AMAZING PAPERS IN NEUROSCIENCE
One Brain. Two Minds? Many Questions.

Victoria Rosen
School of Psychology and Neuroscience, University of St. Andrews, St. Andrews, UK KY16 9JP.

For several decades, split-brain research has provided valuable insight into the fields of psychology and neuroscience. These studies have progressed our knowledge of hemispheric specialization, language processing, the role of the corpus callosum, cognition, and even human consciousness. Following a recent empirical paper by Pinto et al. (2017a) and review by Volz and Gazzaniga (2017), a debate has ensued about the nature of conscious perception of visual stimuli in split-brain patients. This exchange is an ideal platform for generating discussion about both the implications of recent findings and the interpretation of results from split-brain studies in general.

Key words: hemispheric specialization; split-brain; cross-cueing; corpus callosum; cognition; consciousness

From its beginnings fifty years ago, split-brain research has continually proved to be a vital field within the greater scope of psychology and neuroscience. Split-brain research refers to research and insights garnered from studying patients who have had their corpus callosum, a bundle of fibers connecting the two hemispheres of the brain, severed, in most cases to treat severe epilepsy. This unique condition, combined with a novel technique of presenting information to each hemisphere independently, led to a field that has been prominent for five decades, and still continues to produce new and exciting revelations in neuroscience. However, the field also continues to spark debate and controversy. This is best demonstrated by a recent exchange in journal *Brain*.

In a 2017 empirical paper, Pinto and colleagues offer evidence against a dominant view in split-brain research: that after severing the corpus callosum visual information cannot be transferred through other fibers (Pinto et al., 2017a). Going even further, they interpret results indicative of conscious reporting across hemispheres as suggesting the two hemispheres are not separately conscious following the surgery. In their recent review, Volz and Gazzaniga (2017), argue against these interpretations by Pinto et al. Together, these papers triggered a debate within the field leading to further responses in the form of letters to the editor from Pinto et al. (2017b), Volz et al. (2018), and Corballis et al. (2018). Here, I summarize each component of the current debate, and also argue why the exchange as a whole can serve as a valuable teaching tool.

I will start by summarizing sections of the review by Volz and Gazzaniga (2017) that give context to both this exchange and the field as a whole. A group of patients in Rochester, New York in 1939 were the first to undergo surgery designed to treat severe epilepsy by severing the corpus callosum, but these first patients were not actually the first group of split-brain patients that we think of today. That is because though they were studied extensively, these patients appeared not to be significantly different after the surgery compared to before (Akelaitis, 1941). This conclusion was accepted by many for two decades, until a novel experimental design was able to present information to each hemisphere in isolation, which for the first time gave experimenters the ability to observe the two hemispheres individually (Gazzaniga and Sperry, 1967; Volz & Gazzaniga, 2017). I am including this not just as an interesting anecdote, but also because it is a great example of how difficult it can be to design an experiment in split-brain research. In this line of research, it is of the utmost importance that each hemisphere receives information independently. Because of the nature of the condition and the way patients learn to adapt to their new circumstance after surgery, this is not trivial, and therefore relevant for the debate at hand.

Because of the straightforward nature of the visual system when compared with our knowledge of how the other senses are processed, it is commonly used to deliver stimuli in split-brain experiments (Volz and Gazzaniga, 2017). To explain briefly how this works, when an image is shown in right visual field, it is ‘seen’ and processed by the left hemisphere and vice versa. Meaning, if a split-brain patient were to see information only in one half of their visual space, it would be processed only by the contralateral hemisphere (Volz and Gazzaniga, 2017). Interestingly though, when an object is shown in the right visual field and the patient is asked what was seen they can and do answer correctly, but when shown an object in left visual field and asked the same question, the patient will often answer that nothing was seen (Volz and Gazzaniga, 2017). This is because the left hemisphere houses most language capabilities. So, when something is presented in the right visual field (to the left hemisphere) patients are able to respond verbally; however, when an image is presented in the left visual field, though the patient may not be able to respond verbally, they are able to non-verbally. For example, participants can use their left hands (controlled by the right hemisphere) to point out what was seen from a group of objects (Volz and Gazzaniga, 2017).

