No Disconnection Syndrome after Near-Complete Callosotomy

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Abstract

Much of the sensory-motor processing in the human brain is lateralized to either hemisphere, with the corpus callosum integrating these distinct processes into a seemingly unified conscious experience. The corpus callosum is thought to be topographically organized, with different subregions along its anterior-to-posterior axis involved in integrating information across different sensory modalities and cognitive domains. In complete callosotomy patients, where the corpus callosum is fully severed, this integration is typically disrupted across these domains. But which types of inter-hemispheric integration can still be preserved with small posterior callosal remnants? We studied four callosotomy patients—three complete and one partial with approximately 1 cm of preserved splenium—using an array of lateralized visual, tactile, visuospatial, and language tasks. While complete callosotomy patients showed the expected behavioral disconnection effects—performing poorly on tasks requiring inter-hemispheric integration but well on intra-hemispheric ones—the partial callosotomy patient with a preserved portion of the splenium showed no disconnection effects across all tasks. The splenium is traditionally implicated in visual transfer, yet our findings show that minimal splenial preservation maintains functional integration across multiple perceptual and cognitive domains. This is at odds with the presumed topographical organization of the corpus callosum, suggesting a broader inter-hemispheric integrative capacity of the posterior callosal fibers. Structure-function relationships in brain networks are known to be complex and nonlinear—these findings provide novel insights into flexible structural mechanisms for inter-hemispheric communication enabling a variety of integrated behaviors.

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Introduction

When we first began testing a new cohort of callosotomy patients, one patient, BT, stood out with unexpected behavioral outcomes during our initial bedside tasks. On tasks that typically reveal inter-hemispheric disconnections, he showed no signs of impairment, performing comparably to a neurotypical individual with an intact corpus callosum. A closer look at his structural MRI scan and the neurosurgeon's report revealed the source of this surprising observation—a small portion of BT's posterior corpus callosum (part of the splenium) remained intact to prevent surgical complications. This seemingly minor detail would go on to challenge our assumptions about the corpus callosum's functional organization and its mechanistic role in integrating information across the hemispheres.

The corpus callosum (CC) is the largest white matter tract connecting the left and right cerebral hemispheres.[1] Although the functional specificity of the CC remains unclear, callosotomy patients—in whom the CC is surgically severed—provide unequivocal evidence of its importance for unifying (integrating) sensorimotor events across the hemispheres. In lateralized tasks that isolate sensory input and motor output to a single hemisphere, these patients show a profound disruption in inter-hemispheric information flow, known as the *disconnection syndrome*. For example, when a patient with speech areas in the left hemisphere is shown the word "hot" in the left visual field (LVF, processed by the right hemisphere) and the word "dog" in the right visual field (RVF, processed by the left hemisphere), they verbally only report having seen "dog". However, if asked to draw what they saw with their left hand (controlled by the right hemisphere), they draw a fire. Crucially, the emergent, integrated concept of a *hotdog* never emerges, even though each hemisphere accurately processes its respective input.[2,3] This lack of integration and awareness of sensorimotor events in the opposite hemisphere may demonstrate the *disruption* in a unified conscious state when the CC is fully severed.

The CC is thought to be topographically organized, where anterior callosal fibers project to anterior cortical regions like the prefrontal cortex, and posterior fibers project to posterior regions like the occipital lobe.[4] As a result, the CC is argued to have a modality-specific organization with different subsections—from anterior to posterior: rostrum, genu, body, isthmus, and splenium—are hypothesized to facilitate the integration of information across hemispheres in distinct cognitive domains and sensorimotor modalities.[5,6] In some callosotomy cases, the CC can be partially severed rather than fully. Cases of partial

callosotomy may provide causal insights into the functional specificity of CC subregions by examining which types of information can still be integrated and which cannot, based on the location and extent of the resection.[7]

According to the modality-specific framework of the CC, the splenium is typically implicated in visual integration, while the posterior midbody is thought to be involved in tactile integration.[8-11] Partial callosotomy cases sparing these subregions support this prediction. Intact splenium fibers have been reported to readily integrate visual information, while the integration of tactile input has been attributed to the posterior body of the CC.[5,12-14] However, in most partial callosotomy patients, both the splenium and posterior midbody remain intact, rendering a precise functional distinction impossible. The question thus arises: which kinds of information can the splenium *alone* integrate across hemispheres?

Cases in which *only* the splenium is left intact are incredibly scarce. Callosotomies are typically performed in a single stage, where the entire corpus callosum is sectioned, or in two stages, where about one- or two-thirds of the anterior corpus callosum are sectioned first, leaving more than just the splenium intact.[15] Thus, only a few such cases exist in the literature, and their findings are mixed: some show integrated behavior across multiple modalities, suggesting that a small portion of the posterior CC fibers may support broader inter-hemispheric integration beyond visual information.[16] Others reported tactile but not visual disconnection, in line with a linear, topographic model of the CC, where the splenium alone is insufficient to integrate information beyond the visual domain.[17] Importantly, however, in the former case,[16] because no MRI data was available, it remains unclear whether only the splenium was spared or if additional CC structures, such as the posterior midbody, were also preserved. In latter cases,[17] patients were tested shortly after surgery (within less than 6 months), leaving it unclear whether any reorganization occurred over time. Therefore, more evidence is needed to establish the role of a small portion of the posterior CC fibers in inter-hemispheric integration.

Callosotomy research has addressed many specific questions across different cognitive domains, employing diverse methods, procedures, and stimuli with different patients. While these studies have been invaluable, we still lack standardized assessment and a quantitative metric for evaluating the disconnection syndrome, rendering systematic case comparisons challenging. To address this limitation, we introduce a multi-domain approach that quantifies the disconnection syndrome through bedside assessments. This practical methodology requires

minimal equipment and can be quickly administered to establish a comprehensive disconnection profile for each patient (see the *Disconnection Score* in the **Materials and methods** and **Fig. 3** for details).

