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Final dissertation

Split-brain and the intermanual transfer effect

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ABSTRACT

In this thesis, we have explored the split-brain phenomenon and its implications for intermanual transfer of information. Split-brain occurs when the corpus callosum (CC), the commissure that connects the two hemispheres of the brain, is surgically severed to treat certain medical conditions (e.g., epilepsy). As a result, the left and right hemispheres of the brain become functionally independent, leading to a variety of cognitive changes. One of the most interesting effects of split-brain is the *intermanual transfer effect*, where learning and performance on a motor task with one hand can transfer to the other hand, even though the two hemispheres no longer communicate. This effect has been extensively studied in individuals with intact brains, and less is known about its manifestation in split-brain patients.

In the present thesis we have reviewed the existing literature on split-brain patients and their performance on intermanual transfer tasks. Studies of intermanual transfer in groups of split-brain patients have been included and the performance of split-brain patients has been compared to that of control groups with intact brains The findings suggest that the anterior and posterior portions of the CC play a critical role both in sensory and motor integration, as well as in intermanual interactions during motor tasks. In addition, there are limitations in the interhemispheric transfer of tactile information and indications that perceptual priming does not transfer interhemispherically in individuals with acallosal brains. These findings sheds light on the nature of intermanual transfer in split-brain patients and contribute to a better understanding of the functional organization of the brain, emphasizing the importance of the CC in brain function and integration.

Keywords: Split-Brain, corpus callosum, intermanual transfer effect, lateralization, consciousness

CHAPTER 1:

GENERAL INTRODUCTION TO THE SPLIT-BRAIN

1.1 Theoretical Background

The term “split-brain” (i.e., corpus callosotomy) refers to patients in whom the CC (corpus callosum; Goldstein et al., 2022), the main bundle of fibers connecting the two hemispheres of the brain (Figure 1), is cut to treat, in most cases, the effects of severe epilepsy. According to Gazzaniga (2005), by cutting off the entire CC, the interhemispheric transfer of information (sensory, motor, cognitive, etc.) is interrupted, making it possible for scholars to gain insight into the differences between the two cerebral hemispheres and the mechanisms through which they interact.

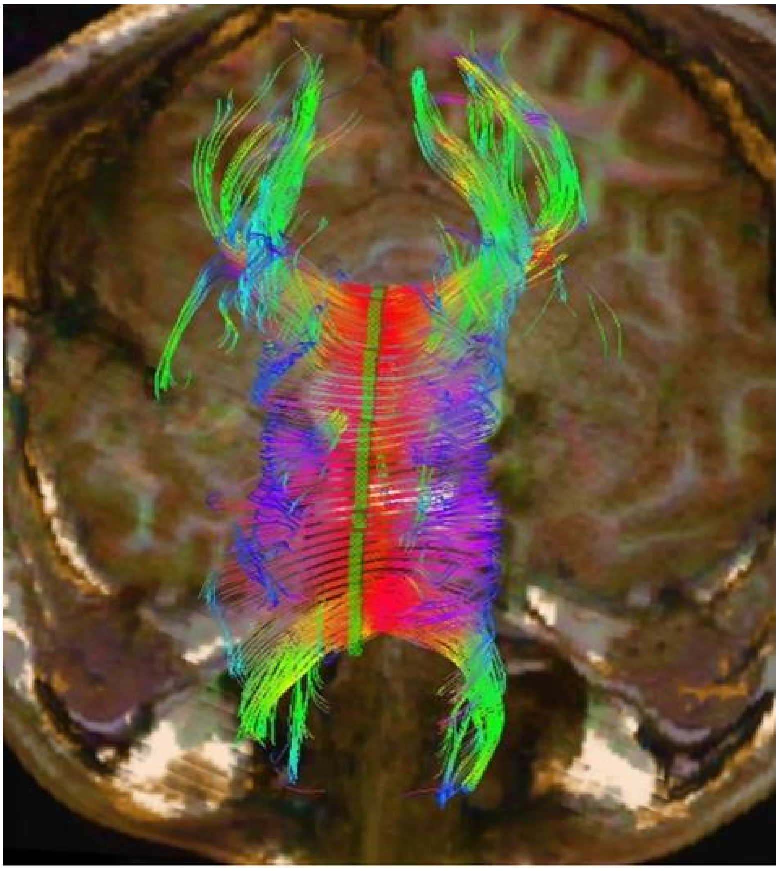

Figure 1. *Diffusion tensor imaging (DTI) of the CC (Goldstein et al., 2022).*

The history of split-brain research begun in 1940, with the first known callosotomy surgeries performed by Van Wagenen and Herren, introducing the concept of split-brain surgery (Figure 2) to control the seizures of patients with epilepsy, who did not respond to pharmacological treatment (as cited in Gazzaniga, 2005). Four years later, Akelaitis, at the University of Rochester, started studying patients from the Van Wagenen and Herren’s cohort. Akelaitis noticed that this type of surgery did not lead to cognitive or behavioral impairment of the patients (as cited in Gazzaniga, 2005).

Between 1956 and 1958, Sperry and colleagues began testing split-brain on non-human animals (i.e., cats, rats, monkeys). This approach was very seminal, because, as a result, more sophisticated techniques, for directly and independently assessing the function of each hemisphere, have been developed (as cited Gazzaniga, 2005). The research of Sperry and colleagues on split-brain in non-human animals opened and paved the way for important future studies on split-brain in humans. Indeed, from 1962 to 1967, Gazzaniga, Bogen, and Sperry adapted the split-brain testing techniques developed in non-human animals for using them in humans (i.e., split-brain patients; Gazzaniga, 2005).

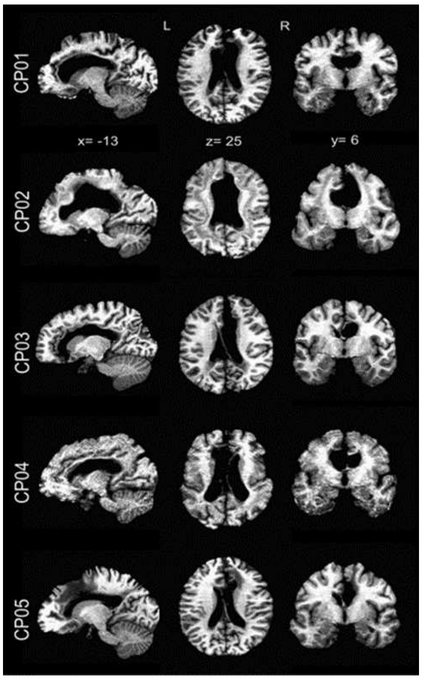

Figure 2. *Anatomical MRI (Magnetic Resonance Imaging) images of split-brain patients. For each patient (CP01– CP05) sagittal, axial, and coronal MRI images are shown in Micro and Nano Imaging (MNI) space. It is possible to appreciate the complete absence of the CC in all cases (Avvenuti et al., 2020).*

1.2 New findings in split-brain research

Over the years, important new findings have been reported about hemispheric dominance and its organization, and new theories about human perception and consciousness have been developed (de Haan et al., 2020). Many of the first studies were focused more on sensory-perceptual processes, such as vision and touch. In these studies, visual and tactile stimuli were presented to the patients so that the stimuli were restricted only to the contralateral hemisphere.