In their 2017 empirical paper, Pinto et al. (2017a) nicely summarize this phenomenon postulating that the left hemisphere can only perceive the right side of visual space with expression through verbal language and the right hand, while the right hemisphere can only perceive the left side of visual space with expression through the left hand. However, following this summary, Pinto et al. (2017a) also mention that though this is widely taught and believed, there are no quantitative data supporting the idea, only clinical observations.

Now I will outline the empirical findings by Pinto et al. (2017a) that have sparked the current controversy. The researchers studied two split-brain patients, and though some of their results replicate past findings, others appear to challenge the status quo in the field. While two patients may seem like a small number, Pinto et al. justify this by explaining that there are very few split-brain patients remaining today. It is also worth noting that both patients were tested at least a decade after surgery. In their first experiment, Pinto and colleagues (2017a) examined if the patients could detect a stimulus and indicate its location when presented in only one visual half field. They asked patients to respond with their left hands, right hands, and verbally. Researchers observed near perfect accuracy for detection of the stimulus, regardless of response type (left hand, right hand, verbal), and well above chance accuracy for indicating location (Pinto et al., 2017a). Even more interesting, however, is that there was no observed interaction between response type and stimulus location (left visual field, right visual field).

This led to further testing to determine if the results above could be due to transfer of visual information across the two hemispheres. In follow-up experiments only one of the patients was asked to compare stimuli across and within visual half fields, as well as name and match pictures within visual half fields. The patient could not compare stimuli across half fields but was able to within half fields. Additionally, the same patient showed better performance when labeling objects presented to the right visual field, and matching objects presented to the left (Pinto et al., 2017a). These findings, consistent with previous research, suggest that visual processing is indeed independent for each hemisphere in split-brain patients. However, the authors note there was still no interaction between response type and visual field. This leaves the question of how patients were able to correctly report what was processed regardless of which side did the processing. To test if this phenomenon was due to conscious or unconscious processes, the experimenters asked the patient to complete similar testing, but this time with confidence ratings. Based on confidence ratings being higher for correct responses, the researchers concluded that the patient was indeed consciously aware of his reporting. Again, there was no interaction between response type and stimulus location (Pinto et al., 2017a).

The authors entertain several interpretations of their data, but ultimately, they take the stance that that visual perception remains divided in split-brain patients, but that in reporting what was perceived, consciousness is undivided. They refer to this as "'split phenomenality' combined with 'unity of consciousness'" (Pinto et al., 2017a). This interpretation lies in direct contrast with both previous theories of processing in split-brain patients and dominant theories of consciousness.

Pinto and colleagues (2017a) go into a lengthy explanation as to why cross-cueing should be ruled out. First, they define cross-cueing as "one hemisphere informing the other hemisphere with behavioral ticks, such as touching the left hand with the right hand" and that it can only transfer "one bit of information" (Pinto et al., 2017a). Using this definition, they claim cross-cueing is not likely responsible for their results. They reason that: 1) cross-cueing could not transfer the amount of information needed for correct responses, 2) there were significant differences in performance on visual tasks between hemifields (this refers to the experiment in which the patient was better at matching objects shown in the left visual field but better at labeling objects shown in the right visual field), 3) the experiment was set up to prevent hands from touching each other, 4) in an experiment of reaction times with a colored circle appearing in either the left or right visual field there were no significant time differences between ipsilateral and contralateral responses, which would be expected if cross-cueing were to take place as it should slow down ipsilateral responses. After this lengthy discussion on cross-cueing, the authors conclude with one final possibility that because testing began several years after the operation and both patients were operated on as young adults, it could be that over time patients develop new structural connections to transfer information across hemispheres (Pinto et al., 2017a).

Switching back to the review by Volz and Gazzaniga (2017), after summarizing basics in the field, the authors take the time to discuss recent findings focusing primarily on the empirical paper by Pinto et al. (2017a). Volz and Gazzaniga (2017) describe cross-cueing as one hemisphere using knowledge gained by perceiving behavioral cues from the other to overcome a challenge or complete a task that would require information to be shared between hemispheres. The authors also note that this is not done actively or consciously and the cues can often be exceptionally subtle. This emphasis on subtle cues marks a difference in definition of cross-cueing between the two sets of authors, which is noted in the review. Volz and Gazzaniga (2017) critique Pinto et al.'s (2017a) willingness to write-off cross-cueing far too quickly. Although Pinto et al. (2017a) used eye tracking technology to ensure the patient was fixating (maintaining visual gaze on a specific location) during stimulus presentation, fixation was not monitored while the patient was responding. According to Volz and Gazzaniga (2017) this meant that cross-cueing could occur in the form of an eye movement when asked to indicate the location of the stimulus.