Here, we report findings from four callosotomy patients: three complete callosotomy cases with total CC resection and one partial case retaining a small portion of posterior CC (splenium). We used an array of lateralized bedside tasks that sample performance across the anteroposterior axis of the CC to identify disconnection syndromes in visual, tactile, and higher-order cognitive functions (e.g., language and visual-spatial processing) to determine where performance breakdowns occur in complete versus partial callosotomy cases (see **Fig. 1**). Based on the framework of the CC's topographic and modality-specific organization, we predicted that complete callosotomy would result in full disconnection syndrome. The partial callosotomy patient with only ~1 cm of splenium intact, on the other hand, would show disconnection in all tasks *except* the visual modality, reflecting restricted inter-hemispheric integration along splenial fibers connecting the visual cortex. As predicted, all complete callosotomy patients exhibited signs of disconnection syndrome. However, contrary to our expectations, the partial callosotomy patient, retaining only a small portion of the splenium, showed no behavioral disconnection effects in any tested domain. We tested this patient six years after surgery, and it suggests two possible interpretations: either the splenium inherently possesses greater capacity for inter-hemispheric integration than previously recognized, or the brain underwent widespread network reorganization over time with the splenium serving as the critical anatomical substrate.[18] While the lack of longitudinal data prevents us from empirically distinguishing between whether this integration was preserved all along or recovered over time, the latter explanation is more plausible based on literature showing that other patients with preserved splenium fibers exhibited selective behavioral disconnections shortly after surgery.[17] In either case, our findings highlight the splenium's unexpected role in supporting inter-hemispheric integration across a range of lateralized tasks, extending beyond the visual domain.

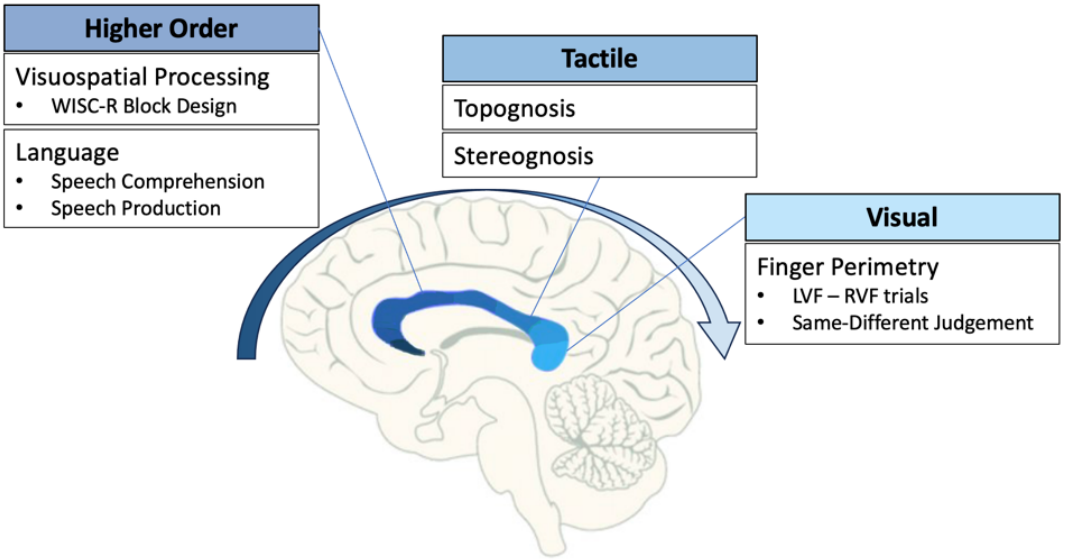


Figure 1 Overview of Bedside Tests and Hypothesized Corpus Callosum (CC) Topography. Assumed relationships between the functional topography of the CC and the cognitive domains and sensory modalities assessed in our bedside tests are shown in accordance with the classical modality-specific framework of CC organization. The splenium, the most posterior section of the CC, is thought to facilitate visual information integration, while the posterior callosal body is usually implicated in inter-hemispheric transfer of tactile information. To assess the modality-specific aspects of interhemispheric integration, we employed simple bedside tests: Finger perimetry for visual integration; topognosis and stereognosis for tactile processing. Additionally, higher-order cognitive functions thought to reflect hemispheric dominance (visuospatial processing and language) were investigated to assess how the performance of the non-dominant hemisphere is affected when it is fully or partially disconnected from the dominant hemisphere. In Finger Perimetry, LVF refers to 'left visual field' trials, and RVF refers to 'right visual field' trials. For further details of the tasks, please see **Materials and methods** section.

Materials and methods

Participants

We tested four patients (BT, NR, TJ, LJ) who underwent callosotomy to alleviate epileptic seizures. Three patients (NR, TJ, LJ) had complete callosotomy, which fully sectioned the corpus callosum. In BT only posterior fibers were left intact due to technical surgical reasons. All patients were tested post-operatively (see **Table 1** for case histories and **Fig. 2** for the anatomical scans). The surgeries effectively reduced drop seizures in most patients. TJ and NR

were entirely drop seizure-free post-surgery (100% reduction), BT experienced a near-complete reduction (98%), and LJ showed moderate improvement with a 20% decrease in drop seizures. No sedation was administered during behavioral testing or MRI scanning procedures. All reported patients here are right-handers,[19] and have language areas in the left hemisphere, confirmed by pre-operative bilateral Wada tests.[20] For ease of comprehension, we will refer to BT as BT* to denote his status as a partial callosotomy patient in contrast to the full callosotomy status of the other patients. Finally, the anterior, posterior and hippocampal commissures remained intact in all patients. The study was approved by the Ethics committee of the University of Münster (2021-523-f-S) and participants provided informed consent before inclusion.

Table 1 Clinical Profiles of Callosotomy Patients

Patient	Age at surgery	Age at testing	Sex	Handedness	Intelligence	Extent of Callosotomy
BT*	22	28	M	Right	Low average	Partial
TJ	49	52	F	Right	Average	Complete
LJ	57	60	M	Right	Low average	Complete
NR	18	18	M	Right	Moderately impaired	Complete

Table 1. Patients Overview. NR underwent testing 6 months after surgery. Patient Intelligence classifications are based on the Stanford–Binet Fifth Edition (SB5) classification.[21,22]

