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PRESERVED GRIP SCALING TO UNSEEN OBJECTS FOLLOWING A UNILATERAL LESION TO V1 FOR IMMEDIATE BUT NOT DELAYED GRASPING

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PRESERVED GRIP SCALING TO UNSEEN OBJECTS FOLLOWING A UNILATERAL LESION TO V1 FOR IMMEDIATE BUT NOT DELAYED GRASPING

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I, Robert Whitwell[1], was the principal author of this thesis and the version submitted to the Journal of Vision. I was involved in all aspects of the project, from design and implementation on through to the analysis of the data and drafting of the initial and revised versions of this thesis and the version submitted to the Vision Research. Dr. Christopher Striemer[1] assisted me with many aspects of the project, including administering the experiments, analysis of the target localisation and fMRI data, and drafting the submitted version. Dr. Melvyn A. Goodale[1] was involved in the design of the experiments and revisions of the submitted manuscript. Dr. David A. Nicolle[2] conducted the tests of static perimetry to define the extent of patient SJ's vision loss.

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Abstract

Patients with damage to V1 can sometimes direct actions towards 'unseen' targets located in areas of the visual field that are deemed 'blind' on the basis of static perimetry tests. Here, we show that a patient with a complete right homonymous hemianopia after a V1 lesion remains sensitive to the width of objects presented in her blind field but only when reaching out to grasp them in 'real-time'. A subsequent fMRI experiment indicated that these preserved abilities are likely mediated by spared extra-geniculostriate pathways, while a small "tag" of occipital cortex located at the occipital pole remained unresponsive. Taken together, the results support the view that visually guided movements can be mediated by pathways that do not support visual consciousness.

Keywords

dorsal stream, grasping, V1, blindsight, perception-action

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CHAPTER 1

Introduction

The deceptively simple act of reaching out and grasping an object is an almost perfect example of what the brain has evolved to do: namely, to control our movements in the world. Vision plays an indispensable role in this skilled behaviour, and over the last three decades, considerable effort has been spent trying to understand the neural substrates of visually guided grasping.

The Perception and Action Model

In 1992, Goodale and Milner proposed that the ventral visual processing 'stream' that arises mainly from primary visual cortex and projects to inferotemporal cortex mediates the recognition and identification of goal objects for action, while the dorsal visual processing stream that arises mainly from primary visual cortex and projects to the posterior parietal cortex (PPC) transforms the particular information about the goal object into the required motor coordinates for action. According to their account, the division of labour between the ventral and the dorsal pathways reflects the different requirements of vision-for-perception and vision-for-action respectively.

The different requirements of vision-for-perception and vision-for-action are also reflected in the way in which each stream makes use of memory of previous visual events. Visual recognition depends on object constancy, the ability to identify the same object from different viewpoints, whereas the visual

control of action requires that the visuomotor transformations reflect the disposition of the goal object with respect to the actor at the precise moment the action is performed. Thus, as Goodale and Milner argue, the dorsal stream has no need for long-term memory because it computes visuomotor transformations *de novo* each time an action is performed. In fact, storing particular visuomotor coordinates would be counterproductive since the disposition of the goal object with respect to the effector to be used can change dramatically in just a few seconds. In stark contrast, visual processing in the ventral stream interacts with long-term memory stores of previous visual experiences to enable the recognition of objects over long periods of time. This means that actions that are performed on remembered objects that are no longer visible must invoke stored visual information originally processed by the ventral stream (for a discussion of these issues, see Milner and Goodale, 2006).

One principal line of evidence for Goodale and Milner's (1992) proposal comes from work with patients with visual form agnosia and optic ataxia. Goodale and Milner have argued that the different patterns of spared visual abilities and deficits in these two patient groups constitute a functional and anatomical double dissociation between vision-for-perception and vision-for-action. One set of findings from this work is particularly relevant to the present set of experiments and involves the differences in the way each patient group deals with temporal delay.

Visual Form Agnosia

Patient DF, for example, who has visual form agnosia as a result of damage to the lateral occipital complex (LOC), a ventral-stream structure (James, Culham, Humphrey, Milner, & Goodale, 2003), is still able to reach out and grasp objects accurately despite the fact that she is unable to report their size, shape, or orientation either manually or verbally. Thus, DF is unable to use her finger and thumb to reliably indicate the width of a target object when asked to give an estimate of its size, but when she reaches out to grasp that same object her grip aperture (the distance between her finger and thumb) smoothly scales in-flight to the object's width (Goodale, Milner, Jakobson, & Carey, 1991; see also patient JS: Karnath, Ruter, Mandler, & Himmelbach, 2009). The authors presumed that her preserved performance during target-directed actions like these is mediated by a largely functioning and intact dorsal stream. Importantly, however, if DF is asked to reach out and grasp an object that she saw only moments before, she no longer scales her in-flight grip aperture to the object's size (Goodale, Jakobson, & Keillor, 1994). This impairment in memory-driven grasping was thought to reflect the fact that, because of her ventral-stream damage, she was unable to perceive the dimensions of the object and store that information in memory.

Optic Ataxia

Optic ataxia is a visuomotor disorder that impairs target-directed actions, such as reaching and grasping. It typically arises following damage to the dorsal stream, particularly in the superior parietal lobule (SPL), intra-parietal sulcus (IPS), and parietal-occipital cortex (POC) (Karnath & Perenin, 2005; Perenin & Vighetto, 1988). Nevertheless, because the ventral stream often remains relatively intact in these patients, they perform reasonably well on perceptual tasks that require object localisation or identification (Jakobson, Archibald, Carey, & Goodale, 1991; Perenin & Vighetto, 1988). Thus, these patients can accurately estimate the size of target objects (Jakobson et al., 1991) and yet show profound deficits in grip formation and coordination when asked to grasp them (Jakobson et al., 1991; Jeannerod, Decety, & Michel, 1994; Milner, Dijkerman, Pisella, McIntosh, Tilikete, Vighetto, & Rossetti 2001; Perenin & Vighetto, 1988). Remarkably, if the task is modified to require the patient to grasp an unseen object viewed two seconds before the response is cued, their performance improves (Milner et al., 2001; Rossetti, Revol, McIntosh, Pisella, Rode & Danckert, 2005). As Milner et al. (2001) noted, these results complement DF's impairment on a similar task (Goodale, Jakobson, & Keillor, 1994). Taken together, these results suggest that skilled target-directed actions depend on intact dorsal stream structures in which visual input is processed the moment an action is programmed, and that actions that follow a delay must be programmed on the basis of remembered visual input which ultimately depends on an intact and functioning ventral stream.

Pathways mediating DF's visuomotor abilities

Although patient DF is able to scale her grip aperture to objects that she cannot recognize, it is unclear what remaining visual pathways are responsible for this remarkable ability. Retinal inputs to primary visual cortex (V1) via the geniculostriate pathway are known to innervate extrastriate regions V2 and V3/V3A, all of which innervate the parietal-occipital cortex (POC) in the dorsal stream. It may be the case that this pathway is critical for DF's preserved visuomotor abilities, particularly since DF's V1 appears to be intact (James et al., 2003; Milner et al., 1991). In fact, because not all of her ventral stream is damaged, DF also has some conscious vision, such as luminance and colour, and is able to report with some accuracy the surface properties of objects.

Blindsight

Although inputs from V1 may well be responsible for the preserved visuomotor abilities in patients with visual form agnosia, there have been reports of similarly preserved visuomotor abilities in patients with visual field loss who do not have access to any conscious vision following damage to V1. Specifically, Weiskrantz and colleagues (Sanders, Warrington, Marshall, & Weiskrantz, 1974; Weiskrantz, Warrington, Sanders, & Marshall, 1974) coined the term "blindsight" to describe patients with visual field loss who deny seeing visual stimuli presented in their affected field but whose voluntary performance can be reliably influenced by this stimulus. Just one year earlier, Poppel, Held, and Frost (1973) showed that four patients with quadrantanopia (as determined with static perimetry) could

scale the amplitude of their saccades to a spot of light flashed briefly (100ms) on any one of the three closest target positions that fell along an oblique meridian within the scotoma.

Action Blindsight

A number of studies have shown that patients with blindsight can reliably detect, discriminate, and/or localize stimuli presented in their affected field using forced-choice methodology, manual pointing (e.g., Danckert et al., 2003; Perenin & Jeannerod, 1975) or eye movements (e.g., Barbur, Forsyth, & Findlay, 1988; Poppel, Held, & Frost, 1973), and that some patients can reliably calibrate their in-flight grip aperture to the size of novel objects located in their blind field when reaching out to pick them up (e.g., Perenin and Rossetti, 1996) (for recent reviews see Cowey, 2010; Danckert & Rossetti, 2005). The particular ability to act on 'unseen' objects has been termed 'action blindsight' (Rossetti & Pissela, 2002; see also Danckert & Rossetti, 2005).

Weiskrantz and his colleagues (1974) were the first to show that a patient, DB, with hemianopia in his left visual field could accurately locate targets presented in his blind field by pointing to them. A few years later, however, Campion, Latto, and Smith (1983) levelled a number of criticisms at these results. The stimuli used for Weiskrantz et al.'s (1974) experiment were white and as bright as the projectors would permit. Thus, light from the stimulus falling on DB's retina corresponding to his blind field might have reflected onto sighted regions of his retina. The characteristics of this reflected light would have varied

with the position of the stimulus and therefore might have cued DB to the position of the stimulus (Campion, Latto, & Smith, 1983). In addition, DB's eye movements were neither recorded nor monitored, and so whether or not DB maintained fixation throughout the experiment was questionable. These criticisms were addressed several years later when Weiskrantz (1987) showed that DB could localize targets accurately when they were presented in the regions of his blind field outside of his optic disc or 'blind spot'. This suggests that light scatter and poor fixation could not account for DB's accuracy, since either of these factors would be equally applicable to a stimulus presented in his blind spot. Furthermore, subsequent studies of several different patients with hemianopia have found that many (though not all) patients retain the remarkable ability to point to targets presented in their blind field (see e.g., Corbetta, Marzi, Tassinari, & Aglioti, 1990; Danckert et al., 2003; Perenin & Jeannerod, 1975; Perenin & Jeannerod, 1978).

As mentioned above, patients with hemianopia show a range of spared visuomotor abilities that are not restricted to saccades and target localisation. Perenin and Rossetti (1996), for example, showed that patient PJG with hemianopia could scale his grip aperture to the width of the objects presented entirely within his blind field yet he could neither 'match' the object size using his thumb and forefinger nor verbally discriminate the objects according to their size. Marcel (1998) tested two patients, one of which was GY, both of whom could scale their grip, categorically, to the diameter of large and small variants of a cylinder and circle. Jackson (1999) tested GY's ability to scale his grip to the

width of novel objects presented in his blind field but also monitored and recorded GY's eye-movements using an infrared eye tracker. Jackson found that although patient GY could not scale his grip aperture to the relevant (varying) dimension of novel objects presented entirely within his blind field, he could in fact do so as long as the 'irrelevant' (i.e., invariant) dimension of the object was located within GY's sighted field. Interestingly, however, under an identical setup, GY failed to estimate the magnitude of the relevant dimension of the objects accurately on a verbal scale of one to six.

Pathways Mediating Action Blindsight

The existence of action blindsight suggests that intact visual pathways outside of the prominent geniculostriate pathway are capable of mediating visually guided actions. One such pathway from the retina courses through the superior colliculus and pulvinar nucleus in the thalamus (i.e., the retino-tectal-pulvinar pathway) to the motion-sensitive area MT and from there on to areas in the dorsal stream (Kaas & Lyon, 2007; Lyon, Nassi, & Callaway, 2010). This pathway is known to convey primarily magnocellular information which has relatively low spatial resolution but is extremely sensitive to changes in contrast. In addition, there are projections from koniocellular cells in the interlaminar regions of the dorsal lateral geniculate nucleus (dLGN) that bypass V1 and project directly to area MT and onward to other regions of the dorsal stream (Sincich, Park, Wohlgemuth, & Horton, 2004). The kind of information conveyed by koniocellular cells depends on which layer of the dLGN they reside in.

Koniocellular cells tend to convey information that is similar to that conveyed by the cells in neighbouring parvocellular or magnocellular layers. Thus, some koniocellular cells convey short-wave length visual information from S-cones of the retina, low spatial acuity, or modulate neurons in the superior colliculus (SC) (Hendry & Reid, 2000). In the monkey, koniocellular, magnocellular, and parvocellular projections from the dLGN to extrastriate regions (those beyond V1) have been shown to survive lesions of striate cortex (Cowey & Stoerig, 1989). Recently, a direct projection from the eye to the pulvinar, and then to MT has been identified in the marmoset (Warner, Goldshmit, & Bourne, 2010) and from the SC to the pulvinar and then on to MT in the macaque (Berman & Wurtz, 2010). Thus, in the absence of V1 input, there appears to be a number of extra-geniculostriate pathways that could continue to provide information about targeted objects to the dorsal stream upon which the transformations required for calibrating grip aperture could be based.

Recent studies of preserved visuomotor abilities in patients with action blindsight have shown that, in addition to the ability to localize targets by eye or hand movements, these patients can also avoid 'unseen' obstacles (de Gelder et al., 2008; Striemer, Chapman, & Goodale, 2009). In short, several studies have demonstrated that patients with action blindsight can carry out rather complex actions in the absence of any conscious vision. Thus, examining patients with action blindsight affords an opportunity to investigate what aspects of dorsal stream function remain in the absence of inputs from V1 and whether these aspects operate only in 'real-time' as Goodale and Milner (1992) suggest.

