propose such a mechanistic model that captures and guides experiments in order to understand changes in human pRF properties. This model will guide further experiments, and in turn the model will be refined as data accumulate. The advantage of model building is that the model that accounts for a broad range of measurements will represent valuable information about the mechanisms underlying pRF dynamics even if the model is incomplete.

In this review, we discuss how neurologic and ophthalmologic disorders can alter pRF properties. First, we review changes of pRF properties in clinical disorders, and following that, we review how pRF properties can change in healthy subjects. Then, we propose a mathematical model that describes how pRFs can alter in healthy conditions. We propose that this model can also be used to guide clinical measurements. Last, we discuss outstanding questions and how such a model-based approach can help to use population-level recordings to infer neural mechanisms.

MEASURING pRFs IN HUMANS

The pRF approach constitutes both a concept and method. The pRF concept is derived from invasive animal research (Jancke et al. 2004, Victor et al. 1994) where a pRF described the average RF of a whole population of neurons at a single measurement location. The method is inspired by prior observations that neuroimaging signals carry information regarding pRF properties (Larsson & Heeger 2006, Li et al. 2007, Smith et al. 2001, Tootell et al. 1997).

The basic pRF analysis is as follows (Dumoulin & Wandell 2008). We define a neural pRF model that summarizes the part of the visual field that the pRF processes (**Figure 1*a***). Next, we predict the fMRI response by a multiplication of the pRF model with the stimulus sequence that varies over space and time and convolve this neural model time course with the hemodynamic response function. We vary the parameters of the neural model, and the optimal model parameters are estimated by minimizing the residual sum-of-squared differences between the predicted and measured fMRI time series, allowing for a scale factor (**Figure 1*b***). We do this for every cortical location. In this type of analysis, the output of the fMRI data analysis is the model parameters. This method has been successfully applied in many fMRI studies and human intracranial electrodes studies. Model parameters of pRFs provide rich information on pRF properties, including on position (Dumoulin & Wandell 2008), size (Dumoulin & Wandell 2008), surround (Harvey et al. 2013b, Zuiderbaan et al. 2012), spatial summation (Kay et al. 2013), cortical representation (Harvey & Dumoulin 2011), and connectivity (Haak et al. 2013).

Variations of pRF size, as estimated using fMRI, show similar trends as the RF estimates from electrophysiological studies (Dumoulin & Wandell 2008, Fracasso et al. 2016b, Kay et al. 2008, Self et al. 2018). There are large differences between different visual field maps, but also within each visual field map, pRF size increases as a function of eccentricity (**Figure 1*c***). These pRF size changes across the visual cortex are reminiscent of a hierarchical organization of the visual field maps in nonhuman primates (Van Essen & Maunsell 1983). The quantitative pRF size estimates are comparable to estimates from human intracranial electrodes (Harvey et al. 2013b, Yoshor et al. 2007) and subjective experience (Winawer & Parvizi 2016).

Traditional stimuli that were used for retinotopic mapping were wedge- or circular-shaped, contrast-defined stimuli, which would cycle through visual space in a periodic fashion (Engel et al. 1994, Sereno et al. 1995). This encodes the pRF position by the response phase of a given cortical location. This simple repetitive stimulus resides in one corner of a space of experimental designs. The opposite corner of this space is occupied by experimental designs that employ extremely rich

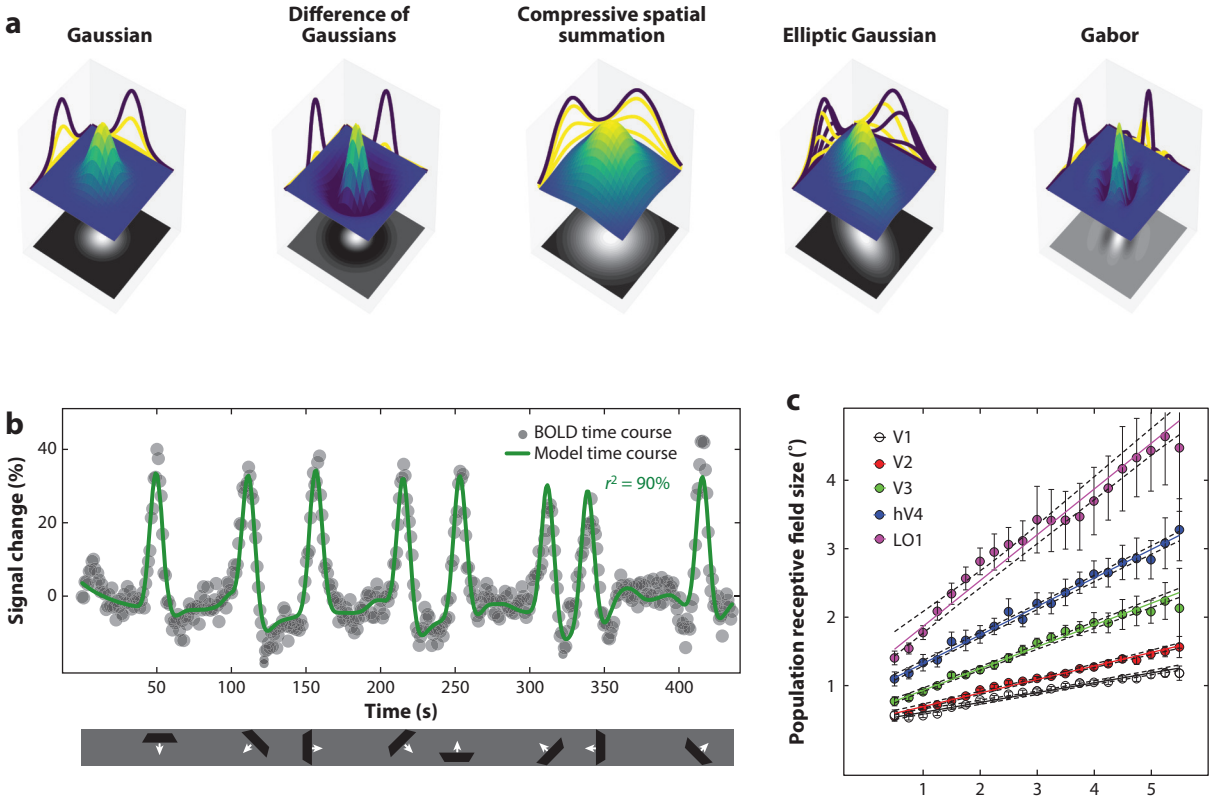

Figure 1

Population receptive field (pRF) models, analysis, and results. (*a*) Different spatial functions have been used to model pRFs. The simplest form is that of a single isotropic two-dimensional Gaussian. This function has three spatial parameters—the *x* and *y* locations of its peak and its width. This simple model has been extended to include suppressive surrounds, compressive spatial summation, and elliptic shapes. On the other end of the spectrum, the pRF has been modeled as a combination of multiple Gabors (Gabor wavelet pyramid). (*b*) BOLD (blood-oxygen-level dependent) time course and best-fitting compressive spatial summation–pRF prediction. The typical pRF mapping experiment features a bar moving through the visual field in different directions (see *bottom panel*). The pRF prediction explains 90% of the variance (r^2). (*c*) pRFs mirror underlying neuronal RFs. The size of pRFs increases with pRF eccentricity within a given visual field map. Furthermore, across the visual field maps, pRF size increases from V1 upward. Both these relations mirror the underlying neuronal RFs, known from single-cell neurophysiology (adapted from Harvey & Dumoulin 2011). Abbreviations: hV4, human visual area 4; LO1, lateral occipital area 1.

stimuli, such as naturalistic images and movies, that are presented only once (Kay et al. 2008). Experimental designs used most for pRF reconstructions lie in between these spaces and typically consist of translating bar stimuli with explicit baseline periods (**Figure 1*b***) (Dumoulin & Wandell 2008), which is necessary to distill pRF parameters, such as size, or surround and compressive nonlinearity parameters. These stimuli are then usually repeatedly presented in multiple runs during one scanning session and averaged. Depending on experimental questions and constraints, the stimuli can be made progressively more complex (Binda et al. 2013, Vanni et al. 2005) or be simplified (Fracasso et al. 2016b).