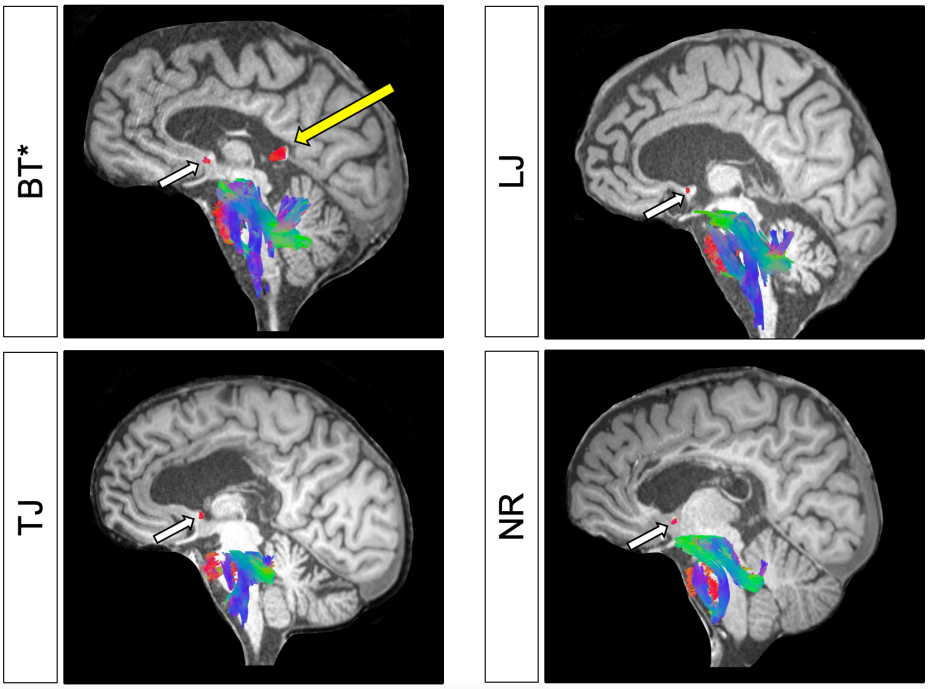


Figure 2 Anatomical Scans of the Patients. Midsagittal T1-weighted MRI images with overlaid DTI-based fiber tractography are shown for each patient. For visualization, only select commissural fibers—the anterior commissure and corpus callosum –as well as some cerebellar and brainstem fibers, are displayed. The fiber orientations are color-coded: red for left-right, green for anterior-posterior, and blue for superior-inferior directions. All patients exhibit an intact anterior commissure (white arrow), but only patient BT* retains a preserved splenium (yellow arrow), in contrast to the complete sectioning of the corpus callosum in the remaining three patients.

Bedside testing of the Disconnection Syndrome

We conducted a total of five bedside tests to sample performance along the anteroposterior axis of the corpus callosum (see **Fig. 1**). The tasks included visual, tactile, language, and visuospatial tasks, described in detail below. Critically, the tasks comprised an *'intra-hemispheric'* condition, where the input and output hemispheres were the same, and an '*inter-hemispheric'* condition, where the input and output hemispheres differed. We operationalized the presence of a disconnection syndrome as *(i)* above chance performance in *intra-hemispheric* conditions with concurrent *(ii)* chance-level performance in *inter-hemispheric* conditions for a given task. This contrast establishes that the patient can understand and perform a given task when it is confined to a single hemisphere (*intra-hemispheric* trials) and only fails to do so if it requires inter-hemispheric integration (*inter-hemispheric* trials).

1. Visual Tasks

Finger Perimetry

The experimenter showed varying numbers of fingers in the patient's peripheral vision (in the left or right visual field) while the patient fixated on the experimenter's nose. Then the patient verbally reported the number of fingers while keeping their gaze fixated at the experimenter (i.e., center of the visual field). Moreover, a same/different version of the task was conducted: The experimenter showed fingers on both sides simultaneously while the patient maintained central fixation and reported whether the numbers were the same or different.

Inter- and intra-hemispheric trials: Since all patients have speech areas in the left hemisphere and this task required verbal responses, RVF trials (processed by the left hemisphere) were *intra-hemispheric* trials, and LVF trials were *inter-hemispheric* trials. In the same/different task, all trials were *inter-hemispheric* in nature.

Chance-level performance was 20%, as patients could guess any number from one to five in each trial. In the same/different version of the task, chance level was 50% when guessing "same" or "different".

Due to LJ's difficulties with maintaining fixation and/or motivation to perform the task, finger perimetry was successfully conducted for BT*, TJ, and NR only.

2. Tactile Tasks

Topognosis—intra- and inter-manual touch localization

The experimenter lightly touched specific points on the fingers of the blindfolded patient's right or left hand. In the intra-manual (i.e., *intra-hemispheric*) condition, the patient used their thumb of the same hand to indicate the stimulated spot; in the inter-manual (i.e., *inter-hemispheric*) condition, the patient used their thumb of the opposite hand to show the corresponding spot on the opposite hand. For example, if the tip of the right index finger was touched, the patient pointed to the tip of the left index finger with their left thumb. Alternatively, in some cases, the patient rested their hands on the table. After the experimenter lightly touched distal segments of the fingers, they indicated its location by raising the corresponding finger. Both versions measure the same underlying ability—tactile localization in intra- and inter-manual conditions. Moreover, the tasks were always compared within subjects—contrasting intra-manual and inter-manual conditions for the same patient—and the task procedure remained

consistent across both intra- and inter-manual conditions within each subject. Thus, the findings remained comparable across conditions, and the chance levels were adjusted according to the specific procedure used for each patient.

Inter- and intra-hemispheric trials: *Intra-hemispheric* trials were the summed intra-manual trials from the left and right hands separately; *inter-hemispheric* trials were inter-manual trials summed across both directions (left-hand stimulated, right-hand responds, and vice-versa).

Chance-level performance: For patients NR and TJ, who completed the task using their thumb (indicating tactile stimulation across four fingers), the chance level was 25%. For patients BT and LJ, who completed the task by raising one of their five fingers to indicate the location, chance level was 20%.

Stereognosis—naming objects held in hand

Blindfolded patients were given common objects (e.g., scissor, spoon, fork, ball) to identify using tactile exploration with one hand at a time, alternating between the left and right hand on separate trials. Then, they were asked to name the presented objects. A towel was used to prevent any auditory cues.

Inter- and intra-hemispheric trials: Since all patients have speech areas in the left hemisphere and this task required verbal responses, right hand trials (processed by the left hemisphere) were *intra-hemispheric*, and left-hand trials were the *inter-hemispheric*.

Chance-level performance was 20% as there were five trials (five objects) per hand.

3. Hemispheric Lateralization of Visuo-Spatial Processing

WISC-R Block Design

The patient was given colored cubes with surfaces that were solid red, solid white, or half red and half white bisected across the diagonal and were shown pictures of patterns. Patients were then asked to replicate these patterns using the cubes.[23] A total of 16 trials were conducted, with eight trials using the right hand and eight using the left hand. The first two trials involved creating simpler patterns using two cubes, while the remaining six trials involved arranging four cubes into 2x2 square patterns.