Overview of Experiments

In the current set of experiments, we extend Perenin and Rossetti's (1996) demonstration that a patient with a hemianopia was capable of calibrating a grasping movement directed towards an 'unseen' object presented in the blind field. We replicated this result in patient SJ, who was left with a right homonymous hemianopia following a stroke which damaged her left occipital cortex. We show not only that SJ can localize 'unseen' stimuli presented in her blind field, but that SJ can scale her in-flight grip to the widths of novel objects located in her blind field when reaching out to pick them up either with (closed loop) or without (open loop) visual feedback, provided the movements are programmed and initiated while vision is available (i.e., in real-time). We move on to demonstrate that SJ's ability to scale her grip aperture is abolished when she is asked to grasp the same objects following a brief delay. Consistent with this latter observation, we further show that she is unable to estimate the widths of objects manually by opening her finger and thumb a matching amount. Importantly, SJ was able to perform all of these tasks perfectly in her sighted visual field. Lastly, we report the results of a functional magnetic resonance imaging (fMRI) study which suggests that SJ's intact extrastriate cortex helps mediate her spared abilities. Taken together, these data provide converging evidence that visuomotor networks in the dorsal stream can operate independently of input from V1, but only in real-time on a moment-to-moment basis.

CHAPTER 2

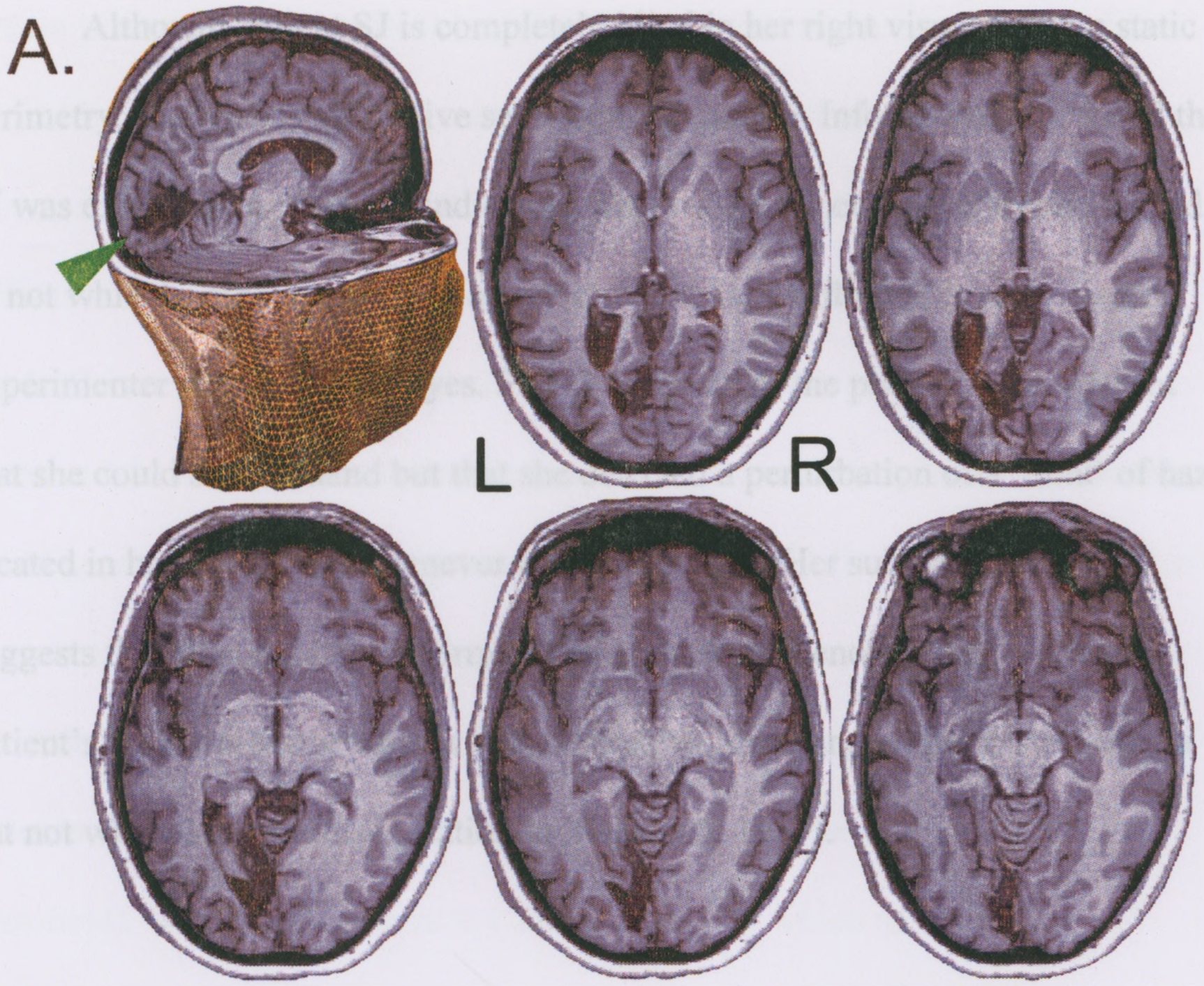
Session One Experiments

To assess patient SJ's ability to process stimuli in her blind (right) visual field, we administered two visuomotor tasks and one target-detection task. SJ localized targets presented in her sighted (left) or blind (right) visual field by pointing to them with her right hand. Next, we tested SJ using the redundant target paradigm. This task requires the participant to respond with a button press as soon as a target appears on the screen. Typically, participants are faster to respond to two targets presented simultaneously than only one (Marzi, Tassinari, Aglioti, & Lutzemberger, 1986). This phenomenon, known as 'redundancy gain', has been linked with the retino-tecto-pulvinar pathway, which is thought to mediate blindsight performance observed in some patients with hemianopia or hemispherectomy (Leh, Johansen-Berg, & Ptito, 2006; Leh, Mullen, & Ptito, 2006; Leh, Ptito, Schonwiesner, Chakravarty, & Mullen, 2009; Marzi, Mancini, Metitieri, & Savazzi, 2009; Tamietto et al., 2010). In addition, this paradigm has revealed residual perceptual processing of visual stimuli presented in the blind field in some patients (Leh, Mullen et al., 2006; Marzi et al., 1986). Finally, SJ grasped solid wooden blocks located in her sighted (left) visual field with her left hand or blind (right) visual field with her right hand.

Methods

Participants

Patient SJ is a 37 year-old right-handed female who has a complete right homonymous hemianopia with no macular or temporal crescent sparing following a left posterior cerebral artery stroke which occurred seven years prior to the time of testing. Her lesion is restricted to the left occipital lobe and optic radiations with some extension into the parahippocampal gyrus (Figure 1a) with a small remaining "tag" of cortex visible at the occipital pole. Visual fields were assessed by a neuro-ophthalmologist (D. Nicolle) using a Goldman Perimeter with III-4 sized targets (Figure 1b). Informed consent was obtained from SJ and all experimental procedures were approved by the University of Western Ontario Health Sciences Research Ethics Board and in full accordance with the Declaration of Helsinki.



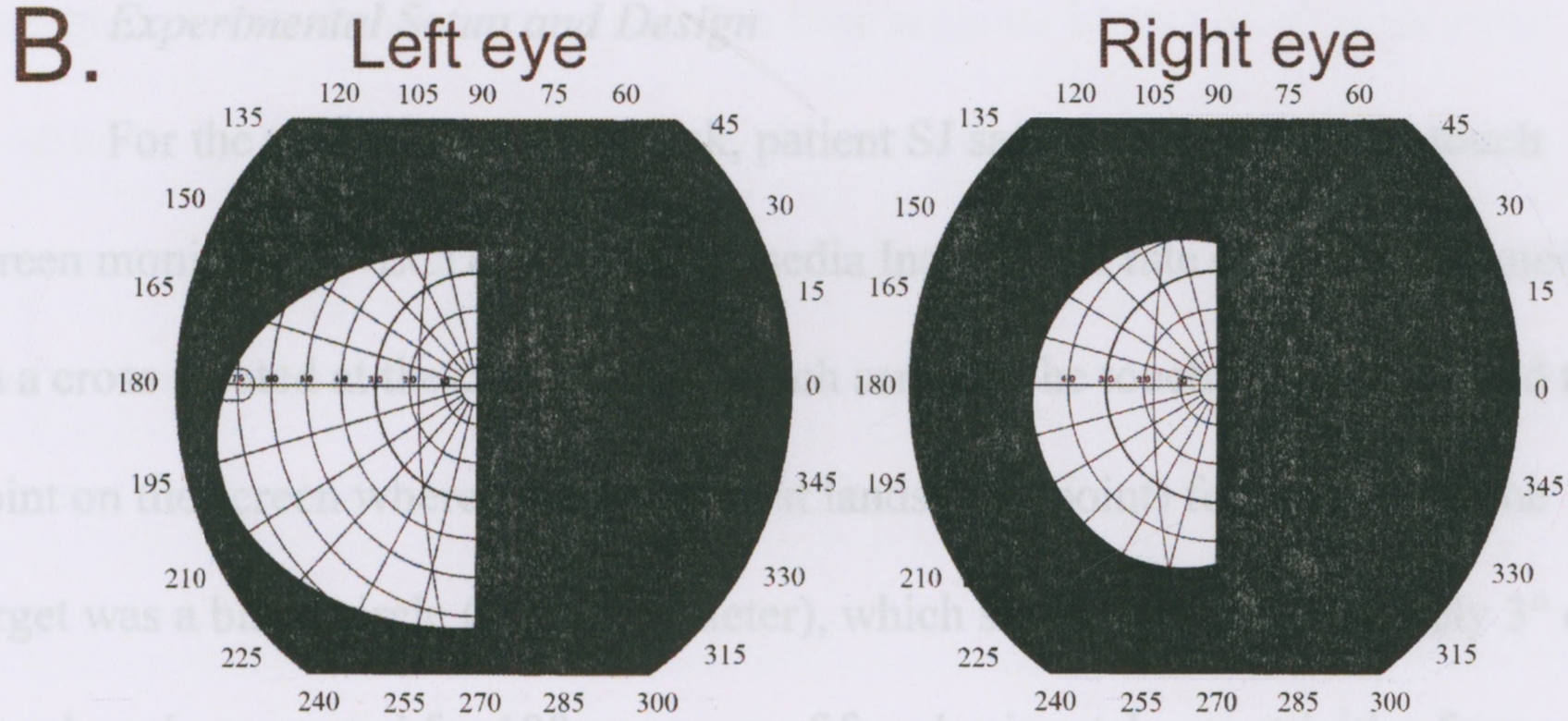


Figure 1. Panel A depicts a saggital and a series of axial slices from a T1-weighted high resolution (192 slice 1mm iso-voxel) anatomical MRI scan of patient SJ's left occipital lesion recently obtained from a 3T Siemens Tim-Trio MRI scanner at the Robarts Research Institute (London, Ontario, Canada). The lesion is restricted to the left occipital lobe and optic radiations with a minor extension into the parahippocampal gyrus. The green arrow indicates the spared "tag" of cortex at the occipital pole. Panel B depicts the results of the visual field testing with SJ. SJ has a complete right hemianopia with no macular or temporal crescent sparing. Data are presented separately for the left and right eyes.

Although patient SJ is completely blind in her right visual field on static perimetry, she reports subjective sensations of motion. Informal testing found that SJ was extremely accurate at indicating whether the experimenter's hand waved or not while he stood facing her across the table in her blind field and a second experimenter monitored her eyes. SJ's description of the phenomenon was not that she could see the hand but that she detected a perturbation of a 'field' of haze located in her blind field whenever the hand moved. Her subjective report suggests that she possesses a form of Riddoch phenomenon, which refers to a patient's ability to sense when a visual stimulus is moving within their scotoma but not when the stimulus is stationary (Riddoch, 1917).

Experimental Setup and Design

For the target localisation task, patient SJ sat 40cm away from a touch screen monitor (32" LCD, Mass Multimedia Inc; refresh rate 60Hz) and fixated on a cross located at the center of the touch screen. The touch screen recorded the point on the screen where SJ's finger first lands (end-point) for each trial. The target was a black circle (2.2cm diameter), which subtended approximately 3° of visual angle presented for 100ms at one of four horizontal eccentricities from fixation (10°, 17°, 24°, or 30°) on a uniform grey background. Each target position was sampled 20 times, and the trial order was pseudo-randomized for target position. The time from trial onset to target onset was randomly varied from 1-3s (in 500ms increments) to minimize the predictability of the target onset. SJ's

eye movements were monitored 'online' by an experimenter and recorded for additional evaluation 'offline' using a video camera zoomed in on one of her eyes.

During the target detection task, patient SJ sat 40cm away from a 32" LCD touchscreen with her head resting in a chin rest. The target was a black circle (2.2cm diameter), which subtended approximately 3° of visual angle presented for 100ms on a uniformly grey background. On a given trial, the target could appear 10° of visual angle to the left or right of a fixation cross located at the center of the screen, on both sides, or not at all. Thus, there were four conditions total. Two 'single target' conditions (left or right hemi-field), one 'double target' condition (two targets presented simultaneously, one in each hemifield), and a blank condition ('catch' trials) on which no target was presented. The task was administered in four separate blocks of 40 trials (four conditions, 10 trials per condition). Trials were presented in a pseudo-random sequence and the time between the onset of the trial and the onset of the target(s) was randomized to last anywhere from 1 – 3s (in 500ms increments). A tone was not used for this task, since SJ was required to respond only when she saw a target.