The experimenter's choice of stimulus can affect the ability to measure specific pRFs. For example, for situations involving retinal lesions, Binda and colleagues (2013) argued that the predictability of the stimuli may be a potential confound, where spatiotemporal nonlinearities,

expectation, and neural filling in can affect responses. Traditional wedges and rings, as well as bar stimuli, have predictable stimulus orders. They favored the randomized multifocal sequences that allowed for more accurate simulated lesion reconstruction presumably because of the lack of predictability. Given more current results of the effect of spatial attention on the pRF properties reviewed in the section titled Cognitive Contributions, a predictable stimulus may invoke attentional mechanisms that follow the stimulus sequence and hence affect the pRF measurements. However, using randomized multifocal sequences comes at decreased signal-to-noise ratios, especially at later visual areas with larger pRFs. This may be in part remedied by collecting more data, but this is not always feasible in patients. A more systematic limitation is that randomized sequences distribute their energy more homogeneously across the visual field, thereby continuously stimulating or suppressing larger pRFs (Tootell et al. 1997). So the inability to reconstruct larger pRFs will be inherent to certain stimulus designs.

Regardless of stimulus design, pRF analysis relates the retinal position of a visual stimulus to the recorded brain responses. Eye movements rapidly change the position of the visual stimulus on the retina. This means that when a participant makes eye movements unbeknownst to the experimenter, this can severely impact results in a pRF mapping experiment. The effects eye movements have on pRF parameters depend on the specific eye movements, but a general result of repeated eye movements in random directions is that this will increase spatial variability of retinal stimulus position and thus result in globally increased pRF size estimates (Hummer et al. 2016, Klein et al. 2014, Levin et al. 2010). Therefore, to interpret global changes in pRF size, one needs to rule out any impact of eye movements on pRF size estimates. This is especially important in clinical populations, since the neural effects of a clinical disorder may also be a global increase in pRF size. When eye movements have been recorded during scanning, correcting for the effects of these eye movements in a post-hoc fashion is possible (Hummer et al. 2016). By translating the visual stimulus sequence with the eye movements, we can essentially subtract the retinal influences of eye movements. This operation can improve the consistency of pRF estimates contaminated by eye movements.

We can estimate pRF properties with or without explicit biologically inspired models about the shape or response properties of the pRF. The most basic model of the shape of the pRF is a Gaussian function (see **Figure 1*a***). The x, y, and standard deviation parameters of the Gaussian function can then be fit to the signal time course by a least squares optimization, using brute-force fitting, gradient descent, Bayesian methods, or a combination. Increasing model complexity—for instance, by adding a surround, compressive nonlinearity, nonisotropic shape, or orientation selectivity—then adds parameters to this fitting procedure. This approach has the advantage of the parameters being readily interpretable, and the parameters can easily be related to the results of simulations (Kay et al. 2013, Klein et al. 2014, van Es et al. 2018). At the other end of the spectrum is the model consisting of a Gabor wavelet pyramid (Kay et al. 2008, Nishimoto et al. 2011). In this case, the number of model parameters is often very large and exceeds the amount of independent measurements, which necessitates the use of penalized regression techniques. Alternative approaches do not assume a specific parameterized pRF description but rather fits weights to each element of the space of interest—for example, pixels in visual space (Greene et al. 2014, Lee et al. 2013). By and large, procedures that do not rely on a specific shape of the pRF have shown that the assumption of Gaussian pRF shape is valid (Greene et al. 2014, Lee et al. 2013). However, if one has reason to believe the Gaussian assumption to be invalid, as in certain clinical conditions (Hoffmann et al. 2012), alternative procedures can provide necessary additional flexibility for exploratory data analysis.

A single pRF represents processing in a circumscribed region of visual space; if a high-contrast stimulus is presented there, the response of the neural population will be high. The pattern of

activity across different pRFs provides information on the incident visual image and can therefore be used to "decode" visual content (Kay et al. 2008, Thirion et al. 2006, Zuiderbaan et al. 2017). As a method for decoding, it has several advantages over so-called classification-based decoding methods. In classification-based decoding, activation patterns are used to train a classification algorithm, which is then used to predict cognitive states from out-of-set activation patterns (Haxby et al. 2001). In this type of analysis, there is no regard for the features that allow for classification, which creates interpretative ambiguities (Naselaris & Kay 2015). Using pRF estimates alleviates these problems because the pRF analysis provides an explicit model of the features through which visual information is encoded, and this model is known and constructed by the researcher. This allows decoding of any image, even those images that the encoding model has not been trained on.

Extending this decoding further, pRFs can also be used to visualize the pattern of activation in visual rather than cortical space (i.e., we may reconstruct visual images and movies from brain activations) (Miyawaki et al. 2008, Nishimoto et al. 2011, Sprague & Serences 2013, van Gerven 2017). One of the advantages of this approach is that it can be used to pool information across recording sessions and subjects into a single visual field representation. This can increase signal to noise and may facilitate analysis of visual information processing on a per-trial basis. In the most basic application of this technique, the encoding model supplies a projection matrix that allows the depiction of cortical responses in visual coordinates (Knapen et al. 2016, Sprague & Serences 2013, Zipser 2017). When cortical responses in visual space are construed in a Bayesian framework, this allows the incorporation of priors on the distribution of stimuli in order to shape the reconstructions (Schoenmakers et al. 2013). More sophisticated uses of explicit encoding models in decoding allow one to explicitly calculate the probability distribution over all possible stimuli, given a pattern of cortical responses. This distribution can then be related to perceptual characteristics. For example, the width of this reconstruction has been shown to provide an index of sensory uncertainty in the orientation domain (van Bergen et al. 2015). We suggest that this common reference frame of visual space allows reconstructions to play an important Rosetta Stone role in future work. For instance, reconstruction provides us with a common reference frame for the comparison of visual processing in different regions in the visual cortex and different experimental conditions. Visual-space reconstructions can even be used to draw together pRF-based recordings from different measurement modalities and facilitate their comparison with modeling results.

pRF CHANGES IN OPHTHALMOLOGICAL AND NEUROLOGICAL DISORDERS

In the following sections, we review how ophthalmological and neurological disorders can alter pRF properties.