Inter- and intra-hemispheric trials: Previous studies using this task suggest a left hand (right hemisphere) dominance over the right-hand trials, potentially because of

the manipulo-spatial superiority of the right hemisphere.[24] Thus, left hand (right hemisphere) trials were considered *intra-* and the right hand (left hemisphere) trials were considered *inter-hemispheric* trials.

Chance-level performance was not clearly defined for this task. Thus, the left hand (intra-hemispheric) and the right hand (inter-hemispheric) trials were contrasted to assess the disconnection syndrome.

4. Hemispheric Lateralization of Language

Language is a classic example of a lateralized cognitive function.[25,26] In most people, the language network is mainly located in the left hemisphere, and the language-related regions in the right hemisphere are smaller and less engaged in language comprehension and production.[27,28] Thus, for all language tasks, *intra-hemispheric* corresponded to right hand response trials (controlled by the left hemisphere) trials and *inter-hemispheric* corresponded to left hand response trials (controlled by the right hemisphere).

Language Comprehension in the form of Speech: Hand Gestures Task

The patient performed hand gestures with either the left or right hand, following verbal instructions, with their eyes closed. The gestures included thumbs up, thumbs down, an okay sign, a fist, and two or four fingers up.

Chance-level performance was not clearly defined for this task. Right-hand trials (*intra-hemispheric*) and the left-hand trials (*inter-hemispheric*) were contrasted to assess the disconnection syndrome.

Control—mimicking task. We included a control task to rule out the possibility of general motor impairments, motivational issues, or a broader inability of the right hemisphere to perform a given task using the left hand—independent of its language processing capabilities. In this task, patients, with their eyes open, were asked to mimic hand gestures demonstrated by the experimenter using their left hand. The ability to successfully mimic the gestures in this control condition but not when following verbal instructions suggested that the deficit was not due to motor impairments, lack of motivation, or general performance difficulties, but rather a difficulty to understand the verbal command. Therefore, performance on this control task was more relevant for the cases where one or both hands failed to perform the main task (i.e., executing hand gestures following verbal commands). In such cases, good performance in this control

task could serve to rule out general motor deficits or motivational issues as potential explanations for poor performance in the main task.

Language Production in the form of Speech

Tasks that require a verbal response to lateralized stimuli (e.g., finger perimetry, and stereognosis) were used to assess speech production from left hemisphere and right hemisphere. While we previously noted that all patients were left hemisphere dominant for speech production, as determined by the Wada protocol prior to surgery, there are reports in the literature suggesting that sometimes the non-dominant right hemisphere can develop the capacity to generate speech years after surgery.[29] Thus, assessing and reporting speech production from both hemispheres is important during periodic post-operative assessments.

Statistical Analyses

We conducted binomial tests to determine whether the patient's performance differed from chance-level performance for *inter*- and *intra-hemispheric* trials. The disconnection syndrome was operationalized as (*i*) above-chance performance on *intra-hemispheric* trials and (*ii*) chance-level performance on *inter-hemispheric* trials for the same task. Significance ($P < 0.05$) indicated that the observed performance was statistically different from chance-level; non-significance ($P \geq 0.05$) indicated that the observed performance did not differ from chance. To account for the fact that all tests were conducted in a clinical setting with a limited number of trials, we also performed Monte Carlo simulations with 10,000 iterations to ensure the robustness of our findings. We generated new data under the null hypothesis (chance-level performance) via simulations to estimate the distribution of outcomes and determine the significance of the observed empirical results. For all tasks, the Monte Carlo simulations produced results consistent with the binomial tests.

For tasks where chance performance was not well-defined (WISC-R Block Design and hand gestures), we used permutation tests to compare performance between the right and left hands. To assess this, we used the absolute difference between the hands' proportion correct scores as our test statistic. The permutation test was implemented with 10,000 iterations. For each iteration, we first created binary arrays representing correct (1) and incorrect (0) trials for each hand. We then pooled all these trials from both hands and randomly reassigned them to either hand while maintaining the original number of trials per hand. For each such permutation, we

calculated the absolute difference in proportion correct between hands. The *P*-value was computed as the proportion of permuted differences that were equal to or greater than the observed difference. This approach allowed us to estimate how likely it would be to observe a difference as large as the one we found if there were no differences between the hands (statistical significance was set at $P < 0.05$).

Lastly, despite the limited trial numbers and small sample size, our statistical inferences were based on within-subject comparisons of *intra-* versus *inter-hemispheric* trials within each task. This approach allowed each patient to serve as their own control. In other words, we used each patient's intra-hemispheric trials as a baseline to compare their inter-hemispheric performance and characterize the disconnection syndrome.

Disconnection Score

To summarize disconnection syndrome across different domains for each patient, a difference score was calculated between intra- and inter-hemispheric conditions, providing a measure of the degree of disconnection (see **Fig. 2**). This *Disconnection Score* was calculated as the proportion-correct in the *intra-hemispheric* condition (ranging from 0 to 1) minus the proportion-correct in the *inter-hemispheric* condition. We computed the proportion-correct scores from the number of correct trials out of the total trials for each condition (**Table 2**). For example, if a patient has a proportion correct of 0.9 in the *intra-hemispheric* condition and 0.1 in the *inter-hemispheric* condition, their disconnection score for that task would be 0.8 (calculated as 0.9 - 0.1).

A Disconnection Score of 0 or closer to 0 indicated no disconnection (i.e., equal performance in intra- and inter-hemispheric conditions); and a Disconnection Score of 1 or closer to 1 indicated full disconnection. Below is a detailed explanation of the methods used to create the Disconnection Score for each cognitive domain and sensory modality.

Visual. The proportion of correct trials in intra-hemispheric (right visual field) trials minus inter-hemispheric (left visual field) trials from Finger Perimetry was used for the visual disconnection score.

Tactile. Topognosis (intra-manual minus inter-manual trials) was used to calculate the tactile disconnection score, which is considered one of the most sensitive tests for assessing tactile disconnections.[30]

Speech Production. For BT*, NR, and TJ, we used Finger Perimetry (RVF minus LVF trials) and Stereognosis (right-hand minus left-hand trials). Difference scores were calculated and averaged for each task. For LJ, only Stereognosis data was available, so the difference score was based solely on this task.