For the reach-to-grasp task, four objects were used each of which was 1.5cm in height, 5cm long, and differed from the others only in width. The smallest object width was 2.0cm with each successively larger object's width incremented by 1.5cm to a maximum of 6.5cm. The objects were painted flat black to eliminate intra-ocular dispersion and padded on the bottom to reduce the sound of contact with the surface of the table on placement. The table top was

covered with white Bristol board to provide a high contrast between the table surface and the black objects. Patient SJ was seated in front of the table with her head positioned in a chin-rest. The chin-rest was attached to the table edge directly in front of the start button, which was 15cm from the table edge. SJ aligned her midline with the start button and the chin rest. The fixation target was centered 30cm directly ahead of the start button and approximately 50cm from the participant's eyes. The inner edge of the objects was placed 8cm either to the left or to the right of fixation, which corresponded to 9° of visual angle to the left or to the right of fixation. The reach-distance from the start button to the center of the edge of the objects facing SJ was approximately 32cm.

Patient SJ's vision was controlled during the grasping session with a pair of PLATO goggles (Translucent Technologies, Toronto, Ontario) worn by the participant. The goggles are equipped with liquid crystal lenses that can switch between opaque and transparent states in less than 6ms. As for the target localisation task, SJ's eye movements were monitored 'online' continuously by one experimenter and recorded for additional evaluation 'offline' using a video camera zoomed in on one of her eyes, while a second video camera recorded her movements. Since controlling SJ's visual input was of utmost importance throughout the studies of grasping, video monitoring and recording of SJ's eyes was the optimal option for two reasons. First, the continuous electrical signal sent to the goggles would 'wash out' those measured by the electrodes using electrooculography (EOG). Second, the available infrared eye-tracking equipment was head-mounted and, therefore, not suitable for use with the goggles.

Moreover, some individuals can find head-mountable eye-tracking equipment cumbersome and distracting, which we felt would be a factor that might have weakened SJ's performance in her blind field.

Patient SJ's performance on visually-guided grasping was tested in blocks of 49 trials administered first in the left visual field and then in the right visual field. Specifically, one block of trials was administered to test SJ's performance with her left hand for objects located in her sighted (left) visual field, and two subsequent blocks of trials were administered to test SJ's performance with her right hand for objects located in her blind (right) visual field. This was done because of the expected difference in effect size between the two fields. Within each block of 49 trials object size was pseudo-randomized such that each object appeared at least 12 times and had an equivalent probability of being preceded or followed by any of the objects. In addition, no object was permitted to occur more than twice consecutively. Thus, the trial order prevented the experience of grasping any particular object on preceding trials from systematically influencing SJ's performance on any subset of the objects. This precaution seemed particularly relevant following recent studies that have shown that the trial history of visual feedback (Whitwell & Goodale, 2009) and indeed that of object size (Dixon & Glover, 2009) can systematically influence grip aperture. The positions of three infrared emitting diodes (IREDs) were recorded in three-dimensional space by Optotrak 3020 (NDI, Waterloo, Ontario) at 200 Hz (one frame every 5 ms) for 3s following the response cue. One IRED was attached to the tip of the thumb, a second was attached to the tip of the forefinger, and a third attached to

her wrist. The IREDs were positioned such that the pads of the forefinger and thumb were unobstructed.

Procedure

First, the touchscreen was calibrated to ensure veridical endpoint measurements. To calibrate the patient SJ's eye movements on the camera monitor, one of the experimenters asked SJ to fixate on the central cross and then noted the position of SJ's iris on the camera display. The experimenter then asked SJ to fixate on the target closest to the fixation cross and again noted the position of SJ's iris on the camera display. This technique was applied for all experiments. For the target-localisation task, each trial began with the target stimulus presented in one of four pre-determined locations for 100 ms coinciding temporally with a 1000Hz tone. The tone cued SJ to both look and point to the target's location. SJ used her forefinger to touch the screen where the target had been presented. Before and after each pointing movement, SJ kept the tip of her forefinger resting on a start position. Her performance was tested in her sighted (left) and then in her blind (right) visual field. SJ was excellent at maintaining fixation.

During the target detection task patient SJ fixated centrally on a cross and pressed a button as soon as she saw a target appear anywhere on the screen. SJ insisted she did not see any targets in her blind (right) visual field with the exception of two discarded single-target trials on which she failed to maintain fixation.

For the grasp task, patient SJ was asked to maintain fixation throughout the test session. The goggles restricted her vision between trials, allowing the experimenter to place the object for the next trial out of sight from SJ. This also meant that SJ could not see the fixation target between trials and as a result SJ was asked to maintain her gaze as best she could by visualizing the fixation target. Before testing commenced, the experimenters explained the nature of the tasks and administered several practice trials to familiarize her with the events and the pace from trial to trial. Throughout these practice trials, SJ reported no difficulty maintaining her gaze on the unseen fixation target between trials. Nevertheless, as mentioned previously, one experimenter monitored her eye movements 'online' on the display of a video camera that was zoomed-in on one of her eyes. A second experimenter concerned himself with placing the objects and observing SJ's performance. Trials during which SJ appeared to move her eyes, fumbled the object, or initiated her movement too early were noted and repeated at the end of the block.

Before the onset of a trial and at the end of each trial, patient SJ depressed the start button with the tips of her thumb and forefinger pinched together while keeping her other hand resting on her lap below the surface of the table. The experimenter initiated each trial which began with a 1s delay followed by a trigger that switched the lenses from their default opaque state to their transparent one, which permitted SJ a view of the workspace with the object located in either her sighted (left) or blind (right) visual field. SJ was instructed to initiate her movement when she could see the workspace (i.e., when the goggles opened).

Patient SJ was asked to reach out and pick the object up off the surface of the table using only her forefinger and thumb such that contact with the object meant that her grip opposition axis spanned the width of the object. The lenses remained transparent for 1s following the release of the start button which permitted SJ a full view of the workspace that included the time taken to obtain the object (i.e., closed loop visual feedback). Note that there was no need to employ a tone "go" cue for this task, since SJ could register a change in the visual input in her sighted (left) visual field as soon as the goggles opened. This was not the case for target-detection and target-localisation tasks, but only the target-localisation task required SJ to respond on each trial. Finally, during testing the experimenters periodically asked SJ if she could see any of the objects to which she answered that she could not.

Data Processing and Analysis

The principal dependent measure for the target-localisation task was computed from the recorded forefinger endpoints, which were converted to a horizontal distance from the fixation cross in visual degree angle. No trials were discarded from the target-localisation task. All statistical analyses were conducted using SPSS version 17.0 (Chicago, Illinois). An Ordinary Least Squares (OLS) linear regression was employed to model the endpoints (in visual degree angle) for each field separately as a linear function of the distance from the fixation cross to the targets (also in visual degree angle).

We report the unstandardized coefficient, *b*, for two major reasons. First, for all behavioural experiments, the variables share the same units. In general, *b* represents the average change in the dependent measure per incremental increase in the independent variable while holding all other variables, when included, constant. For target-directed pointing, *b* reflects the average change in horizontal distance between the endpoint and the fixation cross (in visual degree angle) per incremental increase horizontal distance between the target position and the same fixation cross (also in visual degree angle). For grasping and manual estimates, *b* reflects the average change in grip aperture (depending on task, either peak grip aperture or manual estimate aperture) in millimeters per incremental increase in object width (also in mm). The second reason why we report *b* is because it is recommended over the standardized coefficient, *beta* (which for bivariate models is equivalent to the Pearson product-moment correlation, *r*), for comparisons between or among samples and, therefore, is more appropriate for generalizing to populations at large (Cohen, Cohen, West, & Aiken, 2003; Keith, 2006). This is because the z-transformed scores, from which *r* is derived, rely on the standard deviation of the sample. The standard deviation of the sample will vary from sample to sample and, therefore, incorporate an additional source of variance into *r*, that *b* avoids entirely. The difference between *b* and *r* is not trivial. Given a fixed linear relationship (i.e. signal) between an independent and dependent variable in two independent samples that differ only by virtue of the amount of measurement error (i.e. noise), the OLS regression estimate for *b* will not differ between the two samples, yet the estimate for *r* will. If we are interested in the

OLS relationship between the two variables across numerous independent samples, then clearly we are interested in the mean of the collection of sample estimates (and the variance of this collection). Aggregating across r would needlessly include measurement error.

Despite the advantages of reporting *b*, we also report *r*, because this statistic has been reported across a number of related studies. Note that the t-tests of *b* and *r* against zero for bivariate cases yield equivalent t-statistics and p-values. The Type I error, α, was held at 0.05 for each t-test conducted.

For the target-detection task, trials were removed from the analysis if patient SJ failed to respond or if her reaction time (RT) was more than 2 standard deviations larger then her mean for that condition. As a result, two trials were discarded. The analysis for the target-detection task compared patient SJ's mean RT for single target trials which appeared in her left (sighted) visual field with the mean RT for double target trials (targets appear simultaneously in both visual fields).

In-house software permitted an automated selection of movement onset, movement offset, and the principal dependent measure, peak grip aperture (PGA) for all data from the grasp session. The onset of the movement was defined as the first of 20 consecutive frames during which the velocity of the thumb IRED exceeded 30 mm/s. The offset of the movement was defined as the first of 20 consecutive frames during which the grip aperture velocity fell within ±30 mm/s. The movement onset and movement offset frames were used to define a search

window within which the PGA was selected. Each grip aperture profile was inspected visually to ensure that there were no gross errors made in the selection of PGA. For trials where an erroneous PGA was selected, the number of consecutive frames criterion for movement offset was adjusted by increments of five.

In contrast to the movement onset, the velocity of the thumb IRED (or that of any other IRED) was not used to define the movement offset. This is because the movement to and from the object is fluid and does not cease when the participant obtains the object, which makes the frame selected using a fixed velocity threshold more susceptible to variations from movement to movement. This problem is made more acute when one considers that often times grip aperture is wider when the object is released than when the hand is approaching the object. Fortunately, the velocity of grip opening and closure will necessarily approach zero when the participant establishes a grip on the object independently of whether the hand is still moving. Thus, the grip aperture velocity is a better indicator that the grip has made stable contact with the object under the current task instructions.

Patient SJ committed no errors with her left hand for objects located in her left (sighted) visual field. She did, however, commit four errors with her right hand for objects located in her right (blind) visual field. These trials were discarded from the analysis and their repeats at the end of the block substituted into the analysis.

Ordinary least squares (OLS) linear regression of the width of the object on the current trial on the resultant PGA was used to model PGA as a linear function of the width of the corresponding object for each field separately. The *b* of interest for this analysis represents the average change in the dependent measure (in mm) per incremental increase in the width of the object (also in mm). Since there were two blocks of trials administered to test performance in the right (blind) visual field, this model was tested for the full data set and then once for each block separately.

An additional model of Session 1 PGA was tested that included the width of the object grasped on the current trial and that of the object grasped on the immediately preceding trial. The model, therefore, assesses whether a significant linear relationship between patient SJ's PGA (1) and the width of the current object (2) would remain once the contribution of the width of the object grasped on the previous trial (3) was partialled out of both PGA and the width of the current object. This model was employed as an additional guard against the possibility that SJ may have explicitly or implicitly used the experience with the object on the previous trial to guide her performance on the subsequent trial. Only valid trials that were preceded by a valid trial were included in this analysis. Accordingly, the first trial of each block and each of the four error trials and their subsequent trials were discarded (total of ten). For this second model, we report the βs and partial correlations (e.g., $r_{1.23}$). Given the nature of the trial order it was not surprising to find that the collinearity diagnostic indicated perfect

independence between the current and preceding object widths (*Tolerance* = 1.0). The Type I error, α, was held at 0.05 for each t-test conducted.

Results

Target Localisation

The analysis of patient SJ's performance on target-directed pointing indicated that she was able to localize targets in both her sighted and blind fields (Figure 2).

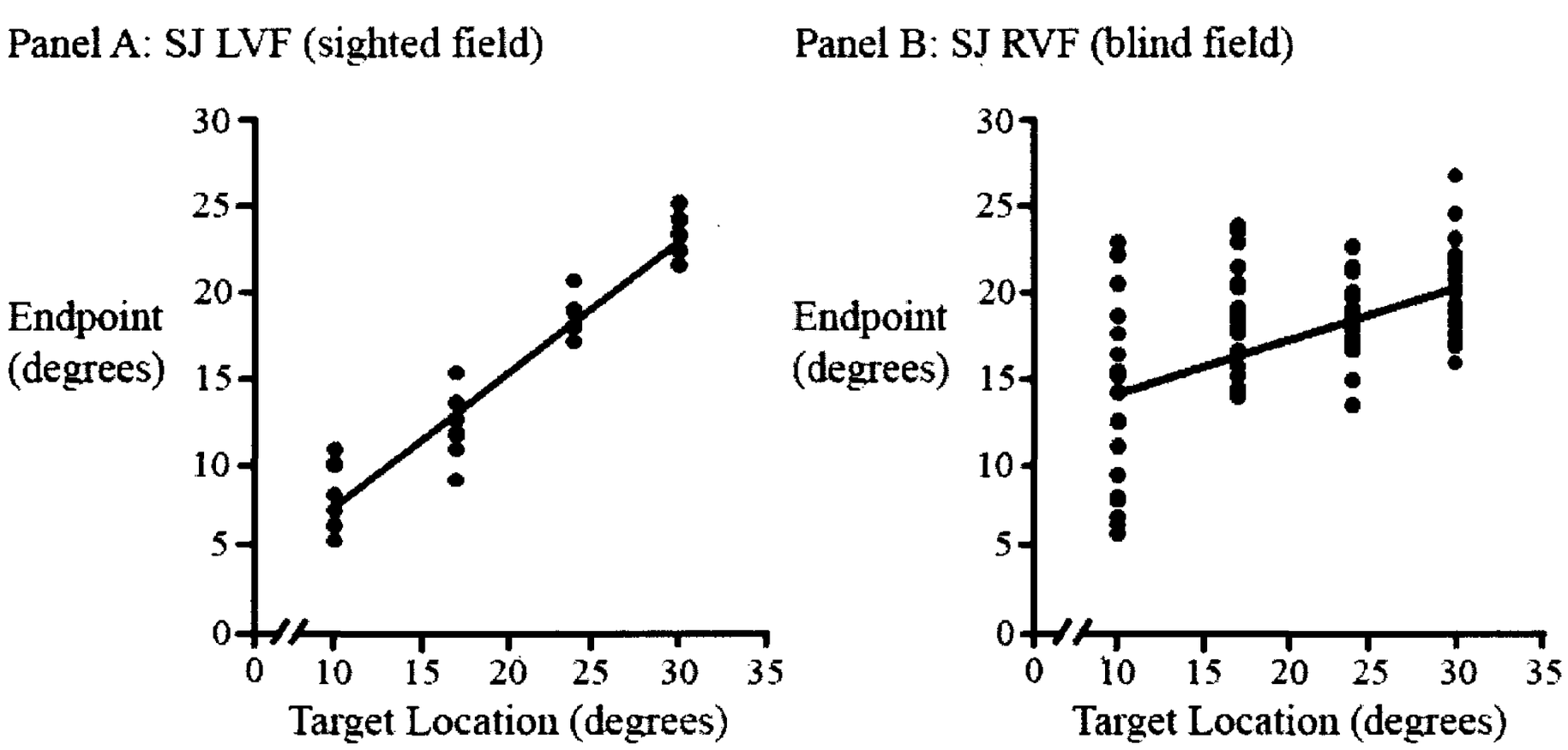


Figure 2. Session 1 horizontal endpoint distance from the fixation cross (endpoint) in visual degree angle from the fixation cross as a function of the target location (also in horizontal visual degree angle from the fixation cross) for patient SJ when pointing to targets in her left (sighted) visual field (LVF) (panel A) and in her right (blind) visual field (RVF) (panel B) with her right hand while vision remained available throughout the movement (closed-loop feedback).

