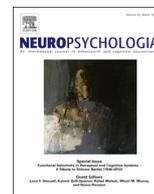




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Which visual functions depend on intermediate visual regions? Insights from a case of developmental visual form agnosia



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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 agnostic 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.

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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

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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);

Table 1
fMRI experiments LG underwent at the age of 18–19^a and experimental findings.

fMRI experiment	Stimuli	Task	Stimulus on-off cycle	Times run	Findings (including abnormalities)	Reported in
Retinotopy	Triangular wedges over upper/lower /right/left portions of the horizontal/vertical meridians	Fixate	18 on 6 off	2	Only V1–V2 retinotopic borders detected, no other more anterior borders found; ventral intermediate areas deactivated to most conditions	Gilaie-Dotan et al. (2009, Supplementary material)
Eccentricity	Colored drawings of objects (foveal circles (1.5° × 1.5°) or peripheral rings (9–16°))	Fixate	18 on 6 off	1	Center-periphery organization in V1; Deactivation both to foveal or to peripheral stimuli in intermediate visual areas	Gilaie-Dotan et al. (2009, Supplementary material)
Motion localiser	Low contrast (6%) rings (motion: expanding/contracting, static: same rings in non-motion appearing order)	Fixate	18 on 6 off	1	Motion-sensitivity in hMT+/V5 expected location; no additional regions show motion sensitivity at lower thresholds	Gilaie-Dotan et al. (2009)
Category localiser	Line drawings of faces, houses, objects, and patterns	1-Back same/different	9 on 6 off	2	V1 above baseline activity; intermediate regions significantly deactivated to all visual stimuli; positive (non-selective) activations in LOC, hMT+/V5, parietal cortex	Gilaie-Dotan et al. (2009)
Category localiser	Grayscale photos of faces, houses, objects, and patterns	1-Back same/different	9 on 6 off	1	Same as above	Gilaie-Dotan et al. (2009)
Category localiser	Video clip of faces, buildings, objects, and navigation	Free viewing	15 on 6 off	1	Same as above , but greater extent of positive visual activation across visual cortex and less deactivations in intermediate visual areas (but no positive activations there)	Gilaie-Dotan et al. (2009)
Completion experiment	Line drawings of animals (whole, partially occluded, scrambled)	Silent naming	9 on 6 off	1	Same pattern as in the category localisers with static images	Gilaie-Dotan et al. (2009)
Imagery	Auditory instructions for imagining 5 domains: faces, objects, places, animals, motion	Close eyes and imagine the described scenarios	15 on (3 s verbal instruct+ 12 s of imagery) 6 off	1	Visual imagery does not generate significant above baseline activity in LG's visual cortex (inc. intermediate visual regions, V1 and high-order visual regions)	Gilaie-Dotan et al. (2013a in main text and Supplementary material)
Resting state ^a	None (eyes closed)	Close eyes and rest	None	1 Run (10 min)	Intermediate visual regions are functionally disconnected from the rest of LG's visual cortex	Gilaie-Dotan et al. (2013a)
Audio-visual	Auditory object sounds and scrambled sounds, visual objects and scrambled objects [as described in Amedi et al. (2002)]	1-Back same/different for all conditions; Open eyes and fixate (vision), close eyes (audition)	12 on 9 off	1–2 Runs	Preliminary analysis reveals no significant auditory activations in intermediate visual areas	Unpublished results
Tactile localizer	Tactile objects and tactile textures every 4 s [as described in Amedi et al. (2002)]	Close eyes; Palpate, recognize and covertly name the object or texture presented	12 on 9 off	2	Preliminary analysis reveals tactile object sensitivity (object > texture) in lateral occipital tactile visual (LOtv) region, and tactile activations in somatosensory, motor, parietal, and visual regions but not in intermediate visual regions	Unpublished results

^a Resting state experiment was run more than a year after the perceptual learning paradigm has begun when LG was 21 years old.

Table 2
Summary of LG's visual functions as an adult between the age of 18 and 26. He started to train on a perceptual learning paradigm at the age of 20. The group number represents the function's classification: 1 – normal in LG, not dependent on V2/V3, 2 – probably normal in LG, probably not dependent on V2/V3, 3 – probably dependent on V2/V3, 4 – impaired in LG even after training, dependent on V2/V3. Dark/light gray shading indicates significant [possible] impairment. Asterisks indicate substantial improvement.

Visual experiment	Group	Before training performance	Visual stimuli/task	After training performance	LG's age when tested	Published in
Probably independent of V2/V3						
1-back same/different	1	Normal	Patterns, faces, houses, and objects (line drawings, grayscale images)		19	Gilaie-Dotan et al. (2009)
Figure-ground organization: using local cues	2		Using local cues (common motion, collinearity, color, blur, orientation and others) to perform figure-ground judgments	Normal	24	Brooks et al. (2012)
Figure-ground organization: convex silhouettes	2		Determine which part of a 2-part unfamiliar convex/concave black/white display is figural	Normal	24	Brooks et al. (2012)
Figure-ground organization: unfamiliar silhouettes	2		Determine which part of a 2-part unfamiliar black/white display is figural	Normal	24	Brooks et al. (2012)
Kanizsa figures – simple	1	Normal	Recognize the shape (triangle, rectangle)		19/20	Gilaie-Dotan et al. (2009)
Object matching across viewpoints	1	Normal	BORB (test 7): match picture of rotated object (distinctive identifying feature obscured due to rotation) to standard view		19	Gilaie-Dotan et al. (2009)
Local global	1	Normal (local 14.7, global 73.3)	Navon (English and Hebrew versions)		19	Gilaie-Dotan et al. (2009)
Place recognition	1	Normal ?? (famous: 11/17, when knows 13/17; neighbourhood: 18/25)	Recognize (from pictures) famous buildings; recognize personally familiar places (pictures) from the neighbourhood		19	Gilaie-Dotan et al. (2009)
Reading	1	Normal but from very close (15–20 cm)	Passionate reader (Hebrew and English); testing included reading passages out loud		19	Gilaie-Dotan et al. (2009)
Masked text (lightly)	1	Normal	Read/identify slightly masked text		19	Gilaie-Dotan et al. (2009)
Writing	1	Normal	Write following dictation		19	Unpublished results
Color	1	Normal	Ishihara and HRR tests		19, 26	Gilaie-Dotan et al. (2009) and unpublished results
Motion detection	2		Detect motion (present/absent, 100% coherence) in the center of a random dot field of flickering dots	Normal	23	Gilaie-Dotan et al. (2011)
Motion coherence	2		Detect direction of coherently moving dots embedded in randomly moving dots (circular display)	Normal	23	Lev et al. (2015)
Biological motion	2		Point light displays: recognition task, perceptual thresholds (direction and detection tasks)	Normal	22–23	Gilaie-Dotan et al. (2011)
Body expressions (in context)	2		Determine emotion conveyed by emotional body images (static stimuli) that appeared with paraphernalia or scene context	Normal	22	Aviezer et al. (2012a)
Stereopsis	1	Normal (30'')	Randot	Improved (to 20'')	20, 26	Gilaie-Dotan et al. (2009) and Lev et al. (2015)
Spatial orientation	1	Normal	Draw the route from your house to the municipality		19	Unpublished results
Space perception	1	Normal	Draw parallel lines		19	Unpublished results
Assortment of "mid-level vision" tasks	2		L-POST (Torfs et al., 2014)	Normal	26	Lev et al. (2015)
Probably dependent on V2/V3						
Near visual acuity (40 cm)	3	Impaired (20/63 or 20/50 for R/L eye)	Recognize letter sequences (40 cm standard ETDRS chart)	Improved* (< 20/40)	21, 22, 26	Lev et al. (2015)
Far visual acuity (3 m)	3	Impaired (20/100 or 20/63 for R/L eye)	Recognize letter sequences (3 m standard ETDRS chart)	Improved* (< 20/40)	20, 21, 22, 26	Gilaie-Dotan et al. (2009) and Lev et al. (2015)
Contrast sensitivity	3	Impaired (oversuppression, no facilitation)	Gabor foveal patches	Improved* (more facilitation, closer to normal)	19, 20, 21, 22, 26	Lev et al. (2015) and unpublished results