We only included disconnection scores for tasks with clearly defined chance levels and binomial test outcomes. WISC-R spatial block design and hand gestures tasks were not included here because the combination of limited trial numbers and undefined chance levels significantly reduced our statistical power, making the statistical detection of disconnection syndrome challenging in these tasks, even though qualitative evidence supports their presence (see **Results**).

Data availability

The authors confirm that the data supporting the findings of this study are available within the article (see **Table 2**). Relevant analysis code is available on GitHub at https://github.com/selinbekir/splitbrain-disconnection-analysis. Patient data that support the findings of this study are available from the corresponding authors, upon reasonable request.

Results

Despite BT*'s near-complete resection, he exhibited no signs of disconnection syndrome in any domain, in contrast to complete callosotomy cases, where disconnection syndrome was observed (**Table 2** and **Fig. 3**).

1. Visual Tasks

In line with our hypotheses, BT*, featuring intact splenium fibers, showed no disconnection syndrome in visual tasks. He performed significantly above chance in both RVF and LVF trials (4/4 correct, $P = 0.002$ for both) and accurately identified whether numbers in his periphery were the same or different (9/10 correct, $P = 0.021$). The complete callosotomy cases, NR and TJ, on the other hand, showed expected disconnections in visual tasks. They could correctly report the numbers shown in RVF trials (4/5 and 3/3 respectively $P < 0.05$ for both), but not in LVF trials (2/5 and 0/3, $P > 0.05$ for both). NR was also unable to report whether the numbers simultaneously presented in the LVF and RFV were the same or different. (4/10, $P = 0.754$).

2. Tactile Tasks

Surprisingly, BT*, despite only having a small portion of the splenium intact, showed no signs of disconnection in any tactile tasks. He correctly located tactile stimulation in inter- and intra-manual trials in Topognosis (10/10, $P < 0.001$ for both), and he correctly named the objects handed to his left hand (4/5) and right hand (5/5, $P < 0.05$ for both).

In contrast to BT*, all complete callosotomy patients (NR, TJ and LJ) exhibited clear signs of disconnection syndrome in tactile tasks. They all failed to cross-locate touch in inter-manual trials (3/8, 4/30, and 0/3 respectively, $P > 0.05$ for all) but they correctly did so in intra-manual trials (7/8, 26/26, and 3/4, $P < 0.05$ for all). They all failed to name the objects placed in their left hands (3/5, 0/1, and 1/5, $P > 0.05$ for all), but were able to correctly name them in their right hands (5/5, 6/6, and 4/5, $P < 0.05$ for all).

Note that with TJ, only one left hand trial could be conducted in Stereognosis because she verbally reported feeling nothing on the left hand. Thus, the remaining trials were abandoned to prevent further frustration. While this limited the statistical analysis (because no meaningful tests could be run with just one trial), it is, in-and-of-itself, an excellent demonstration of the disconnection syndrome. When an object was placed in her left hand—processed by the mute right hemisphere—her disconnected speaking left hemisphere repeatedly insisted she felt nothing. However, during the topognosis task, she performed perfectly fine with her left hand—accurately locating touch stimuli within her left hand. This indicates that she did not have any actual sensory loss in her left hand. Instead, it highlights the disconnection between the hemispheres: her right hemisphere could perceive and process tactile input, but her speaking left hemisphere could not access or verbalize that information.

3. Visuo-Spatial (WISC-R Block Design) Task

BT* showed no disconnection in this task. He correctly completed all 8 patterns with his left and right hands (observed difference in proportion correct = 0, $P = 1$).

TJ showed clear disruption when using her dominant right hand but not her left hand, consistent with previous reports.[24] Although only two trials were attempted with her right hand—limiting statistical analysis—anecdotal evidence highlights her disconnection, and

potentially the involvement of the left hemisphere interpreter.[31] TJ visibly struggled with her right hand. She was incapable of arranging the cubes into a simple 2x2 square, instead repeatedly forming a 3x1 shape, let alone creating the correct patterns. After some effort, she claimed there was something wrong with her vision. Initially, the task was nearly abandoned under the assumption of a general visual impairment. However, when switched to her left hand, TJ quickly and accurately created most of the patterns without difficulty (she completed one as a mirror image, resulting in a score of 5/6). Although this is an anecdotal observation and lacks quantification, it is compelling: her left hemisphere verbally rationalized her right-hand struggles, incorrectly attributing them to vision problems, only for her left hand (mute right hemisphere) to perform the task perfectly. Despite this observation, permutation test showed no statistically significant difference between the hands (observed difference in proportion correct = 0.83, $P = 0.1$), potentially due to the limited trial numbers with the right hand (0/2).

NR, being a complete callosotomy patient, successfully completed this task with both hands. There were no significant differences between hands (observed difference in proportion correct = 0, $P = 1$). His family reported regular rehabilitation exercises involving similar tasks, which may explain his unexpected right-hand performance compared to other complete callosotomy patients in this study and in the literature.[24] Alternatively, it is also plausible that he possesses bilateral representations for visuospatial processing.

4. Language

Language Comprehension in the form of Speech: Hand Gestures Task

BT* successfully carried out hand gestures following verbal commands with his right hand (6/6) and left hand (6/6), showing no difference between the two hands (observed difference in proportion correct = 0, $P = 1$).

In contrast, TJ showed difficulty performing hand gestures with her left hand (4/12) when instructed verbally. For instance, when asked to make a fist, she performed different actions such as opening her hand instead. Remarkably, she easily and accurately performed all gestures when mimicking the experimenter's hand movements with her left hand (9/9), showing no signs of motor or motivational deficits. The difference between her left-hand performance following verbal commands (4/12) and when simply mimicking the experimenter's hand gestures (9/9) was significant (observed difference in proportion

correct = 0.66, P = 0.004). This suggests that her right hemisphere may be limited in its ability to comprehend speech. There was, however, no significant difference between her left-hand trials (4/12) and right-hand trials (3/3) following verbal commands (observed difference in proportion correct = 0.66, P = 0.07). This is likely due to the small and unmatched number of trials despite the observation that her right hand performed the task without difficulty (3/3), while the left hand struggled (4/12). Similarly, even though LJ performed the task well with his right hand (3/4) and struggled with his left hand (0/3), there was no statical difference between the hands (observed difference in proportion correct = 0.75, P = 0.15).