Specifically, SJ's endpoint distance increased with the target positions located in her sighted (left) visual field ($r(29) = 0.96$, $b = 0.76$, $p < .001$) and again with the same targets when located in her blind (right) visual field ($r(78) = 0.52$, $b = 0.31$, $p < .001$). During the testing SJ insisted that she saw nothing. On a few of the trials in which the target was presented 10° from the fixation cross, she remarked that she "felt" like she "saw a shadow". However, when asked to describe the phenomenon she replied that she could derive no shape or form from the impressions. Her description suggests a type II blindsight, which reflects an awareness of visual stimulus without a concrete description (e.g., a 'gut' feeling see Cowey, 2010). Moreover, nearly identical subjective reports like these are reported frequently in blindsight literature (see Zeki & Ffytche, 1998).

Target Detection

In addition to examining patient SJ's ability to localize targets in her blind field, we also tested her on the redundant target paradigm. SJ was not reliably faster at responding to two simultaneously presented targets (one in each visual field) ($M = 349$ ms, $SD = 54$ms) than to one target presented in her left (sighted) visual field ($M = 357$, $SD = 54$ms) ($t(69) = 0.66$, ***ns***). She did not respond on any of the blank 'catch' trials.

Grasping with Visual Feedback

Figure 3 depicts patient SJ's PGA as a function of the width of the object located in her sighted (left) visual field and grasped with her left hand (panel A) and with her right hand in her blind (right) visual field (panel B).

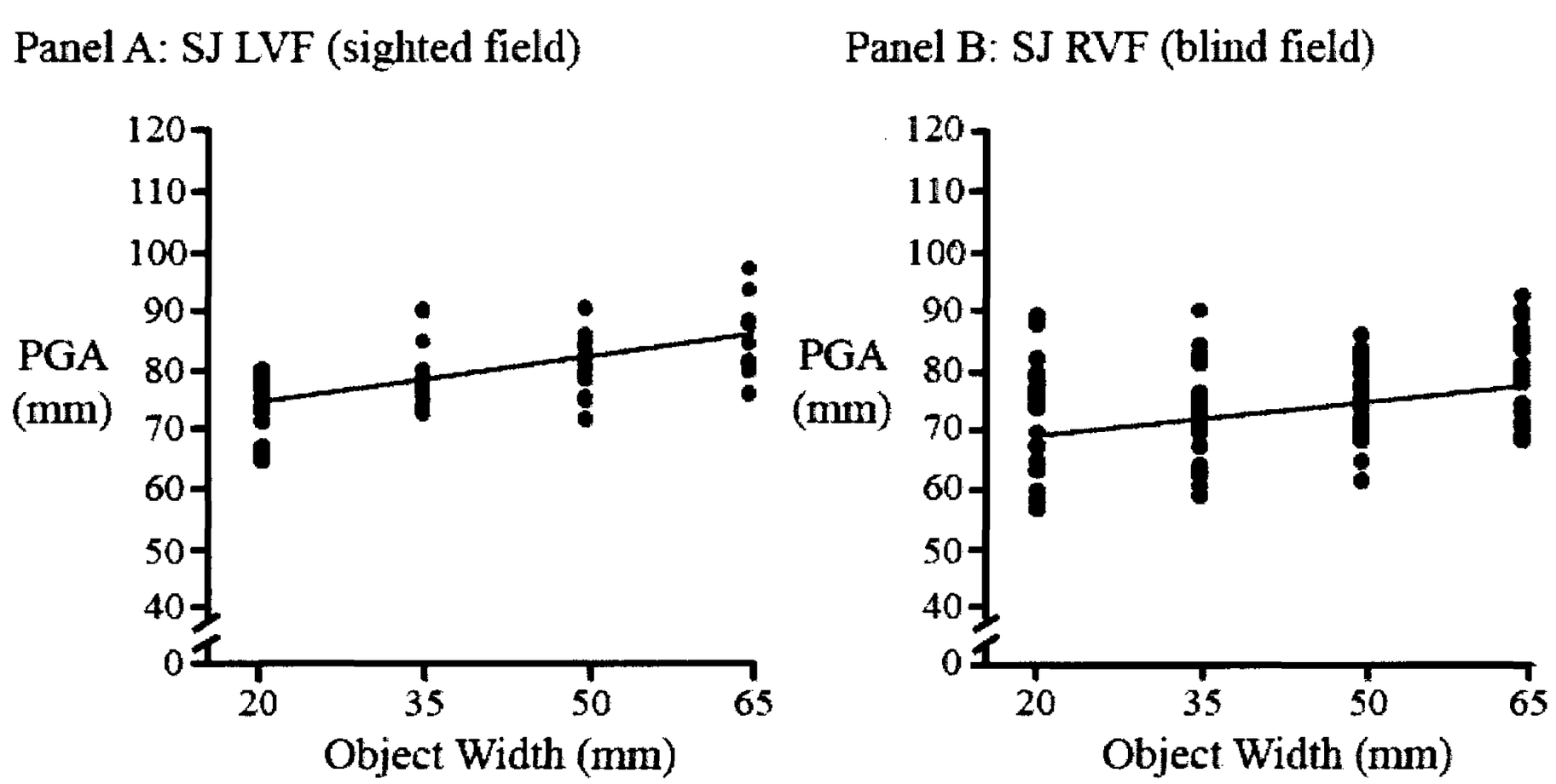


Figure 3. Session 1 PGA as a function of object width for patient SJ when grasping objects located in her left visual field (LVF) with her left hand (panel A) and in her right visual field (RVF) with her right hand while vision remained available throughout the movement (closed-loop feedback). SJ shows a reliable sensitivity to the width of objects presented in her sighted and blind fields.

As expected, PGA increased linearly as a function of the width of the object located in her sighted (left) field, ($r(47) = 0.60$, $b = 0.25$, $p < .001$). Critically, PGA also increased linearly as a function of object width in her blind (right) field ($r(96) = 0.35$, $b = 0.17$, $p < .001$). Subsequent analyses of SJ's performance in her blind (right) field indicated a significant linear relationship between PGA and

object width for each block separately (first block, $r(47) = 0.40$, $b = 0.21$, $p < .005$; second block, $r(47) = 0.30$, $b = 0.13$, $p < .05$).

The analysis of PGA (1) as a function of the width of the object grasped on the current trial (2) and the immediately preceding trial (3) indicated that patient SJ's PGA increased with the width of the current ($r(85)_{12.3} = 0.34$, $p < .001$) and previous objects ($r(85)_{13.2} = 0.41$, $p < .001$; $r(86)_{23} = 0.01$, *ns*) located in her blind (right) visual field. This suggests that both the visual information from the current object and experience with the object on the previous trial made unique and significant contributions to the programming of grip aperture for the object on the current trial. An influence of the width of the previous object was not observed when SJ grasped objects located in her sighted (left) visual field. Accordingly, SJ's PGA increased with the width of the current ($r(46)_{12.3} = 0.63$, $p < .001$) but not the width of the previous objects ($r(46)_{13.2} = 0.28$, *ns*; $r(47)_{23} = 0.1$, *ns*).

Discussion

The endpoints of patient SJ's pointing movements were clearly guided by the location of the targets in both her left (sighted) and right (blind) visual field. When asked to reach out to pick up novel objects located in her blind (right) visual field with her dominant (right) hand, SJ adjusted her grip aperture with the width of the target object. Interestingly, the results of the second model that included the width of the object grasped on the previous trial indicated that SJ,

either explicitly or implicitly, used the experience gleaned from the previous trial to inform her performance on the following trial when reaching out to pick up objects located in her right (blind) but not her left (sighted) visual field. Critically, however, visual information about the width of the current object accounted for a nearly identical amount of variance in her performance on the current trial. Although the slopes governing the relationship between object width and PGA appear to be comparable across hands, it is likely that had SJ been tested with her dominant (right) hand for both fields, a larger difference would have emerged. Nevertheless, the slope determined for SJ's blind (right) field is in good agreement with that observed for patient PJG (Perenin & Rossetti, 1996).

At the same time, patient SJ's spared performance in these visuomotor tasks did not appear to depend on her ability to 'see' the targets or, for the purposes of grip scaling, perceiving their width, shape, or form; in fact, SJ never reported seeing a target when it was presented by itself in her blind field nor was she reliably faster at responding to a target in her good field when an additional target was presented in her blind field during the target-detection task. SJ did, however, report a "shadow-like" impression during the target-directed pointing task for some trials when the target was located 10 degrees of visual angle into her blind (right) visual field while insisting, when pressed, that she did not see the target. The difference in performance and phenomenology between the target-detection and target-directed pointing tasks may have resulted from the change in the mode of response from a simple button press in the target-detection task to a combined saccade and pointing movement in the target-directed pointing task

(Corbetta et al., 1990). Alternatively, SJ's performance and subjective reports on this task could be the result of premature saccades.

Although EOG or infrared eye-tracking equipment was not used in the present experiments, it seems unlikely that patient SJ failed to fixate properly for a number of reasons. First, the timing of the onset of the tone and target during the target-directed pointing task was unpredictable. Second, as mentioned previously, SJ's eye movements were monitored online and recorded for offline evaluation. The tone can be heard clearly on the record, and SJ's saccades appear to occur after the tone. Finally, subjective descriptions of impoverished perceptual experiences related to visual stimuli presented in the affected portions of patients' visual fields are reported frequently in the literature even under stringent monitoring of eye position (see e.g. Cowey 2010; Zeki & Ffytche, 1998). For example, Blythe, Kennard, and Ruddock (1987) used EOG to track the eye movements of their participants, whom were asked to saccade to briefly flashed targets presented in their sighted and 'blind' fields. Interestingly, the patients with medial-occipital lesions reported identical experiences to that of SJ whom also possesses a lesion to the medial-occipital cortex.

It is important to note, however, that patient SJ's failure to show a target redundancy effect does not mean that she is insensitive to targets located in her blind-field when responding with button presses. SJ may very well exhibit better-than-chance levels of performance if tested on forced-choice paradigms.

Nevertheless, there was no evidence that she was visually conscious of any targets in her blind field even though she showed clear evidence for action blind-sight.

CHAPTER 3

Session 2 Experiments

Approximately four months following the Session 1 test sessions, we tested patient SJ again for replicability of our initial findings and to explore the limitations of her grip scaling in her blind field with three additional tasks. Thus, in separate testing blocks SJ grasped objects located in either her left or her right visual field with (closed loop) and without (open loop) visual feedback and following a 2s delay without feedback. In addition, as a control task, we asked SJ to manually estimate the width of the same objects presented within her sighted (left) and blind (right) visual fields. In all cases, SJ used her right hand.

Methods

Participants

In addition to patient SJ we also tested a right-handed female control participant, BJ who was roughly the same age (40 years) and who had normal vision and no prior neurological or neuropsychological history. In each experiment, the control participant performed the tasks under exactly the same conditions as SJ. Informed consent was obtained from SJ and the control participant and all experimental procedures were approved by the University of Western Ontario Health Sciences Research Ethics Board and in full accordance with the Declaration of Helsinki.

Experiment Setup and Design

The Session 2 setup required few changes from those used for Session 1 grasping. A new set of four black objects was used. The object height remained the same as those used on Session 1 (1.5cm), but the lengths were increased to 6cm and the widths were reduced by 0.5cm each such that the shortest object width was 1.5cm and the longest 6cm. The Session 2 objects were instrumented so that the time at which contact was made with the objects could be recorded electronically. Additionally, rather than keeping the location of the fixation target constant and varying the object's position as was done on Session 1 testing, the location of the fixation target varied while the location of the target object remained constant. Thus, all grasps and manual estimates were executed with the right hand while the participant fixated to the left or to the right of the object. This ensured that the biomechanical requirements for the action within each field were identical. The objects were located such that centre of the edge of the object facing the participant was 30cm from the start button. Patient SJ was seated as on Session 1. The distance from her eyes to the front edge of the object was 50cm. The fixation points were located 10cm from the leftmost or rightmost edge of the object. The distance, therefore, between the fixation target and the closest edge of the object subtended 11° of visual angle.