Table 2 (continued)

Visual experiment	Group	Before training performance	Visual stimuli/task	After training performance	LG's age when tested	Published in
Contrast sensitivity	4	Impaired (lower than normal for 9–18 cpd)	Full-field sinusoidal gratings in a temporal 2AFC	Impaired (lower than normal for 4–18 cpd)	19, 21	Gilaie-Dotan et al. (2009) and unpublished results
Crowding	3	Impaired (0.3 log units)	Tumbling E	Close to normal	19, 20, 22, 24, 26	Gilaie-Dotan et al. (2009) and Lev et al. (2015)
Lateral interactions	3	Impaired (no collinear facilitation)	Gabors	<i>Improved*</i>	20, 21, 22, 26	Gilaie-Dotan et al. (2009) and Lev et al. (2015)
Contour in noise card test	3	Impaired (ratio ~1, i.e. 5–6 year olds level)	Detect closed contour made of Gabor patches in random background of Gabor patches (Kovacs et al., 2000)	Normal	19, 21, 26	Gilaie-Dotan et al. (2009) and Lev et al. (2015)
Figure-ground organization: using contextual cues	4		Using remote cues (common motion and collinearity) to perform figure-ground judgments	Impaired	24	Brooks et al. (2012)
Kanizsa figures – complex	3	Impaired	Recognize the shape (Star of David)		19/20	Gilaie-Dotan et al. (2009)
Object perception	3		Visual Object and Space Perception Battery (VOSP)	At lower end of norm	26	Lev et al. (2015)
Object naming	3	Somewhat impaired? (only failed on some low frequency objects)	Boston naming set		18	Gilaie-Dotan et al. (2009)
Object recognition – perceptual organization	4	Impaired (12.5/30: 'very high probability of impairment') Geo. shapes: no mistakes but impaired RT ratio 1:1.6; Letters: 16/180 mistakes, RT 1:2.8 for pairs; Objects: 4/72 mistakes; RT 1:2.7	Hooper visual organization test (name line drawn objects from their fragmented parts) BORB (test 6): naming overlapping geometric shapes, letters, or overlapping line drawn objects	Impaired (20/30: 'moderate probability of impairment') Geo. shapes: 1 mistake, RT ratio 1:1.5; Letters: 6/180 mistakes, RT 1:2.3 for pairs; Objects: 3/72 mistakes; RT 1:2.3	19, 24, 26	Gilaie-Dotan et al. (2009) and Lev et al. (2015)
Line drawn animal recognition	4	Impaired (63%) Impaired (17%) Impaired	Recognized whole animal line drawings Recognize occluded animal line drawings	Impaired (72%, 67%) Impaired (25%, 50%)	19, 24	Gilaie-Dotan et al. (2009) and Lev et al. (2015)
Masked text (heavily)	3		Read/identify heavily masked text (normals can recognize it)		19	Gilaie-Dotan et al. (2009)
Figure-ground organization: familiar silhouettes	4		Determine which part of a familiar 2-parts black&white display is figural (100 ms exposure)	Impaired	24	Brooks et al. (2012)
Figure-ground organization: familiar silhouettes naming	4		Name a familiar 2-parts black-&white display (unlimited exposure)	Impaired	24	Brooks et al. (2012)
3D structure-from-motion	4		Discriminate rotating sphere/cylinder in random dots display (various speeds, dot density, dot lifetime)	Impaired	23	Gilaie-Dotan et al. (2011)
Visual memory: cars	4		Cambridge car memory test (from different angles, viewing conditions, and noise (Dennett et al., 2012))	Impaired (38/72, > 2 SDs below controls' mean)	28	Unpublished results
Visual memory: bodies	4		Cambridge body memory test (from different angles, viewing conditions, and noise (Susilo et al., 2015))	Impaired (33/72, > 2 SDs below controls' mean)	28	Unpublished results, Tirta Susilo and Brad Duchaine, personal communications
Visual memory: hair styles	4		Cambridge hair memory test (from different angles, viewing conditions, and noise)	Impaired (42/72, > 2 SDs below controls' mean)	28	Unpublished results, Brad Duchaine, personal communication
Face memory and matching: unfamiliar faces	4	Impaired (33/54: severely impaired) (faces: 37/50, 53 rd percentile, words: 47/50, 4 th percentile) (34/75)	Benton face recognition (match unfamiliar faces) Warrington Face/Word (short memory test) Cambridge face memory test (from different angles, viewing conditions, and noise)	Impaired (Original CFMT: 31/72, CFMT-Aus: 25/72: ~4 SDs from controls)	19, 24, 28	Gilaie-Dotan et al. (2009), Lev et al. (2015) and unpublished results

Table 2 (continued)