Ophthalmological Disorders

Retinal lesions. The study of how receptive fields and cortical visual organization are altered was pioneered using invasive nonhuman animal neurophysiology. In these cases, the retina is experimentally lesioned and is, as such, not the consequence of a disorder. There is a large and lively debate regarding these experiments, which are covered in several review articles (Gilbert et al. 1996, Wandell & Smirnakis 2009). We briefly review the main arguments, as they are relevant for how pRF changes may follow disorder-induced retinal lesions.

Gilbert & Wiesel (1992) noted remarkable RF changes in adult V1 following experimentally induced damage to the retina (**Figure 1*a***). They found that neurons with RFs near the edge of the

lesion projection zone increase their RF sizes, whereas neurons initially silenced by the lesion can recover with their RFs now representing visual field locations surrounding the lesion projection zone. They suggested that the movement of RFs indicated a reorganization of the RF properties that were most likely due to synaptic changes intrinsic to the cortex.

This conclusion was strongly contended in a combined fMRI and neurophysiological study (Smirnakis et al. 2005a), sparking a passionate debate (Calford et al. 2005, Sereno 2005, Smirnakis et al. 2005b). Smirnakis and colleagues found that adult macaque V1 does not approach normal responsivity during 7.5 months of follow up after retinal lesions and that visual-field-maps representation does not change. They suggested that the reported RF changes may be restricted to a few sparsely distributed neurons sampled in previous neurophysiological experiments and may reflect activity arising in the far reaches of the RF of cortical cells. This activity may initially be subthreshold, then rise above threshold after lesioning through gain adjustments or downregulation of inhibition, causing it to masquerade as cortical reorganization. In other words, cortical reorganization is not required to explain the changed RF properties arising from experimentally induced retinal lesions.

In humans, simulations of blind regions in the visual field have been a powerful tool to assess their effects on pRF measurements. These blind regions have been simulated by removing the visual stimulus at a given location (Baseler et al. 2011, Binda et al. 2013, Haak et al. 2012, Papanikolaou et al. 2015) or under low-light conditions when only rods are operating (Barton & Brewer 2015). Under low-light conditions, cones are silenced and rods are not present in central retina, thereby creating a naturally occurring and reversible central blind region (Barton & Brewer 2015, Baseler et al. 2002). A consistent observation of these simulations is that pRF measurements change around the simulated lesion site. In all cases, simulations of blind regions resulted in reduced signal amplitudes, shifted pRFs, and scaled pRF sizes. The simulation of lesions in healthy adults provides further evidence that changes in pRF sizes arising from lesions are not unique identifiers of cortical reorganization.

Macular degeneration. Macular degeneration (MD) is a disorder that impairs function of the central retina, also known as the foveal or macular retina. This impairment creates a visual blind spot (scotoma) in central vision and can be thought of as a naturally occurring retinal lesion. Central vision loss is particularly problematic because the fovea is a specialized region that represents the image with the highest spatial acuity. Age-related MD is the leading cause of visual impairment in people over the age of 50 (Leibowitz et al. 1980). Juvenile MD is a group of inherited disorders affecting the macula during development. Juvenile MD is not as common as age-related MD but is often studied in scientific research. We speculate that the initial use of patients with juvenile MD over patients with age-related MD may be related to patient access. Regardless, juvenile versus age-related MD is an important distinction when considering how cortical organization may be altered because of different causes and considering that developmental mechanisms likely influence how the cortical organization adjusts.

The interest in MD, and specifically how MD may alter cortical organization, was sparked by Baker and colleagues (2005). They observed that the foveal cortical representation, or lesion projection zone, that receives no input from the eye can nevertheless respond to visual stimuli. They concluded that these results demonstrated large-scale reorganization of visual processing in MD. Although this phenomenon does not occur in every subject with MD (Sunness et al. 2004), Masuda and colleagues (2008, 2010) replicated this finding both in MD and in other retinal disorders. They found that these foveal signals do not depend on visual inputs but instead on the task the subjects perform. The foveal signals appeared only when subjects were asked to make attention-demanding judgments on the stimuli but not during passive viewing. Masuda and colleagues argued that this task dependence of foveal signals speaks against an alteration of cortical

organization. Rather, they suggested that these task-dependent foveal signals are suppressed in normal visual function and come to light by the deletion of afferent inputs. Importantly, in this hypothesis, no alteration of cortical organization is required.

Baseler and colleagues (2011) measured pRF properties in the foveal region of subjects with MD and found alterations in pRF location and size around the fovea. However, control subjects with a simulated foveal scotoma showed the same pattern of results. Several groups have now confirmed the observation of altered pRF properties in healthy subjects around a simulated scotoma (Baseler et al. 2011, Binda et al. 2013, Haak et al. 2012, Papanikolaou et al. 2015). This observation, that simulated lesions in healthy subjects produce similar pRF changes as experimentally induced lesions, underscores the argument that the cortical organization does not have to change to give rise to different (p)RF measurements. Consequently, they argued for a lack of cortical reorganization in MD.

The above-described arguments debate the degree to which a change in pRF measurements reflects cortical reorganization, if it has an effect at all. If it does not, an altered response may be elicited by a stable cortical organization that can respond differently with different pRF values in different experiments following alterations of its input. A complicating factor is that cortical reorganization and related concepts of plasticity are ill defined. Reorganization ranges from adaptation to changes in connection strength, to growing new connections between neurons, to growing new neurons altogether. These interpretations vary from being generally accepted to highly controversial. For example, on one hand, almost all neural systems incorporate a form of adaptation that decreases sensitivity to static stimulation and increases sensitivity to change. On the other hand, evidence for growing new neurons in the adult brain is limited to the granule cells of the dentate gyrus and olfactory bulb (Rakic 2002). We propose that the field needs to take steps to specify the implied mechanism (Wandell & Winawer 2015), and here, we propose a mathematical model that specifies how pRF properties can change in healthy subjects.

Amblyopia. Amblyopia, also known as lazy eye, is a disorder associated with a reduction in best-corrected visual acuity in one eye. Amblyopia is the most common cause of visual impairment in children and young adults (prevalence of about 3%). The deficit of amblyopia is thought to be in the brain rather than in the eye. Reconstructing pRF in human strabismic amblyopes, Clavagnier and colleagues (2015) measured larger pRF sizes elicited from viewing the stimuli through the amblyopic as compared to the fellow eye in the early visual cortex (V1/2/3). Importantly, they also measured fixation stability in both eyes and were able to discount the contributions of eye movements. Consequently, they attributed this to a neural deficit related to loss of neural resolution or neural disorganization, both of which could increase pRF sizes.

Sight recovery from blindness. Most studies we discuss focus on how visual cortical organization is altered as a consequence of ophthalmological or neurological disorder. However, visual cortical organization also responds to the recovery of sight. This is a rare but increasingly relevant situation, given current restoration approaches using retinal prosthetic devices, stem cell transplantation, and genetic therapies. Subject MM lost one eye and became blind in the other owing to corneal damage at the age of 3. At age 46, MM regained his retinal image through a corneal stem cell eye transplant, but his visual abilities remain severely limited and he does not rely on vision for daily life.