NR, in contrast, had no difficulty performing hand gestures with his left and right hand following verbal instructions (4/5 and 5/5, observed difference in proportion correct = 0.16, P = 1), suggesting that he might have bilateral representations for speech comprehension.

Language Production in the form of Speech

Tasks that required a verbal response to lateralized input to a hemisphere (Finger Perimetry and Stereognosis) were used to assess speech production from the left and right hemispheres.

BT* was able to verbally respond to all inputs, whether presented to the left or right hemisphere. This was likely due to his intact splenium, which facilitated the integration of visual and tactile information across hemispheres. While the splenium's role in visual information integration is well-established, his topognosis performance showed he could also cross-localize tactile stimuli. As a result, it was not possible to lateralize any visual or tactile inputs in his case. This likely allowed him to verbally respond accurately to all stimuli.

In contrast, all complete callosotomy cases demonstrated a clear disconnection syndrome, suggesting that the speech production is still exclusively controlled by the left hemisphere. They could verbally respond only to inputs presented to their left hemispheres (e.g., RVF trials in Finger Perimetry and right-hand trials in Stereognosis), but not to their right hemispheres (e.g., LVF trials in finger perimetry and left-hand trials in Stereognosis).

Table 2 Individual Performance on Disconnection Assessments

			Patients			
Domain	Task	Condition	BT*	NR	TJ	LJ
Visual	*Finger Perimetry*	*Intra (LVF)*	**4/4** *P* = .002	**4/5** *P* = .007	**3/3** *P* = .008	NA
		Inter (RVF)	**4/4** *P* = .002	2/5 *P* = .263	0/3 *P* = 1	NA
	Same-Diff.	*Inter-*	**9/10** *P* = .021	4/10 *P* = .754	NA	2/4 *P* = 1
Tactile	*Topognosis*	*Intra-manual*	**10/10** *P* < .001	**7/8** *P* < .001	**26/26** *P* < .001	**3/4** *P* = .027
		Inter-manual	**10/10** *P* < .001	3/8 *P* = .422	4/30 *P* = .204	0/3 *P* = 1
	Stereognosis	*Intra (right hand)*	**5/5** *P* < .001	**5/5** *P* < .001	**6/6** *P* < .001	**4/5** *P* = .007
		Inter (left hand)	**4/5** *P* = .007	3/5 *P* = .058	0/1	1/5 *P* = 1
Visuo-spatial	Block Design	Intra (left hand)	8/8	8/8	5/6	NA
		Inter (right hand)	8/8 *P* =1	8/8 *P* =1	0/2 *P* = 0.105	NA
Language	Hand Gestures	Intra (right hand)	6/6	6/6	3/3	3/4
		Inter (left hand)	6/6 *P* =1	5/6 *P* =1	4/12 *P* = 0.076	0/3 *P* = 0.14

Table 2. Performance of each patient across tasks and conditions. The table presents the number of correct trials for each patient, with scores listed under their respective columns. Tasks in *italic* (e.g., Visual and Tactile tasks) were analyzed using binomial tests to assess whether performance exceeded chance-level. **Bold** scores indicate above-chance performance ($P < 0.05$), while non-bold scores reflect chance-level performance. Notably, BT* consistently performed at ceiling levels in both *inter-* and *intra-hemispheric* conditions. In contrast, complete callosotomy patients generally struggled with *inter-hemispheric* tasks but performed well on *intra-hemispheric* trials. Block Design and Hand Gesture tasks were analyzed using permutation tests to compare the left- and right-hand performances, with a single *P*-value reported for each comparison. While BT* and NR showed no differences between hands, TJ and LJ exhibited trends suggestive of differences. However, due to limited and unmatched trial numbers (e.g., 5/6 vs. 0/2 for TJ), none of the comparisons were statistically significant ($P > 0.05$). Some tasks were aborted early (e.g., 0/2) when patients showed visible struggles, to prevent further frustration. These methodological limitations are discussed in the Results and Discussion sections.