Visual experiment	Group	Before training performance	Visual stimuli/task	After training performance	LG's age when tested	Published in
Face matching (identity, expressions): unfamiliar faces	3	Impaired (close to chance level on all tasks)	(Levy and Bentin, 2008): Match facial identity (static faces) Match facial expression (static faces)		18	Unpublished results
Face recognition: familiar faces	4	Impaired (no family members were recognized from photos; famous faces: recognized 4/53, while has semantic knowledge of 52 of them and thinks he can recognize 41 of them)	Recognize personally familiar people; Recognize famous faces	Impaired	19, 26	Gilaie-Dotan et al. (2009), and informal observations at the age of 26
Facial expressions: unfamiliar faces	4		Determine facial expression based on isolated faces or in the context of emotional bodies (static stimuli)	Impaired	22	Aviezer et al. (2012a)
Facial expressions: unfamiliar faces	4		Recognize and match emotion based on diagnostic or non-diagnostic face components	Impaired	24	Aviezer et al. (2012b)

Lev et al., 2015)], and “high-level” as object, place, and face-perception (Gilaie-Dotan et al., 2009; Lev et al., 2015), including processing of emotional faces, affective body perception (Aviezer et al., 2012a, 2012b), and reading abilities (Gilaie-Dotan et al., 2009). At the age of 20, amidst some of these studies, LG started to train on a perceptual learning paradigm in an effort to improve his visual functions. The training procedure was similar to previous training studies (Polat et al., 2004) and was done monocularly or binocularly from a viewing distance of 150 cm, in 30 min sessions, 3 times a week. It included contrast detection of foveal Gabor targets (with or without lateral (spatial) or backward (temporal) masking), covering a range of spatial frequencies, Gabor orientations, and temporal modulations (see more details in Lev et al. (2015)). The training lasted approximately 9 months and was effective in improving LG's low-level and some of his intermediate-level visual functions (see Table 2; Lev et al., 2015).

3. Classifying visual functions according to their dependency on intermediate visual regions

In light of the abnormality observed in LG's intermediate visual areas it is surprising that some visual functions are completely normal in LG. Expectedly, his performance in some of the tested visual functions was adversely affected. Consequently, it is possible to classify the perceptual visual functions that LG was tested on according to their dependencies on intermediate visual areas in the following way:

1. Visual functions that are independent of intermediate visual areas with high probability (group 1 in Table 2). These functions were already normal in LG even before he began the training and therefore were not affected by the perceptual training, and probably not affected by his abnormal intermediate visual regions' function (although compensatory mechanisms cannot be ruled out). These include 1-back same/different image judgements (Gilaie-Dotan et al., 2009), color perception [binocularly (Ishihara, 1917; Gilaie-Dotan et al., 2009) and

monocularly (HRR color test,¹ richmondproducts.com, unpublished results)], naming simple Kanizsa figures (Gilaie-Dotan et al., 2009), object matching across viewpoints (BORB test 7; Riddoch and Humphreys, 1993; Gilaie-Dotan et al., 2009), reading (albeit from a short distance; Gilaie-Dotan et al., 2009), reading from lightly masked text (Gilaie-Dotan et al., 2009), writing (from dictation, unpublished results), stereopsis (Randot Stereo Test; Gilaie-Dotan et al., 2009; Lev et al., 2015), spatial orientation (drawing the route from one place to another, unpublished results), spatial perception (drawing parallel lines, unpublished results), and local–global effect (Navon, 1977; Gilaie-Dotan et al., 2009). I am also including place recognition here, as although LG's performance on these tests was not perfect (see Table 2; Gilaie-Dotan et al., 2009), he did perform rather well, possibly within the normative performance range (his performance was not compared to any normative data).

2. Visual functions that are independent of intermediate visual areas with medium probability (group 2 in Table 2). LG's performance on these functions was normal. However as he was tested on them only after the training ended, the influence of the visual training cannot be ruled out as a contributing factor. These include figure-ground assignment based on local or on convexity cues (Brooks and Driver, 2010; Brooks et al., 2012), motion detection (Gilaie-Dotan et al., 2011, 2013c), motion coherence (Meteyard et al., 2008; Gilaie-Dotan et al., 2013b, 2013c; Lev et al., 2015), biological motion perception from point light displays (Johansson, 1973; Saygin, 2007; Gilaie-Dotan et al., 2011, 2015), recognizing body expressions in context from static images (Aviezer et al., 2012a), and performance on the L-POST testing for assortment of midlevel visual functions (Torfs et al., 2014; Vancleef et al., 2014; Lev et al., 2015).

3. Visual functions that are dependent on intermediate visual

¹ LG was tested monocularly at the age of 26 on the HRR color vision test and performed normally in each eye.

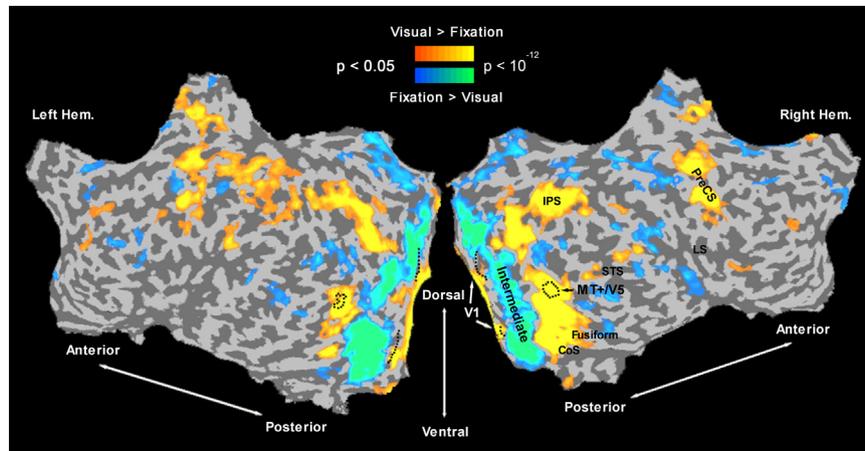


Fig. 1. LG's BOLD responses to visual stimuli. While LG's V1 is activated above baseline (depicted in orange to yellow, see scale bar), LG's intermediate visual areas show significantly abnormal deactivations to visual stimuli relative to fixation baseline (blue to green, see scale bar). Note that despite these significant deactivations, high order visual regions, as in controls, are activated above baseline including ventral, motion-sensitive, and dorsal regions, and even more anterior regions outside the visual cortex. The statistical map is based on three runs of the category localizer experiment (line drawn or grayscale images of faces, houses, objects, or textures, see Table 1) that LG underwent. Black dotted lines represent the retinotopic borders of LG's V1–V2 (defined by the retinotopic experiment) and motion-sensitive MT+/V5 (defined by the motion localizer experiment). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