According to de Haan et al. (2020), in these early studies, stimuli, such as objects, presented to the left hemisphere either tactually in the right hand or as an image in the right visual hemifield, could be easily named (because the left hemisphere is dominant for language) or pointed to with the right hand (which is controlled by the left hemisphere). By contrast, when the same stimuli were shown in the left visual hemifield or placed in the left hand, the patient's behavior changed dramatically. The patient, then, seemed to be unaware that any stimulus had occurred. Nonetheless, the patient was still able to choose the correct object from a variety of options (i.e., the target stimulus among distractors) presented to the left hand or the left visual hemifield.

One example of this kind of experiment was conducted with the famous patient called "Joe". The patient drew a cowboy hat with his left hand in response to the word "Texas" presented in his left visual hemifield. Nonetheless, the patients left verbal hemisphere showed a complete absence of knowledge about why his left hand had drawn this cowboy's hat (de Haan et al. 2020). According to de Haan et al., these preliminary findings suggested that split-brain patients do not have a meaningful communication between the two hemispheres. This gave rise to the theory that there may be two distinct conscious agents. On the other hand, there is the verbal left hemisphere that can communicate and explain what it sees and feels. On the other hand, there is the non-verbal right hemisphere that is "mute", but can nonetheless demonstrate that it has perceived and recognized words and objects.

Though this is an interesting theory, it is not surprising that some irregularities were found within the years of research on this subject; especially because after surgery the patients, for example, seemed to behave normally in everyday life activities (de Haan et al. 2020). Even though the experiments in the laboratory suggested that consciousness is split, the observation that split-brain patients frequently behave and feel normally seems incompatible with a breakdown of consciousness' unity. Indeed, it appears implausible that both the patients and those in close contact with them failed to notice that after the CC was surgically removed, the patient only perceived half the visual field and controlled half the body (de Haan et al., 2020).

Even when explicitly probed, the patients maintain that they still have complete control over their body. In addition, it has been observed that both the task and the patient can influence the communication capacity between the two hemispheres (de Haan et al., 2020). An example is the ability of some patients to compare visual stimuli across the midline. As explained by de Haan et al. (2020), the patient is unable to accurately distinguish between two stimuli when one is presented to the left visual hemifield and the other to the right one. Nevertheless, the patient is able to do so when both stimuli are presented in the same visual hemifield, independently whether it is the left or the right hemifield.

This is consistent with the idea that each hemisphere perceives the contralateral visual hemifield independently, and that an intact CC is required for integration. But now comes the interesting part. Even though we would logically expect that, after severing the CC, the perceptual information would not be able to cross over to the other hemisphere, the opposite has been shown by a few split-brain patients. In fact, Johnson (1984; as cited by de Haan et al., 2020) showed that some patients had had an intact ability to compare stimuli across the midline.

Another example of this phenomenon, where split-brain patients appear to be able to compare or integrate particular types of stimuli across the two visual hemifields, has been observed in apparent motion and good line continuation studies. Most patients display an integration of these features (de Haan et al. 2020). For example, when tested with apparent motion, split-brain patients were presented with two dots in succession at a short distance. These patients could tell whether the dots caused apparent motion or if, instead, the dots were presented simultaneously or with delays too long to cause apparent motion. Split-brain patients could perform this task even when one dot appeared in the left visual hemifield and the other in the right visual hemifield (de Haan et al., 2020).

In the good line continuation experiment, the split-brain patients were presented with two tilted lines with a gap between them. The lines, according to de Haan (2020), were positioned in such a way that extending them across the gap would either cause the lines to coincide or to run in parallel. Split-brain patients were highly accurate at indicating whether the lines were parallel or coincident, even when each line segment was displayed in a different visual hemifield (de Haan et al., 2020).

Another aspect that influences the hemispheric response to different stimuli is whether the split-brain patient is right-handed or left-handed. Most people show a left-hemisphere dominance for language, but, in a minority of people, the opposite can also be observed.

According to Knecht et al. (2000), a systematic relation between handedness and language dominance has long been suggested because of the increased occurrence of atypical right-hemispheric language in left-handed neurological patients.

In right-handed individuals, language functions are typically located in the left hemisphere, while spatial abilities are typically located in the right hemisphere (de Haan et al. 2020). As a result, when split-brain patients are presented with stimuli that are presented only to one visual field (e.g., only to the left visual field), the information is processed primarily in the opposite hemisphere (e.g., the right hemisphere; de Haan et al., 2020). In right-handed individuals, this means that information presented to the left visual field (which is primarily processed in the right hemisphere) may not be able to be verbally reported, because the language centers are located in the left hemisphere (de Haan et al., 2020). However, they may be able to respond to the stimulus using their left hand (which is controlled by the right hemisphere), indicating that the right hemisphere has processed the information.

Conversely, information presented to the right visual field (which is primarily processed in the left hemisphere) may be verbally reported by the individual, but they may not be able to use their left hand to respond, because the motor control for the left hand is located in the right hemisphere (de Haan et al. 2020). The opposite pattern might be observed with those of left-handed patients who have language dominance in their right hemisphere. These findings suggest that handedness can influence the behavior of split-brain patients by affecting which hemisphere processes certain types of information and which hand is used to respond to that information. Nevertheless, it is worth noting that the relationship between handedness and split-brain patient behavior is complex, and not all studies have found consistent results.