Levin and colleagues (2010) found, in addition to abnormalities in cortical connectivity, several abnormalities in cortical organization. The visual field maps were abnormal in V1, where pRF sizes were increased near the fovea, and they were unable to measure a V1 foveal response. Higher-order visual field maps did show unusually large foveal representations. They suggested that MM

selectively lacks V1 neurons with small receptive fields. These neurons may have been lost because, at the time of his accident, these neurons were not fully mature.

Congenital Visual Pathway Disorders

The organization in the early visual system reflects the spatial layout of the retina, with visual processing taking place on so-called retinotopic maps. These maps are a direct consequence of the retino-cortical projections that preserve the retinal layout. Consequently, congenital disorders that affect the retino-cortical projection can have a large impact on the cortical organization.

These congenital pathway disorders are albinism, achiasma, and hemihydranencaphaly. Albinism is an inherited disorder typically associated with reduced pigmentation of the eyes, skin, and hair. It is also associated with a variety of ocular symptoms, one of which is increased crossing at the optic chiasm. That is, visual information predominantly projects from each eye to the contralateral hemisphere. Conversely, achiasma, or nondecussating retinal-fugal fiber disorder, is characterized by an absence or decreased crossing at the optic chiasm so that no or less visual information projects to the contralateral hemisphere. Last, hemihydranencephaly is a rare disorder associated with a complete or near-complete absence of one hemisphere of the cerebral cortex due to an insult in utero. In this case, the eye or eyes project to the remaining hemisphere; in other words, all surviving eyes project to the same hemisphere.

Typically, each visual hemifield from both eyes projects to the contralateral hemisphere (i.e., each eye projects roughly half of its information to the contralateral hemisphere). This is done in such a way that each hemisphere combines the information from the contralateral visual fields of both eyes. These congenital disorders are a notable exception, as in all cases, at least one visual hemifield in each eye projects to the ipsilateral hemisphere. Consequently, each hemisphere receives input from the ipsi- and contralateral visual hemifield. In other words, each hemisphere represents—at least partly—both left and right visual hemifields.

The cortical visual field maps from opposite hemifields appear macroscopically to be arranged as overlays, with two bilateral pRF regions mirrored around the vertical meridian in the left and right hemifield (**Figure 2*b***) (Fracasso et al. 2016a; Hoffmann & Dumoulin 2015; Hoffmann et al. 2003, 2012; Muckli et al. 2009). This cortical mapping scheme is only one of three typically observed in animal models. Humans appear to converge to the same alternative cortical organization in all congenital disorders described here (Hoffmann & Dumoulin 2015).

The properties of overlapping ipsilateral and contralateral visual field maps combined with bilateral pRFs are clearly beyond the realm of typical cortical organization. Yet we believe that there is no large-scale reorganization. When measured, pRF sizes and the properties of all major visual pathways appear normal. Hoffmann and colleagues (2012) speculated that these results can be explained by conservative developmental mechanisms that largely preserve the normal visual pathways beyond the lateral geniculate nucleus. As a consequence, a conservative geniculostriate projection would yield interdigitated representations of the contra- and ipsilateral fields in V1, as those would occupy the former ocular dominance columns (Dell'Osso & Daroff 1998, Olman et al. 2016). Thus this hypothesis suggests that ocular dominance columns are replaced by hemifield columns. Ultra-high-field fMRI has provided preliminary evidence for the existence of hemifield columns (Olman et al. 2016). We speculate that visual function is preserved by reorganization of intracortical connections instead of large-scale reorganizations of the visual cortex.

The notable exception to this proposal is the patient of Fracasso et al. (2016a). This is the only case where both eyes and both hemifields project to the same hemisphere, thus where ocular and hemifield information coexist. In this patient, a similar organization was recovered, but tremors of the patient—involuntary movements—precluded detailed investigations.

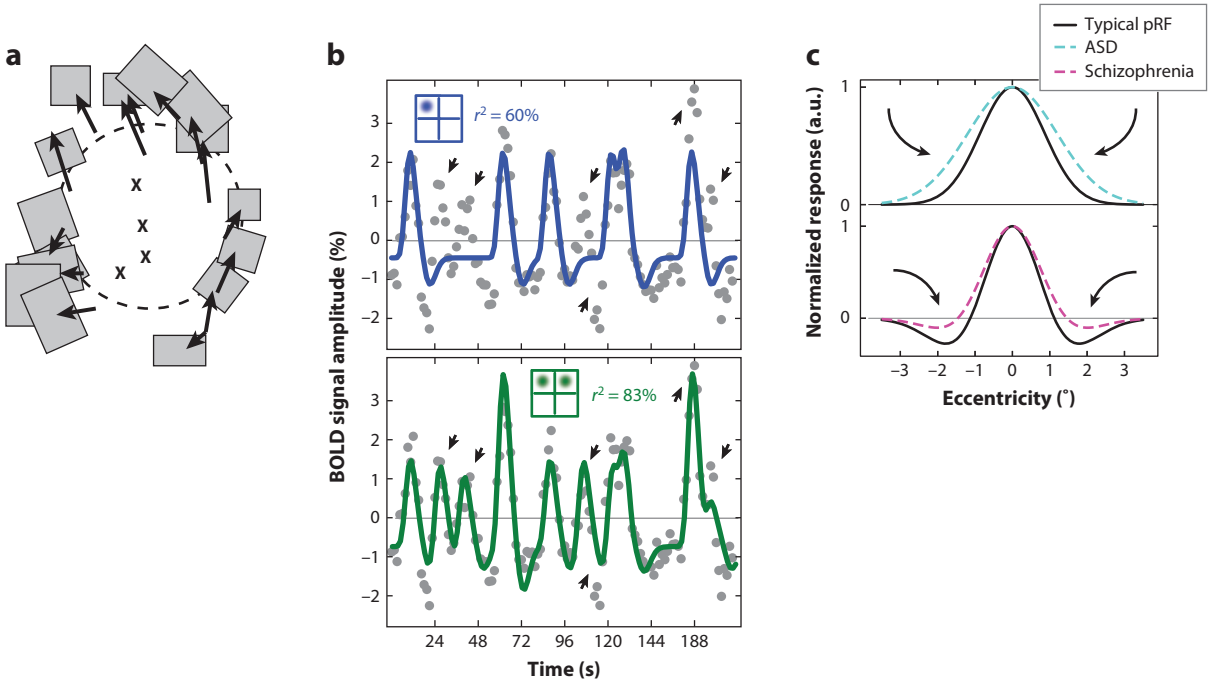

Figure 2

Clinical effects on population receptive fields (pRFs). (*a*) Creating a retinal scotoma causes cortical receptive fields to shift away from the scotoma (adapted from Gilbert & Wiesel 1992). Xs denote unresponsive units. (*b*) Measurements and fits of pRFs in a patient with achiasma. A fit of the blood-oxygen-level-dependent (BOLD) time course with a single-pRF model shows systematic deviations between predicted and measured time courses (see *arrows*). These discrepancies are resolved when a dual-pRF model is used to fit the BOLD time course. The models explain 60% (*left*) and 83% (*right*) of the variance in the same time course (r^2). This analysis indicates that in achiasma, a single cortical location has multiple pRFs, whose positions are mirrored in the vertical visual field meridian (adapted from Hoffmann et al. 2012). (*c*) Systematic changes in pRF shape occur in different neurological disorders. Patients with autism spectrum disorder (ASD) (*top panel*) show larger pRFs primarily in the extrastriate cortex, whereas in schizophrenia (*bottom panel*), the strength of the suppressive surround of pRFs is attenuated (adapted from Schwarzkopf et al. 2014 and Anderson et al. 2017, respectively). This latter pRF change has a close behavioral correlate, as it is mirrored in the perceptual effects that also occur in schizophrenia.