areas with medium probability (group 3 in Table 2). LG's performance on these functions was impaired before the training began, and following the training, reached normal or almost normal performance. I also include in this group three functions (matching static faces based on identity or expression, reading heavily masked text, and recognizing complex Kanizsa figures) that LG was impaired in before training, and was not tested on after training, as I find that their perceptual demands resemble those of tasks that LG is still impaired in (face perception, and shape recognition from incomplete information), yet I cannot rule out a possible post-training improvement, had LG been retested on these functions post-training. Explicitly, this group includes contrast sensitivity (Polat et al., 2005; Gilaie-Dotan et al., 2009; Lev et al., 2015), near and far visual acuity (Gilaie-Dotan et al., 2009; Lev et al., 2015), crowding (Bonneh et al., 2004; Gilaie-Dotan et al., 2009; Lev et al., 2015), lateral interactions (Polat and Sagi, 1993; Gilaie-Dotan et al., 2009; Lev et al., 2014, 2015), identifying contour in noise (Kovacs et al., 2000; Gilaie-Dotan et al., 2009; Lev et al., 2015), reading heavily masked text (Gilaie-Dotan et al., 2009), recognizing complex Kanizsa figures (Star of David; Gilaie-Dotan et al., 2009), object perception from atypical silhouettes (Visual Object and Space Perception Battery; Lev et al., 2015), object naming of low frequency objects (Boston Naming Test; Kaplan et al., 1983; Gilaie-Dotan et al., 2009), and matching static faces based on identity or expression (unpublished results following paradigm by Levy and Bentin (2008)).

4. Visual functions that are dependent on intermediate visual areas with high probability (group 4 in Table 2). LG's performance on these functions was abnormal even following the visual training. These include figure-ground organization based on contextual cues (Brooks and Driver, 2010; Brooks et al., 2012) or on familiarity of silhouettes (Peterson and Gibson, 1994; Peterson et al., 1998; Brooks et al., 2012), figure-ground segmentation of overlapping line drawn geometric shapes, letters, or objects (BORB test 6; Riddoch and Humphreys, 1993; Gilaie-Dotan et al., 2009; Lev et al., 2015), naming animals from complete line drawings or partly occluded by a grid (Lerner et al., 2002; Gilaie-Dotan et al., 2009; Lev et al., 2015), object recognition from fragmented parts (Hooper Visual Organization Test; Hooper, 1983; Gilaie-Dotan et al., 2009), object recognition from short-term memory [Cambridge Memory Tests (LG's results on these are unpublished): Car – Dennett et al., 2012; Body – Susilo et al.,

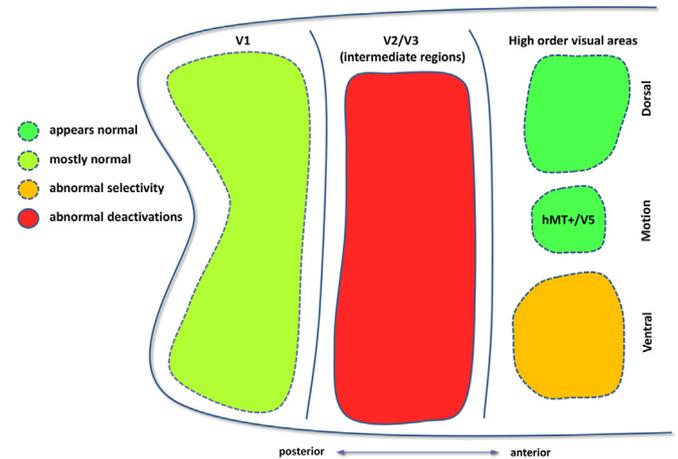


Fig. 2. Schematic illustration of LG's abnormal visual cortex function on a cartoon of the posterior aspects of a flattened right cortical map. While V1 (in light green) showed the expected pattern of significant positive BOLD activations in response to visual stimuli (although with increased magnitude and a slight delay), intermediate visual areas (in red) unexpectedly showed significantly abnormal BOLD deactivations to visual stimuli (across different paradigms, stimuli, and tasks (Gilaie-Dotan et al., 2009) and abnormal functional connectivity to the rest of LG's visual cortex in the absence of visual stimulation (Gilaie-Dotan et al., 2013a)). Despite this abnormal upstream activity, higher-order visual regions showed positive BOLD activations (Gilaie-Dotan et al., 2009). Specifically, dorsal regions and motion-sensitive hMT+/V5 (both colored in dark green) showed the expected functional connectivity patterns to the fronto-parietal system while LG was watching video clips (Gilaie-Dotan et al., 2011), and motion-sensitivity was found in the expected middle temporal hMT+/V5 location. On the other hand, LG's ventral regions specializing in form processing (colored in orange) did not show the expected selectivities to faces and objects (Gilaie-Dotan et al., 2009). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

2015; and Hair – Brad Duchaine, personal communication], recognizing 3D structure-from-motion (Singer and Sheinberg, 2008; Gilaie-Dotan et al., 2011, 2013c), face matching and short-term memory of unfamiliar faces (Warrington, 1984; Benton et al., 1994; Duchaine and Nakayama, 2006; Levy and Bentin, 2008; Gilaie-Dotan et al., 2009; McKone et al., 2011; Lev et al., 2015), identifying facial expressions from static images (Aviezer et al., 2012a, 2012b), and recognition of famous or personally-familiar faces (Gilaie-Dotan et al., 2009) including informal observations at the age of 26).