1.3 Understanding split-brain phenomena: unity, hemispheric specialization, and mechanisms of communication

In summary, as mentioned before, the task, which has been mostly used in split-brain patients to test their sensory-motor and cognitive changes after split-brain, is the *"response vs. visual hemifield interaction"*, where a visual stimulus is presented either to the left or the right visual hemifield (Pinto et al. 2017). On this task, split-brain patients can show the following hallmarks (Figure 3):

1. When a stimulus is presented to the left visual hemifield, patients can only respond adequately with their left upper limb. When the same stimulus is presented to the right visual hemifield, patients can only respond adequately with their right upper limb.
2. Patients show hemispheric specialization, referring to the differential role of the left or right hemisphere in processing a specific task or showing a behavior. The left hemisphere excels at language, math, and detailed processing, among other things. The right hemisphere is better at visuo-spatial tasks, temporal awareness, and causal inferencing. This suggests that each hemisphere operates independently of the other, creating consciousness autonomously.
3. Patients can show post-hoc confabulations after performing actions with their left hand, where the left hemisphere of the brain tries to explain the action of the left hand by fabricating a story.
4. Patients' performance suggests that each hemisphere may have its own independent focus of spatial attention.
5. Patients are incapable of comparing stimuli across the visual midline. This makes sense, if two independent conscious agents perceive half of the visual field and are unable to communicate their perceptions to each other. Although, it is important to

take into consideration that there are indeed prominent examples of some patients who can compare stimuli across the midline (de Haan et al. 2020).

According to Pinto et al. (2017), these five hallmarks have produced what we refer to as the classic models deriving from studies on split-brain patients. There are two classic models of brain functioning in split-brain patients. The first model, called the *"partial consciousness model"*, expresses the idea that only the left hemisphere is conscious, whereas the right hemisphere works unconsciously (Pinto et al. 2017). The second model, called the *"split consciousness model"*, argues for the existence of independent, separate hemispheric consciousnesses (Pinto et al. 2017). Because *"three of the five hallmarks (hemispheric specialization, post hoc confabulations, and split attention) also exist in healthy adults with unified consciousness"* these models require further elaboration (Pinto et al. 2017).

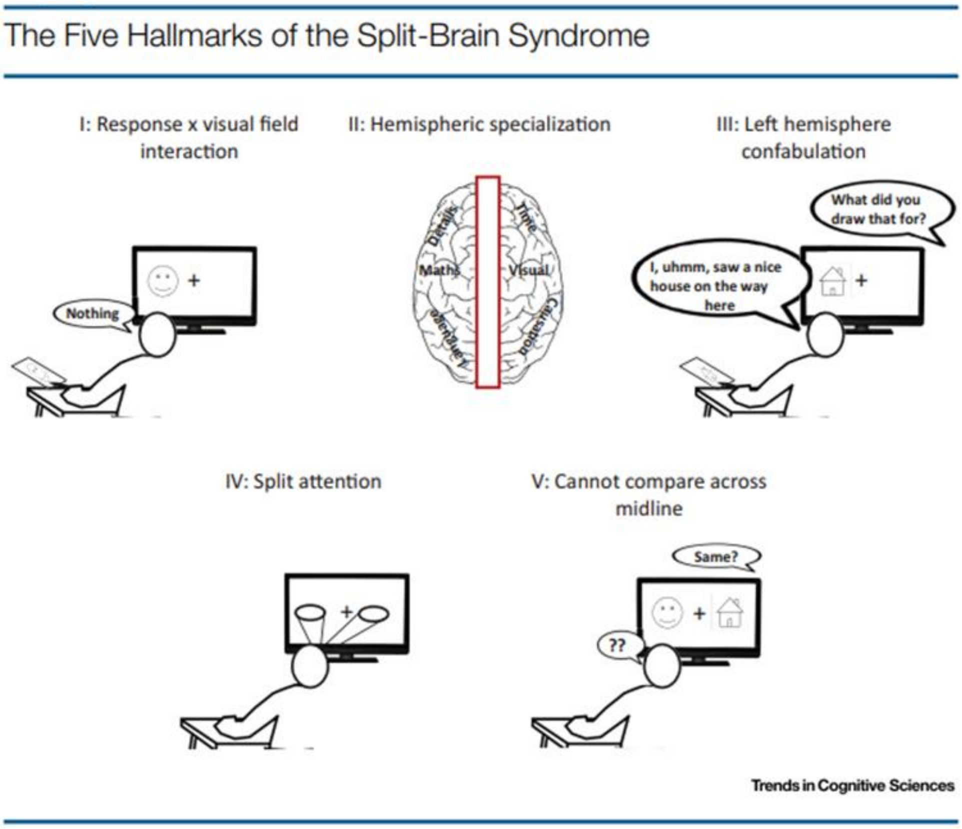

Figure 3. *The classic models of brain functioning in split-brain patients assert that conscious unity is disrupted in this syndrome. The evidence for this view comes from five hallmarks (Pinto et al. 2017).*

In general, it can be stated that, in split-brain patients, the presence of divided processing is not enough to be used as evidence about whether these patients have one or two types of consciousness (de Haan et al. 2020). Maybe, it can be sustained that both models of consciousness (*"partial consciousness model"* and *"split consciousness model"*) are valid and that all depends on the measures used, because it seems that some measures indicate unified consciousness while others do not.

But how is it possible for split-brain patients to show and feel such a unity in their behavior in everyday life? Researchers have asked themselves this question and as reported by de Haan et al. (2020), there are three competing, but complementary hypotheses for the mechanisms underlying the split-brain preservation of unity.

1.4 Unity of mind in split-brain patients: exploring three hypotheses on transfer, control, and communication

The *first hypothesis* suggests that information is transferred subcortically between the hemispheres (de Haan et al., 2020). This means that it is possible that many subcortical connections, which were not separated in split-brain patients, are the ones making it achievable for information to be transferred from one hemisphere to the other (de Haan et al., 2020). These subcortical connections are numerous commissures (white matter tracts connecting homologous structures on both sides of the brain) and decussations (bundles connecting different structures on both sides) that connect nuclei known to be involved in perceptual processing (e.g., the superior colliculus, inferior colliculus, lateral geniculate nucleus, etc.; de Haan et al. 2020). According to de Haan et al., Trevarthen and Sperry (1973) emphasized the importance of these commissural connections in transferring visual information in split-brain patients.

The *second hypothesis* is that unity in action control is based on ipsilateral motor control (de Haan et al., 2020). This finding might explain why split-brain patients could respond equally well with both their hands on certain tactile and visual tasks. According to de Haan et al. (2020), the proximal (but not the distal) regions of the arm are controlled bilaterally, and manual movement is not strictly lateralized.

The *third hypothesis* suggests that, in addition to any direct neuronal connection that might exist between the hemispheres, these may communicate with one another through strategic cross-cueing mechanisms (de Haan et al. 2020). For instance, the split-brain patients had split-brain many years before been tested. Consequently, their distinct perceptual systems, in each hemisphere, had, indeed, plenty of time to learn how to adapt for the lack of callosal connections (de Haan et al. 2020).