In addition to closed-loop visual feedback, we also asked patient SJ to perform grasps without visual feedback (open loop). For this condition, the trial events occurred as before, but vision was removed once the participant released the start button at the onset of the movement rather than remaining open for an

additional second. Grasping was also tested in a delay condition in which vision was permitted for one second and the response cued two seconds thereafter by an auditory tone. All grasping tasks were administered in separate blocks of 65 trials each, while manual estimates were tested in a block of 33 trials. The trial order was constructed using the same criterion used for Session 1, except that each object was sampled 16 times for each grasping task and 8 times for manual estimations.

Procedure

For all tasks, the sighted (left) visual field was tested before the blind (right) visual field to further familiarize patient SJ with the requirements. The same order was used for the control participant. Both participants adopted the same starting hand configuration SJ used on Session 1. For the immediate grasping and manual estimation tasks, the participants were instructed to initiate their grasps when vision was permitted (i.e., when the goggles opened). For manual estimates, the participants used their forefinger and thumb to indicate the width of the target object and once satisfied with their estimate kept their fingers as stable as possible until vision was occluded by the goggles. The bottom of their hand remained rested on the table, which prevented them from inadvertently directing their hand towards the object. Immediate grasping with closed-loop visual feedback was tested first, then manual estimations, followed by immediate grasping in open loop (i.e., movements without visual feedback), and then delayed grasping. As on Session 1, trials during which SJ appeared to move her

eyes, fumbled the object, or initiated her movement too early were noted and repeated at the end of the block.

Data Processing and Analysis

For immediate and delayed grasping tasks, grip aperture was defined as the peak vector distance between the IRED placed on the forefinger and the IRED placed on the thumb. Movement onset corresponded to the frame at which the start button was released. The movement offset corresponded to the point at which contact was made with either the front or back sides of the object. The independently determined movement onset and offsets were used to restrict the search window within which the peak grip aperture (PGA) was selected.

The principal dependent measure for manual estimation was the manual estimate aperture (MEA) which was defined as the first of 30 consecutive frames during which the speed at which the thumb and finger closed or opened fell below 30 mms. This threshold reflected a point at which the grip aperture remained highly stable and was thought to best reflect the participant's estimate of the object's width given the experimenter's instruction to preserve their estimate until vision was occluded.

The data were analyzed using the first model employed on Session 1, which described PGA as a linear function of the width of the object grasped on the current trial. For grasps executed with closed-loop visual feedback, patient SJ committed seven errors in her sighted (left) visual field and five in her blind (right) visual field. The control participant committed one error in her left field

and three errors in her right field. For grasps executed without visual feedback (open loop), SJ committed one error in her sighted (left) field and two errors in her blind (right) field. The control participant committed one error in her right visual field. Finally, for delayed grasps, SJ committed two errors in her sighted field and three errors in her blind field. The control participant committed one error in her right visual field. As on Session 1, all error trials were discarded from the analysis and the missing values replaced with the data from the corresponding trials that were repeated at the end of the block.

Results

Grasping with Visual Feedback

As panels A and B of Figure 4 suggest, similar to the results from Session 1, patient SJ's PGA scaled with the width of objects located in her sighted (left) ($r(63) = 0.72$, $b = 0.39$, $p < .001$) and blind (right) ($r(63) = 0.33$, $b = 0.14$, $p < .01$) visual fields when she grasped the objects with visual feedback (i.e., closed loop). For comparison, PGA for the control participant is shown in panels C and D of Figure 4 (left visual field: $r(31) = 0.82$, $b = 0.67$, $p < .001$; right visual field: $r(28) = 0.94$, $b = 0.71$, $p < .001$).

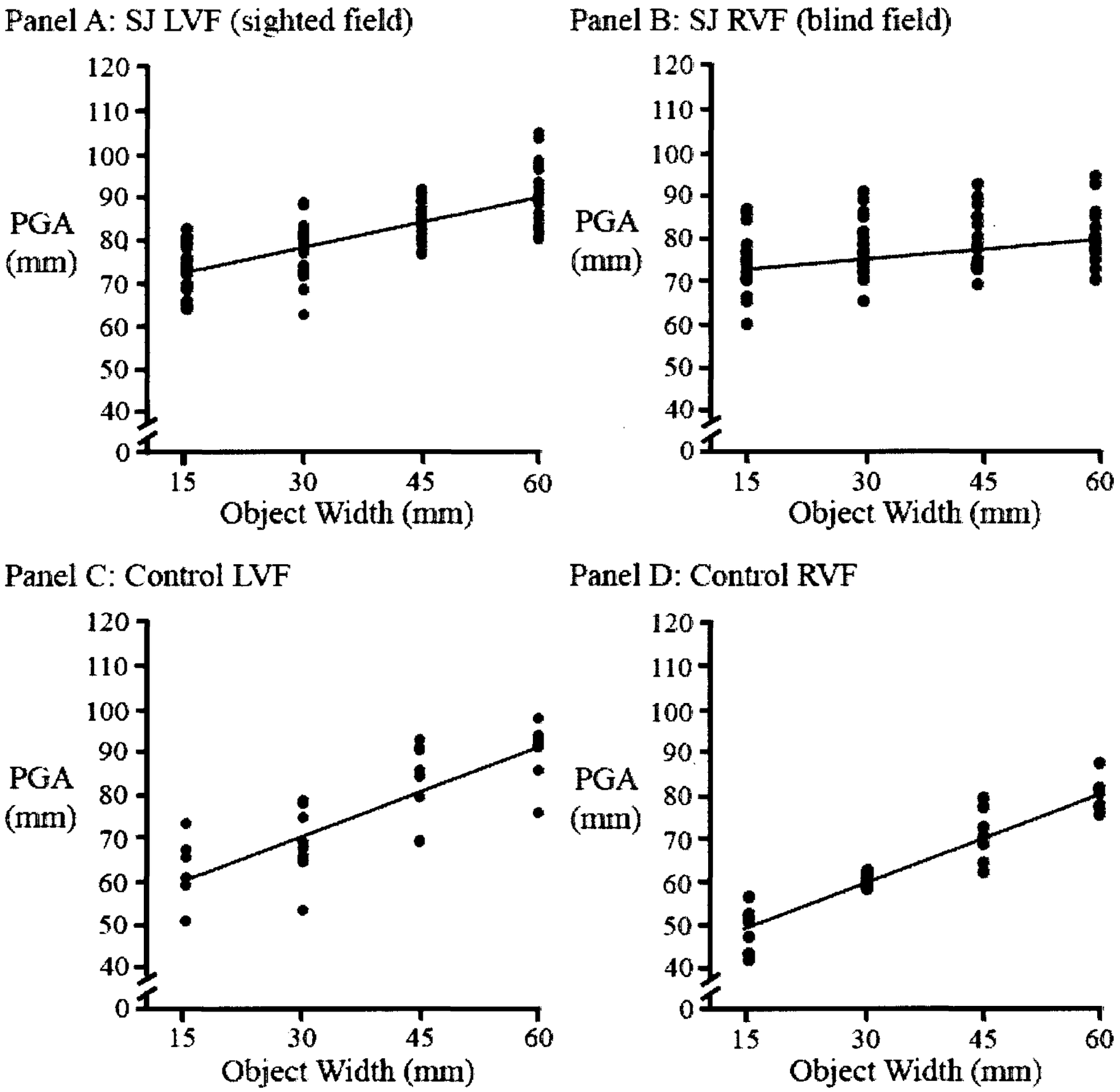


Figure 4. Session 2 PGA as a function of object width for patient SJ (panels A and B) and the control participant (panels C and D) when grasping objects located in the left visual field (LVF) (panels A and C) and right visual field (RVF) (panels B and D) with the right hand while vision remained available throughout the movement (closed-loop feedback). Similar to the Session 1 results, SJ's grip aperture shows a reliable sensitivity to the width of objects located in her blind and sighted fields.

Grasping without Visual Feedback

In general, patient SJ's performance when grasping without visual feedback (i.e., in open loop) resembled her performance with closed-loop feedback albeit with a slight decrease in sensitivity. Accordingly, PGA increased with the width of objects located in her sighted (left) ($r(63) = 0.74$, $b = 0.35$, $p < .001$) and blind (right) ($r(63) = 0.26$, $b = 0.12$, $p < .05$) visual fields (see panels A and B in Figure 5).

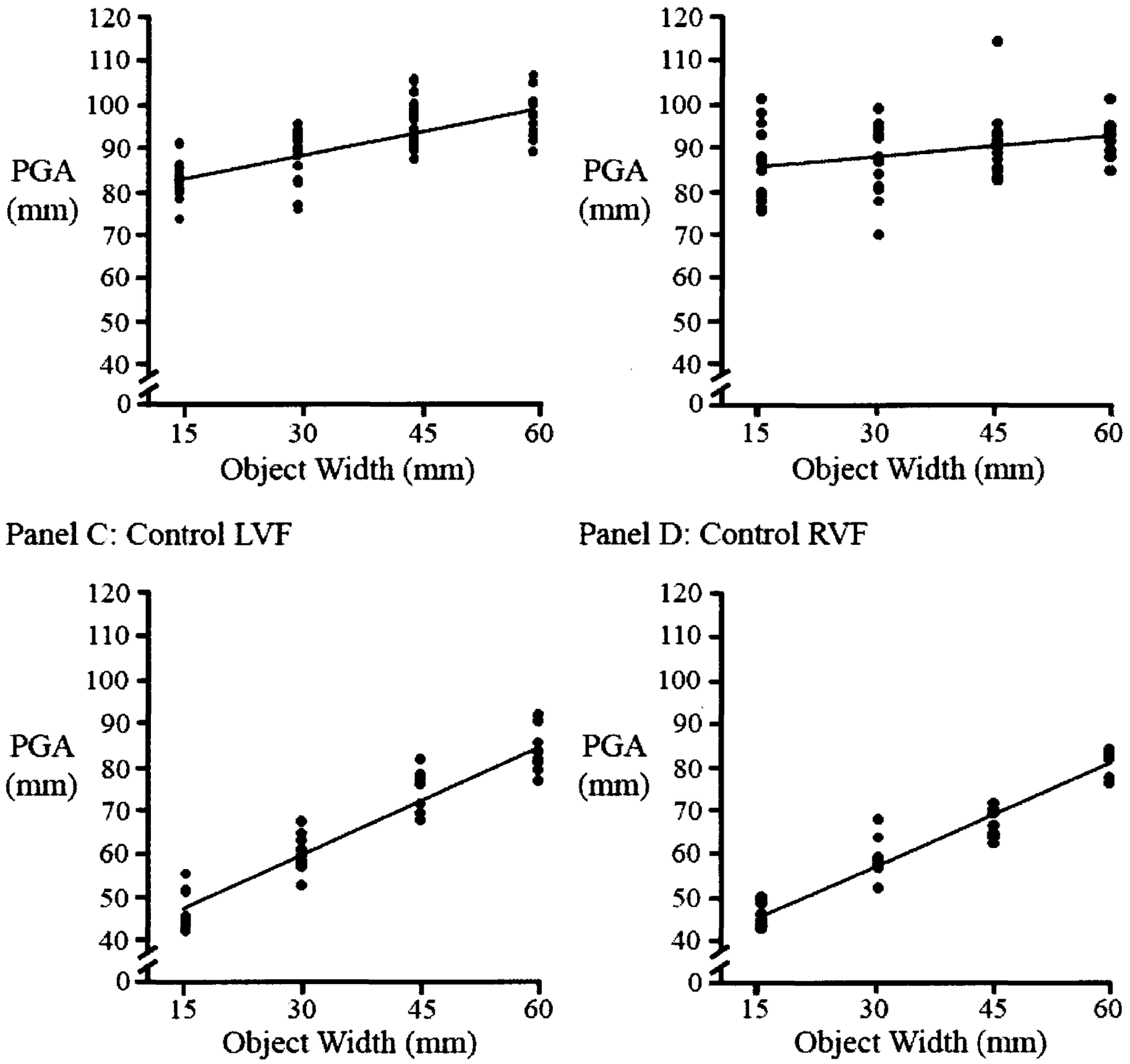


Figure 5. Session 2 PGA as a function of object width for patient SJ (panels A and B) and the control participant (panels C and D) when grasping objects located in the left visual field (LVF) (panels A and C) and right visual field (RVF) (panels B and D) with the right hand while vision was unavailable from movement onset onwards (open-loop feedback). SJ's grip aperture remains sensitive to the width of objects located in her sighted and blind fields

For comparison, PGA for the control participant is shown in panels C and D of Figure 5 (left visual field: $r(31) = 0.94$, $b = 0.82$, $p < .001$; right visual field: $r(31) = 0.96$, $b = 0.78$, $p < .001$).

Delayed Grasping without Visual Feedback

Consistent with the results from closed and open-loop grasping, when patient SJ grasped objects following a 2s delay where vision of the object was unavailable, PGA increased with the width of objects presented in her sighted (left) visual field ($r(63) = 0.51$, $b = 0.30$, $p < .001$). In striking contrast, SJ's PGA showed no sensitivity to the width of objects presented in her blind field ($r(63) = 0.11$, $b = -0.04$, *ns*) (panels A and B in Figure 6).