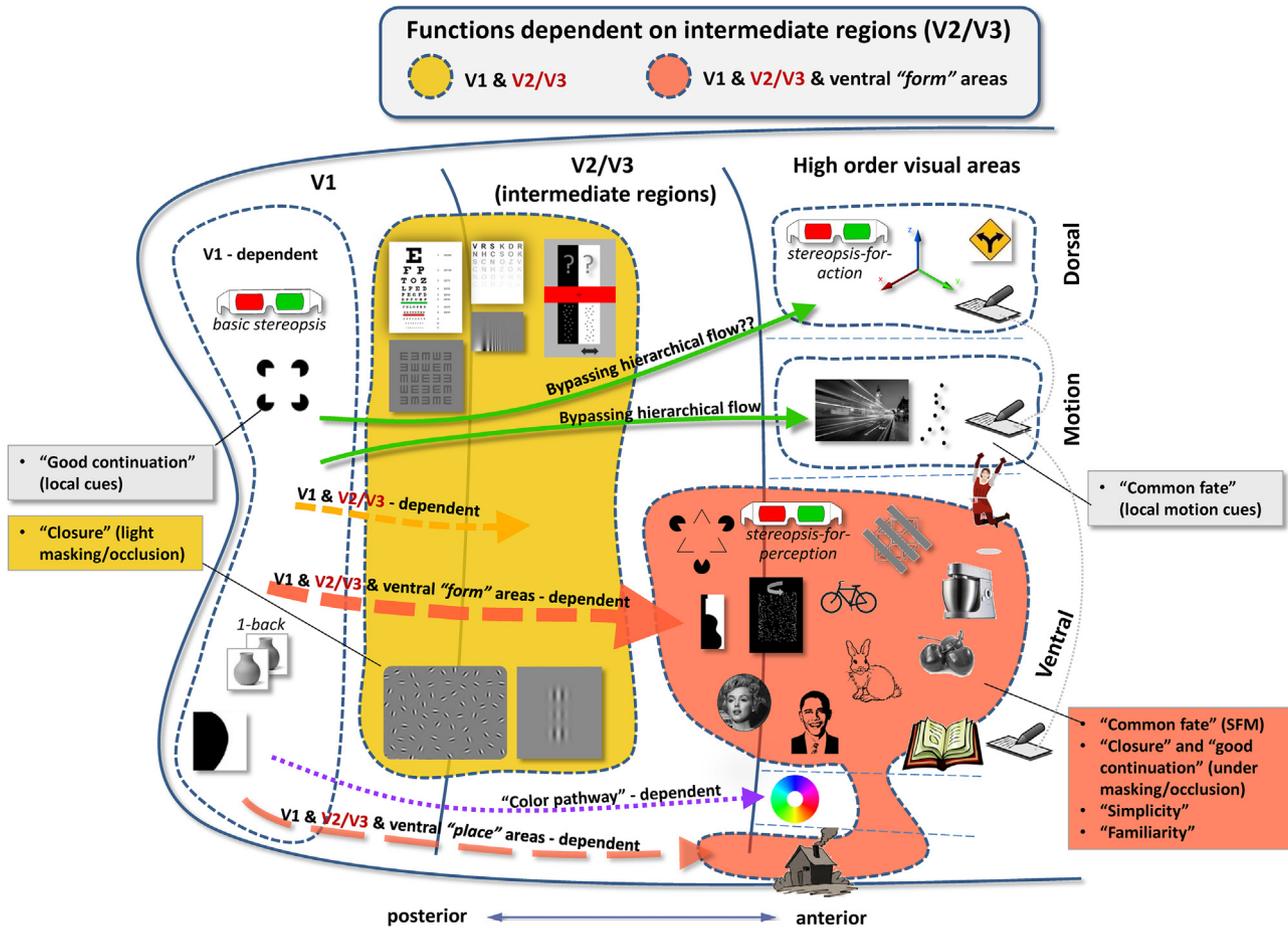


Fig. 3. Proposed grouping of visual functions with the brain regions they rely on, based on LG's case and previous studies. Grouped functions are suggested to rely on common mechanisms and are superimposed on a schematic cartoonish flattened cortical right hemisphere (posterior aspects, not to scale, as in Fig. 2) to illustrate the cortical regions that each is proposed to rely on. Functions are depicted by icons (see sections 4 and 5 for full details). Colored background indicates dependency on intermediate visual regions (V2/V3) and arrows indicate information flow from V1 into the visual cortex. In yellowish-orange are functions that I suppose rely on V1 and on V2/V3 ("V1 & V2/V3 - dependent"; e.g. require normal feedforward to or feedback from V2/V3 to develop properly, see orange dashed arrow). In pinkish-orange are functions that are critically dependent on V2/V3 for mid-level or higher-order form-based representations ("V1 & V2/V3 & ventral "form" areas - dependent"; e.g. objects, faces, here presented together) performed in ventral cortex based on hierarchical information flow (depicted by thick arrow passing through V2/V3). Note that (i) place perception might be less dependent on V2/V3, perhaps similar to local-global effects, (ii) reading might be less reliant on V2/V3, and (iii) writing might rely on reading (ventral), visuo-motor skills (dorsal cortex), and motion-sensitive cortex (see Open questions). Functions in non-colored sections do not critically depend on V2/V3. These include the V1-dependent functions, functions dependent on V1 and on motion or dorsal high-order regions but not on V2/V3 (see green arrows; dorsal inputs might rely on direct V1 and MT connections), or the color processing network that traverses intermediate visual regions (see purple arrow) in an independent route (blobs, thin stripes, globs). Some of the Gestalt grouping principles are associated with the different groups (see text). Three stereopsis functions (depicted by red-green glasses) rely on different mechanisms (see text for more details). The visual functions presented here are limited to the ones LG was tested on. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

The above classification makes a broad distinction between two classes of functions: those that probably do not depend on V2/V3 (groups 1 and 2 in Table 2), and those that probably do depend on V2/V3 (groups 3 and 4 in Table 2).

A few observations stand out from this classification and from LG's performance. **First**, some functions that seem to rely on very proximal or even joint mechanisms do not show similar performance in LG. So for example, figure-ground processes based on local cues were found to be normal in LG, while when based on contextual cues – even when the contextual cues were only slightly more distant than the local cues (0.15° apart), LG's performance was significantly impaired (Brooks et al., 2012). In a similar fashion, LG performed very differently on simple and complex Kanizsa figures. While he instantaneously correctly identified simple geometric shapes (e.g. rectangles, triangles) from Kanizsa figures, he misidentified the more complex shape of the Star of David (which is composed of two opposite triangles superimposed on each other) as a diamond, and only after being provided with feedback and tracking it with his finger did he get it right. And another example relates to his performance on object tests, where

he performed normally on some tests, as when being required to match an image of an object from a rotated view to "standard" image of the same object (but without having to name it) or when asked to name the line drawings in the Boston naming test and succeeded in all but the infrequently occurring objects (Gilaie-Dotan et al., 2009). In other object-related tests he shows significant impairments as when required to name overlapping line drawings of objects, letters, or geometric shapes, or to name full animal line drawings (Gilaie-Dotan et al., 2009; Lev et al., 2015). **Second**, early mechanisms that were assumed to be associated with and rely predominantly on V1, which is for the most part normal in LG (see Figure 2), such as contrast sensitivity, crowding and lateral interactions (Polat et al., 1998; Chen et al., 2001; Mizobe et al., 2001) were impaired in LG before he began training (Gilaie-Dotan et al., 2009; Lev et al., 2015). **Third**, certain mechanisms that are assumed to rely on higher-order visual mechanisms beyond intermediate visual regions, seem to be normal in LG despite his abnormally functioning visual cortex. These include color perception that is assumed to rely on human ventral occipital cortex or macaque posterior IT (Beauchamp et al., 1999,

