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Abstract: Each cerebral hemisphere primarily controls and receives sensory input with regard to the contralateral hand. In the disconnected brain (split-brain), when the hands are uncrossed, direct visual access to each hand is available to the controlling (contralateral) hemisphere. However, when a hand crosses the midline, visual and tactile information regarding the hand are presented to different hemispheres. It is unknown how a contralateral hemisphere codes the position and orientation of a visually inaccessible hand in the disconnected brain. The present work addresses this issue. We ask how each hemisphere represents "its" hand across hand positions that span the midline in the absence of cortical input from the contralateral hemisphere. In other words, when a hand is placed across the midline and is visually inaccessible, is it represented by the controlling hemisphere: (1) in accordance with its new position with respect to the body (e.g. a left hand "becomes" a right effector when it crosses the midline), (2) with left/right position information unaltered (e.g. the left hand is represented as "left" regardless of its location), or (3) stripped of its location information altogether? The relationship between hand position and the spatial codes assigned to potential responses (an index of hand representation) was investigated in two split-brain patients using direct (Experiment 1) and orthogonal (Experiment 2) S-R compatibility paradigms. S-R compatibility effects in split-brain patients were consistent with those displayed by typical individuals. These findings suggest that position-based compatibility effects do not rely on cross-cortical connections. Rather, each hemisphere can accurately represent the full visuomotor space, a process that appears to be subserved by subcortical connections between the hemispheres.

July 6, 2018

Dear Dr. Vuilleumier,

In response to your May 30, 2018 request for revisions of manuscript CORTEX-D-18-00289, "Attention and Awareness: Representation of visuomotor space in split-brain patients," for publication in *Cortex* as part of the special issue "Attention and awareness: a special issue in honour of Dr. Robert Rafal."

We include both "clean" and track-changes copies of the revised manuscript, as well as a detailed response to the two expert reviewers concerning our changes. Specifically, our changes include: reshaping the introduction to clarify the overall argument and significance of the work, the addition of a methods figure in the introduction to make key comparisons more clear, expansion of the discussion of how our work speaks to other special populations (notably those with neglect and optic ataxia), and additional precision in our reporting of variance and trial exclusions. There is no question that the comments and constructive suggestions we received have strengthened our paper, and we believe, and hope you agree, that it is now ready to be disseminated into the broader community.

We look forward to hearing from you soon.

Sincerely,

Jill Dosso
For authors: Jill Dosso, Romeo Chua, Daniel Weeks, David Turk, Alan Kingstone

***Detailed Response to Reviewers**

Comments from the Reviewers:

Reviewer #1: The authors examined the relation between hand position and space (using classic S-R compatibility tasks) to determine how such relations are processed in the absence of cross-cortical input (i.e., in the famous corpus callosotomy patient JW). Essentially, how are hand-centered reference frames processed and controlled when the hand is not directly visible to the controlling hemisphere? Stimuli were presented along the vertical meridian with judgments of top and bottom made when the hand was either within the same hemisphere (e.g., left hand in left space) or crossed (e.g., left hand in right space). Results of study 1 showed comparable compatibility effects for either hand regardless of where in space the hand was positioned. Study 2 tested 2 split brain patients with left-right key responses instead of up/down. Here the results suggested that spatial position of the hand was the important determinant of the compatibility effect.

The paper is well written although I have to confess to finding this work a little mind-bending - keeping track of what is crossed and which information is contained within which hemisphere is challenging in these two studies. Ultimately, if the outcome is that we discover that each hemisphere can represent "hand position with respect to a target" I suspect that this is largely based on proprioceptive reference frames and is not at all surprising (see my comment below). So perhaps the piece would benefit from some clarity with respect to the theoretical import of the finding.

I found myself wondering particularly how remarkable the finding was for Study 1? Essentially, JW knows his hand is crossed over (he has visual access to his elbow at the very least and certainly would have proprioceptive signals telling him where his hand was in space). So the fact that he shows a compatibility effect regardless simply confirms that I, with my intact CC, can tell you what my hand is doing when it is out of view. I may be missing something here - but why would we have expected vision of the hand to be so critical to this effect?

In a related sense, how does the healthy brain do on this kind of task? Here you would likely need to occlude vision of the hand in some way - but if there were effects in the healthy brain that did not mirror what is seen here with JW, then the result would be more interesting.

For study two I was also scratching my head trying to figure out the import. It is sold as the right hand becoming a left effector and vice versa - but I don't see how the data has supported such a claim.

Authors: Thank you very much for these comments. We agree with the reviewer that JW's performance in E1 is not surprising and is consistent with performance among healthy controls. Overall, we have endeavored to clarify that E1 is more of a control experiment to ensure that split-brain patients can do this sort of task, and to make our expectations with respect to healthy intact control data more explicit. Overall, the results of E2 are the most central to our claims, so we have reorganized the introduction (and made minor changes throughout the manuscript) to better set up this narrative so that it is clear to the reader why the E2 results (though they match what would be expected in healthy intact individuals) are surprising and novel when shown in split-brain patients. To recap, the use of the orthogonal SR task in E2

allows us to assess whether hands that cross the midline take on a new left/right code (e.g. right hand becomes a left effector). We find that, even in split-brain patients, this happens. This is surprising because others have suggested that one or both hemispheres might not 'recode' the spatial representation of 'its hand' when a hand crosses the midline into ipsilateral space, especially in the absence of cross-cortical input.

I didn't see the direct relevance of the discussion on neglect literature - yes, they fail to orient contralaterally, but in most patients this deficit is most prominent in the visual domain. Their success in adapting to prismatic lenses suggests that for many neglect patients proprioceptive signals are unaffected (or at least less affected). So I didn't see how this related to the current findings.

Authors: Thank you for this comment. We have modified the relevant text to acknowledge that neglect can be primarily visual. We also mention that unilateral sensory neglect has been shown in other domains (e.g. proprioception: Karageorgiou, 2015). However, even if proprioception is preserved in neglect patients when parietal function is unilaterally damaged, this does not mean that each hemisphere can support accurate hand position *in the total absence of cross-cortical connections*. It is the potential role of these connections that split-brain patients allow us to test, and we expand on this in the general discussion (p 26).

So clearly, I have been a little underwhelmed by this paper. Is this a valid reason to reject? Not in my view - I might simply not be getting it. If the authors feel like they could hammer home the key message in a more obvious way, perhaps I would see the light. But in terms of design and execution, the work is fine and so if it fits in with the tenor of other contributions to this special issue then I see no problem with publishing it.

Authors: Thank you. This is very helpful and, as mentioned, we have reshaped the argument of the paper in a way that we hope speaks to the problem of messaging.

Minor points:
The trimming of RT distributions was a little crude - could RTs that were 2 or 3 SDs outside the subject's mean (per condition) be removed instead? With patients (not sure about JW given his surgery was so long ago) long RTs are not unusual - certainly longer than 1,000 ms. Alternatively, if this trimming only chopped a small percentage of RTs then reporting that would be helpful.

Authors: Exclusions made up a relatively small proportion of RTs:

	Incorrect	Timing
E1 JW	2.3%	1.1%
E2 JW	3.3%	1.8%
E2 VP	3.7%	3.1%

We have also updated the manuscript to include these values (pages 10, 18).

Could variance measures be included on Figures?

Authors: Yes! We now include standard error bars on Figures 2.2 and 3.2.

Reviewer #2: Manuscript Number: CORTEX-D-18-0028
The authors examine whether the S-R spatial compatibility effects are preserved in split-brain patients when the hand providing the two-choice button response is located in the controlateral visual field and thus, spatially, in the hemisphere ipsilateral to the hand, while the somatosensory and motor representation is supposed to lie in the hemisphere controlateral to the hand. In all experiences, the visual target that the patient was required to respond to was presented in the visual midline (top or bottom location). The authors show the preservation of the S-R compatibility effects and conclude that "hand-centred" visuomotor representations of a given hand are present in both hemispheres.

I am not familiar enough with S-R spatial compatibility effects but for me the interpretation in terms of "hand-centred" visuo-motor representation is not straight forward. Please explain a bit more how the ability to select one finger or the other with respect to the visual target location (top-down) has to rely on "hand-centred" representations rather than simple allocentric or semantic spatial coding and association to specific fingers.

Authors: The hand- versus body-centred distinction was intended to help clarify matters for readers, and obviously that goal was not achieved. As it is not critical to the main argument of our paper, we have removed this language throughout. Instead, we focus on the representation of the hand as a whole as it moves across space. We have further clarified throughout the manuscript that E1 is primarily a control experiment while E2 is the critical manipulation (and we have reworked the messaging somewhat, especially in the introduction), which might help the reader track our argument more clearly.

It would be interesting that the authors discuss their results about visuomotor space with respect to studies on optic ataxia (patients whose parietal lesions affect pointing movements). These studies have underlined that the lesion of one hemisphere has two consequences: one related to the contralesional hand accuracy (hand effect) and another related to the coding of hand and target within the contralesional space (field effect). See Blangero et al. NeuroImage 2007

Authors: Thank you very much. This is a very nice connection, and we have now added reference to this population and its relationship with our data on page 26.