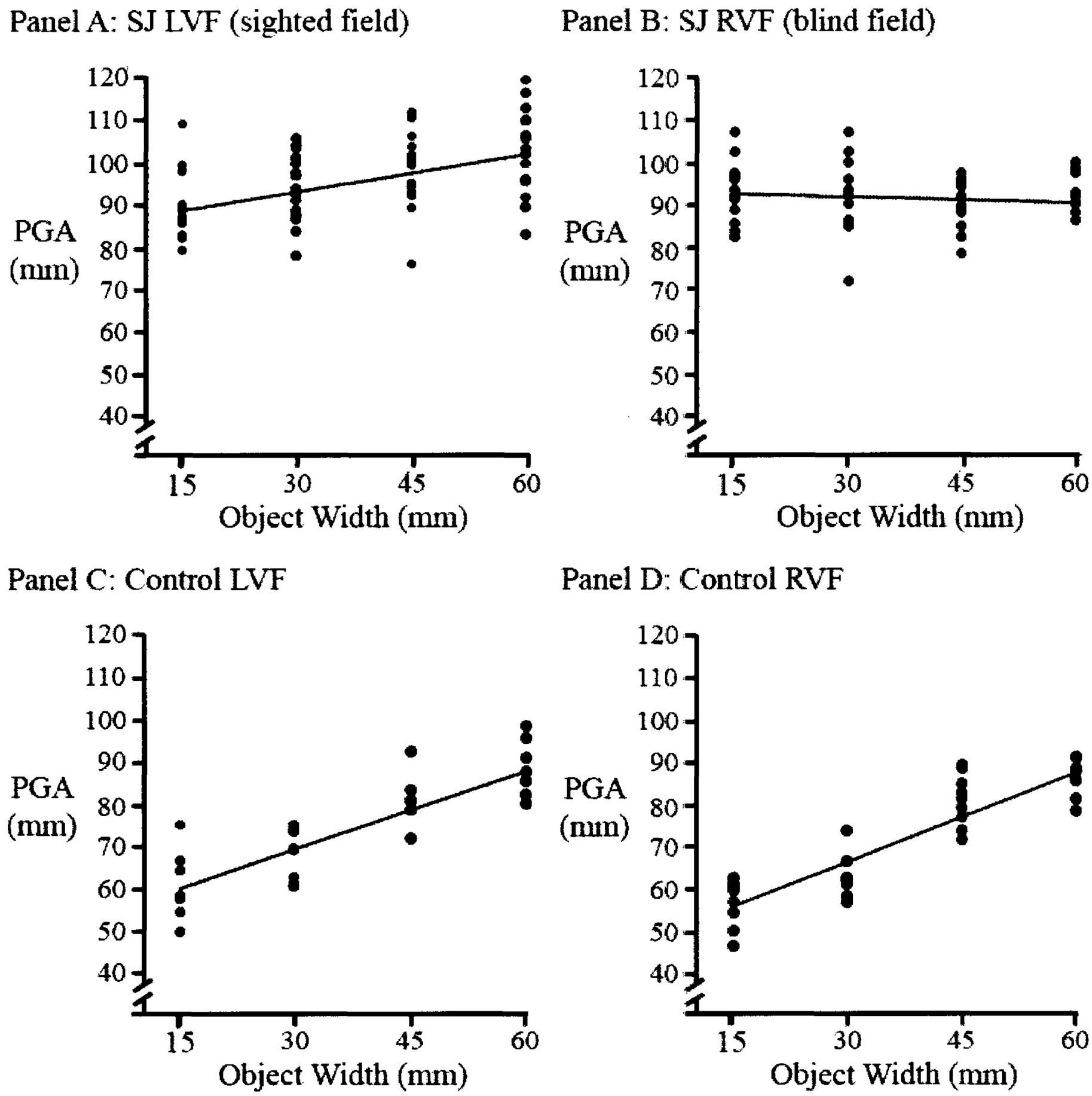


Figure 6. Session 2 PGA as a function of object width for patient SJ (panels A and B) and the control participant (panels C and D) when cued to grasp objects located in the left visual field (LVF) (Panels A and C) and right visual field (RVF) (Panels B and D) following a 2s delay. SJ's PGA is sensitive to the width of objects when they are located in her sighted field but not when the objects are located in her blind field.

As expected, PGA for the control participant increased with the width of objects located in either her left ($r(31) = 0.86$, $b = 0.63$, $p < .001$) or right visual field ($r(31) = 0.89$, $b = 0.64$, $p < .001$) (panels C and D in Figure 6).

Manual Estimations with Visual Feedback

The pattern of results observed for manual estimation was similar to those for delayed grasping. Accordingly, patient SJ was able to scale her MEA accurately to the width of objects presented within her sighted (left) visual field ($r(31) = 0.84$, $b = 0.99$, $p < .001$), however; her MEA showed no sensitivity when the very same objects were presented within her blind (right) visual field ($r(31) = 0.08$, $b = -0.11$, *ns*) (panels A and B in Figure 7).

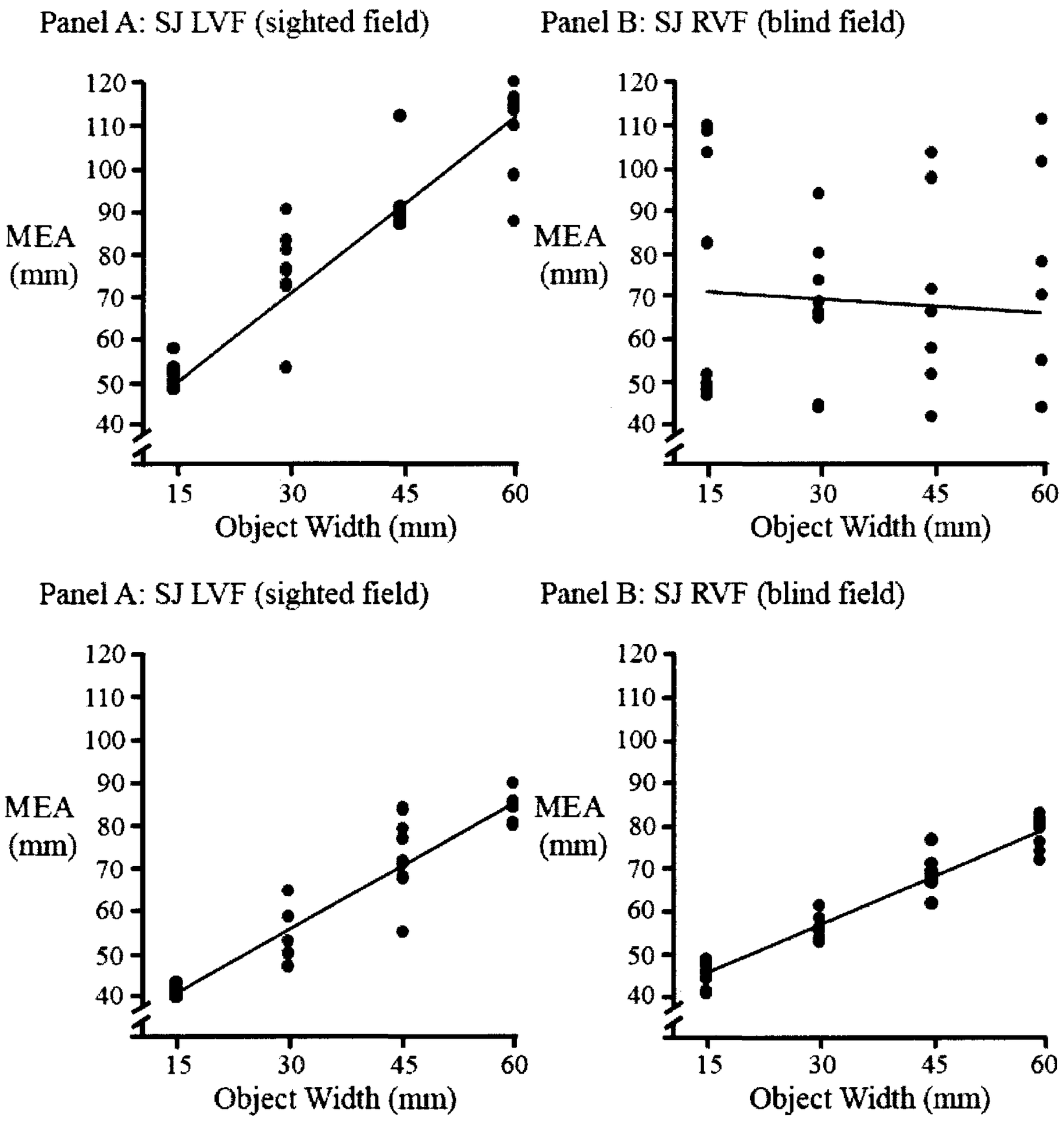


Figure 7. Session 2 MEA as a function of object width for patient SJ (panels A and B) and the control participant (panels C and D) when manually estimating the width of objects located in the left visual field (LVF) (panels A and C) and right visual field (RVF) (panels B and D) with the right hand when vision remained available throughout the movement (closed loop feedback).

As expected the control participant accurately estimated the width of objects when they were presented within her left ($r(31) = 0.94$, $b = 0.99$, $p < .001$) or right visual field ($r(31) = 0.97$, $b = 0.74$, $p < .001$) (panels C and D in Figure 7).

Discussion

The results of the Session 2 testing again show that patient SJ is remarkably sensitive to the widths of novel objects located in her blind (right) visual field when she reaches out to pick them up, but not when she used the same digits to make manual estimates of their widths. Although SJ appears not to be as sensitive to the width of object's placed in her blind (right) visual field as she is to the width of objects presented in her sighted field, this pattern is consistent with the fact that the dorsal stream functions optimally under normal circumstances under which input from V1 is readily available. Importantly, SJ's sensitivity to object width deteriorated dramatically when she was cued to reach out and pick up the same objects two seconds after vision had been removed.

Patient SJ's pattern of spared visuomotor abilities and deficits fits well with Milner and Goodale's (2006) perception and action model. Milner and Goodale argue that it is the ventral stream that is engaged when one makes a manual estimate of the width of a novel object, although bottom-up visual input from the retina about the object is available to both the ventral and dorsal stream. Since this task does not require a visuomotor transformation to direct the limb and hand to the object's location, the dorsal stream remains largely disengaged. SJ's inability to scale her manual estimate aperture to the width of objects presented in her blind (right) visual field suggests that inputs from V1 to the ventral stream are required for performing this behaviour. Presumably, the motor outputs that mediate her manual estimates do not receive the requisite information from the

ventral stream. A similar account explains SJ's deficit with delayed grasping. When one reaches out to pick up a novel object that is no longer in view, the usual bottom-up input from the retina about the size of object as well as its disposition with respect to the hand is no longer available to either the ventral or the dorsal stream. Instead, the delayed grasp must use stored or rehearsed information about the size and position of the object that was initially processed by the ventral stream. Again, in SJ's case, it appears that inputs from V1 to the ventral stream are necessary for the mediation of delayed grasps.

Patient SJ's grip-scaling to novel objects with and without visual feedback was sensitive throughout the movement suggest that the dorsal stream can exploit bottom-up sources of visual information that do not rely on V1 and that do not mediate a conscious visual experience of the object. As just discussed, the results also suggest that V1 is a necessary but not sufficient structure for mediating grip scaling to object width during memory-driven grasping. It is important to note that these results do not rule out the possibility of observing preserved performance for other delayed tasks that do not require explicit rehearsal of object form or other features that do not depend on location. A stimulus flashed in the blind field could elicit a visual or somatosensory-related experience that cues the participant to the target location, for example, through awareness of an orienting response or saccade to the target's position as may well have been the case for the target-directed pointing task on Session 1 testing. Under such circumstances it would hardly be surprising that this information, while not visual in nature, could be rehearsed for later use. Nevertheless, conscious awareness of a target's

location is not necessarily conscious awareness of other stimulus specific features such as size or width, which must be processed for accurate in-flight grip scaling when reaching out to pick up an object.

CHAPTER 4

Session 3 Experiment

Approximately five months following Session 2 testing, we brought patient SJ back for an MRI session to acquire high resolution anatomical images and measure blood oxygen-level dependent (BOLD) signalling related to moving stimuli in her blind and sighted visual fields. Our aim was to test whether moving visual stimuli would invoke BOLD signalling in SJ's intact extrastriate regions and the spared tissue around the V1 lesion, particularly for stimuli presented in her blind field. We used moving stimuli because motion stimuli have been shown to reliably elicit neurovascular responses in extrastriate regions including MT reliably across numerous neuroimaging studies of blind sight (e.g., Barbur, Watson, Frackowiak, & Zeki, 1993; Baseler, Morland, & Wandell, 1999; Goebel, Muckli, Zanella, Singer, & Stoerig, 2001)

Methods

Participants

Patient SJ participated in this session. No other individuals were tested. Informed consent was obtained from SJ and all experimental procedures were approved by the University of Western Ontario Health Sciences Research Ethics Board and in full accordance with the Declaration of Helsinki.

Data Acquisition

The fMRI data were collected on a 3 Tesla Siemens Tim-Trio MRI scanner at the Robarts Research Institute (London, Ontario) using a 32-channel head coil. To collect functional data we used a T2* weighted single shot EPI imaging sequence (TR = 2, TE = 30ms, 36 slices, 3mm iso-voxel, flip angle 90°, in place resolution 80 x 80, FOV=240x240). The functional data were aligned to a high resolution (1mm iso-voxel) 192 slice T1 anatomical scan. The slices of each volume were collected in an ascending interleaved order.