1.5 Unveiling subtle signals and cross-cueing: insights into communication in split-brain patients

Subtle signals may be provided by small movements of the eyes or of the facial muscles of the patient. These movements cannot even be visible to an external observer, but they are capable of encoding, for example, the position of a stimulus for the hemisphere that did not "see" the stimulus. For example, if a patient is shown a stimulus in his/her left visual field (processed by the right hemisphere) and asked to indicate the stimulus position without being able to directly access that information, they might make a subtle movement with their left hand (controlled by the right hemisphere) that encodes the position of the stimulus. This movement may not be visible to an external observer, but it can still provide a cue that indirectly communicates the position of the stimulus to the hemisphere that did not "see" it. Additionally, a cross-cueing mechanism might enable one hemisphere to inform the other about which of a small number of known items had been displayed (de Haan et al. 2020).

Cross-cueing occurs when one hemisphere attempts to communicate with the other hemisphere by utilizing external factors to “cue” the opposite hemisphere. As an example, there is one split-brain behavior which has been observed by Bogen (1990; as cited in, Downey, 2018). This behavior involves patients stabbing themselves with a pencil in their left hand (alien hand phenomenon). This stabbing action sends tactile information to the left hemisphere, which then realizes the left hand is holding a pencil. Specifically, the patient is asked to close their eyes and reach for an object (such as a pencil) placed in front of them using their left hand. The patient then stabs themselves in the hand with the pencil, causing a sharp pain.

Despite the pain, the patient does not let go of the pencil. This is because the right hemisphere (which controls the left hand) does not understand why the left hand is in pain and does not have access to the language centers in the left hemisphere to understand what happens. Instead, the left hemisphere (which controls the right hand) may try to help by reaching over and removing the pencil from the left hand. Nevertheless, the left-hand resists and may even grab onto the right hand in an attempt to prevent it from removing the pencil. This behavior can be seen as evidence of the lack of communication between the two hemispheres in split-brain patients and the separate sense of agency that each hemisphere has over its respective hand.

In summary, there are many hypotheses and observations regarding how the mind may remain unified or not in the case of split-brain patients. One of these observations that has not been mentioned here yet, is the intermanual transfer effect.

CHAPTER 2:

SPLIT-BRAIN AND THE INTERMANUAL TRANSFER EFFECT

2.1 Commissural pathways and interhemispheric communication: insights from callosal lesions

The CC is the main commissural pathway between the two cerebral hemispheres (Friedrich et al. 2020). According to Caillé et al. (2005) callosal fibers are distributed rostro-caudally. Different parts of the CC can be correlated with fibers bridging specific cortical regions. Therefore, fibers from the prefrontal cortex cross in the rostrum and the anterior part of the genu. Fibers connecting the premotor and the supplementary motor areas run through both the genu's middle and posterior parts, as well as along the most rostral part of the body. The middle portions of the body contain fibers connecting primary motor and somatosensory areas (Figure 4). Callosal regions caudally to the posterior part of the body, the isthmus, and the splenium are occupied by fibers connecting the parietal, temporal, and occipital regions respectively (Figure 5).

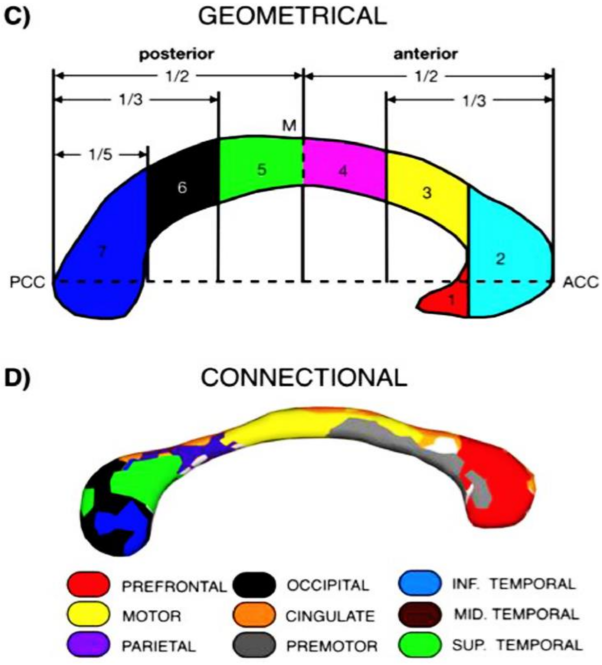

Figure 4. *Parcellations of the CC along the midsection (right view). C) Geometrical division: a parcellation generating seven parcels, by equally diving the midsection, is depicted. ACC: most anterior point of the CC; PCC: most posterior point of the CC; M: middle of the CC. D) Connectional division: the parcellation of the connected cortex, based on diffusion tractography, is depicted (Friedrich et al. 2020).*

It has been mentioned earlier that the complete split-brain eliminates or reduces the ability to transfer information between the cerebral hemispheres. These deficits in communication between the two hemispheres can be demonstrated via restriction of input to a single hemisphere when the non-stimulated hemisphere must respond, or when both hemispheres must respond simultaneously (Caillé et al., 2005). This is especially true for the motor and sensory modalities, which are essentially lateralized and in which the distal parts (hands and feet) are not bilaterally represented, but rely on the commissures for interhemispheric communication (Caillé et al., 2005).

In general, however, many studies have failed to link the location of a callosal lesion to specific signs of interhemispheric disconnection (Caillé et al., 2005). In accordance with the results of most studies (e.g., Gazzaniga 1995; Provinciali et al. 1990), only a complete split-brain, including the posterior third of the CC, particularly the splenium, results in clear signs of hemispheric disconnection, whereas a section of the anterior CC does not result in any long-term interhemispheric deficits (Caillé et al., 2005). There were, nonetheless, short-term deficits. As cited by Caillé et al. (2005), Provinciali et al. (1990) found *"only mild and transient linguistic, praxic, and somesthetic disturbances in patients who underwent anterior callosotomy"*. These short-term symptoms are believed to be associated with the surgery process and the degree of damage that existed before the surgery, rather than to hemispheric disconnection (Caillé et al. 2005).