*Title page

ATTENTION AND AWARENESS: REPRESENTATION OF VISUOMOTOR SPACE IN SPLIT-BRAIN PATIENTS

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ABSTRACT

Each cerebral hemisphere primarily controls and receives sensory input with regard to the contralateral hand. In the disconnected brain (split-brain), when the hands are uncrossed, direct visual access to each hand is available to the controlling (contralateral) hemisphere. However, when a hand crosses the midline, visual and tactile information regarding the hand are presented to different hemispheres. It is unknown how a contralateral hemisphere codes the position and orientation of a visually inaccessible hand in the disconnected brain. The present work addresses this issue. We ask how each hemisphere represents "its" hand across hand positions that span the midline in the absence of cortical input from the contralateral hemisphere. In other words, when a hand is placed across the midline and is visually inaccessible, is it represented by the controlling hemisphere: (1) in accordance with its new position with respect to the body (e.g. a left hand "becomes" a right effector when it crosses the midline), (2) with left/right position information unaltered (e.g. the left hand is represented as "left" regardless of its location), or (3) stripped of its location information altogether? The relationship between hand position and the spatial codes assigned to potential responses (an index of hand representation) was investigated in two split-brain patients using direct (Experiment 1) and orthogonal (Experiment 2) S-R compatibility paradigms. S-R compatibility effects in split-brain patients were consistent with those displayed by typical individuals. These findings suggest that position-based compatibility effects do not rely on cross-cortical connections. Rather, each hemisphere can accurately represent the full visuomotor space, a process that appears to be subserved by subcortical connections between the hemispheres.

Keywords: split-brain; S-R compatibility; visuomotor space; spatial coding

INTRODUCTION

The present set of studies examines if, and how, information about hand position is integrated with information about objects in the environment within and between the cerebral hemispheres. Spence, Kingstone, Shore, and Gazzaniga (2001) addressed this issue with a split-brain patient, J.W., and found that when a hand does not cross the midline, visual information near the hand interferes with the processing of tactile information on the hand. The same result occurs for intact control participants. Indeed, controls are still affected by near-hand visual distractors when their hand crosses their midline. However, when J.W. placed his hand across his body, responses to tactile information were unaffected by nearby visual distractors. Spence et al. concluded that when J.W. placed his hand across the midline, visual information was received by one cortical hemisphere while tactile information was received by the other, and J.W.'s disconnection prevented normal multisensory integration by bimodal neurons. What this study does not tell us, however, is how each hemisphere, when isolated, represents "its hand" when the hand is placed across the midline. Of course, in intact individuals, the issue is trivial, because when a hand crosses the midline, cross-cortical connections allow the two hemispheres to communicate about the hand's new position. When the corpus callosum is sectioned, however, how a hand that crosses the midline is represented is an open, and to date, unanswered question. The present studies sought to resolve this issue.

In the typical population, the coding of hand position has often been examined in the context of stimulus-response (S-R) compatibility paradigms. Participants respond to a stimulus more quickly when there is spatial alignment between the stimulus and the response effector than when there is misalignment (Fitts & Seeger, 1953; Proctor & Cho, 2006; Weeks, Proctor, & Beyak, 1995). Importantly, this stimulus-response (S-R) compatibility effect is typically effector-

independent (Wallace, 1971, 1972). For example, in Figure 1.1, trials that employ the incompatible mapping should be performed more slowly than trials that employ the compatible mapping, regardless of whether hands are crossed or uncrossed. Thus, for intact healthy participants, these tasks seem to rely on brain regions that represent the hand by its position rather than its identity. In other words, compatibility effects are driven primarily by the location of the response effector (e.g. a right hand located in left space is treated as compatible with a left-side target rather than a right-side target). By manipulating hand and stimulus location in split-brain patients, perceptual inputs from the hands and from the stimuli can be separated systematically into the two non-communicating hemispheres, allowing the hand-target relationship to be assessed.

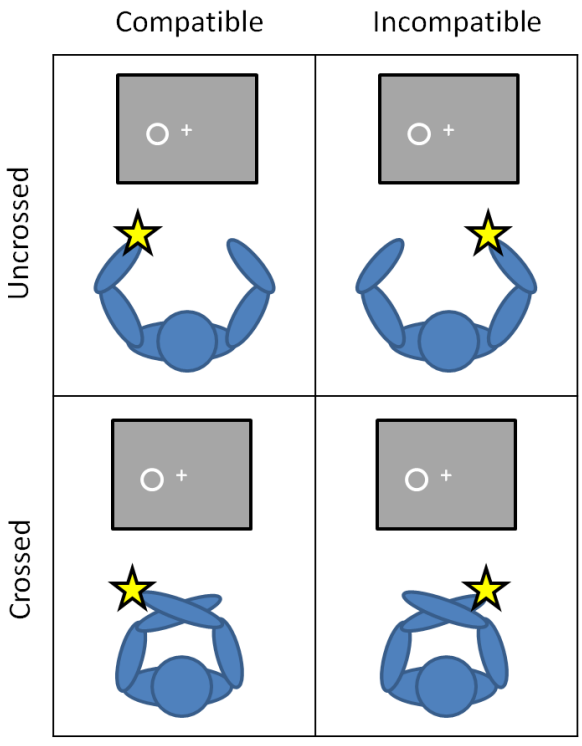

Figure 1.1. Schematic representation of testing conditions used in previous S-R paradigms with intact and split-brain individuals (Aglioti et al., 1996; Mooshagian et al., 2009; Wallace, 1971). Yellow stars indicate the designated response effector.

Of special interest to the present work, Aglioti and colleagues administered an S-R compatibility task to four individuals with varying degrees of corpus callosum disconnection (Aglioti, Tassinari, & Berlucchi, 1996). In their task, target location (left or right), hand posture (both hands crossed, or uncrossed), and stimulus-response mapping (spatially aligned (compatible) or spatially misaligned (incompatible)) were manipulated, mirroring the earlier S-R work. Similar work, again with split-brain patients, has also been conducted more recently by Mooshagian, Iacoboni, and Zaidel (2009). In both investigations, on some key trials, the hemisphere controlling the responding hand did not have direct access to the visual stimulus to which it was required to respond (e.g. in Figure 1.1, the incompatible-uncrossed and compatible-crossed trials). Surprisingly, split-brain patients were still able to respond effectively on these trials. This fact seems incongruent with the findings of Spence and colleagues, who demonstrated that visual and tactile information presented near a crossed hand were not integrated (Spence et al., 2001). While the authors of the compatibility papers interpreted the responses on these trials as involving the subcortical transfer of target information, we note that they could also represent correct guesses, as a warning tone preceded each target trial and catch trials (to assess response guessing) were not provided. For example, in the previous S-R split-brain studies, the right hemisphere could correctly infer that the absence of a visible left-side target meant that a right-side target had been presented. In short, correct responses need not reflect the subcortical transfer of target information. In addition, interpretation of the results is complicated by the fact that both studies involved patients crossing the hands; thus, not only does

each hemisphere lose visual access to the contralateral hand that it controls, each hemisphere sees an "intruder hand" in its contralateral visual field. Even in typical participants, crossing the hands is associated with a reaction time penalty, possibly due to the unfamiliarity of this situation (Brebner, Shephard, & Cairney, 1972).

Thus, current evidence about the nature of hand representation in the disconnected brain is mixed. There are at least two possibilities. When the hand crosses the midline and is no longer directly visible to the controlling contralateral hemisphere it is possible that positional information about the hand is still maintained even though the spatial location of the hand is now felt but not seen. Alternatively, the controlling hemisphere might simply cease to represent the position of "its hand" in any specific way beyond "not visible." To apply this to a specific scenario: when the left hand is located near a left-side target, the hand and target can be perceived as "aligned" or "compatible," even for split-brain patients. However, when the left hand is located in right space, away from left-side targets, target position can be mismatched with hand position one of two ways: the hand position might be known to be incongruent with target position (e.g. the hand is known to have a rightward position, which is incongruent with the leftward stimulus), or specific hand position information may be absent.

To resolve our question about hand representation across the visuomotor space while avoiding concerns about patients guessing, the present work employed S-R paradigms with two special features. First, the stimuli were presented centrally, and so were simultaneously available to both hemispheres of the patients. Second, a two-alternative choice response was required by the responding hand (and thus the controlling hemisphere), thereby ensuring that response guesses would result in errors while also allowing for each hemisphere to be tested in isolation.

In sum, the present work sought to determine how hand position and orientation are represented by the controlling, contralateral hemisphere when the hand is located across the midline in the absence of cross-cortical input. Put another way: how do hand-target relationships change (or stay the same) as the hand crosses the midline, and how is this informed by cross-cortical input?

