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Which visual functions depend on intermediate visual regions? Insights from a case of developmental visual form agnosia

Sharon Gilaie-Dotan

UCL Institute of Cognitive Neuroscience, 17 Queen Square, London WC1N 3AR, UK

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ABSTRACT

A key question in visual neuroscience is the causal link between specific brain areas and perceptual functions; which regions are necessary for which visual functions? While the contribution of primary visual cortex and high-level visual regions to visual perception has been extensively investigated, the contribution of intermediate visual areas (e.g. V2/V3) to visual processes remains unclear. Here I review more than 20 visual functions (early, mid, and high-level) of LG, a developmental visual agnosic and prosopagnosic young adult, whose intermediate visual regions function in a significantly abnormal fashion as revealed through extensive fMRI and ERP investigations. While expectedly, some of LG's visual functions are significantly impaired, some of his visual functions are surprisingly normal (e.g. stereopsis, color, reading, biological motion). During the period of eight-year testing described here, LG trained on a perceptual learning paradigm that was successful in improving some but not all of his visual functions. Following LG's visual performance and taking into account additional findings in the field, I propose a framework for how different visual areas contribute to different visual functions, with an emphasis on intermediate visual regions. Thus, although rewiring and plasticity in the brain can occur during development to overcome and compensate for hindering developmental factors, LG's case seems to indicate that some visual functions are much less dependent on strict hierarchical flow than others, and can develop normally in spite of abnormal mid-level visual areas, thereby probably less dependent on intermediate visual regions.

1. Introduction

Throughout the day we are continuously required to carry out a variety of multifaceted visual tasks. These include walking through the environment while maintaining body balance without bumping into undesired obstacles (a chair, street pole or passing car), interacting and acting upon target items (reaching for a coffee cup, opening a doorknob, swiping a smartphone), viewing and understanding other people's actions and facial expressions, reading emails, searching for items ("Where've I put my keys?"), driving while following traffic signs, and many other visual tasks.

The visual system that allows us to perform all these tasks is predominantly hierarchical (Felleman and Van Essen, 1991). Visual inputs entering primary visual cortex (V1), the first stage of the visual cortical hierarchy, continue through intermediate visual areas (V2 and V3/VP) and into higher-order and more specialized visual and other multisensory regions [e.g. object-sensitive LOC (Malach et al., 1995; Grill-Spector et al., 1998), face-sensitive "FFA" (Kanwisher et al., 1997; McCarthy et al., 1997; Levy et al., 2001) and "OFA" (Gauthier et al., 2000), place-sensitive "PPA" (Epstein and Kanwisher, 1998; Levy et al., 2001; Malach et al., 2002), motion-sensitive MT+/V5 (Zeki, 1974; Zeki et al., 1991; Rees et al., 2000) and biological motion-sensitive pSTS (Grossman et al., 2000; Hoffman and Haxby, 2000)]. Along the hierarchical levels the sensitivity becomes more complex [V1 is sensitive to very small and local elements in the visual field, and higher levels are sensitive to larger and more complex elements in the visual field (Hubel and Wiesel, 1968; Lerner et al., 2001; Avidan et al., 2002; Grill-Spector and Malach, 2004)], receptive field sizes become progressively larger (e.g. Kastner et al., 2001; Smith et al., 2001), and response latencies increase (Schmolesky et al., 1998; Lamme and Roelfsema, 2000). The visual hierarchy is divided into two main parallel processing streams, the ventral "what"/"perception" visual stream in the ventral aspects of the visual cortex processing cues related to form and shape, and the dorsal "where"/"action" visual stream in the dorsal aspects of the visual cortex processing cues related to space, navigation, and preparation for action (Mishkin et al., 1983; Milner and Goodale, 1993).

While V1, at the bottom of the visual hierarchy, and specialized regions at the top of visual hierarchy have been extensively investigated with respect to their involvement in specific perceptual

E-mail address: shagido@gmail.com

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processes and even in visual awareness [e.g. motion perception (Zihl et al., 1983; Newsome and Pare, 1988; Salzman et al., 1992; Schiller, 1993; Gilaie-Dotan et al., 2013c), object, face and word perception (Behrmann and Kimchi, 2003; Barton, 2011; Konen et al., 2011; Behrmann and Plaut, 2014), and awareness (Lamme and Roelfsema, 2000; Silvanto et al., 2005; Silvanto, 2014)], investigating the contribution of intermediate visual regions to our visual perceptual experience lags behind and therefore remains unclear.

One major contribution proposed for the role of intermediate visual areas involves integrating the basic information units from the visual field into more meaningful or useful data chunks that are used by higher order regions to lead to perceptual experiences and behavioral performance. In line with this idea, midlevel visual processes as figure-ground segmentation, edge-assignment, and perceptual grouping (e.g. Gestalt grouping principles) have been hypothesized to be supported by the function of intermediate visual regions. But whether these are performed locally in V1 or together with V2/V3 early in the visual process ("the first/forward sweep"), or rely on contextual, top-down influences (as attention or past experience) from higher-order regions (Lamme and Roelfsema, 2000; Hochstein and Ahissar, 2002; Kubilius et al., 2014), remains unknown (for an overview see Brooks et al. (2012)). Furthermore, even if these midlevel processes are computed in intermediate visual regions, whether they rely on a single mechanism, are performed in parallel in a similar fashion (e.g. all relying on feedback from higher regions), or dissociate, is also unclear. So for example, an influential model suggests that intermediate visual regions, as part of the visual hierarchy, support multiple predominantly segregated processing routes (DeYoe and Van Essen, 1988; DeYoe et al., 1994b), where on the one hand, color and form are supported by distinct populations *within* the ventral pathway, and on the other hand the same visual attribute can be processed in duplicate parallel routes (e.g. stereo or orientation are each processed both in the form parvocellular interblob pathway, and in the magnocellular motion pathway).