In summary, congenital visual pathway disorders have revealed a remarkably different cortical organization from typical controls. In contrast to animal models, humans appear to converge to the same cortical organization of overlapping visual fields and bilateral pRFs. The current hypothesis is that in humans, the plasticity of thalamocortical connections appears limited, thus demonstrating the importance of cortical adaptations. Remarkably, this organization can support relatively normal visual perception.

Neurological Disorders

Brain lesions. Injury to the early visual cortex or pathways from the eye to the brain leads to a loss of conscious vision in the corresponding region of the visual field. In other words, a scotoma is generated akin to scotomas resulting from retinal lesions. Unlike retinal lesions, cortical insults may initiate cortical repair mechanisms, which could widen the opportunity for reorganization. In animal models, RFs near the lesion have been reported to change, and in particular to enlarge. Akin to the retinal lesions, the changes in RF properties, on one hand, could be interpreted as a

reorganization of the underlying circuitry as a result of the insult. On the other hand, a change in the balance between inhibitory and excitatory processes surrounding the lesion could also result in changing RF properties, an explanation that requires no reorganization of the underlying circuitry.

A few studies have investigated the consequences of human brain lesions on pRF properties. In most cases, the lesion resulted in a blind quadrifield or hemifield. A blind quadrifield or hemifield is the hallmark of a lesion in the brain, as this reflects the organization of visual field maps and cortical tracts in the early visual cortex (i.e., visual field maps are organized as quadrifields and hemifields). Dilks and colleagues (2007, 2009) studied one patient with a lesion in the optic radiations. This lesion caused blindness in the upper-left visual field but left V1 otherwise intact. They reported that the fMRI representation of the lower visual field extended into the upper visual field. Interestingly, they also measured distorted perception in the lower visual field; stimuli appeared vertically elongated, toward and into the blind upper-left visual field. They suggested that adult cortical reorganization caused the perceptual distortions; however, they found similar effects around the blind spot, suggesting that "filling in" mechanisms known to operate in the healthy visual system may underlie the reported neural and perceptual distortions.

Papanikolaou and colleagues (2014) measured human pRF properties in five patients with partial or complete quadrantic visual field loss as a result of partial V1+ or optic radiation lesions. They compared the results with healthy controls deprived of visual stimulation in one quadrant. They reported no large changes in spared-V1 representation. However, they did report small changes in pRF properties, where the distribution of pRF centers in spared V1 was shifted slightly toward the scotoma border in two patients, a slight increase of pRF size near the lesion border, and slightly enlarged pRF sizes in the contralesional hemisphere.

Hemispherectomy. In hemispherectomy, one hemisphere is surgically removed. Hemisphere removal is reserved for the most extreme scenarios, most often as a last resort to treat a variety of seizure disorders where the source of epilepsy is localized to the broad area of one hemisphere. This is done only when the seizures are unresponsive to medications or less invasive surgeries and significantly impair functioning or put the patient at risk of further complications.

Hemispherectomy is conceptually similar to hemihydranencephaly, discussed above, in that both are associated with the loss on one hemisphere. However, hemihydranencephaly occurs in utero before the connections between the eye and brain have been established, whereas hemispherectomy is performed in children or young adults, thereby also destroying connecting fibers between the eye and brain. Consequently, hemispherectomy results in hemianopia (i.e., blindness in the contralateral visual field), whereas the vision of patients with hemihydranencephaly extends significantly into the contralateral visual field to the extent that patients have full visual fields.

Haak and colleagues (2014) studied a single patient who underwent hemispherectomy surgery at the age of three. They reported normal visual field map organization but with an exceptionally large representation of the central visual field and with pRF sizes that were significantly smaller in lateral occipital visual field maps but not in early visual field maps. They speculated small receptive fields were a consequence of the pRFs being deprived from input from the opposite cerebral hemisphere. However, this missing input from the opposite cerebral hemisphere cannot explain the enlarged representation of the central visual field. The authors suggested that this may be a consequence of arrested development when the patient underwent surgery at the age of three, akin to the sight-recovery patient described above. In contrast, the authors also could not rule out that the removal of the opposite hemisphere caused the neurons in the lateral occipital cortex to malfunction, which in turn resulted in a redistribution of these neuronal resources among other visual functions requiring a very detailed processing of the central visual field.

Schizophrenia. Schizophrenia is a neuropsychiatric disorder in which patients interpret reality abnormally. It is typically associated with hallucinations, delusions, and extremely disordered thinking, accompanied by behavior that impairs daily functioning. Schizophrenia is also associated with abnormal visual perception apart from its characteristic hallucinations. For example, Dakin et al. (2005) used a visual illusion where the surrounding context influences the perception of the center. They showed behaviorally that schizophrenia patients are less susceptible to this illusion (i.e., the perception of the center is less strongly influenced by the surrounding context than in controls). This perceptual effect is thought to be due to an imbalance between cortical excitation and inhibition.

Anderson and colleagues (2017) built on this observation using pRF mapping, with a focus on measuring the center-surround configuration of pRFs. They found smaller pRF sizes in the early visual cortex compared to control subjects. This size difference was largely due to reduced suppressive surrounds. They suggested that the imbalance between cortical excitation and inhibition drives the change in pRF center-surround configuration and ultimately explains the visual deficits experienced in schizophrenia.

Autism spectrum disorder. Autism spectrum disorder (ASD) is a disorder in social cognition, communication, and repetitive behaviors. ASD is also associated with abnormal visual perception, such as a sharper spatial selectivity. Schwarzkopf and colleagues (2014) measured pRFs in the early visual cortex and reported larger pRF sizes in the extrastriate cortex but not V1 and V3A, as compared to control subjects. Because these deficits are localized to specific visual field maps, the results are not likely due to global confounding factors such as eye movements. They suggested that the abnormal cortical organization may be characterized by extrastriate cortical hyperexcitability or differential attentional deployment.

Alzheimer's disease. Alzheimer's disease is a degenerative brain disease that usually starts in late middle age or in old age. Alzheimer's disease is characterized by progressive cognitive deficits, including disturbances in memory, language, executive function, and vision. The general nature of cognitive deficits is reflected histologically in the degeneration of neurons throughout the cerebral cortex. There is one feasibility report suggesting possible altered pRF properties in one patient with Alzheimer's disease (Brewer & Barton 2014). Brewer and Barton also pointed out that to study pRF properties in Alzheimer's disease or in related disorders, we must characterize the pRF changes as a function of age, as most studies are performed in healthy young adults or specific patient populations. Comparing elderly with young, healthy subjects, Brewer & Barton (2012, 2014) noted a decrease of V1 central representation and an increase in pRF sizes. Therefore, they underscored the importance of understanding the extent of pRF changes that occur in normal aging to understand aging patients suffering from age-related visual and cortical disorders.

pRF CHANGES IN HEALTH

Here we consider two sources of pRF changes in healthy subjects—those elicited by different visual pathway contributions and those elicited by cognitive contributions.