Pinto and colleagues (2017b) subsequently responded to Volz and Gazzaniga's review in a letter to the editor of *Brain*. In this letter they once again assert why they believe cross-cueing is an unlikely explanation, responding more specifically to points brought up in the review. They contend that even cross-cueing cannot explain the lack of an interaction between response type and location. Though they do give way that an alternative explanation broached by Volz and Gazzaniga (2017) (transfer through subcortical routes) could be more likely, they assert that there is a larger problem in the whole interpretation framework, namely that the term cross-cueing is not clearly defined (Pinto et al. 2017b). In a subsequent reply to Pinto et al. (2017b), Volz and colleagues (2018) concede that the lack of a formal definition of cross-cueing is a significant issue, but still reassert their stance. They emphasize that due to the passing of time between the patients' surgery and testing, they could have learned much more subtle and efficient ways to transfer information through behavioral cues. In a final response in the form of a letter to the editor, a third party weighs in. Corballis and colleagues (2018) cite the ongoing debate and argue that it is a mistake to focus so heavily on cross-cueing. Instead the authors assert that both groups should return to the idea of subcortical routes. The authors provide anatomical evidence citing a 'second visual system' pathway involving midbrain structures. This pathway is believed to go through the superior colliculi, the pulvinar nuclei, and subsequently to the parietal lobes with a subcortical interhemispheric connection at the collicular commissure (Trevarthen and Sperry, 1973; Corballis et al., 2018). In addition to the anatomical evidence, Corballis et al (2018) summarize results from previous behavioral experiments involving split-brain patients that support this possibility. Overall the authors make a strong case for subcortical connections as a possible explanation for Pinto and colleagues' (2017a) observations.

VALUE

The above exchange serves as an example of a lively and provocative conversation in neuroscience emerging from competing interpretations of published data. The value of this exchange as a teaching tool comes not from which interpretation (if any) the reader chooses to accept, but rather from understanding why these different interpretations exist, and how each group of authors was able to use scientific evidence to support their ideas. In a classroom setting, research is often presented as producing facts, but it is important to remember that different scientists can draw different conclusions from the same data. This means that our interpretations of scientific work are just as much a part of science as the actual evidence. Though this may seem obvious to researchers, it is something that is often overlooked by students.

The current debate in split-brain research brings the audience's attention to critical components of scientific research in general, including experimental design and interpretation, as well as communication within the field. Though the separate sets of authors may disagree, they communicate effectively and publicly, and in doing so demonstrate that there can be wide variation in interpretation of scientific evidence which can largely affect the implications of a study as well as guide future research.

In addition to being a great teaching tool for the aspects mentioned above, this exchange is also useful in that it can introduce students to a variety of publication types. The inclusion of an empirical paper, a review, and responses in the form of letters to the editor, teaches students that scientific research is not done in isolation, and shows how and when to use different forms of publication.

AUDIENCE

I believe there is a place for this set of papers in almost any introductory psychology or neuroscience class, as well as cognitive neuroscience classes. Additionally, this exchange could be especially useful in upper level psychology and neuroscience classes with a focus on evaluating scientific literature, interpretation, or experimental design. The authors' emphasis on critical thinking and interpretation creates a springboard for classroom discussion and ideas for future directions in the field.

If I were to teach this exchange in a classroom, I would have students read these manuscripts in the order I have presented them here: starting with the review by Volz and Gazzaniga which contains relevant background of the field, followed by the empirical by paper by Pinto et al. (2017a). I would then ask the students to discuss if they believe the criticism in the review was fair and why (or why not). Afterwards, I would follow up the discussion with the three letters to the editor and ask the students to decide which interpretation they side with and why, or to come up with their own interpretation supported by empirical evidence.

Regardless of how this set of papers is taught, it has the potential to stimulate thought and discussion. It will be exciting to see how this debate continues to develop over time.

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Address correspondence to: Victoria Rosen, School of Psychology and Neuroscience, St Mary's Quad, South Street, St Andrews, Fife, KY16 9JP. Email: vr38@st-andrews.ac.uk