Neuroimaging studies can typically provide correlative measures but lack the ability to provide causal brain–behavior relations. Lesion studies, even when the lesions are focal and non-diffuse (Girard and Bullier, 1989; Merigan et al., 1993; Cowey and Vaina, 2000), do not typically follow precise functional regional boundaries and thus may be limited in providing specific region-behaviour causality measures. While atypical visual development may involve plasticity and compensatory mechanisms, it has proven effective in highlighting neurofunctional and neuroanatomical contributions to visual performance, as in the case of face perception (Bentin et al., 1999, 2007; Avidan et al., 2005; Garrido et al., 2009; Thomas et al., 2009). Therefore here, I review an extensively investigated case of developmental visual form agnosia with clear abnormal function of intermediate visual areas, and taking into account many earlier findings, I put forward a model that associates a host of visual functions to visual regions, highlighting the role of intermediate visual regions (V2, V3/VP) in supporting these functions.

2. LG – a short overview

LG is a young intelligent and completely independently-functioning adult (now 28 year old), who suffers from developmental visual agnosia and prosopagnosia. He was diagnosed with visual form agnosia as a young boy before the age of 8 (Ariel and Sadeh, 1996), following an extensive neuropsychological examination. That study found that LG had significant impairments in object and face perception, as well as a difficulty in overcoming occlusion (as when text or objects are partially covered), in contrast to his adequate social skills and normal or above normal performance on tests assessing intelligence (within the superior range in the verbal skills), language (reading, writing, verbal), basic and spatial vision, visual imagery, and short-term visual memory.

When he was 18, we initiated a series of studies to investigate his visual functions, starting with extensive neuroimaging and neuropsychological examinations (see Tables 1 and 2). Importantly, the critical finding for this review is that these studies revealed that LG's intermediate visual regions consistently function in a significantly abnormal fashion (see Fig. 1 and an illustration in Fig. 2), i.e. show significant BOLD *deactivations* to any visual stimulation (Gilaie-Dotan et al., 2009), in contrast to the positive BOLD activations that are observed in neurotypical adults. It is important to emphasize that this abnormal BOLD deactivation response does not include LG's V1 but starts at the expected location of V2 (as evident by superimposing his functional V1/V2 retinotopic border on his activation maps, see Fig. 1), and most probably also includes V3, that is, his intermediate visual regions. These uncharacteristic findings in LG were replicated across a set of fMRI visual experiments using a variety of paradigms, stimuli, and tasks (see Table 1), and were confirmed in electrophysiological measurements (Gilaie-Dotan et al., 2009) and in a resting state functional connectivity fMRI study (Gilaie-Dotan et al., 2013a).

In additional unpublished fMRI studies using tactile and auditory stimuli (Amedi et al., 2002), there were no indications that LG's intermediate visual regions developed as part of another non-visual brain system (see Table 1 (Amedi et al., 2003; Raz et al., 2005)). This thus provides further support that LG's intermediate visual regions are part of LG's visual system that developed in an abnormal fashion.

Two issues require drawing attention to. First, while this abnormality in LG's intermediate visual cortex is very robust and therefore likely to represent the activity of the majority of the neurons in these regions, subpopulations within these regions could still function normally (e.g. at the submillimeter range) yet go undetected due to the spatial and temporal limitations of the imaging techniques. Second, LG's V1 is not entirely normal, as its response amplitude is higher and slightly delayed than would be expected (Gilaie-Dotan et al., 2009), possibly resulting from deficient feedback from intermediate regions, thus perhaps indicating on plasticity.

Still, this most conspicuous functional irregularity of LG's visual cortex (i.e. in his intermediate visual regions) is of great importance, even if additional regions within LG's visual system have developed differently than in the neurotypical brain for compensatory purposes. Predominantly, it allows examining which visual functions are more dependent on normally functioning intermediate visual regions and less likely to gain from compensatory mechanisms, and which visual functions are less dependent on intermediate visual regions and can develop normally despite such abnormality (even if reliant on compensatory mechanisms).

It is also important to emphasize that even though no structural abnormality was detected in LG's brain (as determined by a neuroradiologist blind to LG's condition (Gilaie-Dotan et al., 2009, 2011)), I do not assume that LG's intermediate visual regions' abnormality is merely functional, as the integrity of these regions is as important as their functionality.

A series of behavioural studies were carried out to investigate various aspects of LG's visual perceptual abilities. These studies started when LG was 18 year old and are still ongoing. Here I describe all the studies that were done until he reached the age of 26 (see Table 2), and a few of the more recent unpublished results. These include visual functions that are considered "early" (e.g. acuity, crowding, lateral interactions (Gilaie-Dotan et al., 2009; Lev et al., 2015)), "mid-level" [e.g. figure-ground segmentation (Brooks et al., 2012), motion perception abilities (Gilaie-Dotan et al., 2011;