2000; Bouvier and Engel, 2006; Conway and Tsao, 2009); stereopsis, which on top of V1 is assumed to rely on multiplicity of regions including ventral V4 and LOC in the ventral stream (Covey and Porter, 1979; Janssen et al., 2000; Gilaie-Dotan et al., 2002; Roe et al., 2007) and regions in the dorsal pathway (Marotta et al., 1997; Roe et al., 2007; Georgieva et al., 2009); visual motion relying on a multitude of regions including MT+/V5, pSTS, vPMC, and even ventral visual cortex (Zihl et al., 1983; Newsome and Pare, 1988; Salzman et al., 1990; Celebrini and Newsome, 1995; Saygin, 2007; van Kemenade et al., 2012; Gilaie-Dotan et al., 2013c; Zihl and Heywood, 2015); and reading, which is assumed to rely on ventral occipital regions (Seghier et al., 2012; Behrmann and Plaut, 2014). **Fourth**, it is unlikely that all the functions within each class/group rely on joint mechanisms. For example, basic visual motion, 1-back task and reading, all grouped into group 1, are probably supported by different mechanisms.

4. Associating visual functions with visual regions

Therefore, based on LG's results and previous studies, in Fig. 3 I propose a partition of visual functions into groups that rely on similar mechanisms, along with a neural correlate for each group. Functions that were classified as **independent of V2/V3** (in non-colored zones of Fig. 3 and in groups 1 and 2 in Table 2) are those that are (i) assumed to *rely solely on V1-related* (or earlier) mechanisms [on the left zone of Fig. 3 labeled "V1-dependent", e.g. 1-back same/different, simple Kanizsa figure, and figure-ground assignment based on local or convexity cues], (ii) those that seem to rely on *non-hierarchical information flow to motion or to dorsal high-order areas*, probably bypassing V2/V3 (on the top right zones of Fig. 3), or (iii) *color perception* (bottom right of Fig. 3). Examples of non-hierarchical functions bypassing V2/V3 (ii) are visual motion functions that seem normal in LG (motion detection, motion coherence) and aspects related to stereopsis. Indeed, visual motion cues progress directly from V1 to MT/V5 (Ungerleider and Desimone, 1986; Van Essen et al., 1986; Rockland, 1989; Movshon and Newsome, 1996), which can explain how LG's hMT+/V5 seems to show the expected motion selectivity and functional connectivity (Gilaie-Dotan et al., 2009; Gilaie-Dotan et al., 2011). Stereopsis was found to be completely normal in LG as established by a stereopsis test commonly used in the clinical setup and administered from near vision (Fricke and Siderov, 1997; Birch et al., 2008), however global stereopsis and grasping or prehension have not been tested in LG, and these critically rely on stereo vision (Covey and Porter, 1979; Marotta et al., 1997) and are supported by high order visual cortex (Zeki, 1978; Janssen et al., 1999; Gilaie-Dotan et al., 2002; Roe et al., 2007; Georgieva et al., 2009). Therefore, I propose that *basic stereopsis* abilities are supported by V1-based mechanisms, in line with LG's normal performance on the Randot stereo test before the training began. In addition, I classified *stereopsis-for-action* under the dorsal stream functions that do not rely on V2/V3, again in line with LG's unimpaired space perception and orientation and his reliance on visuo-motor behaviour (including tactile inputs) to compensate for his perceptual impairments (Gilaie-Dotan, unpublished). His normal stereo performance might also be supported by the V1 to MT/V5 route (Zeki, 1978; Maunsell and Van Essen, 1983; Ungerleider and Desimone, 1986; Rockland, 1989; DeAngelis et al., 1998) or by binocular inputs reaching higher order regions through a route that bypasses V1 (Girard et al., 1991; Sincich et al., 2004). In addition, I assigned a third stereo-related classification (*stereopsis-for-perception* or "*global stereopsis*") to the ventral stream functions that are dependent on intermediate visual regions (see in pinkish-orange in Fig. 3) in line with earlier studies (Covey and Porter, 1979) and with my hypothesis that *stereopsis-for-perception* might be impaired in LG.

Multiple scenarios can lead to **dependency on V2/V3**. First, functions that are assumed to rely on V1 mechanisms as visual acuity, contrast sensitivity, crowding and lateral interactions (Polat et al., 1998; Chen et al., 2001; Mizobe et al., 2001), but were significantly impaired in LG before he started training, might actually rely on an *indirect secondary contribution of intermediate visual regions* to these functions ("V1 & V2/V3 - dependent", colored in yellowish orange in Fig. 3), probably depending on normal feed-forward and feedback information flow between V1 and V2/V3 (Ahissar and Hochstein, 1997; Hochstein and Ahissar, 2002). This is in line with the improvements in these visual functions that LG experienced following the visual training, as the training is assumed to strengthen lateral connections in and mechanisms associated with V1 (Polat et al., 1998; Chen et al., 2001; Mizobe et al., 2001; Lev et al., 2015), which might have not developed properly due to the abnormality in his intermediate areas and the abnormal flow of information between V1 and V2/V3 (Gilaie-Dotan et al., 2009). Grouped with these functions is also figure-ground organization based on close contextual cues, and contour in noise (Kovacs et al., 2000) which might be considered to rely on V2/V3, yet since it has improved to normal performance following training, I assume it also relies on V1.

A visual function would also rely on V2/V3 if it directly supports form-based midlevel visual representations, or if it is a high-order visual function (e.g. face perception) relying on normal buildup of information along the visual hierarchy. However, my underlying hypothesis is that most computations are not completed in intermediate visual cortex, and therefore most information that flows downstream through intermediate visual cortex reaches high order cortex (except for V1-dependent and V1 & V2/V3-dependent groups for very limited form-based computations (see Fig. 3)). As a consequence, and taking into account previous knowledge, I assigned most of the functions that LG is still impaired in (or that I think he is likely to be impaired in) to one group "V1 & V2/V3 and ventral "form" areas - dependent", (colored in pinkish-orange in Fig. 3), as I assume that each of these functions *relies on normal function of both intermediate visual areas and high order visual cortex specializing in form perception* (including faces and objects together here). Note that it is likely that all these functions actually rely on a subsystem within intermediate visual areas, for example one that is color-blind and sensitive to orientation, edges, and surfaces, such as the proposed parvocellular inter-blob system (DeYoe and Van Essen, 1988).