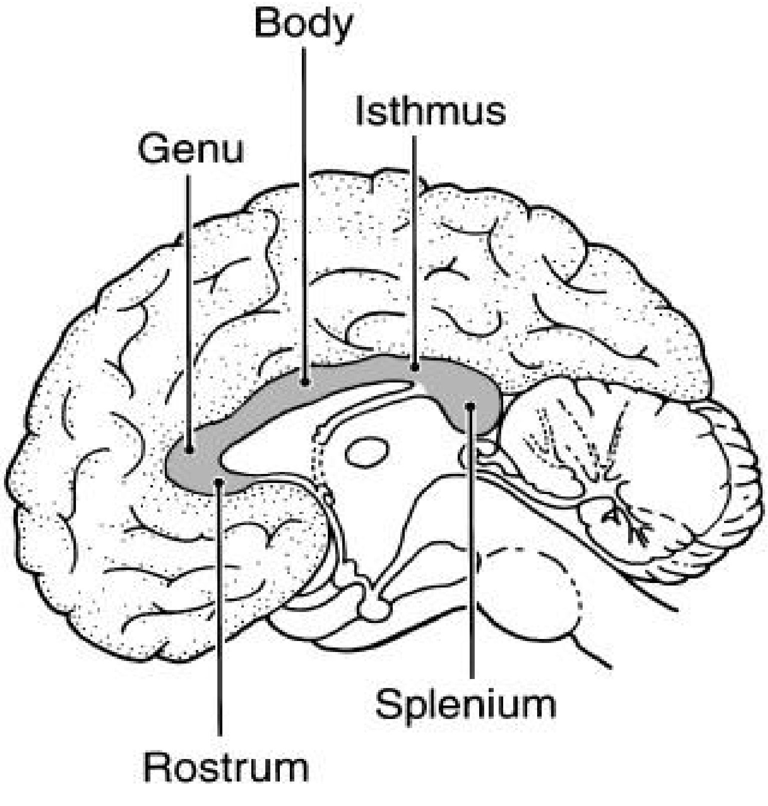

Figure 5. *Sagittal section of the brain with major divisions of the CC labeled (Baynes, 2002).*

In contrast, these largely negative findings are surprising considering the neuroanatomical data obtained from studies in monkeys and human participants, which have indicated that the interruption of specific portions of the anterior callosum results in distinct disconnection deficits in the motor and somatosensory modalities (Caillé et al. 2005). Nonetheless, as highlighted by Caillé et al. (2005), most disconnection deficits, after callosal section, are very difficult to be observed and they can only be detected under highly controlled experimental conditions. Thus, it appears that the effects of callosal sectioning on interhemispheric communication may be more complex than previously thought and may depend both on the specific location and the extent of the lesion, as well as on individual differences in brain structure and function.

As a result, it is necessary to use tasks that are sensitive enough to detect the abovementioned types of deficits. In this context, several recent studies (Caillé et al., 2005), by using a broader range of tasks, have shown the presence of interhemispheric disconnection symptoms following partial split-brain involving only anterior portions of the CC (Caillé et al. 2005). For example, lesions to the anterior third of the CC have been shown to impair interhemispheric motor integration, whereas lesions of the CC`s body have been shown to impair somesthetic transfer (Caillé et al. 2005). Indeed, many of the previous studies were exclusively focused either on sensory functions (somesthetic and/or visual) or on motor functions (Caillé et al. 2005), without elaborating on integration and transfer.

2.2 Motor and Somesthetic Tasks for Assessing Intermanual Transfer Deficit

The term *intermanual transfer deficit* refers to the impaired ability of one hand to learn and perform a motor task after the same task has been learned by the other hand. There are three motor tasks and three somesthetic tasks used by Caillé et al. (2005) that are, among others, sensitive enough to detect signs of interhemispheric disconnection.

The motor tasks are:

1. *The Purdue Pegboard Test* (Figure 6). This test measures primary motor integration and synchronous bimanual coordination. The participant must quickly place small metal pegs of different shapes in the respective holes laid out in two vertical rows. The task is completed first with the preferred hand, then with the non-preferred hand, and finally with both hands at the same time. The

score is determined by the number of pegs correctly placed in 30 seconds in each condition (Caillé et al., 2005).

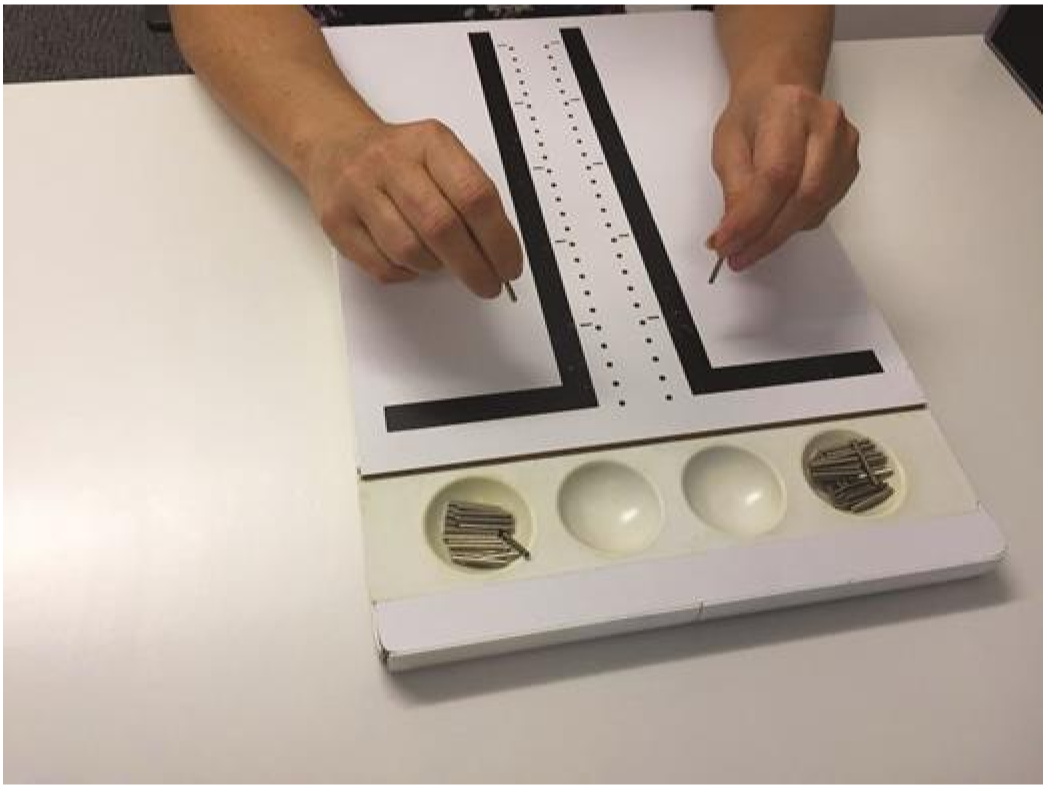

Figure 6. *The Purdue Pegboard Test (Lawson, 2019).*

2. *The Preilowski's test* (Figure 7). This test assesses asynchronous motor coordination and necessitates extensive feedback from both cerebral hemispheres (Caillé et al. 2005). This test was administered by Caillé et al. using a computerized version. Participants drew a line on an x-y plotter connected to an IBM-PC microcomputer that matched a sample line as closely as possible. Afterwards, participants had to control the x axis by rotating one knob with their index and thumb of one hand and the y axis with their index and thumb of the other hand to achieve accurate performance. Each hand operates independently, requiring coordination between the two hemispheres of the brain. The relative

speed at which participants turn each knob determines the angle and position of the line they draw in relation to the sample line. This means that the speed and coordination of hand movements play a role in accurately reproducing the line. Each condition was composed of five trials per line (left and right), for a total of 30 trials; the time for execution was limitless, meaning there is no time constraint placed on participants. (Caillé et al. 2005).

normal control　　　　patient 4

patient 2　　　　patient 1

patient 3 pre-surgery　　　　patient 3 post-surgery

Figure 7. The Preilowski's test. Typical examples of the performance of split-brain patients and one normal control. For Patient 3, both pre- and postoperative data are presented. Three patients (1–3) manifested a deficit on this task. Typically, they produced an impaired design, which looked as a staircase(Caillé et al., 2005).