Experimental Setup and Design

The stimuli used during the MT localizer scans were displayed on a 15x20cm screen using an LCD projector (AVOTEC Silent Vision Model 6011). SJ viewed the stimuli on a screen through a front surface mirror mounted on top of the head coil and was instructed to fixate on a red dot (0.5°) presented at the centre of the screen. An MR-compatible infrared camera was used to monitor her eye movements online. Each scan began with the first of nine blocks of 16s of baseline stimuli interleaved with eight blocks of 16s of motion stimuli. The baseline stimuli consisted of a pseudo-random pattern of white dots (diameter 0.1 degrees visual angle and spaced, on average, 1° of visual angle apart) that flickered at 1Hz against a black background. The motion stimuli consisted of the same pattern of white dots translating coherently across the visual field in a random direction. The direction of the moving dots changed randomly every

second. The sighted and blind fields were tested in separate scans of 136 volumes (i.e., 4.53 minutes) each.

Data Processing and Analysis

Data were analyzed using the BrainVoyager QX 2.1 (Brain Innovation, Maastricht, The Netherlands). The data were pre-processed prior to the statistical analysis. First, the raw signal of each scan was slice scan time corrected using a cubic-spline interpolation. Next, the volumes for each functional scan were transformed to coincide spatially with the first volume of the scan closest to the high-resolution anatomical scan using a trilinear-sync interpolative motion-correction method. The trilinear nearest-neighbour algorithm detected spatial discrepancies between temporally adjacent volumes, and a sync-interpolative method estimated each of six rigid-body parameters (three rotations and three translations) used to align the volumes. Finally, each scan was temporally high-pass filtered by regressing the blood oxygen-level dependent (BOLD) time course on a Fourier basis set composed of two sine and cosine functions and a linear component. Thus, the resultant data set reflected the residuals, that is, the difference between the predicted BOLD and the measured BOLD. No smoothing kernel was applied to the data.

Statistical analysis was conducted separately for each scan using multiple regression of the percent transformed measured BOLD signal time course on the expected fluctuations in BOLD time course attributable to the motion stimulus and six additional timecourses attributable to patient SJ's movement during the

scan which corresponded to the six rigid-body parameters estimated during the pre-processing motion correction. The expected BOLD timecourse for the motion stimuli assumed a constant value above zero (baseline) for those volumes during which the stimulus were moving and was convolved using the default double gamma hemodynamic response function. The resultant timecourse was scaled to a peak response value of one. The six timecourses corresponding to the motion parameter estimates were then added to the model. These six covariates were included to minimize misattribution of head movement related fluctuations in measured BOLD to fluctuations invoked by the moving stimuli (see e.g., Johnstone et al., 2006).

Accordingly, the dependent measure of interest used for statistical analysis is the unstandardized regression coefficient for the motion stimuli (β_{motion}). Thus, β_{motion} represents the average measured change in percent BOLD signal per incremental increase in expected BOLD signal while all other variables are held constant. The resultant statistical parametric maps reflect the t-value returned from the t-test of β_{motion} against zero and will be referred to hereafter as 'activation'. This test assesses whether or not the BOLD signal reliably increased or decreased linearly with the expected increase in BOLD signal while all other variables are constant. The statistical maps were thresholded using a cluster extent determined using an extension of Forman et al.'s (1995) Monte Carlo method (see Goebel, Esposito, & Formisano, 2006) with the cluster-level per-family error rate (α) held to 0.01 or less.

Results

As can be seen in Figure 8a and 9a, moving stimuli presented in SJ's sighted (left) visual field elicited functional activation in and around intact cortical tissue forming the calcarine sulcus (i.e.,striate cortex V1) of SJ's right hemisphere.

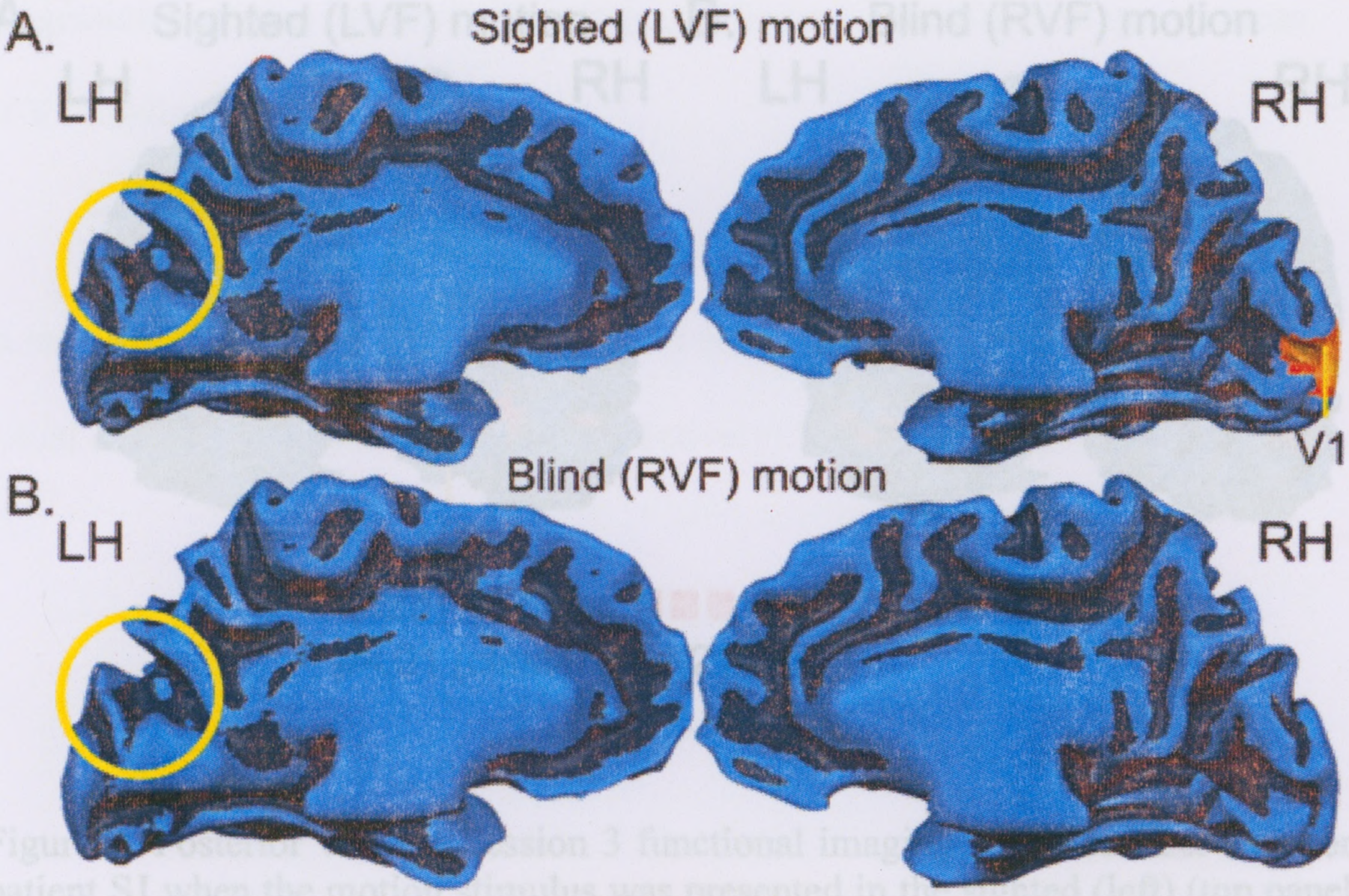


Figure 8. Medial view of Session 3 functional imaging MT+ localizer data for patient SJ when the motion stimulus was presented in the sighted (left) (panel A) or blind (right) visual field (panel B). The data are displayed on a segmented and smoothed version of SJ's brain to allow easier viewing of the sulci (dark blue) and gyri (light blue). The yellow circles depict the site of SJ's occipital lesion. Abbreviations: LH = left hemisphere, RH = right hemisphere, LVF = left visual field, RVF = right visual field, V1 = primary visual cortex. Note the absence of any activation in V1 in the damaged (left) hemisphere when the motion stimulus was presented within her blind (right) visual field. In comparison, when the same stimulus was presented within her sighted (left) visual field, it resulted in robust V1 activation in the normal (right) hemisphere.

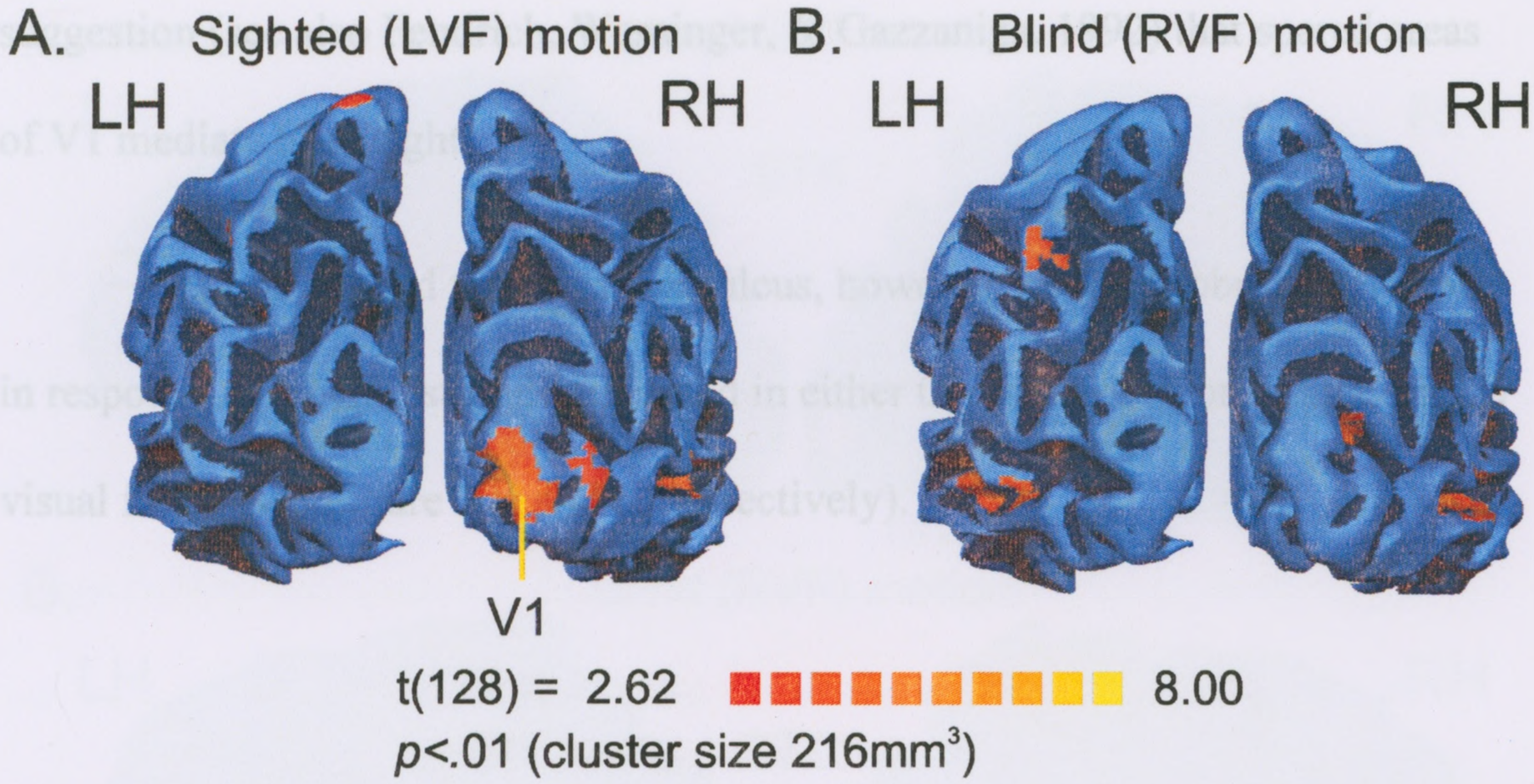


Figure 9. Posterior view of Session 3 functional imaging MT+ localizer data for patient SJ when the motion stimulus was presented in the sighted (left) (top panel A) or blind (right) visual field (bottom panel B). The data are displayed on a segmented and smoothed version of SJ's brain to allow easier viewing of the sulci (dark blue) and gyri (light blue). Abbreviations: LH = left hemisphere, RH = right hemisphere, LVF = left visual field, RVF = right visual field, V1 = primary visual cortex. Note the lack of significant activity in and around the left occipital pole for visual stimuli presented in SJ's blind (right) visual field.

In contrast, moving stimuli presented to SJ's blind (right) visual field failed to invoke activation in any of the grey tissue immediately surrounding SJ's lesion in her left hemisphere (see Figure 8b and Figure 9b), even at an uncorrected threshold of $p < .01$ (Stoerig, Kleinschmidt, & Frahm, 1998).

Thus, the vascular response and underlying metabolic activity of the remaining portion of cortex at patient SJ's occipital pole is not influenced by moving stimuli. This result does not lend support to Campion et al.'s (1983)

suggestion (see also Fendrich, Wessinger, & Gazzaniga, 1992) that spared areas of V1 mediate blindsight.

Regions beyond the calcarine sulcus, however, showed robust activation in response to moving stimuli presented in either the blind (left) or sighted (right) visual fields (see Figure 10a and b, respectively).