5. Open questions

Still, some issues remain puzzling. It is surprising that some functions that require spatial integration over occlusion or absent information are normal in LG following training (contour integration in noise), while other very similar functions show impairments (figure-ground based on contextual cues or recognition over occlusion). These *perceptual "discrepancies"* in LG could suggest that the classical Gestalt intermediate grouping mechanisms ("laws of grouping", e.g. by proximity, similarity, symmetry, continuity) may actually rely on multiple different mechanisms (rather than on one common mechanism), some of which rely on intermediate visual regions and some of which do not. For example, "*the law of common fate*", which might typically be considered a single mechanism, seems to break down in LG (see boxes on the right side of Fig. 3). While some tasks based on the common fate principle seem normal in LG [e.g. coherence (Lev et al., 2015), edge-region grouping based on local cues (Brooks et al., 2012) and biological motion from point-light-displays (Gilaie-Dotan et al., 2011)], in line with findings from late-acquired or late-restored vision (Fine et al., 2003; Ostrovsky et al., 2009), suggesting

predominant reliance on motion-based mechanisms independently of intermediate visual regions, other common fate-related tasks are impaired in LG and are probably significantly dependent on intermediate visual areas and perhaps on ventral object-related regions (2D and 3D non-biological structure-from-motion such as polygons, spheres or cylinders (Gilaie-Dotan et al., 2011), and edge-region grouping based on very close contextual cues (Brooks et al., 2012)). The “law of closure” and the “law of good continuation” might be significantly dependent on intermediate visual areas, especially in more complex situations (vs. simple Kanizsa figures) as when heavy masking (heavily masked text) or occlusion are present [e.g. line drawing naming (Gilaie-Dotan et al., 2011) or edge-assignment over occlusion (Brooks et al., 2012)]. This is also in line with recent studies that investigated individuals who acquired or restored their vision late in life (Fine et al., 2003; Ostrovsky et al., 2009), further suggesting that the underlying mechanisms supporting these laws are based on visual perceptual representations that are acquired across development. LG’s compromised object perception and perceptual organization performance [e.g. Hooper visual organization test (Hooper 1983), BORB-6 (Riddoch and Humphreys, 1993; Gilaie-Dotan et al., 2009; Lev et al., 2015), and figure-ground based on familiarity silhouettes (Brooks et al., 2012)] might also indicate that the “law of simplicity” (aka the “law of good figure” or “law of Prägnanz”) and the “law of familiarity” might actually rely on previously stored perceptual representations and thus be significantly dependent on intermediate as well as on ventral object-related regions (Ostrovsky et al., 2009), whether for the creation and storage of these perceptual representations or for their retrieval. Object perception and even more so face perception, may be considered as extreme cases of the law of familiarity, in which case it is not surprising that LG’s performance on a variety of these tasks is significantly impaired (see Table 2) and even resembles that of 6–8 year olds on a face memory test (Duchaine and Nakayama, 2006; Mardo et al., 2015). These dissociated Gestalt heuristics have been added to Fig. 3 in four boxes accordingly.

Another such unresolved issue is that LG’s color vision appears to be normal. One possibility is that although we used two different tests to assess his color vision (Ishihara (1917) and HRR²), they both lacked the sensitivity to reveal LG’s color perception deficits. However, this might not be the most compelling explanation. Another possibility is that color is processed in a segregated route, such as the parvocellular-blob stream proposed by DeYoe and Van Essen (1988), and this route is not adversely affected in LG’s visual system. And indeed, color information processing begins at the retinal level (cone receptors, parvocellular and bistratified ganglion cells) and remains somewhat segregated through LGN (parvocellular and koniocellular layers), early visual cortex (V1’s color blobs and V2’s thin stripes; Wong-Riley, 1979; DeYoe and Van Essen, 1988; Lu and Roe 2008), and even within downstream regions in the ventral pathway (V4 and PIT globs; Conway et al., 2007; Conway and Tsao, 2009), where color “columns” resembling the perceptual color space are organized within color-sensitive cortical regions (Conway and Tsao, 2009). These color-sensitive regions have relatively weak shape-selectivity, whereas nearby shape-sensitive regions have relatively weak color-selectivity (Conway et al., 2007; Lu and Roe, 2008, Lafer-Sousa and Conway, 2013), suggesting that color and shape are predominantly processed in parallel within the ventral stream. Since the abnormality in LG’s visual cortex was revealed with fMRI and EEG (Gilaie-Dotan et al., 2009), both methods averaging across extensive neural populations, and since the network supporting color processing constitutes a minor portion of the visual cortex

(Lu and Roe, 2008; Lafer-Sousa and Conway, 2013) which in V1 and V2 is rather uniformly distributed (Lu and Roe, 2008), LG’s color system, even if normally functioning, might have gone undetected under these circumstances. And lastly, direct subcortical projections (e.g. LGN or pulvinar) to V4 and possibly to additional regions downstream (Ninomiya et al., 2011) might provide sufficient color information to allow normal color vision. The idea that color processing might be dissociated from shape processing is in fact supported by some cases of *acquired* visual agnosia, who, despite their lesions and form perception deficits, retained their color perception (Adler, 1950; Efron, 1968; Milner and Heywood, 1989; Grossman et al., 1997; Mapelli and Behrmann, 1997). In light of the 3-stream model for motion, form, and color (DeYoe and Van Essen, 1988), LG’s perceptual profile raises the possibility that despite the functional abnormality observed in his intermediate visual regions, his magnocellular pathway for motion and space and parvocellular-blob pathway for color are somewhat preserved, while his parvocellular-interblob system for form functions abnormally.