In our first experiment we ensure that split-brain patients are capable of performing two-choice S-R tasks with variation in responding hand position. We expected that split-brain performance on this control task (Experiment 1) would match what is typically seen in healthy intact control individuals.

2.1 Experiment 1

As reviewed above, existing work on S-R compatibility in split-brain patients has been concerned primarily with questions regarding the interhemispheric transfer of information, and has employed conditions in which both hands are crossed over the midline at the same time (Aglioti et al., 1996; Mooshagian et al., 2009). This present study examines the potential impact on task performance of moving the responding hand with respect to the stimulus while keeping both visual access to the target and control of the responding hand in the same hemisphere. If direct S-R compatibility effects (i.e. faster responding when top stimuli are matched with top as opposed to bottom response options) are observed across hand locations, this would suggest that each hemisphere can represent response options within the hand as "top" and "bottom" without visual access to the hand. This procedure therefore allows one to characterize potential changes in the way that the controlling hemisphere represents its responding hand in the absence of cross-cortical inputs when the hand is and is not directly visible.

This experiment distinguishes between two hypotheses. First, it could be that when the hand is placed across the midline and is no longer visible to the controlling hemisphere, no information about hand position is maintained. If this were the case, one would expect normal S-R compatibility results when the hand does not cross the midline (i.e. faster responding to a top stimulus when using the top response option rather than the bottom response option) but no S-R compatibility when the hand was crossed over the body. A second possibility is that hand position information is maintained regardless of hand position, in which case normal S-R compatibility effects should persist across all hand positions. Note that a combination of results could also be possible: one hemisphere but not the other might be capable of representing hand position information in this way (Kinsbourne, 1970).

2.1.1 Materials and Methods

2.1.1.1 Participants

J.W. is a right-handed male who underwent callosotomy in 1979. Details about his neurological history have been reported previously (Gazzaniga, Nass, Reeves, & Roberts, 1984; Sidtis, Volpe, Wilson, Rayport, & Gazzaniga, 1981). J.W. was 46 years old at the time of testing.

2.1.1.2 Apparatus and Stimuli

Stimuli were presented on a 14 inch computer monitor. A stimulus square subtending 1˚ was presented white on black, 4˚ above or below a central white fixation cross (subtending 0.3˚). Responses were collected using a generic computer keyboard.

2.1.1.3 Procedures

The display was located at the midline approximately 57 cm in front of the participant. The stimulus array was presented along the vertical meridian of the display. J.W. performed speeded top and bottom key-press responses while maintaining central fixation. He placed the

index and middle fingers of the responding hand on the spacebar (bottom) and "b" (top) keys of the keyboard. As illustrated in Figure 2.1, three response locations were used, where the keyboard was centred either in left space (30 cm left of midline), at the midline, or in right space (30 cm right of midline) (see Figure 2.1).

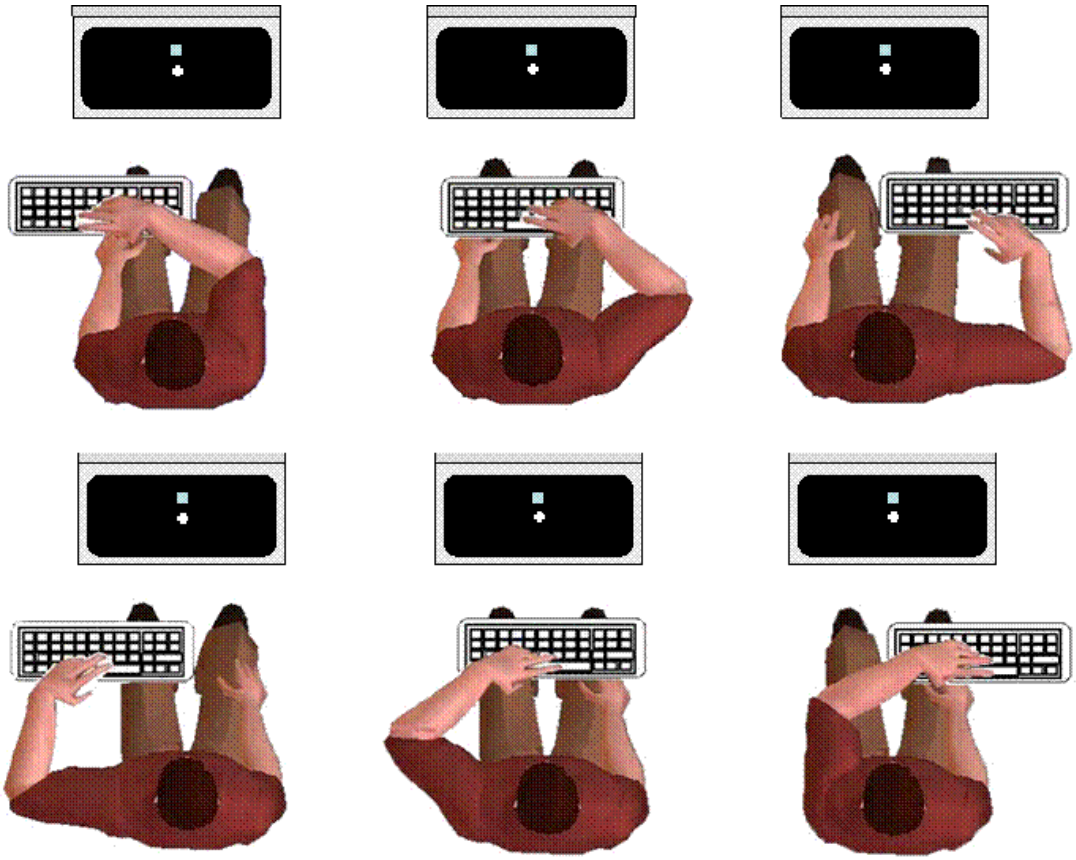

Figure 2.1. Illustration of experiment set-up and design.

J.W. responded according to two spatial mapping rules: a compatible mapping, in which the top and bottom stimuli were paired with top and bottom responses respectively; and an incompatible mapping, in which the top and bottom stimuli were paired with bottom and top responses respectively. Each mapping rule was performed in a separate block of trials. For each mapping rule, J.W. performed separate blocks of trials with each hand at each of the three

response locations, for a total of 12 blocks. Each block consisted of 70 trials, with the stimulus appearing an equal number of times at each position.

2.1.2 Results

All data are available at https://osf.io/g8mhs/. Mean reaction times (RTs) were derived for each unique combination of the factors of Response Hand (left, right), Response Location (left, midline, right), and S-R Mapping (compatible, incompatible). Trials in which the RT was less than 100 ms or greater than 1000 ms (1.1% of trials), or in which the wrong key was pressed (2.3% of trials), were counted as errors and excluded from analysis. The mean RTs and errors for J.W. as a function of the experimental conditions are presented in Table 1.1. The compatibility effects (Incompatible RT - Compatible RT) are illustrated in Figure 2.2. The results clearly show that RTs were faster when the spatial mapping was compatible, yielding a robust spatial compatibility effect (e.g., Fitts & Seeger, 1953).

Table 1.1. Mean (and SD) reaction time (ms) and error rates for JW as a function of Response Hand, Response Location, and S-R Mapping.

S-R Mapping		Compatible			Incompatible	
Response Location	Left	Middle	Right	Left	Middle	Right
Left Hand	441.9	438.9	451.5	612.0	596.2	529.1
	(84.8)	(50.4)	(94.4)	(104.0)	(108.5)	(115.4)
Right Hand	397.7	419.4	377.8	664.8	631.6	578.1
	(72.7)	(72.0)	(56.1)	(131.9)	(80.4)	(99.0)

S-R Mapping		Compatible			Incompatible	
Response Location	Left	Middle	Right	Left	Middle	Right
Left Hand	1.4	0.0	1.4	4.3	4.3	7.1
Right Hand	1.4	0.0	1.4	12.9	1.4	4.3

All analyses were conducted as single-subject analyses using trials rather than participants as the random variable. To confirm the spatial compatibility effect for each response hand, a univariate analysis of variance (ANOVA) was performed on the cleaned reaction time data (Figure 1.2) with two factors: compatibility (compatible versus incompatible mapping between stimulus and response) and response location (left, middle, right). For both hands, there was a large main effect of spatial mapping ($F(1, 407)=205.7$, $p<.001$, $\eta p2=.34$; $F(1, 405)=675.6$, $p<.001$, $\eta p2=.63$ for left and right hands respectively) with incompatible trials eliciting slower responses than compatible trials. There was also a main effect of response location ($F(2, 407)=5.4$, $p=.005$, $\eta p2=.03$; $F(2, 405)=15.0$, $p<.001$, $\eta p2=.07$) and a response location by mapping interaction ($F(2, 407)=9.4$, $p<.001$, $\eta p2=.05$; $F(2, 405)=5.5$, $p=.005$, $\eta p2=.03$), but these effects were much smaller in magnitude than the mapping effect. Descriptively, the main finding of these data was that compatible trials were always performed more quickly than the equivalent

incompatible trials, regardless of response location or hand used (i.e. in Figure 2.2., deltaRT is always meaningfully positive), including the critical cross-midline hand positions. Thus, the top and bottom of the hand (designations that can only be defined if hand orientation is known) were represented across the full visuomotor space.