Visual Pathway Contributions

Evidence is accumulating that, in healthy adults, the measured pRF properties depend on the stimulus properties (Dumoulin et al. 2014, Harvey & Dumoulin 2016, He et al. 2015, Yildirim

et al. 2017). These changes in pRF properties are substantial and can alter the pRF properties up to 30–40% from their typical values.

Typically, the stimulus for these pRF measurements travels systematically throughout the visual field and can take different shapes (e.g., wedge, ring, or bar shaped). Since the introduction of the bar-shaped stimuli (Dumoulin & Wandell 2008), this has become a very popular way for pRF estimation and visual field mapping (for a review of the advantages, see Wandell et al. 2007). The stimulus consists of two components: the carrier and the aperture. The carrier is the background pattern that predominantly drives neuronal activity. The (bar-shaped) aperture reveals the carrier. In essence, the aperture is used to selectively stimulate different parts of the visual field based on which pRF properties are estimated.

As we change the carrier, we can elicit responses from different neuronal populations (**Figure 3*a***). The change in neuronal population will cause the neural RF to change, which causes the pRF model estimates to change. For example, we expect pRF sizes to vary as we change properties of the carrier. This change in the pRF size should be carried by changes in the neural RF only, because we have not altered the neural population size or cortical location we measure from.

Changing the orientation of contours, Dumoulin and colleagues (2014) showed that the pRF size depends on the orientation of the contours relative to the pRF measurement. In these experiments, the carrier consisted of contours. The orientation of the contours was manipulated relative to the bar-shaped aperture. If the contours were oriented parallel to the bar-aperture motion direction (i.e., in the direction of the pRF measurement), the pRF sizes were estimated to be larger than when the contours were oriented orthogonal to the bar-aperture motion direction. They speculated that contour integration mechanisms (i.e., a direction-specific communication between neighboring RFs) (Field et al. 1993) can increase the net pRF size. Harvey & Dumoulin (2016) performed a similar experiment using motion direction instead of contour orientation and found comparable increases in pRF sizes that depend on the motion direction relative to the bar-shaped carrier.

Yildirim and colleagues (2017) replaced the contrast-defined bar stimulus with an orientation-defined bar stimulus. They reported a strong decrease in pRF sizes. Gabors were presented throughout the visual field, defining the bar-shaped aperture with orientation differences but allowing the carrier to cover the entire visual stimulus extent. This narrowband stimulus evokes responses from a limited neural population, presumably much smaller than the broadband contrast-defined moving checkerboard carrier. Consequently, they concluded that the most plausible cause for this reduction is that this stimulus mainly drives a subset of the neurons sensitive to orientation contrast.

Cognitive Contributions

Information represented in the visual system depends also on the cognitive state of the viewer. Measurements of pRFs are thus also likely to be influenced by cognitive manipulations. As pRF properties are spatial in nature, the prime candidate for cognitive influences on these properties is spatial attention.

Covert spatial attention allows specific visual locations to be analyzed preferentially. As a result of the application of spatial attention, perceptual performance at an attended location is higher than at other locations. This is thought to be the result of spatial attention drawing processing resources toward the focus of attention to the detriment of processing at other locations (Anton-Erxleben & Carrasco 2013).

Neurally, spatial attention is thought to be implemented as a gain field (i.e., a visuospatial profile that scales responses of neurons depending on the overlap between their receptive fields