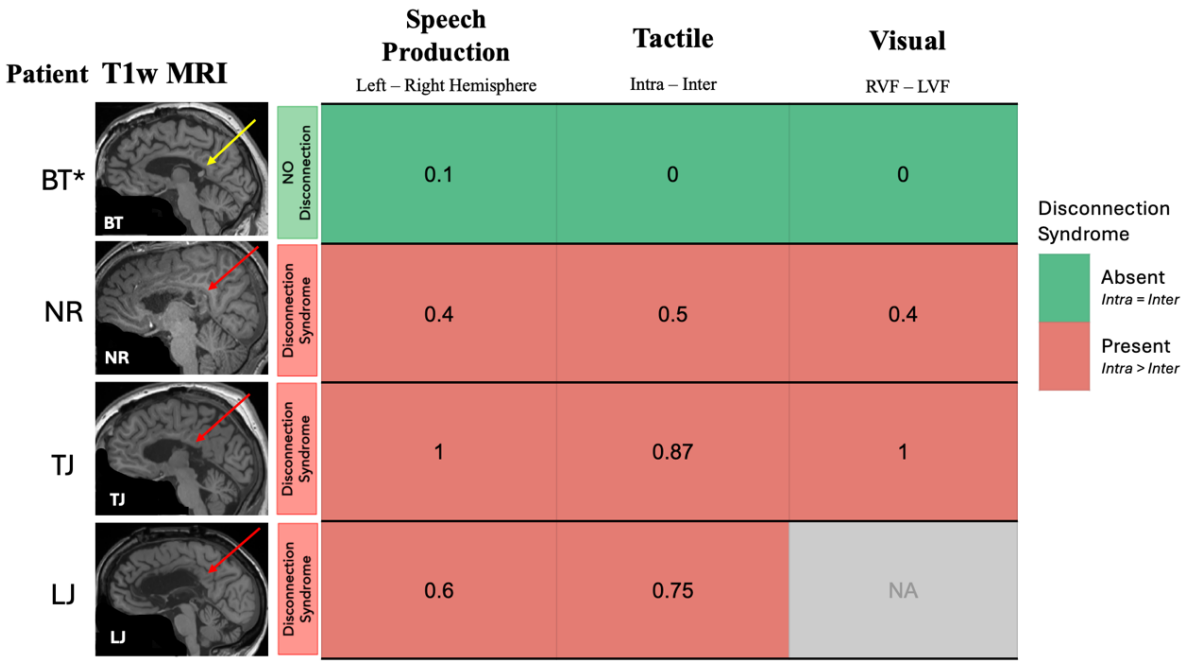


Figure 3 Disconnection Scores. Binary color-coded representation of the disconnection syndrome. *Red* indicates the presence of the disconnection syndrome, defined by above-chance performance in intra-hemispheric trials ($P < 0.05$), and chance-level performance in inter-hemispheric trials. *Green* indicates no disconnection, with above-chance performance in both inter- and intra-hemispheric conditions. *Gray* indicates no available data. Disconnection Scores range from 0 (equal performance in inter- and intra-hemispheric conditions) to 1 (perfect intra-hemispheric performance with chance-level inter-hemispheric accuracy). Structural MRIs with red arrows indicate complete callosotomies, while the yellow arrow indicates partial callosotomy. Patient BT*, while structurally more similar to complete callosotomy cases with the majority of the CC severed, exhibited no disconnection syndrome, performing equally well in inter- and intra-hemispheric conditions.

Discussion

Given that BT* retained only a small posterior portion of the splenium, we expected signs of a disconnection syndrome, such that visual information integration would remain intact (facilitated by the splenium), while more anterior functions such as tactile integration would be disrupted. This prediction was based on the assumed functional topography of the CC, which primarily associates the splenium with visual information integration, and the posterior body with tactile integration.[5] Yet, BT* showed no such disconnections. This result was surprising, especially when compared to previous splenium cases (see **Fig. 4** for case comparisons). First, we discuss three factors that may explain the discrepancy between BT* and previous splenium cases with selective disconnections: (a) the timing of testing, (b) the extent of the CC

preservation, and (c) the direction of resection. Second, we consider how our current data speaks to recent debates about perceptual and motor unity in callosotomy patients. Third, we discuss the implications of our comprehensive metric for the disconnection syndrome. Finally, we compare BT*'s findings with other cases of callosal disruptions caused by pathological lesions, distinguishing these from callosotomy cases.

Reconciling BT*'s Performance with Existing Evidence on CC Topography

The Timing of Testing and The Potential for Network Reorganization Over Time

BT* was tested six years post-surgery, and this may have allowed enough time for brain network reorganization to occur. This contrasts with previous splenium cases showing selective disruptions when tested a few months after surgery (e.g., Case 9,[17] see **Fig. 3B**). In those cases, it is unclear whether any recovery occurred over time. Other splenium cases, such as JKN,[32] also exhibited a selective disconnection syndrome; though his exact post-operative testing time is unclear, it is most likely within the first year (see **Fig. 3D**).

The Extent of the CC Preservation and the Possibility of a Threshold Effect

Some partial cases, even when tested years post-surgery, showed persistent disconnections. Why, then, does network reorganization fail to occur in these cases? We suggest that a threshold effect may explain this observation. Network reorganization may depend on a critical threshold, and such reorganization may fail to occur if the number of intact fibers falls below this threshold. Threshold effects are common in complex systems, where gradual changes often produce no noticeable impact until a critical point is reached, leading to a sudden state shift.[33] For example, although we cannot draw reliable conclusions from a single image, patient JKN,[32] may have a smaller intact portion of the splenium compared to BT* (see **Fig. 3D**). This smaller intact portion may have fallen below the critical threshold needed for reorganization, leading to persistent disconnection symptoms.

Direction of the Resection and the Role of the Anterior CC in Cognition

The direction of the resection—anterior-to-posterior versus posterior-to-anterior—is a critical factor in partial callosotomy patients. The behavioral effects of posterior callosotomy are more drastic than anterior callosotomy.[7] One of the proposed evolutionary origins of the CC is argued to be midline fusion for the sensory cortices,[1] and humans rely heavily on sensorimotor processes to interact with the world. Thus, posterior inter-hemispheric integration might better

preserve system integrity and may allow more effective compensation than the other way around. What, then, is the role of the anterior CC? Our tasks may have been insensitive to effectively probe this question. More rigorous testing with BT* is needed to better investigate the role of the anterior CC in cognition. It is, however, methodologically harder to probe any higher-order disconnections, especially if the posterior sensorimotor integration is intact. This intact sensorimotor integration prevents the lateralization of input and output during behavioral testing, making it difficult to isolate and identify potential disconnections in higher-order functions.

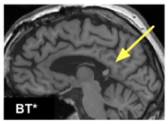
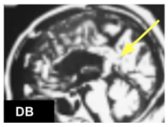
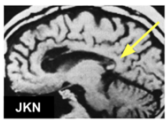
		Patient	Testing Time Post-Surgery	Disconnections	Factors That May Explain Discrepancies	MRI Reference Sources
A		BT*	6 years	Visual. NO Topog. NO Stereog. NO	-	The Current Study
B		Case 9	2-6 months	Visual. NO Topog. YES Stereog. YES	Timing of Post-Surgery Testing	Risse et al., 1989
C		DB	12 years	Visual. NO Topog. NA Stereog. YES**	**Unclear behavioral reports	Fabri et al., 1999
D		JKN	Probably < 1 year†	Visual. NO Topog. NA Stereog. YES	Timing of Post-Surgery Testing and/or Extent of Preserved CC fibers	Gazzaniga, 1988

Figure 4 Case Comparisons: Splenium Patients. Overview of previous partial callosotomy cases similar to BT*, with testing times since surgery, observed selective disconnections, and potential factors explaining differences in disconnection profiles. "Topog." refers to topognosis, "Stereog." to stereognosis tasks, and "No" indicates the absence of disconnection syndrome. For case JKN, the testing time is probably within the first year (†Prof. Gazzaniga, personal communication). For case DB, stereognosis performance is unclear. See **Discussion** Section for further details.

Neural Correlates of BT*'s Intact Performance

Incorporating neuroimaging methods alongside behavioral measures could provide additional insights into mechanisms associated with BT*'s integrated performance. While we have not yet conducted an event-related fMRI study with BT*, a closely comparable case, DB (see **Fig. 3C**), was previously investigated.[11] In this fMRI study, tactile stimulation of either of DB's hand produced only ipsilateral but not contralateral activations.[11] This suggests disrupted inter-hemispheric transfer of tactile information. However, DB's behavioral stereognosis

performance is not clear-cut. While described as showing disconnection syndrome in stereognosis, she successfully named objects with her left hand 75% of the time. This relatively high success rate, if statistically above chance, suggests her tactile processing may be more similar to BT*'s preserved abilities than to the clear deficits typically seen in complete callosotomy patients. The discrepancy between intact tactile behavior and ipsilateral-only activations might suggest alternative mechanisms supporting this function. A similar tactile fMRI study with BT* would be highly illustrative to conduct and compare.