In addition, similar univariate ANOVAs were performed for each hand on the error data. For the left hand, there was a main effect of mapping ($F(1, 420)=4.6$, $p=.03$, $\eta p2=.01$), with more errors made in the incompatible trials. For the right hand, there was a main effect of response location ($F(2, 420)=3.2$, $p=.04$, $\eta p2=.02$), with errors made most frequently when the hand was placed in the left location. No other main effects or interactions were found.

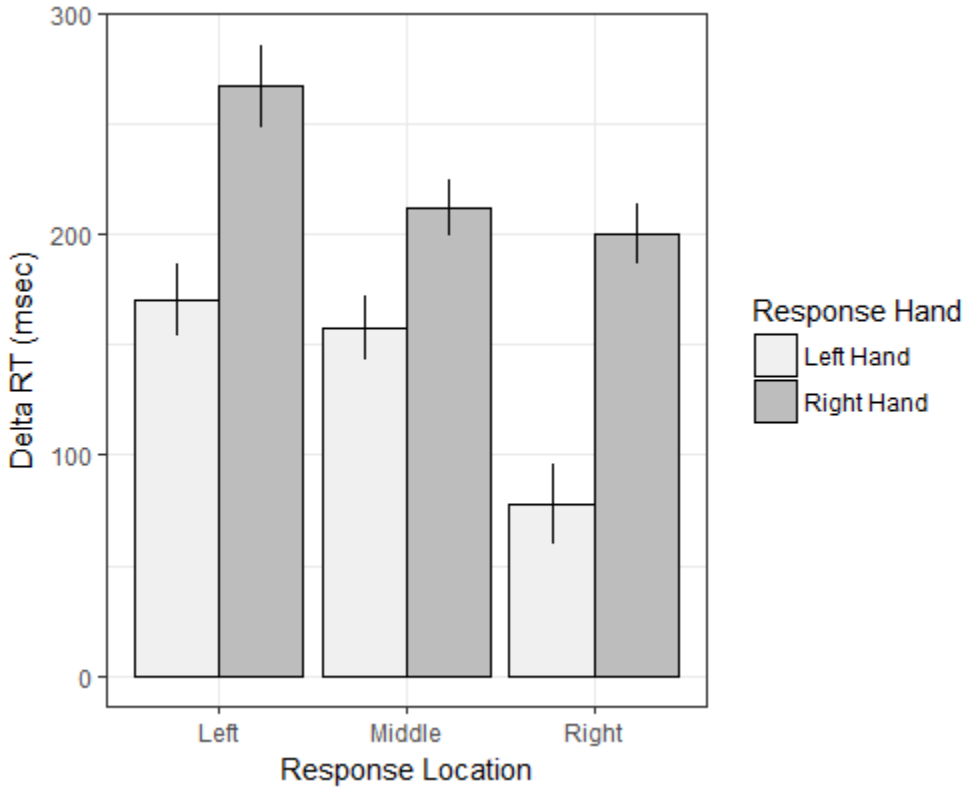

Figure 2.2. Influence of spatial S-R mapping expressed as the reaction time difference (delta RT ± SE) between incompatible and compatible mappings across response locations and effectors.

2.1.3 Discussion

Experiment 1 assessed direct top-bottom compatibility effects for each hand and on either side of the midline. This was done in order to investigate the extent to which each hemisphere maintained a representation of the two response options as "top" and "bottom" based on felt hand orientation in the absence of direct visual access to "its" hand. Because the two response options were located within a single hand and stimuli were presented at midline, each hemisphere could be tested in isolation, excluding the possibility of cross-cortical input. We did not predict that J.W.'s performance would differ from that typically seen among healthy subjects (Weeks & Proctor, 1990; Weeks et al., 1995), but we performed this experiment to ensure that split-brain patients could perform this type of direct S-R compatibility task before examining the critical orthogonal mapping in Experiment 2.

Overall, the data show that direct compatibility effects exist for both hands and on either side of the midline for split-brain patient J.W. Like typical subjects, J.W. responded more quickly and more accurately when employing a compatible S-R mapping (e.g. responding to top stimuli with his top finger) than when employing an incompatible S-R mapping (e.g. responding to top stimuli with his bottom finger). Importantly, this was the case for both hands and for all hand positions, including when the hand was placed across the midline. Because the stimuli were always located at midline, they were visually available to both hemispheres (Fendrich & Gazzaniga, 1989). For J.W., visual and tactile information from the hand are located in the same hemisphere when the hand is located on the ipsilateral side of the body. When the hand crosses the midline, visual access is no longer available to the hand-controlling hemisphere (Spence et al., 2001).

Thus, these results indicate that vision of the hand is not necessary for the S-R compatibility effect, and this is consistent with data in normal intact individuals (Wallace, 1972).

Moreover, the "top" part of the hand is a relative designation that is determined by hand orientation. These data therefore suggest that each hemisphere can independently represent response options within the hand as "top" and "bottom" based on proprioceptive information regarding the hand's orientation without direct visual access to the hand in question. These response codes could be maintained without online visual access to information about hand orientation.

3.1 Experiment 2

Experiment 1 established that vertical (top/bottom) response codes are maintained as the hands move across the midline in split-brain patient J.W. This served as an important manipulation check indicating that S-R compatibility effects can be measured using a two-choice paradigm and single-hand responding in split-brain patients. In Experiment 2, we performed the critical measure: each hemisphere's representation of left and right spatial codes were examined as the hands moved across the midline in a pair of split-brain patients. Specifically, we investigated if each hemisphere could maintain updated hand position information in the same coordinate system as the target information, in the absence of cross-cortical input, even when the hand crossed the midline and was no longer visible. Put another way, when a right hand crosses the midline, can it become a left effector from the perspective of its controlling hemisphere? Or does it simply cease to be a right effector without taking on a new specific spatial position? Existing data on cross-midline hand positions are not able to answer this question; a visuotactile integration task indicated the new hand position cannot be integrated with tactile information at the new location (Spence et al., 2001), but it does not speak to how the hand is represented. While compatibility paradigms seem to show a reaction time advantage when hand-target

alignment exists (Aglioti et al., 1996; Mooshagian et al., 2009), these latter tasks may be confounded by the possibility of patients guessing on critical trials.

To address this issue, an orthogonal S-R compatibility paradigm was employed. This task is a variant of the typical S-R compatibility paradigm and involves stimuli and responses that are orthogonal to one another rather than organized in the same plane (i.e., up and down stimuli are mapped to left and right responses). This paradigm indicates whether an effector is represented to be relatively leftward or rightward based on the finding that top is compatible with a left keypress (and bottom with a right keypress) when the response pad is on the left; and top is compatible with a right keypress (and bottom with a left key press) when the response pad is on the right (Proctor & Cho, 2006; Weeks et al., 1995). The general principle is that the top stimulus is more compatible with the more salient referent (left keypress when the response pad is on the left; right keypress when the keypad is on the right). For intact controls, and in keeping with the standard S-R compatibility paradigm, this robust orthogonal compatibility mapping phenomenon occurs even when a hand crosses the body (Weeks et al., 1995). –Thus, by comparing the reaction time associated with the top-left/bottom-right mapping versus the top-right/bottom-left mapping under the same conditions, we obtain an index of the relative salience of "left" and "right." Importantly, in healthy intact individuals, it is effector location (left or right side of space) and *not* effector identity (left or right hand) that determines the preferred mapping (Wallace, 1971; Weeks et al., 1995).

The question is: what will the case be for split-brain patients? If, for example, the right hand can be represented as a "leftward" effector by its controlling left hemisphere when it is placed across the midline in the left position, one would expect that the preference to map the top stimulus with a left keypress (and the bottom stimulus with a right keypress) to be maintained,

resulting in faster responding than when the mapping is reversed (i.e., top with a right response and bottom with a left response). Such a result would be consistent with performance of intact individuals (Weeks et al., 1995) and would suggest that cross-cortical connectivity is not necessary for normal task performance. Alternatively, if the right hand is always represented as "right" then top should prefer to map with the right keypress (and bottom with the left keypress). This scenario would be aligned with work suggesting the each hemisphere preferentially attends only to the contralateral side of space (Cohen, Ivry, Rafal, & Kohn, 1995; Posner, Walker, Friedrich, & Rafal, 1987). A third possibility is that when the hand crosses the midline, its mapping is disrupted because information about its position is simply unavailable to the controlling hemisphere, in which case there should be no discernable compatibility effect. And finally, it could also be possible that the two hemispheres might differ in their ability to represent the full visuomotor space; for example, it has been suggested that only the right hemisphere supports orienting to both sides of space (Karnath & Rorden, 2012).