Another unclear finding relates to *LG’s reading*, as it is not clear which mechanisms allow LG to compensate for his atypical information processing to achieve normal reading (even if from a close distance). Patients with lesions in their left ventral visual cortex suffer from pure alexia which is characterized by the difficulty to read (e.g. Barton, 2011; Habekost et al., 2014). It is true that due to LG’s developmental origins plasticity might have been involved in facilitating normal reading despite abnormal left ventral visual function. The fact that plasticity was not effective in assisting him in object and in face recognition might perhaps have to do with the different spatial frequencies associated with text vs. those associated with facial or object stimuli, with the real-world dimensionality of these different categories (2D for text vs. 3D for faces and objects), with different viewing distances that each category is acquired with (near vision for reading, far vision for faces and objects; interestingly, LG finds it difficult to read street signs or distant text), with simpler and more definite high-contrast based edge-assignment and figure-ground segmentation for text, or with different processing demands such as different receptive field sizes that are required to succeed in these different tasks. But again, it is probably not only about receptive field sizes, stimulus dimensionality or viewing distances, as when tested with static pictures, LG seems to be able to recognize correctly body expressions (when in context) but not facial expressions (Aviezer et al., 2012a, 2012b; see also Table 2), and he also performs normally on whole-body motion perception (Gilaie-Dotan et al., 2011) when bodies take up a bigger portion of the visual field than faces. I hypothesize that LG’s normal writing relies on his normal reading combined with his probably adequate visuo-motor coordination abilities (see Figure 3).

Lastly, *LG’s local-global performance* in the Navon task (Navon, 1977) is also not easy to explain, especially since it appears normal showing the local-global effect, unlike typical visual agnosics (Behrmann and Kimchi, 2003). However, since a recent developmental study shows that local-global effect magnitude is age-dependent, reducing with age (Mardo et al., 2015), there is a possibility that LG’s effect magnitude actually matches that of younger age groups, corresponding to his underperformance in other high-level visual functions. If that is the case, then the mechanisms giving rise to local-global effects could be placed in the proposed model under “V1 & V2/V3-dependent” or “V1 & V2/V3 & ventral form areas-dependent” mechanisms. Alternatively, local-global effect could be driven by the “gist of the scene” or “vision at a glance” percept (Hochstein and Ahissar, 2002) that is hypothesized to occur early in the visual process by high-level implicit processes. However, it is unclear which brain mechanisms or more specifically high-order areas give rise to this ability. Could

² <http://www.richmondproducts.com/>.

magnocellular transient processes suffice to support this ability, perhaps explaining how even in LG's case of hindered downstream flow, such "vision at a glance" might function normally? Interestingly, a recent framework for midlevel vision computations (Kubilius et al., 2014) proposes that the gist of the scene can be achieved in a pre-attentive manner by pooling together information from multiple sources (color, orientation, natural statistics of the scene and so on). For such a framework to support "vision at a glance" (Hochstein and Ahissar, 2002; Kubilius et al., 2014), it would be reasonable to assume that such pre-attentive computations should occur fast and based on coarse spatial resolution, as is the case with the magnocellular pathway (Schmolesky et al., 1998; Lamme and Roelfsema, 2000) which appears to function normally in LG (Gilaie-Dotan et al., 2009, 2011). Another such processing route that might also be normal in LG (see place recognition in Table 2), might rely on peripheral form-based computations, which are suggested to respond transiently (Gilaie-Dotan et al., 2008) and rely on coarse spatial resolution (Levy et al., 2001, 2004; Dumoulin and Wandell, 2008). This might actually suggest that local-global effects are driven by peripheral coarse vision integrating over space, possibly relying on the same mechanisms as those for place recognition. Lastly, while LG's color perception seems normal, since investigations of the color processing network are still in their infancy, it is hard to predict if color could additionally support "vision at a glance".

Although LG has been tested on many visual functions, there are still many visual functions that his performance on remains unknown and also unpredictable. While most investigations on LG have focused on tests normally administered to visual agnostic individuals and thus concern functions associated with ventral stream, much less is known about his dorsal related mechanisms, and about his visual motion perception (e.g. Vaina et al., 1999).

6. Conclusions

Here I had the opportunity to review a set of studies that we carried out on an individual with no apparent brain damage to examine which of a wide range of visual functions are adversely affected by his abnormally functioning intermediate visual areas.

While LG is a singular case study, and his visual functioning and visual cortex cannot be directly compared to the neurotypical visual system, the results reviewed here allow examining which visual functions are more likely to overcome hindering factors (associated with intermediate visual areas) and reach normal performance even if relying on plasticity, and which visual functions are more vulnerable and less likely to benefit from compensatory mechanisms when intermediate visual areas function abnormally.

Although some issues remain unclear or puzzling, it seems that LG's biggest problems are on the one hand related to spatial integration, especially over occlusion or inadequate visual inputs, leading to holistic shape and spatial percepts; and on the other hand, related to retaining in or retrieving from memory representations of such percepts [as evident by his performance on short-term memory face or object tests (see Table 2; Warrington, 1984; Benton et al., 1994; Duchaine and Nakayama, 2006; McKone et al., 2011; Dennett et al., 2012; Susilo et al., 2015)]. This suggests that the main functions that V2 and V3 are involved in, or more precisely the network associated with the parvocellular inter-blob "form" system within V2/V3 (DeYoe and Van Essen, 1988; DeYoe et al., 1994a), are to integrate form and structure information over space, probably in the service of memory.

Thus, although spatial integration may be considered a homogenous process, it might actually be a family of different processes modulated by different task demands (e.g. object perception,

scene perception, spatial attention, multiple object tracking, optic flow, etc.), and therefore more specific terminology would be appropriate (e.g. 'spatial integration for structure perception'). The results reviewed and the model proposed here might provide challenging insights about dependencies of visual processes on visual regions (with a special emphasis on intermediate visual regions) that might also serve computational vision neuroscience.

Acknowledgments

This paper is dedicated to the dear Prof. Shlomo Bentin, may his soul rest in peace. Shlomo was an enthusiastic scientist who was keen and thrilled about scientific explorations. He was fascinated by LG the person and by his peculiar vision, and kept himself occupied in trying to find a remedy for LG's vision. The visual improvements that LG experienced following the perceptual learning paradigm he trained on (Lev et al., 2015) filled Shlomo with joy. Shlomo also suggested to LG another training paradigm aimed at improving facial recognition skills. However, after training for quite some time with no feeling of improvements in facial recognition, LG decided to stop training on that paradigm. I would like to thank you, Shlomo, for teaching me so many things, introducing me to new scientific territories that were so fascinating, challenging me and at the same time applauding, criticizing and supporting me. I also thank the editors for giving me the opportunity to write this review, LG and his family for their wonderful and heart-warming willingness to continue and participate in our long-lasting scientific investigations, Juha Silvanto and Joseph Brooks for their insightful and helpful comments on the manuscript, Anat Perry, Yoram Bonneh, and Hillel Aviezer for assisting me in retrieving some details for this manuscript, all my collaborators on all of these studies, Constantin Rezesescu for assistance with the Cambridge Memory tests, and two anonymous reviewers who have provided me with insightful comments and feedback allowing me to crystalize the ideas presented in this paper.

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