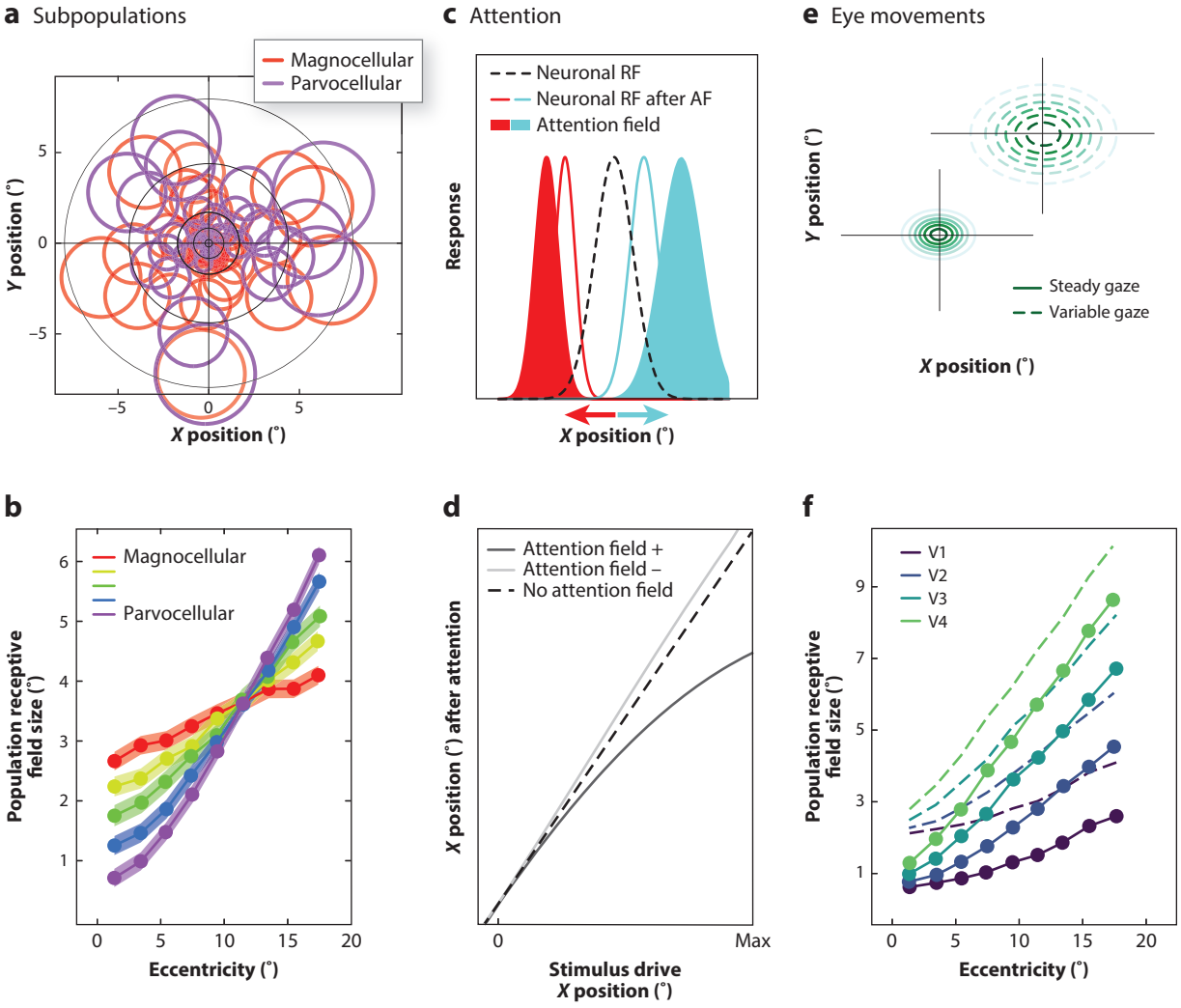

Figure 3

Modeling population receptive field (pRF) dynamics. Changes to different elements of the model have differentiable effects on pRF estimates. (*a*,*b*) Subpopulations. From a recording site, we measure the weighted average of several subpopulations of neurons. One example of different subpopulations that can be present is the magno- and parvocellular processing streams in, for instance, V1. These magno- and parvocellular subpopulations tile the visual field differently [i.e., parvocellular receptive fields are, compared to magnocellular receptive fields (RFs), smaller near the fovea and larger in the periphery] (Cheong et al. 2013). Clinical disorders or changes in the stimulus can change the effective contributions of different subpopulations to the measured pRFs. This means that the offset and the slope of the relation between the eccentricity and size of the pRF may change as a function of these factors. (*c*,*d*) Cognitive factors. Cognitive factors such as attention influence the estimates of pRFs. Spatial attention, modeled as an attention field (AF), interacts with receptive fields through gain-field interactions and draws the RFs toward the AF. As a result, pRF estimates shift toward the locus of attention. Differentially allocating attention to opposite locations in the visual field (attention field + and –) then draws larger, more eccentric pRFs toward the AF more strongly than smaller, more foveal pRFs do. (*e*,*f*) Methods and nuisance factors. Eye movements displace the visual image on the retina. If, over the course of an experiment, an observer makes relatively many, even small, eye movements, this effectively blurs the visual image in the pRF analysis. In terms of pRF estimates, the pRF size parameter increases with a constant throughout the visual cortex (*dashed lines* in panel *f*).

and the gain field). This type of interaction is known to subserve the integration of information in different reference frames and can explain findings in motor control, multisensory integration, and neurophysiological and behavioral experiments on attention (Pouget et al. 2002; Reynolds & Heeger 2009; Salinas & Abbott 2001; Womelsdorf et al. 2006, 2008). How does a gain field shift neuronal preferences and, consequently, pRFs? In the example implementation we use here (Womelsdorf et al. 2008), both the pRFs outside the focus of attention [referred to as stimulus drive (SD)] and the attentional gain field have a Gaussian shape for reasons of mathematical simplicity. Then, the interaction between SD and gain field is modeled by the multiplication of the two Gaussians, which itself also has a Gaussian shape. The resulting pRF, measured under the influence of attention, lies in between the AF and the SD, meaning that shifting spatial attention will change the location of the measured pRF (see **Figure 3*b***). Second, a more precise AF will produce larger shifts in the measured pRF profiles. Furthermore, larger pRFs will be drawn more strongly to the focus of spatial attention than small pRFs will, an effect that would also become evident across different eccentricities.

Klein and colleagues (2014) showed that the pRFs indeed shift according to this gain-field model. That is, pRFs shifted toward the lateral focus of attention, with more eccentric (and thus larger) pRFs experiencing greater shifts. These attentional shifts were also greater in higher-order visual areas than they were at lower levels of the visual system. Moreover, with the model in hand, they could quantify (*a*) the width, or precision, of the attention field per visual field map, which they found to be highly similar throughout the visual cortex and (*b*) the parameters of pRFs outside the influence of attention—a situation that is impossible to achieve by experimental means alone. More recent studies have manipulated spatial attention by directing it to the bar stimulus or to fixation and found hemispheric asymmetries in the effects that spatial attention has on pRFs in intraparietal sulcus (Sheremata & Silver 2015). Furthermore, by directing attention to different features in the bar stimulus, van Es (2018) showed that pRF changes are determined by interactions between feature-based and spatial attention throughout the visual cortex. Interestingly, manipulating attentional load causes effects that run counter to predictions by this attention field model (de Haas et al. 2014). The simple Gaussian attention field mechanism may need to be extended, however, as an elegant study by Puckett & DeYoe (2015) has revealed that the effects of attention on pRFs are best explained by an attention field with a suppressive surround. The common implications of these pRF changes at the level of entire visual field maps is that spatial attention improves the sampling of visual space at the attended location (Sprague & Serences 2013, Vo et al. 2017). Similarly, spatial uncertainty is reduced in face-selective visual regions when attention is directed toward faces (Kay et al. 2015).

In sum, the cognitive state (in particular, spatial attention) influences pRF properties. Consequently, if the clinical disorder alters the cognitive state, it can influence the pRF properties and masquerade as cortical reorganization.

TOWARD A MODEL OF pRF PLASTICITY AND STABILITY

We propose a mechanistic model that captures several sources of short-term and long-term pRF plasticity. The model links different neural mechanisms to the properties of pRFs that are recorded in experiments. By providing this link, the model can guide experiments and allow researchers to connect patterns of pRF changes to specific neural mechanisms, facilitating a mechanistic stance. The model accounts for a broad range of measurements, but it will represent valuable information about the mechanisms underlying pRF dynamics even if the model is incomplete.

The model of pRF dynamics is built on the concept of a pRF (Dumoulin & Wandell 2008, Jancke et al. 2004, Victor et al. 1994) and the pRF analysis (Dumoulin & Wandell 2008). Our

model is based on the idea that pRF dynamics (g_{pRF}) can be captured by two principal components (also see Equation 1 below):

1. The neural subpopulations carrying the signal affect the average pRF properties (**Figure 3*a***). Different neural populations (p) and their individual neural properties [$g_{nRF}(p)$] process different information, and we propose that the net population properties are determined by their weighted (w) average [$\sum_p(w(p) \cdot g_{nRF}(p))$]. In the section above, we have already determined that different neural populations can yield different pRF estimates. Specifically, we propose that pRF dynamics are made possible by changing the balance between stable neural populations and a reweighting of the neural connections by the stimulus, task, or disorder (if applicable). Furthermore, the pRF is also influenced by the total size of the neural population ($g_{population}$), whose effect is modeled by convolution (*). The neural population size depends on neural interactions (i.e., stronger neural interactions will increase the neural population size but are also affected by measurement parameters such as spatial resolution). Conversely, atrophy may essentially alter the total size of the neural population represented in a given cortical recording site.
2. The cognitive task can affect the pRF properties. As the pRF definition most used here is spatial, cognitive tasks that manipulate spatial importance will influence the pRF properties most. We model this as an additional spatial component (g_c). In the section above, we have already determined that changing the task can yield different pRF estimates. Specifically, we propose that alterations in task demands can provide a gain modulation on the individual RFs' spatial layout and, more speculatively, can bias the neural responses to certain subpopulations.