3.1.1 Materials and Methods

3.1.1.1 Participants

J.W. was tested again. We also tested split-brain patient V.P., a right-handed female who both underwent callosotomy in 1979. Details of both patients have been reported elsewhere (Gazzaniga et al., 1984; Sidtis et al., 1981). V.P was 47 years old at the time of testing.

3.1.1.2 Apparatus and Stimuli

The apparatus and stimuli were the same as in Experiment 1.

3.1.1.3 Procedures

The procedure matched that used in Experiment 1, with the exception that participants now performed speeded left and right key-press responses. They placed the index and middle

fingers of the responding hand on the "b" (left) and "n" (right) keys of the keyboard. Three response locations were used again (left, middle, right; see Figure 2.1).

Participants responded according to two orthogonal S-R mapping rules: a top stimulus being assigned to the left (b) key, the bottom stimulus assigned to the right (n) key; or vice versa. Each mapping was performed in a separate block of trials. For each mapping, participants performed separate blocks of trials with each hand at each of the three response locations, for a total of 12 blocks. Each block consisted of 70 trials, with the stimulus appearing an equal number of times at each position. Data were collected from V.P. in a single session. J.W. participated in two sessions, conducted over two days, providing twice as much total data. Data for J.W. are collapsed over the two sessions.

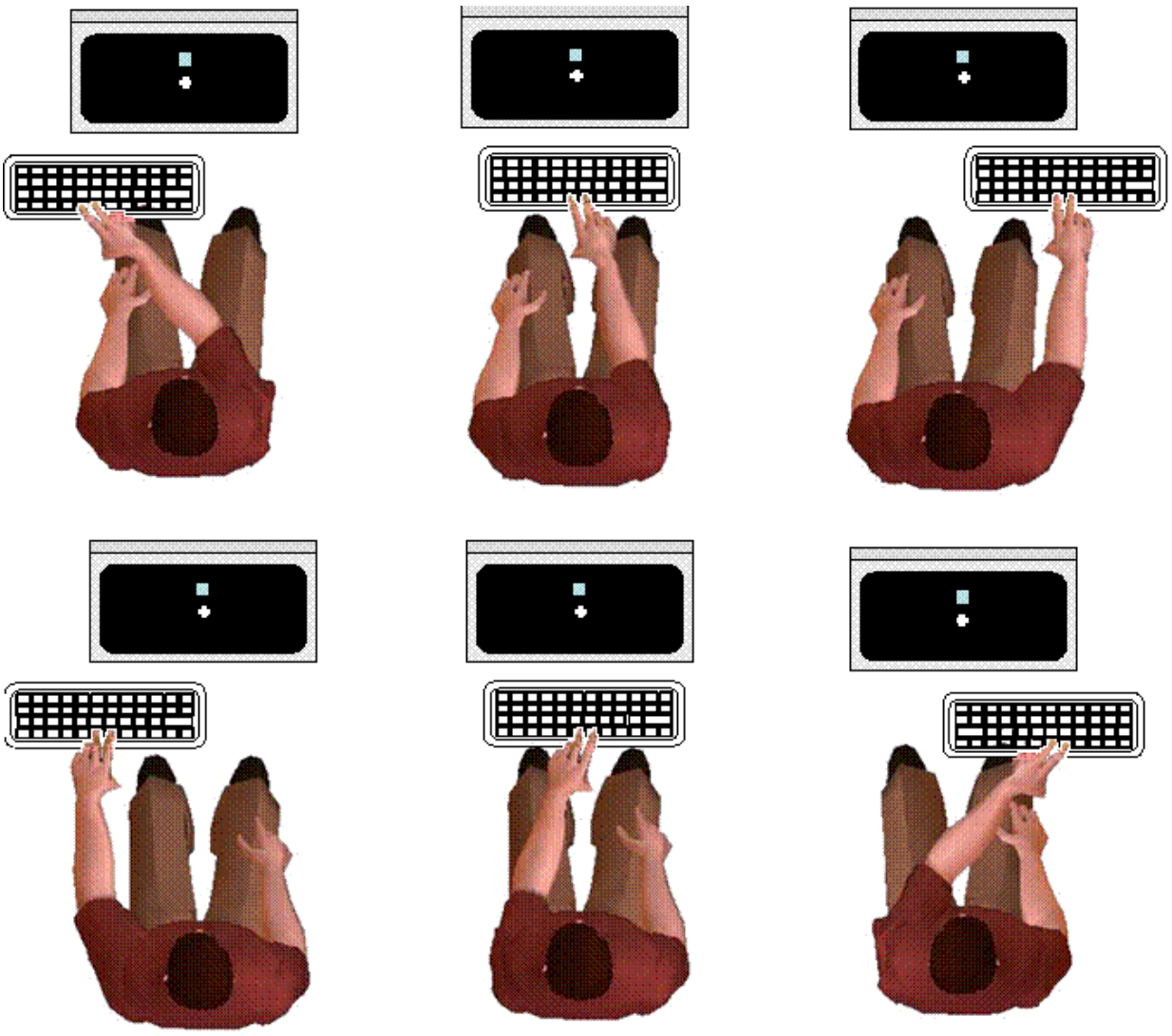

Figure ~~2~~3.1. Illustration of experiment set-up and design in Experiment 2.

3.1.2 Results

Mean RTs were derived for each unique combination of the factors of Response Hand (left, right), Response Location (left, midline, right), and S-R Mapping (top stimulus-left response/bottom stimulus-right response, or vice versa). Data handling was as before; trials were excluded if they resulted in incorrect keypresses (3.3% and 3.7% of trials for J.W. and V.P. respectively) or had an RT less than 100 ms or greater than 1000 ms (1.8% and 3.1% of trials for J.W. and V.P. respectively). Table 2.1 shows the mean RTs and error rates for J.W. and V.P. as a

function of the experimental conditions. Figure 3.2 displays the mean RT differences (delta reaction times) between the two orthogonal mapping conditions. The S-R mapping that produced the fastest reaction time shifted as a function of response location for both response hands.

Table 2.1. Mean (and SD) reaction time (ms) and error rates for BP and JW as a function of Response Hand, Response Location, and S-R Mapping.

Participant: J.W.

S-R Mapping	Top-Left / Bottom-Right			Top-Right / Bottom-Left		
Response Location	Left	Middle	Right	Left	Middle	Right
Left Hand	494.7	592.1	630.3	583.8	524.2	528.2
	(106.2)	(137.2)	(138.4)	(145.8)	(128.1)	(122.4)
Right Hand	525.6	523.1	520.1	592.1	515.0	468.6
	(115.0)	(124.2)	(118.7)	(140.1)	(112.8)	(101.6)
S-R Mapping	Top-Left / Bottom Right			Top-Right / Bottom Left		
Response Location	Left	Middle	Right	Left	Middle	Right
Left Hand	2.1	7.9	13.6	7.1	2.9	8.6
Right Hand	1.4	2.9	2.9	6.4	3.6	1.4

Participant: V.P.

S-R Mapping	Top-Left / Bottom-Right			Top-Right / Bottom-Left		
Response Location	Left	Middle	Right	Left	Middle	Right
Left Hand	490.8	497.8	601.9	602.2	493.9	487.9
	(166.9)	(132.6)	(161.7)	(190.0)	(134.5)	(138.1)
Right Hand	466.7	441.0	531.4	519.1	448.9	475.4
	(106.9)	(89.5)	(173.7)	(143.8)	(121.0)	(117.8)
S-R Mapping	Top-Left / Bottom Right			Top-Right / Bottom Left		
Response Location	Left	Middle	Right	Left	Middle	Right
Left Hand	11.4	4.3	12.9	8.6	8.6	8.6
Right Hand	4.3	4.3	10.0	1.4	2.9	4.3