We have, however, conducted a resting-state functional connectivity study with this cohort, which revealed that BT*'s inter-hemispheric connectivity was largely sustained.[18] Various measures of functional network integration resembled that of healthy controls with an intact corpus callosum—in stark contrast to complete callosotomy patients. These observations show that even small posterior callosal remnants can sustain widespread inter-hemispheric functional couplings, consistent with his intact behavioral performance (see Santander *et al.*[18] for a detailed discussion).

Is the Motor and Perceptual Unity Hanging by the Thread of the Splenium?

The unity of consciousness in callosotomy patients has recently been revisited and debated.[34-39] This debate primarily revolved around two types of unity: motor versus perceptual,[38] also similarly referred to as behavioral versus representational,[40] or, agency-based versus experience-based conceptions of conscious unity.[34] The recent debate was sparked by the observation of a complete callosotomy patient's motor unity—that is, the ability to respond to any lateralized inputs with either hand.[38] Here, we did replicate the classical findings with a new cohort of complete callosotomy patients: all complete callosotomy cases showed the typical pattern of motor disunity, characterized by accurate performance on intra-hemispheric trials (stimulus and response within the same hemisphere) but poor performance on inter-hemispheric trials (stimulus and response in different hemispheres). We also showed that all complete callosotomy cases exhibited the typical pattern of perceptual disunity—none of them were able to compare visual inputs presented simultaneously to both visual fields, nor did they exhibit any awareness or above-chance performance in response to sensorimotor events occurring in the opposite hemisphere. BT*, on the other hand, with his remaining splenium, demonstrated preserved motor and perceptual unity across all tasks, performing similar to neurotypical individuals with an intact CC.

A Comprehensive Metric for Disconnection Syndrome: Addressing Limitations in Case Comparisons

The heterogeneity of assessment methods in split-brain research renders case comparisons across studies challenging. While in-depth, domain-specific investigations have provided valuable insights into specific aspects of callosal function, we still lack a standardized disconnection profile metric that could be reported for each patient regardless of the study's primary focus. Such standardization would facilitate case comparisons and help establish common ground when evaluating findings across different studies. Our multi-domain assessment approach addresses this limitation by providing a standardized framework for quantifying disconnection severity. By assessing performances across visual, tactile, and higher-order cognitive domains using simple bedside tests, this method aims to provide an initial "disconnection profile" for each patient. Moreover, the tasks are simple enough for patients with intermediate cognitive impairment to perform. Notably, since the characteristics of the disconnection syndrome can change over time, conducting these simple and quick bedside assessments longitudinally post-surgery is crucial for providing a more comprehensive understanding of a patient's disconnection profile.

Other Cases of Partial Callosal Disruption

Patients with callosal disruptions caused by pathological lesions generally exhibit selective functional disruptions consistent with the topographic organization of the CC.[9] However, these patients' behavioral outcomes often differ from those observed in callosotomy cases.[16] This distinction likely stems from fundamental differences in how the CC disruption occurs: callosotomy involves sudden, targeted disruption of white matter, whereas pathological lesions often develop gradually and may include extra-callosal damage. After callosotomy, the system suddenly and specifically loses the callosal fibers through a very targeted surgical resection, to which it may respond differently as compared to gradual, diffuse disruption. This is also similar for agenesis of the corpus callosum cases, where individuals are born without a corpus callosum.[41] In such cases, the developmental trajectory is fundamentally different from having a fully developed corpus callosum that is then suddenly disrupted in adulthood through surgery, which could explain differences in behavioral outcomes.

Limitations

Here we consider two important limitations. First, the *lack of longitudinal* data prevents us from determining whether BT*'s intact performance reflects a general absence of disconnection symptoms or their recovery through network reorganization over the six years post-surgery. While network reorganization remains the most plausible explanation given the existing reports of selective impairments in other splenium cases, we cannot definitively establish BT*'s symptom trajectory. Second, several factors limit the *generalizability* of our findings: the single-subject nature of BT*'s case, and the limited number of trials due to clinical testing constraints—which significantly reduced statistical power. Nonetheless, several aspects of our study design strengthen the validity of these findings. The within-subject design offers robust control over individual variability, and the selective disruption observed in complete callosotomy cases—only in inter- but not intra-hemispheric conditions—suggests a targeted impairment in tasks requiring inter-hemispheric transfer or integration, rather than a general deficit. This pattern of selective disruption stands in clear contrast to BT*'s intact performance across similar tasks.

Conclusion

Our study shows the remarkable functional capabilities of a small, intact posterior callosal remnant years after surgery. In contrast to complete callosotomy cases, BT*, with only ~1 cm of splenium intact showed no disconnections in any of our cross-modal disconnection assessments. While BT* is a single case, and the absence of longitudinal data prevents us from determining whether this integration was preserved immediately post-surgery or emerged through network reorganization over time, this observation nevertheless highlights the splenium's remarkable role in such integration. This finding supports the claim that structure-function relationships in the human brain do not follow a linear pattern where behavioral functional deficits scale with the extent of structural (callosal) resection. Instead, we showed that minimal preserved structural connectivity may maintain broad integration beyond that which our classical anatomical models predict.

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Competing interests

The authors report no competing interests.

Author contributions

S.B., J.L.H., T.P., A.R., H.E.S., B.G., C.G.B., O.S., M.S.G., L.J.V., and M.B.M. conceived and planned the experiments. T.P., V.M.W., J.L.H., A.R., F.G.W., C.G.B., and L.J.V. assisted with patient recruitment and were responsible for data collection. T.K. performed the callosotomy surgeries. S.B., T.S., L.J.V. and M.B.M. conceived the data analysis strategy; S.B. contributed to analysis code and executed the data analysis pipeline. S.B. wrote the manuscript with contributions from T.S., C.G.B., M.S.G., L.J.V., and M.B.M. The project was supervised by A.R., C.G.B., L.J.V., and M.B.M. Funding was secured by B.G., L.J.V., and M.B.M. All authors assisted with manuscript revision and approved the final submitted version. L.J.V. and M.B.M. contributed equally.

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