3. *The Thurstone's uni- and bimanual performance test* (Figure 8). This specific test requires motor coordination, motor planning, and mental flexibility, which are all associated with prefrontal activity (Caillé et al. 2005). In the unimanual condition of this task, the participant must tap, as quickly as possible, with a stylus, on four numbered sectors located on one of two metal plates in ascending numeric order. The stylus is linked to a counter that records each contact with the plate (Caillé et al. 2005). Within 30 seconds, the participant's accurate contacts (taps) are counted. In the unimanual condition, the preferred hand is used for two consecutive trials, followed by the non-preferred hand (Caillé et al. 2005). In the bimanual condition, the participant must simultaneously tap on two numbered plates, while holding a stylus in each hand (Caillé et al. 2005). The fact that the numbers on the sectors on the two plates are not in the same place, in space, adds another layer of difficulty to this situation and requires asynchronous hand movements. The total number of simultaneous, correctly timed taps made in 30 seconds over the course of two trials determines the final score (Caillé et al. 2005).

Figure 8. *The Thurstone's uni- and bimanual performance test. (Hernandez et al., 2002).*

The examples below can help understand better the nature of the tasks involved:

- Unimanual task examples:
    I. Tapping: participants may be asked to tap their fingers individually or in a specific pattern on a designated surface.
    II. Buttoning: participants could be required to button or unbutton a series of buttons using only one hand.
    III. Writing or drawing: participants may be asked to write a sentence or draw a simple figure using only one hand.
    IV. Pegboard Manipulation: Participants might be tasked with inserting small pegs into holes on a pegboard using only one hand.

- Bimanual task examples:
    1. Archery: participants could be asked to hold and draw a bowstring with one hand while aiming and releasing the arrow with the other hand.
    2. Folding clothes: participants may be required to fold a piece of clothing using both hands simultaneously, with each hand performing a specific folding action.
    3. Typing: participants could be asked to type a given sentence on a keyboard using both hands simultaneously, with each hand responsible for specific keys.
    4. Playing piano: Participants may be tasked with playing a simple melody on a piano, where each hand plays different keys simultaneously.

These examples represent common tasks that require different levels of motor coordination, ranging from simple finger movements to more complex actions involving the manipulation of objects.

The somesthetic tasks are:

1. *The somesthetic interhemispheric transmission time (Caillé et al., 2005).* The stimuli are short bursts of air lasting 150 milliseconds. They are delivered in a random order to the center of the palm, via tubes connected to a gas tank. Participants are instructed to respond as soon as the stimulus appears, by pressing one of two response keys with their index finger. On this task, the interhemispheric transmission time (IHTT) is calculated. Responses to stimuli processed in the same hemisphere (uncrossed or intrahemispheric condition) are faster than responses to stimuli received in the opposite hemisphere (crossed or interhemispheric condition). The IHTT is then calculated by subtracting intrahemispheric response times from interhemispheric response times.
2. *The tactile localization task (Caillé et al., 2005).* This task, which requires the transfer of a tactile stimulus between the hands, has been shown to be particularly sensitive to disconnection deficits. It is frequently performed at the bedside of patients who have had split-brain to assess the extent of deficit and follow the path of recovery. On this test, both simple and serial finger stimulations are used. A screen obscures the participants' hands, which rest on a table with palms exposed and fingers slightly extended. In this experiment, both simple and serial finger stimulations were used. The experimenter uses the point of a sharpened pencil to make a brief, light touch on the distal segment of one or two of the participants' fingers. In the tactile localization task, participants were assigned to two conditions: intramanual and intermanual. In the intramanual condition, participants were instructed to designate the locus of stimulation using the thumb of the stimulated hand. So, if the stimulation was applied to the participant's right hand, they would

use their right thumb to indicate the exact spot where they felt the stimulation. Conversely, in the intermanual condition, participants were asked to designate the same locus on the corresponding finger(s) of the non-stimulated hand using the thumb of this latter hand. For example, if the stimulation was applied to their right hand, they would use their left thumb to indicate, on the right hand, the corresponding location on the finger(s) touched on their left hand. Prior to the actual testing, participants engaged in practice trials, which were conducted in full view, allowing them to observe their hands and the areas being stimulated. This practice session aimed to ensure that participants could successfully complete the task with accuracy.

3. *The intra- and intermanual comparisons of shapes.* This task is frequently used in split-brain research. The participant must decide whether two stimuli, presented in each hand out of view, are the same or different. The stimuli are three-dimensional wooden shapes (e.g., star, square) measuring, on average, 5 X 5 X 2 cm. In the intermanual condition, both hands touched the stimuli simultaneously. In the intramanual conditions, each hand explored the two shapes sequentially. In each of the three conditions, twenty pairs of stimuli (i.e., ten identical pairs and ten different pairs), were presented randomly: intermanual; intermanual right hand; and intramanual left hand. For each trial, the participant's verbal responses (match or no-match) and response times were recorded.

On the tasks described above, not only response accuracy was measured, but also the response time, in patients in whom different portions of the anterior CC (genu and/or body) were sectioned in a surgical approach (Caillé et al., 2005). The reason is that another limitation of previous studies on interhemispheric coordination, is that performance was measured solely in terms of response accuracy, without incorporating measures of response times. The difference in response times between patients during intrahemispheric and interhemispheric processing is assumed to reflect the interhemispheric transmission time (i.e., the extra time required for information to reach the opposite hemisphere via the CC).

If the CC is not available, patients either cannot perform the interhemispheric task correctly or they use alternative routes or mechanisms of transfer that are thought to be more time consuming than the direct callosal route. In fact, as cited by Caillé et al. (2005), according to Jeeves et al. (1986), experimental paradigms that are limited to measure only response accuracy may miss more subtle performance decrements that become apparent only when response time is considered.