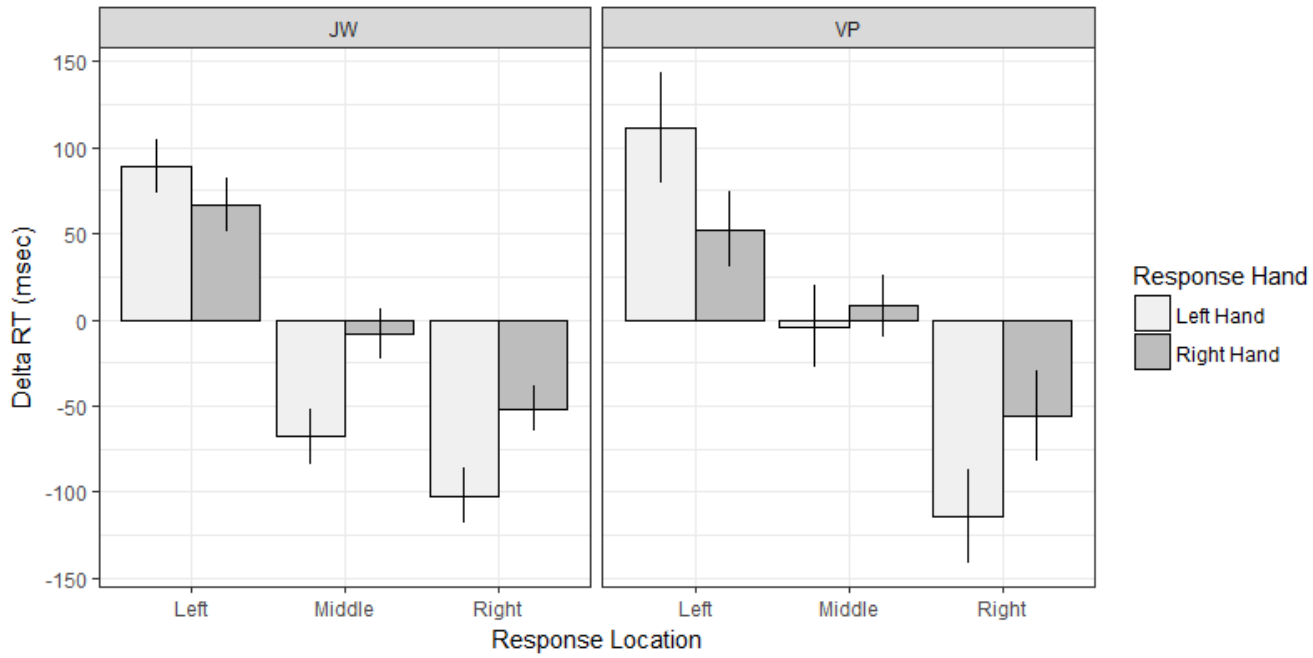

Figure 3.2. Influence of S-R mapping expressed as the reaction time difference (delta RT ± SE) between the Top-Stimulus Left-Response / Bottom-Stimulus Right-Response mapping (Top-Left/Bottom-Right), and the Top-Stimulus Right-Response / Bottom-Stimulus Left-Response mapping (Top-Right/Bottom-Left) as a function of response location and hand.

To confirm this pattern for participant and each response hand, a univariate ANOVA was performed on the cleaned reaction time data (Figure 3.2) with two factors: mapping (top-left/bottom-right versus top-right/bottom left) and response location (left, middle, right).

Patient J.W. For the left hand there was a main effect of mapping ($F(1, 781)=8.4$, $p=.004$, $\eta p2=.01$); responses were faster with the top-right/bottom-left mapping. There was no significant main effect of mapping for the right hand ($p>.05$). Each hand displayed a main effect of hand position on RT ($F(2, 781)=6.1$, $p=.002$, $\eta p2=.02$; $F(2, 814)=20.2$, $p<.001$, $\eta p2=.05$ for left and right hands respectively). In both cases, responses were made more quickly when the hand was located in ipsilateral space as compared to when the hand was located across the midline. Most importantly, both hands displayed a mapping by hand position interaction ($F(2,$

781)=40.2, p<.001, ηp2=.09; F(2, 814)=17.0, p<.001, ηp2=.04, left and right hands respectively). The top-left/bottom-right mapping resulted in faster responses when either responding hand was located in left space. Conversely, the top-right/bottom-left mapping resulted in faster performance when responses were made by either effector in the rightward response location. This is consistent with performance seen in typical individuals (Weeks et al., 1995).

Patient V.P. The RT data for V.P. told a similar story. A main effect of hand position was seen for both hands (F(2, 382)=4.4, p=.01, ηp2=.02; F(2, 401)=7.9, p<.001, ηp2=.04 for left and right hands respectively). Both hands showed their shortest RTs when located at the centre position. There was no main effect of mapping for either hand (both p>.05). Again, the most notable result was the hand position x mapping interaction seen for both hands (F(2, 382)=16.6, p<.001, ηp2=.08; F(2, 401)=6.0, p=.003, ηp2=.03 for left and right hands respectively). As was the case for J.W., the preferred mapping in each condition was dependent on effector location (left or right hemispace) rather than effector identity (left or right hand).

The error data for both participants and each hand was also analyzed using a univariate ANOVA with mapping and hand position as factors. Only J.W.'s left hand showed any significant results: a main effect of mapping (F(1, 840)=5.1, p=.02, ηp2=.01), a main effect of hand position (F(2, 840)=4.5, p=.01, ηp2=.01), and a hand position by mapping interaction (F(2, 840)=3.8, p=.02, ηp2=.01). As can be seen in Table 2.1, J.W. most frequently erred with his left hand located in right space, especially when using the less compatible and slower top-right/bottom-left mapping. Thus there was no evidence of a speed-accuracy tradeoff. There were no main effects or interactions concerning errors made with his right hand, nor were there any significant results involving either of V.P.'s hands (all p>.05).

3.1.3 Discussion

Experiment 2 examined the representation of "left" and "right" in the disconnected brain as the hand moves through space. With two split-brain patients we asked whether a hand placed across the midline, for example the left hand placed on the right, is represented based on its body-centred position (right effector), or without left/right position information. This was accomplished using an orthogonal S-R task in which stimuli above and below fixation were assigned to left and right responses (Proctor & Cho, 2006; Weeks et al., 1995).

The results clearly show that the mapping rule which yielded the shortest RTs depended on the location of the responding hand. When J.W. and V.P. carried out their responses in left space, the compatible top-stimulus left-response (bottom-right) mapping resulted in a RT advantage compared to the less compatible top-stimulus right response (bottom-left) mapping. When responses were carried out in right space, the reverse mapping yielded an advantage (top-right/bottom-left RT < top-left/bottom-right RT). This reversal of the mapping effect was independent of the hand used to respond, and was apparent for both patients.

These results are consistent with previous work on orthogonal S-R compatibility in normal intact subjects (Weeks et al., 1995). This suggests that both hemispheres are independently capable of representing "their" hand as either a leftward effector or a rightward effector, even without visual access to the hand. The spatial position of the hand, not its identity, determines the compatibility effect. Thus, hand and target could be coded in the same coordinate system by each hemisphere, even when the hand crossed the midline and was not visually accessible.

4.1 General Discussion

The present work investigated the representation of hand position in the left and right cortices in the absence of interhemispheric cortical connections. Results indicated that hand

position with respect to a target can be coded by each hemisphere, without cross-cortical input, across hand positions that span the midline. This suggests that when the hand crosses the midline, though it is no longer directly visible to the controlling hemisphere, its position and orientation can be accurately represented in the same coordinate system as a stimulus presented at midline.

Previous work has asked split-brain patients to respond to stimuli in both hemispaces with crossed and uncrossed hands, often with the aim of determining the time taken for information to transfer from one hemisphere to the other cross-cortically. These experiments typically consider cases in which perception of the stimulus and control of the responding hand may be located in different hemispheres (Aglioti et al., 1996; Mooshagian et al., 2009; Spence et al., 2001). This was not the focus of the present work. Here the focus was on how each hemisphere would cope with the situation in which "its" hand was located across the midline in the invisible hemispace. Tactile input from the hand is received normally in this situation (Spence et al., 2001). However, it was unknown whether features like hand orientation or hand position with respect to visible or invisible objects can be represented by each hemisphere when the hand crosses the midline. Unlike previous S-R compatibility work in this population, a unimanual task was used, allowing each hemisphere to be tested in isolation. This task therefore allows for the examination of intrahemispheric spatial coding of the hand while removing any potential contributions of a "neural pathway effect" due to the lack of information transfer between cerebral cortices.

Experiment 1 looked at whether the top and bottom of the hand continued to be represented by the controlling hemisphere across hand positions based on felt hand orientation. Specifically, split-brain patient J.W. was presented with stimuli in two locations (top/bottom) at

midline, and he was asked to provide responses (top, bottom) with a single hand that varied in location relative to the screen (left, midline, right). He was faster to respond when stimulus and response were compatible than when they were incompatible. Importantly, this was the case for both hands and regardless of hand position with respect to the midline. This suggests that both hemispheres are capable of representing vertical responses in hand-centered coordinates even when the hand crosses the midline and is not visually available. This set the stage for the critical second experiment, which asked about representations of left and right across the visuomotor space, a topic for which existing literature is contradictory.

Experiment 2 asked whether the hand could be coded as a leftward or rightward effector depending on its position when responding to centrally presented stimuli. Split-brain patients J.W. and V.P. were presented with stimuli in two locations (top/bottom) at midline. They provided unimanual responses that were orthogonal to the stimuli (i.e. left/right) with either hand and at locations on either side of midline. Both patients were faster to respond when the top stimulus was mapped onto the response option within the hand that matched hand location (Proctor & Cho, 2006). In other words, responses to the top stimulus were speeded for the left response option (and the bottom stimulus for the right response) when the hand was located in left space, and responses to the top stimulus were speeded for the right response option (and the bottom stimulus for the left response) when the hand was located in right space. This pattern of results supports the claim that each hemisphere flexibly codes "its" hand based on the hand's spatial location, even when the hand crosses the midline and is no longer visually accessible.