We assume that we can, akin to the pRF approach, approximate all components by Gaussian functions. Consequently, we propose that we can capture pRF dynamics in the human brain by a relatively simple equation:

$$g_{pRF} = \sum_p (w(p) \cdot g_{nRF}(p)) \cdot g_c * g_{population} + k \qquad 1.$$

We propose this particular model of pRF dynamics because it is the most basic combination of the hypothesized two components. In addition, methods affect pRF measurements [e.g., through subject motion, data-acquisition parameters, and blood-brain relationships (k)]. In essence, the model proposes that pRFs consist of different neural subpopulations and that changing the balance between these neural subpopulations can yield different pRFs. This model provides a starting point, which can be refined and extended as data accumulate. In addition, different models may be required for different parts of the brain. As data accumulate, we expect that the model will be extended—analogous to the initial pRF model (Dumoulin & Wandell 2008) and extensions (Kay et al. 2013, Zuiderbaan et al. 2012). Furthermore, this model of pRF dynamics relates to the spatial dimension of the pRF, but a similar approach can model pRF dynamics in terms of other visual dimensions, such as orientation or temporal channels.

We can evaluate the model's accuracy by its ability to explain the variance of independent data sets. Furthermore, a direct comparison of the independent subsets provides information on the total explainable variance (i.e., the maximum explainable variance or noise ceiling given the noise in the data) (Machens et al. 2004, Mante et al. 2005). Importantly, the model then allows us to summarize findings from a collection of up to thousands of pRF estimates in a small number of parameters that are readily interpretable in a mechanistic and neurally plausible way. The model not only predicts the results of single-pRF measurements but can be used to simulate many separate pRFs in parallel and generate model-based reconstructions.

CONCLUSIONS AND FUTURE DIRECTIONS

We have reviewed the patterns of changes in pRF estimates in a variety of cognitive and clinical situations. In developmental disorders, marked changes have been observed that far exceed the range observed in healthy subjects. However, in the adult brain, a controversy surrounds observations that pRFs can change. The question is whether altered pRF parameters reflect cortical reorganization or whether the pRF changes may be explained by the same neural circuitry operations present in healthy subjects.

Several limitations cause this long-standing controversy to endure. Dynamic pRF changes were pioneered in animal experiments, which were until recently the only way to measure pRFs. However, animal experiments allow only limited measurements of perceptual consequences. Furthermore, lack of computational descriptions of the circuitry and its perceptual consequences limit interpretations. Here, we propose a model-based framework for the assessment of these changes, which will allow researchers to more specifically pinpoint the mechanisms underlying recorded pRF changes. We emphasize that this is a direct result of explicitly modeling these mechanisms in a framework that allows one to formulate precise predictions.

We assert that we can correctly interpret the pRF changes in clinical disorders only if we establish the capabilities and limitations of pRF dynamics in healthy humans with mechanistic models that provide quantitative predictions. In essence, we propose that visual cortical organization in ophthalmological and neurological diseases could be altered in two principal ways.

First, pRF organization could be altered using the mechanisms that are also operating in healthy subjects (i.e., a different balance of visual pathways and changes in cognitive mechanisms will yield different pRF estimates). Specifically, certain visual pathways are thought to be selectively impaired in certain conditions. For example, magnocellular pathways are thought to be selectively impaired in dyslexia (Stein 2001), whereas attention may be altered in autism (Schwarzkopf et al. 2014). Either will result in different pRF estimates, but the model allows us to link these effects on pRF estimates to different neural elements, thereby bringing us closer to finding the origin of the disease.

Secondly, apart from disorders in which the model makes specific patterns of pRF changes interpretable in terms of underlying neural factors, certain disorders will produce pRF estimates whose changes from controls are not captured by the model. For example, the dual pRFs observed in congenital visual pathway disorders are clearly beyond the range of pRF dynamics observed in healthy subjects and must invoke alternative mechanisms (Hoffmann & Dumoulin 2015) that extend the model. It is important to relate these changes to a control group, which provides a null distribution for the model parameters to compare measurements from the clinical group to. The model can be quantitative (i.e., the parameters are defined in interpretable units), which facilitates comparisons across different experiments and labs.

Arguably, the model we propose hinges on population properties, with explicit parameters of neural populations and population size. However, given that a single neuron has about 1,000 synaptic inputs (Braitenberg & Schuz 1998), we argue that even single neuron properties reflect the properties of neighboring neurons. In line with our argument, pRF properties are similar to single-neuron measurements (Dumoulin & Wandell 2008), although no simultaneous recordings have been performed. Furthermore, population properties are thought to drive behavior and therefore may also be more relevant when assessing the impact of stability and plasticity in clinical conditions.

This approach is not limited to vision. Estimates of pRFs were conceived by analogy to single-neuron visual receptive fields, but the pRF technique has proven to be amenable also to other modalities. Researchers have moved from location-based pRF models to the incorporation

of visual primitives such as orientation and motion direction (Nishimoto et al. 2011, St-Yves & Naselaris 2018), as well as the duration of visual stimuli (Stigliani et al. 2017, Zhou et al. 2017). Population receptive fields have been used to describe sensory information processing in the auditory and somatosensory domains (Thomas et al. 2015) and in the domain of numerical cognition (Harvey & Braddick 2008; Harvey & Dumoulin 2017; Harvey et al. 2013a, 2015). Furthermore, nonparametric modeling of fMRI responses to semantic categories in video and auditory stimuli have been shown to explain responses throughout the brain (Huth et al. 2012, 2016). The RF analogy has been instrumental in the evolution of fMRI from a signal-amplitude (phrenology) method to a method that allows for the investigation of neural information processing.

The spatial precision of fMRI presently serves the majority of human neuroscience well, but its slow measurement timescale obscures faster neural processes important for cognition, vision, and their disorders. The recent extensions of pRF methodology to other, faster measurement modalities carry such promise. Recent findings using intracranial electrodes in humans have shown good correspondence between pRFs estimated from fMRI data (Harvey et al. 2013b, Winawer et al. 2013), buttressing the assumptions of the pRF method. Furthermore, pRF measurements have been proposed using MEG recordings (Nasiotis et al. 2017). These developments extend the possible use of pRF methodology to shorter timescales and will likely bring faster neural processes, such as sensorimotor interactions, and temporal pRF changes within reach. Furthermore, the quantitative pRF parameters allow researchers to bridge measurement modalities, making them increasingly complementary.

Last, human measurements allow easy access to cognition and behavior. We argue that another important direction to push this debate forward is to link it to perception. The functional anatomy of one's visual cortical organization correlates with how one perceives the world (Schwarzkopf et al. 2011), and changes in cortical organization are implicated in certain visual illusions (He et al. 2015). In certain disorders, changes in pRF properties have been linked to perception (Anderson et al. 2017, Witthoft et al. 2016), but in many others, this link remains elusive. Specifically, cortical reorganization implies a functional or perceptual benefit for this reorganization. There is also a lot of potential in linking perception to brain activations on an instantaneous level and in individual subjects. Estimates of pRFs, especially when combined into a reconstructed visual image, can provide single-trial estimates of the state of neural processing from a given visual region. These reconstructions can then be compared to perceptual outcomes during those same trials (van Bergen et al. 2015) and used in the modeling of cognitive and perceptual processes (Kay & Yeatman 2017).

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