Through the three motor tasks and the three somesthetic tasks used by Caillé et al. (2005), important findings were reported. On the Purdue Pegboard Test, each patient's performance on the number of pegs that they were able to place in 30 minutes was compared to normative data taken from the test manual. Two patients had a deficit in the bimanual condition of the test because their scores were below the cutoff score, even though all four patients received scores that were within normal limits in the unimanual conditions (preferred hand and nonpreferred hand).

In the Preilowski Task, by looking at the lines that the patients drew in each of the 30 trials, performance was qualitatively assessed. Figure 7 presents the performance of the patients and that of one control participant. It was also possible to assess the performance of Patient 3, before and after surgery (extension of the callosal section: middle and posterior genu, anterior body). The ability to perform this task was impaired in three out of the four patients (Patients 1-3), who had trouble coordinate their hands to work together well enough to draw a straight line. Indeed, the produced line usually looked like a staircase. Moreover, a deficit on this task was not present before the operation, but it was found in Patient 3's postoperative performance. As mentioned by Caillé et al. (2005), preoperative practice with this task was ineffective for the patient. Furthermore, on the Thurstone’s Uni- and Bimanual Performance Test, even though one patient (Patient 1) performed worse in the bimanual condition, the performance of the remaining patients was intact.

In summary, on the motor tasks, three patients (Patients 1-3) showed deficits in at least one of the functions on the motor coordination tasks. The middle section of the genu, which is the point where the fibers bridging the premotor and supplementary motor areas in both hemispheres cross in the CC, was affected in all these patients. These parts of the CC were only spared in patient 4, who, therefore, did not show any deficits on these tasks (Caillé et al. 2005).

On the somesthetic tasks, only one patient (Patient 4) showed signs of a disconnection deficit. Indeed, Patient's 4 somesthetic interhemispheric transmission time was abnormally long, and he performed poorly on the tactile localization task. These two activities require basic tactile perception (detection and localization of tactile stimuli). By contrast, this patient performed normally on the interhemispheric comparison task, which calls for more sophisticated perceptual abilities (discrimination of tactile stimuli).

Patient's 4 callosal section affected the midbody. The only section in the sample that was compatible with a break in the transfer between primary somesthetic areas was the section that was the furthest posterior. This posterior section is associated with the transfer of information between primary somesthetic areas of the brain. The interruption in this specific callosal section resulted in the observed deficits in tactile localization and prolonged IHTT for Patient 4. The other patients, in whom this callosal portion was spared, did not show these deficits.

Caillé et al. (2005) concluded that anterior callosal sections could cause deficits in motor behavior and transfer of somesthetic information. Caillé et al. (2005) also suggested that these deficits can be linked to lesions of specific portions of the anterior CC. The results tend to support on a behavioral level, the findings regarding the antero-posterior topography of anterior callosal fibers revealed in studies with non-human animals.

According to Caillé et al. (2005): *"bimanual coordination seems to be mediated primarily through callosal fibers crossing in middle portion of the genu, whereas asynchronous bimanual coordination requiring motor planning and mental flexibility seem to cross anteriorly to those fibers"*. In addition, as the complexity of the motor task increases and more extensive motor planning and control is required, it is possible to assume that interhemispheric information transfer and integration occurs in more anteriorly located portions of the CC genu (Caillé et al. 2005).

More posterior sections, including the anterior portion of the CC body, appear to abolish interhemispheric transfer of simple somesthetic information (touch perception), but not tactile discrimination (intermanual shape comparisons), which appears to be transferred through the caudal region of the CC body (Caillé et al. 2005). Moreover, the deficits are consistent with the antero-posterior topography of anterior callosal fibers, highlighting the functional importance of these fibers in bilateral integration of motor functions and somesthetic information (Caillé et al. 2005).

2.3 Intermanual interactions in split-brain patients: exploring the role of rhythmic and discrete movements in bimanual coordination

There are some very interesting studies exploring the intermanual transfer effect in split-brain research. For instance, Sternad et al. (2007) explored the intermanual interactions during initiation and production of rhythmic and discrete movements in individuals lacking the CC. According to Sternad et al. there are significant contrasts between these two types of actions (i.e., rhythmic vs. discrete movements).

Rhythmic movements, on the one hand, are typically continuous. Furthermore, they have an invariant period and amplitude, and they are created in extrinsic space without explicit targets; for example: moving in a structure of patterns in time or the pattern produced by emphasis and duration of notes in music. *Discrete movements*, on the other hand, have clearly defined initiation and termination landmarks. According to Cordo et al. (1995) an example of discrete movement is *"...defined as a movement with a single goal that involves a series of overlapping joint rotations. Reaching-and-grasping and throwing are examples of discrete movement sequences"*.

It has been claimed that rhythmic and discrete movements are two basic units of action, and that control operations differ depending on whether the movements are produced in a smooth continuous manner or by discrete salient events. Neuroimaging and neuropsychological research have yielded evidence that supports both hypotheses (Sternad et al., 2007).

Rhythmic and discrete movements are necessary for many tasks. As mentioned by Sternad et al. (2007), we can use one hand to stir the soup, while using the other hand to pick up a saltshaker, actions which fall under the category of bimanual actions. It is logical to assume that the different actions of the two hands would be relatively independent or they would exhibit attenuated forms of coupling compared to conditions in which both hands produce either rhythmic movements or discrete movements. As reported by Sternad et al., if the control of discrete and rhythmic movements is performed by distinct neural mechanisms, one should wonder how the human brain produces actions that combine discrete and rhythmic components.

In this context, individuals without the CC provide an intriguing chance to investigate bimanual coordination, because of the lack of direct connectivity between the brain hemispheres. Kennerley et al. (2002; as cited in Sternad et al. 2007) tested three split-brain patients on a bimanual circle drawing task (e.g., both drawing circles or both tapping). For these tasks, the focus is on the limitations that occur when a second movement is added to a continuing rhythmic movement. Moreover, the main comparison is between instances where the secondary movement is rhythmic and those where it consists of a quick, distinct movement. Under such conditions, spatiotemporal coupling was considerably reduced. In fact, the two limbs moved at separate rates in some instances. Because circle drawing requires multi-joint coordination, a second experiment was carried out in which all the movements featured rhythmic finger movements.

In the second experiment (Kennerley et al. 2002), the performance of rhythmic movements with smooth transitions between flexion and extension was compared to intermittent or discrete-like movements with a pause before each flexion phase. This seemingly little distinction resulted in a significant difference in performance: coupling was significantly more prominent in the discrete condition than in the continuous one. From this finding is possible to conclude that the processes underlying spatio-temporal coupling observed during continuous movements interact via signals sent across the CC. In contrast, discrete movements that are either produced alone or as part of a rhythmic pattern are associated with the subcortical locus for spatio-temporal coupling.