These findings can be considered in the context of previous work on other groups of patients with attentional impairments. Neglect patients typically have right hemisphere brain lesions, resulting in a failure to orient to events contralateral to their lesion, though this bias

seems to exist primarily in the visual domain (Chokron et al., 2002). On the other hand, unilateral deficits in position and movement senses have also been reported, associated with one-sided damage to the inferior parietal cortices (Karageorgiou, 2016). It has been demonstrated that patients with unilateral parietal injuries show impairments in contralesional attentional shifts (Cohen et al., 1995; Posner et al., 1987 but see Danziger, Kingstone, & Rafal, 1998), suggesting that in the intact brain each hemisphere might preferentially attend contralaterally, and that ipsilateral attention might be supported by inputs from the parietal counterpart in the other hemisphere. Alternatively, it has been suggested that a right hemisphere network supports the processes involved in spatial orienting to both sides of space (Karnath & Rorden, 2012). While patients with unilateral parietal damage lack contributions from the corresponding contralateral parietal lobe (or the damaged component of this lobe), they continue to receive inputs from the remainder of the contralateral hemisphere. Split-brain patients are unique in that all communication typically supported by the corpus callosum is interrupted. Therefore, what is unique about the present work is that each hemisphere can be tested in complete isolation. In the present work, then, it was uncertain whether each hemisphere would be able to represent the ipsilateral hemispace when the hand crossed the midline to this position. Overall, our findings converge on the conclusion that both hemispheres can represent the position and orientation of "their" hand, based on proprioceptive information alone, even when it is located in ipsilateral space in the absence of cross-cortical input. Specifically, the top and bottom of the hand are represented based on hand orientation and the hand overall is treated as a leftward or rightward effector based on its position with respect to the body midline. This is consistent with work in patients with optic ataxia (Blangero et al., 2007) indicating that the parietal lobe integrates proprioceptive information about the contralateral hand with near-hand visual information,

regardless of whether the hand is located in ipsilateral or contralateral space. However, data from these patients did not speak to the question of whether cross-cortical connections are necessary inputs for this parietal function. The present work indicates that cortical connections are not necessary. This provides novel evidence that, even in the disconnected brain, the full visuomotor space is represented in each hemisphere, a process that appears to be performed through subcortical rather than cortical connections.

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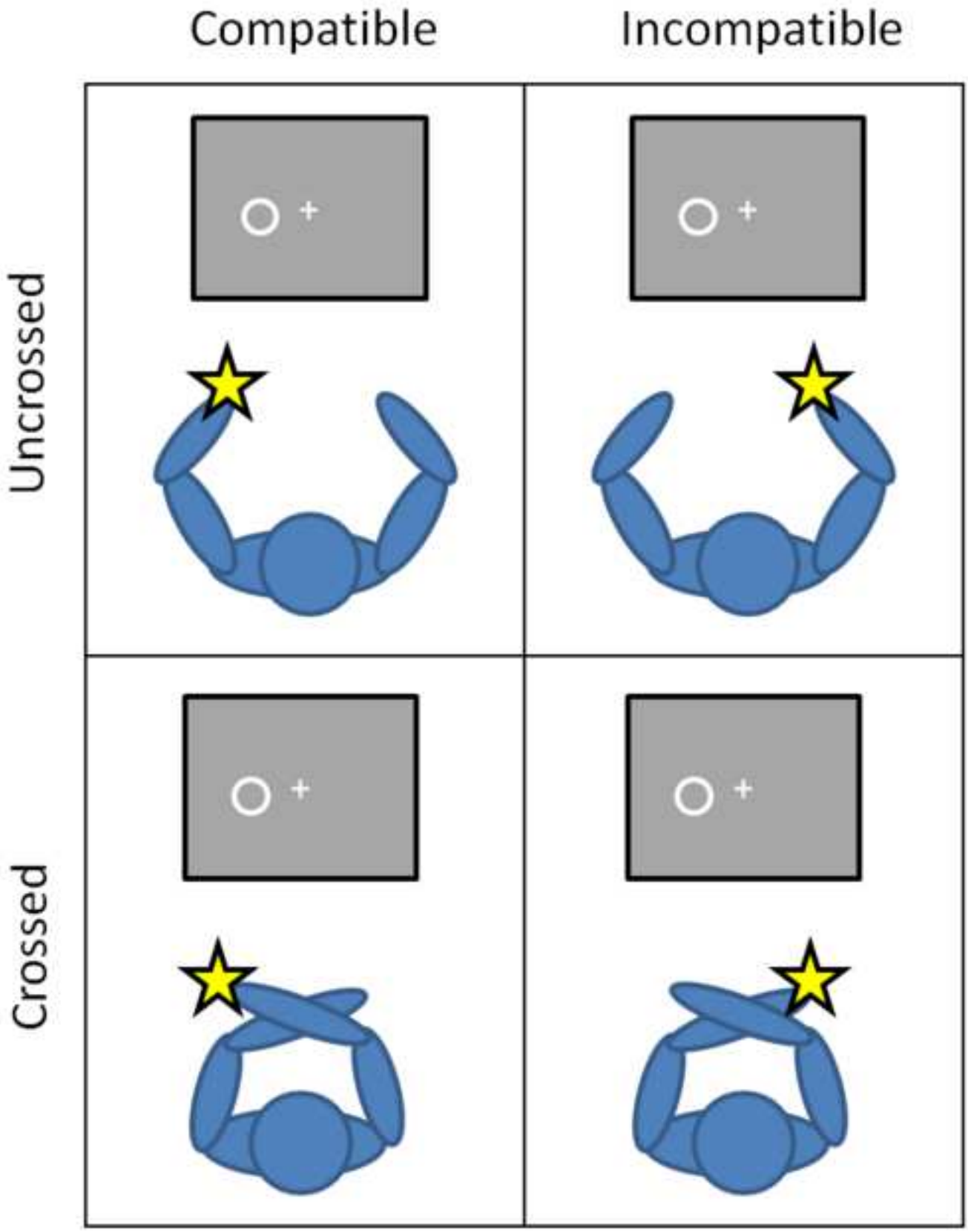

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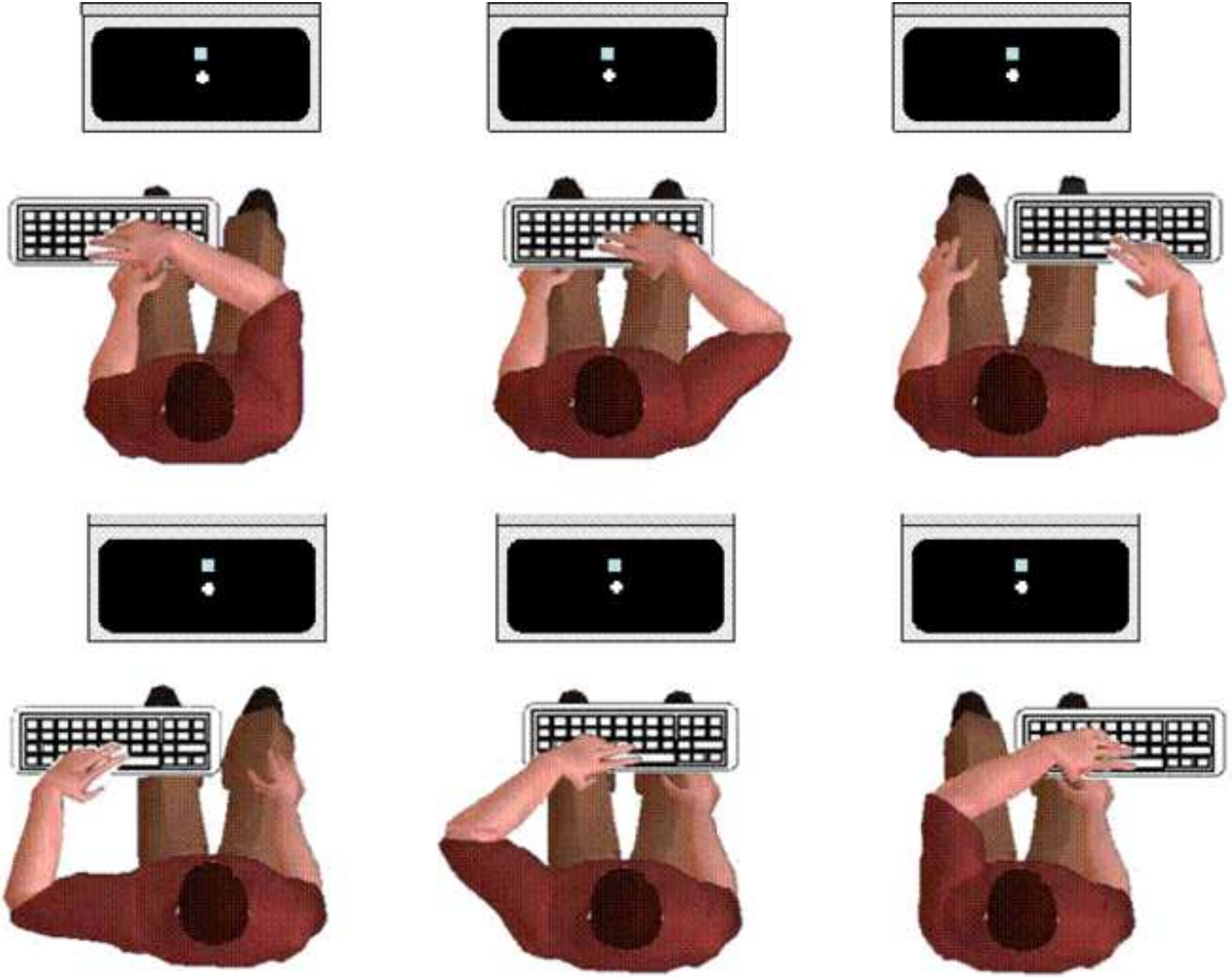