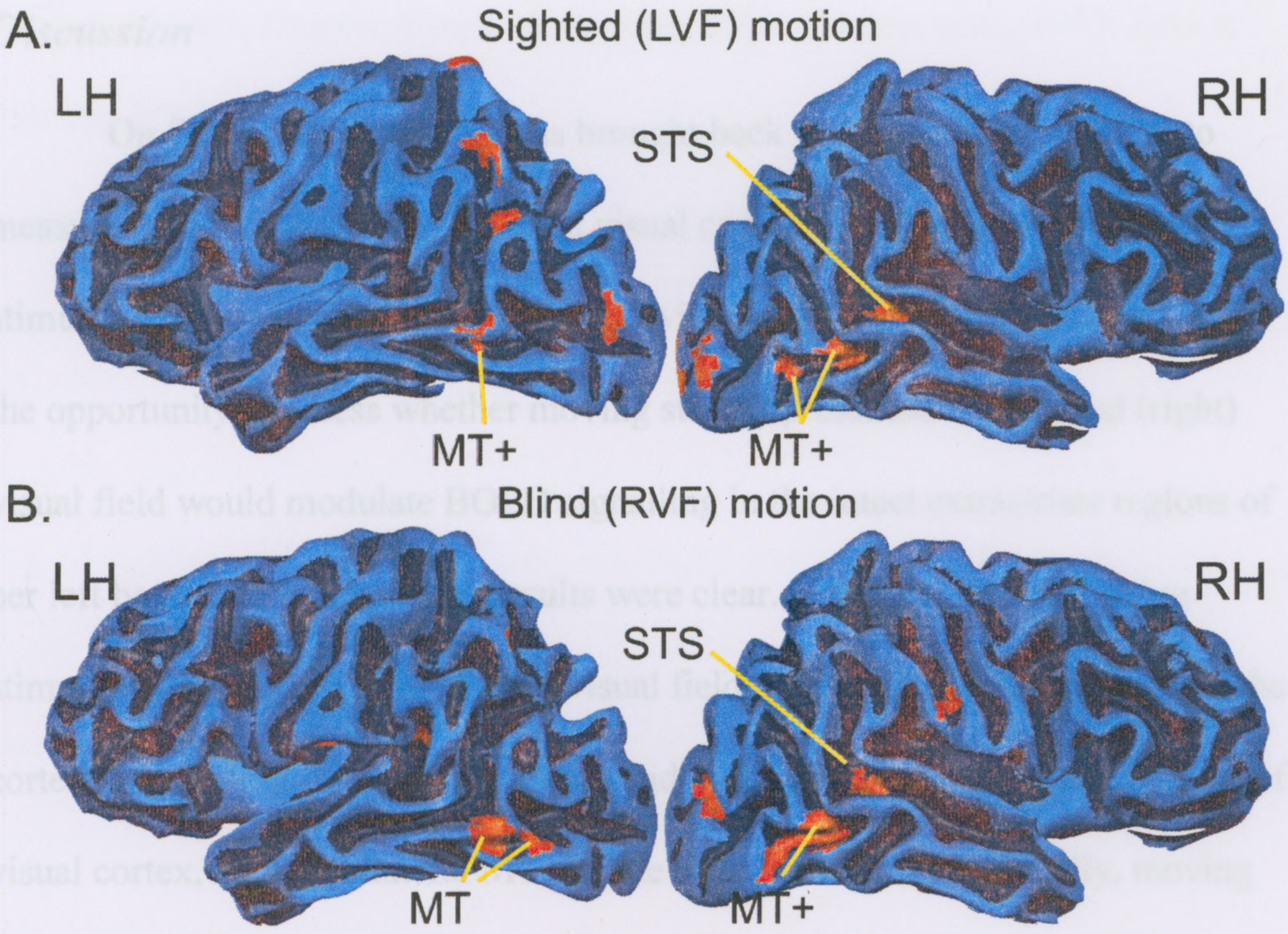


Figure 10. Lateral view of Session 3 functional imaging MT+ localizer data for patient SJ when the motion stimulus was presented in the sighted (left) (panel A) or blind (right) (panel B) visual field. The data are displayed on a segmented and smoothed version of SJ's brain to allow easier viewing of the sulci (dark blue) and gyri (light blue). Abbreviations: LH = left hemisphere, RH = right hemisphere, LVF = left visual field, RVF = right visual field, MT+ = middle-temporal cortex, STS = superior temporal sulcus. Note the significant bilateral activation in the motion sensitive complex MT+ regardless of whether the motion stimulus appeared with SJ's sighted (left) or blind (right) visual fieldBilateral activation was found in motion-sensitive extrastriate regions corresponding to the middle temporal and superior temporal gyri (MT+ and STS, respectively). As expected, moving stimuli presented in SJ's sighted (left) visual field invoked bilateral activation in the motion sensitive areas MT+ and STS of the right hemisphere (see Figure 10a) (Culham, He, Dukelow, & Verstraten, 2001; Dukelow et al., 2001; Watson et al., 1993).

Discussion

On Session 3, patient SJ was brought back for an fMRI experiment to measure how SJ's intact and lesioned visual cortices would respond to moving stimuli presented in her sighted and blind visual fields. The experiment afforded the opportunity to assess whether moving stimuli presented in her blind (right) visual field would modulate BOLD signalling in the intact extrastriate regions of her left hemisphere or not. The results were clear. Not surprisingly, moving stimuli located in SJ's sighted (left) visual field increased BOLD signalling in the cortex surrounding the calcarine sulcus and in the expected extrastriate regions of visual cortex, namely bilateral MT+ of the right hemisphere. Critically, moving stimuli presented in SJ's blind (right) visual field failed to modulate BOLD signalling in the cortical tissue surrounding SJ's lesion yet these same stimuli elicited a robust response bilaterally in MT+. These findings suggest that SJ's spared visuomotor abilities could be mediated by these extrastriate regions.

Overall, the results appear to be consistent with patient SJ's subjective descriptions of her ability to sense that things are moving within her blind visual field. Indeed, at the end of the experiment SJ mentioned that on some occasions she felt like something was moving in her blind field but that she could not "see" it. Overall, these results resonate with previous neuroimaging work that has shown that BOLD signalling in extrastriate regions including MT+ is modulated by moving stimuli restricted to the blind field of patients with hemianopia (Barbur, Watson, Frackowiak, & Zeki, 1993; Baseler, Morland, & Wandell, 1999;

Goebel, Muckli, Zanella, Singer, & Stoerig, 2001; Watson et al., 1993; Zeki & Ffytche, 1998).

CHAPTER 5

Summary and Discussion

Previous work has demonstrated that patients with damage to ventral aspects of the occipital and temporal cortex who present with visual form agnosia are able to grasp objects accurately despite being unable to estimate their size (Goodale et al., 1991; Karnath et al., 2009). In contrast, patients with lesions to POC, IPS, and SPL often present with optic ataxia – an inability to accurately reach towards objects – despite a preserved ability to recognize objects and estimate their size (Jakobson et al., 1991; Perenin & Vighetto, 1988). In addition, while patients with visual agnosia are unable to scale their grip aperture to remembered objects previewed a few seconds before (Goodale et al., 1994), patients with optic ataxia show an improvement in grip scaling following a delay (Milner et al., 2001).

This neurological double dissociation has been used to argue in favour of the notion that the ventral visual stream (extending from V1 to the inferior temporal cortex) is primarily concerned with conscious vision, object recognition, and the ability to create long-term visual memories, whereas the dorsal visual stream (extending from V1 to dorsal aspects of the posterior parietal cortex) is thought to be primarily concerned with visuomotor control in "real-time" (Goodale & Milner, 1992; Milner & Goodale, 2006). Although patients with visual form agnosia are able to grasp objects accurately that they are unable to identify, the pathways that mediate their preserved abilities have not been

specified. In monkey, and presumably in humans, the PPC receives most of its input from V1, MT, and other extrastriate areas, which may provide the necessary information with which to calibrate grip aperture to object size. Presumably, all these pathways, including those that arise from V1, are intact in patients with visual form agnosia who show spared visuomotor behaviour.

There are several potential alternative routes from the retina to the PPC that may bypass V1 altogether. In monkey, the SC projects, via the pulvinar nucleus of the thalamus, to the motion sensitive area MT, which itself sends projections to dorsal structures in the PPC (Kaas & Lyon, 2007; Lyon et al., 2010). Recently, Berman and Wurtz (2010) provided neurophysiological demonstration of a route from the SC to MT through connected neurons in the pulvinar of the macaque. Specifically, Berman and Wurtz (2010) elicited responses in neurons in the pulvinar with orthodromic stimulation (propagation forward to the axon terminal) of innervating SC neurons and antidromic stimulation (propagation back towards the cell body) of the terminal projections of the pulvinar neurons in MT. Moreover, these connected pulvinar neurons satisfy the 'collision test'. Thus, the responses of these neurons are suppressed when their terminal projections in MT are stimulated immediately after either the pulvinar neurons fires spontaneously or when their SC afferents are stimulated. In addition, it has recently been demonstrated histochemically that there are direct projections from the retina to the pulvinar – and then to area MT – in the marmoset (Warner, Goldshmit, & Bourne, 2010). Finally, the interlaminar layers

of the dLGN form a koniocellular pathway which also projects to extrastriate regions that include area MT (Sincich et al., 2004; Vakalopoulos, 2005).

Some recent behavioural and fMRI studies of the macaque monkey following a unilateral lesion to V1 have shed new light on the subcortical structures and pathways currently believed to underlie preserved processing observed in the affected visual field. Schmid et al. (2009) have shown that while BOLD signalling in extrastriate regions drops substantially in early extrastriate areas of V2 and V3 following unilateral lesion to V1, residual signalling remains one month post-surgery and is maintained for several months thereafter for all post-surgical testing dates. The authors confirmed their functional results with multi-unit recordings taken from the lesion projection zone of V2 of one of the monkeys tested. Importantly, Schmid et al. (2009) observed robust signalling in these regions even when the stimulus was presented entirely within the monkey's scotoma. In a subsequent study, Schmid et al. (2010) used fMRI to study the stimulus-invoked activity in the intact cortical regions of two macaques before and after deactivation of the dLGN. Following surgery, the monkeys could successfully detect and direct saccades to stimuli presented in the monkeys' scotoma. Furthermore, stimuli presented in the monkey's scotoma elicited functional activation of extra-striate regions outside of V1 (e.g., V23, V4, and MT). Critically, however, deactivation of the monkeys' dLGN using the $GABA_A$ agonist THIP abolished not only the behavioural performance but also the residual functional activity of the extrastriate structures of the two monkeys investigated.

Any or all of these routes could potentially provide the dorsal stream with the necessary input to accurately calibrate grip aperture to object size. In the current experiment, we investigated whether or not routes such as these which bypass V1 could play a role in the visual control of grasping by examining the grasping ability in patient SJ, who developed a homonymous right-visual field hemianopia following damage to the left occipital cortex. Preliminary testing indicated that SJ was able to localize targets in her blind field by pointing to them. Subsequent testing revealed that SJ was able to accurately scale her grip to objects presented entirely within her blind field with and without vision throughout the movement, provided the visual sensory input was available when the response was cued. Functional-MRI indicated that moving visual stimuli presented in SJ's blind field invoked activity bilaterally in extrastriate regions that likely correspond to the motion sensitive area MT+. Importantly, no activation was observed in the remaining tissue in the occipital pole immediately adjacent to her V1 lesion. On the basis of these findings, we conclude that SJ possesses action blindsight (Danckert et al., 2003; Rossetti & Pesilla, 2002). Critically, SJ's ability to scale her grip aperture to objects in her blind field was abolished when the cue to respond followed a 2s period during which vision was unavailable.

Throughout both testing days patient SJ repeatedly insisted that she "saw nothing" in her blind field. These claims were further validated by the fact that SJ was unable to manually estimate the width of the very same objects when they were presented within her blind field. Importantly, SJ was able to perform all of these tasks perfectly in her sighted visual field. In addition, an age-appropriate

control participant was able to perform all of the tasks perfectly regardless of which visual field the objects were presented in.

These findings have a number of important implications for our understanding of which visual pathways are required for accurate grip scaling as well as the time constraints under which these pathways operate. First, our results suggest that neither conscious vision nor input from V1 is required in order to accurately scale one's grip to object size. In addition, the fact that patient SJ was able to scale her grip to objects in her blind field even when vision was removed at movement onset (i.e., open-loop) shows that the pathways to the dorsal stream that do not depend on V1 can generate reliably scaled grasping without visually-driven 'on-line' control. Perhaps the most interesting finding in the current set of experiments is the fact that SJ could not scale her grip aperture to the width of objects presented in her blind field when a 2s delay was introduced prior to the cue to respond. These findings resonate with recent observations of patient CB who has a hemianopia and is able to avoid unseen obstacles presented in his blind field in "real-time" but not following a 2s delay period in which vision of the obstacles was removed (Striemer et al., 2009). Taken together, these two studies provide converging evidence that the extra-geniculostriate pathways and/or the koniocellular inputs to extrastriate visual areas that project eventually to the dorsal stream operate solely in real-time on a moment-to-moment basis based on information immediately available on the retina (Rossetti, 1998; Striemer et al., 2009). This is consistent with Milner and Goodale's contention that the dorsal stream does not store visuomotor transformations for later use, but rather,

computes them on demand depending on current task requirements (Milner & Goodale, 2006).

Important questions for future research are 1) to what extent can the dorsal stream extract the necessary information to grasp more complex objects that have constrained grasp points (e.g., the "Blake shapes") and 2) what are the temporal intervals over which the visual pathways that bypass V1 operate? In other words, if these pathways and the dorsal stream operate on the basis of real-time visual input exploited at movement onset then if *any* (even minimal) delay is introduced, patient SJ's grip scaling in her blind field should be eliminated (e.g., Westwood & Goodale, 2003). On the other hand, if very short delays (e.g., 250ms) reveal some residual sensitivity to the size of objects in her blind field then it would provide the first evidence for the existence of a kind of information persistence for object form in the dorsal stream. Finally, it will also be important for future studies to try and further delineate the brain regions and visual pathways that subserve action blindsight using functional brain imaging and diffusion tensor imaging, similar to recent efforts that have helped identify the neural substrates responsible for attention blindsight (Leh, Johansen-Berg et al., 2006; Leh et al., 2009; Tamietto et al., 2010).

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