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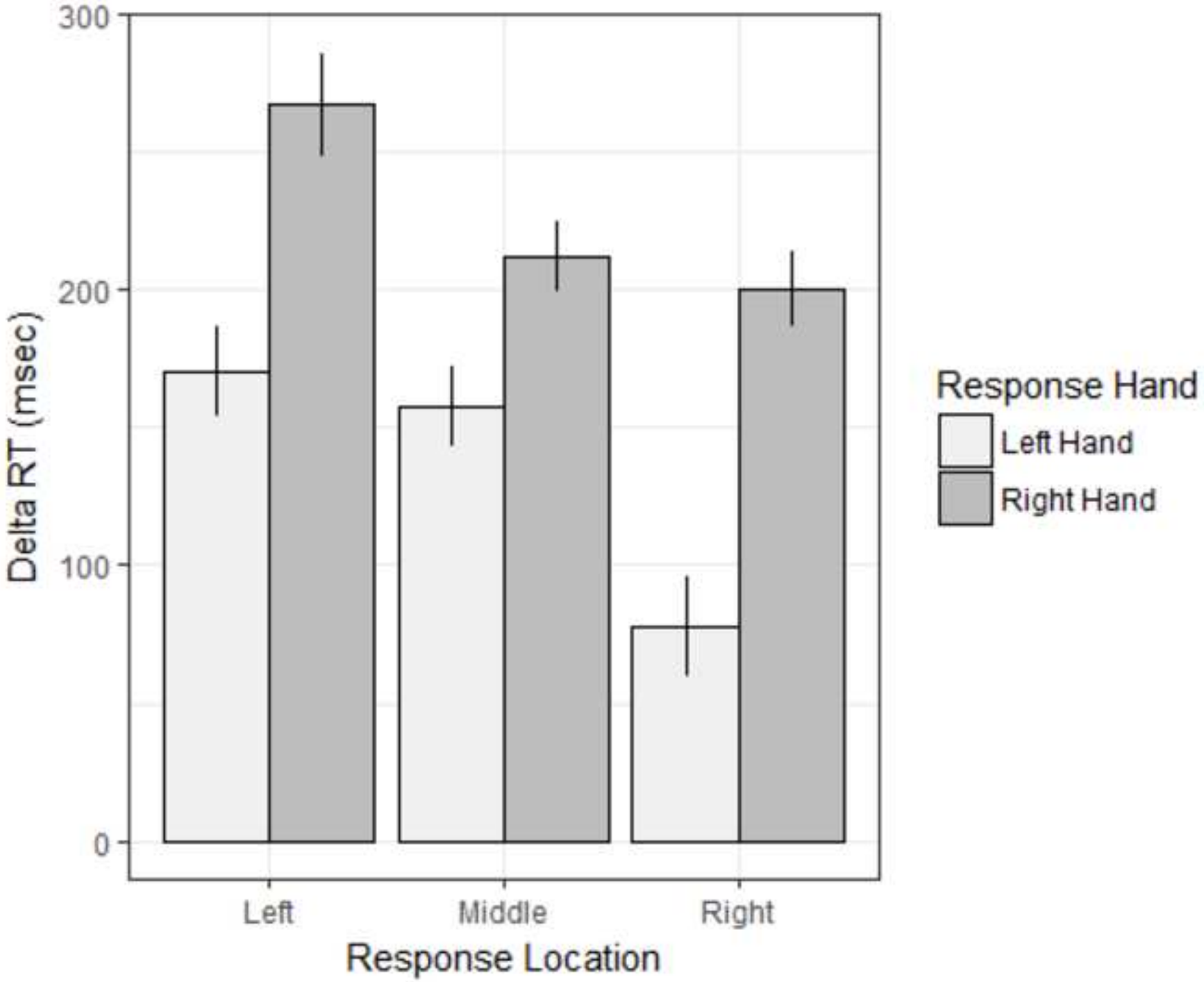

Figure 3.1

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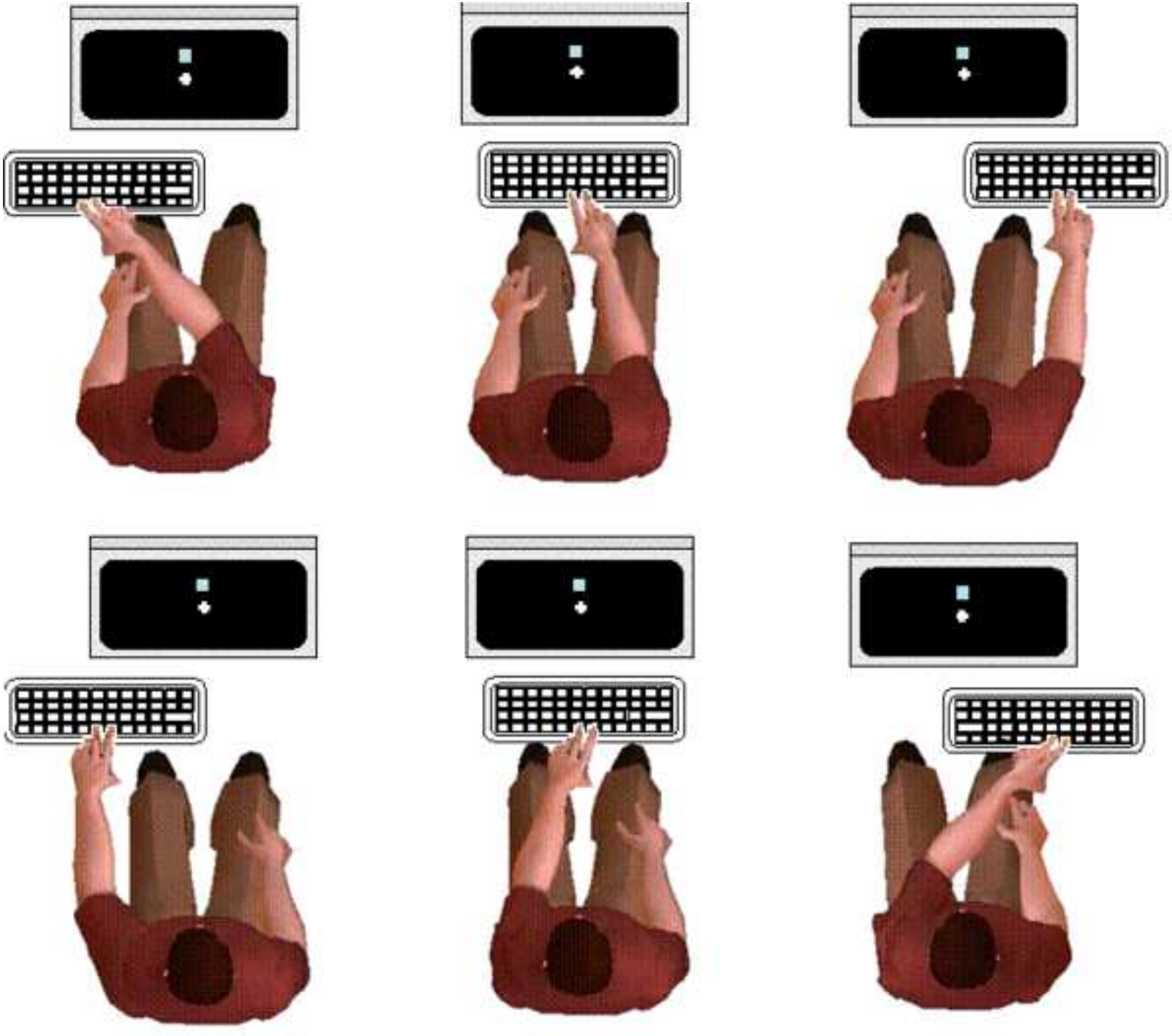

Figure 3.2

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