The term *"subcortical locus"* refers to a specific region or area within the subcortical structures of the brain. The subcortical structures are located beneath the cerebral cortex and play a vital role in various functions, including movement control, emotion regulation, and sensory processing; these structures may include the basal nuclei, the cerebellum, the thalamus, etcetera. It is important to mention that in the context of discrete movements and rhythmic patterns, the CC may not be necessary for coordination. This is because these movements can be primarily controlled and coordinated within each hemisphere, utilizing the structures mentioned above. Thus, in the absence of the CC, these subcortical connections could offer a route via which signals to the two hands could communicate (Sternad et al. 2007).

Typically, in previous investigations with split-brain patients, the task utilized required both hands to do similar movements and that were started at the same time (Sternad et al. 2007). As mentioned before, three acallosal patients were tested on bimanual tasks. For these tasks, the emphasis was on the limitations that occur when a second movement is added to an ongoing rhythmic movement. Moreover, the main comparison was between instances where the secondary movement was also rhythmic or when it was a quick, discrete movement. It is important to note that in this study two of the acallosal patients were split-brain patients and one was a patient with callosal agenesis.

Figure 9 shows the experimental setup and coordinate definitions for data analysis. As reported by Sternad et al. (2007), the participants sat at a table, with both their elbows resting on the table surface. The movements were carried out by flexing and extending the elbow joint. For data analysis, the movement data was projected onto the best fitting line that described the main movement orientation.

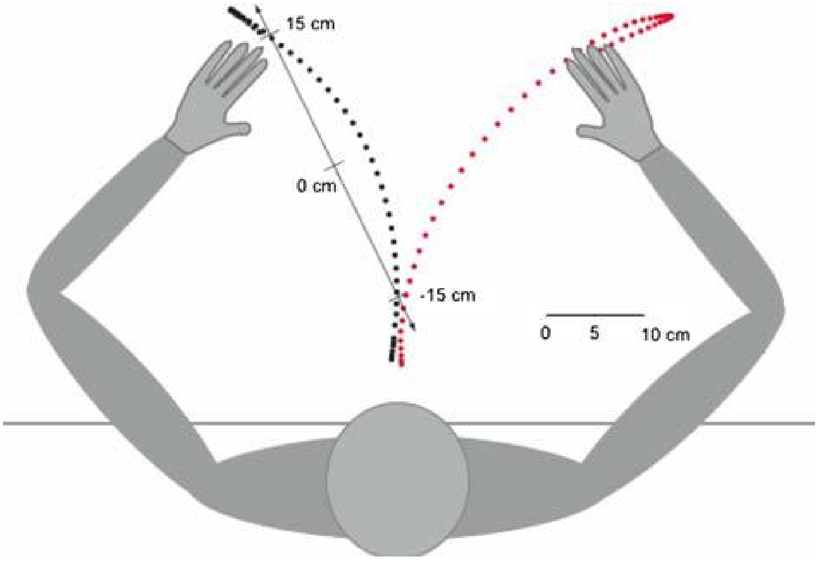

Figure 9. *Experimental setup and coordinate definitions for the data analysis. The participants sat at a table, with both elbows resting on the table surface. Movements were executed by flexion and extension about the elbow joint. For data analysis, the movement data was projected onto the best fitting line that describes the main movement orientation (Sternad et al. 2007).*

Figure 10 shows a segment of the time series of three exemplary trials with rhythmic and discrete initiation (Sternad et al. 2007). In segment **A,** the split-brain patient JW performed a rhythmic initiation trial. The rhythmic base movement cycles produced by the left arm are shown in the upper trajectory, whereas the secondary movement cycles produced by the right arm are shown in the lower trajectory. Vertical lines indicate the imperative signal and the moment when the secondary movement begun. The vertical dotted lines during the bimanual movement epoch were aligned to peak flexion of the left arm and illustrate the wandering relative phase between the two arms.

On this trial, the metronome pacing period was 300 ms (Sternad et al. 2007). It is possible to observe that before and after the imperative signal, the participant's movement period was a little bit slower than the target pace. Segment **B** shows the discrete initiation trial of the same acallosal patient and segment **C** shows the unsuccessful trial where the acallosal patient failed to perform the instructed discrete movement and to simultaneously stop the continuous movement (Sternad et al., 2007).

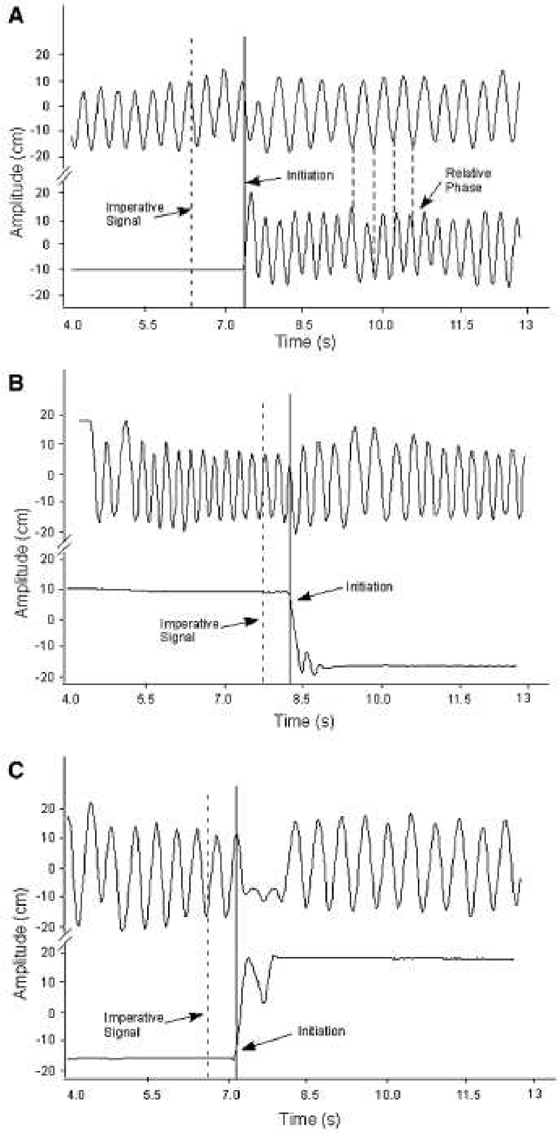

Figure 10*. A segment of the time series of three exemplary trials with rhythmic and discrete initiation (Sternad et al., 2007).*

Figures 10a and 10b illustrate that, although the initiation phase and period of the secondary rhythmic and discrete movements are independent of the base movement, the base movement still experiences a brief perturbation at the time of the onset of the secondary movement. Once established, the two rhythmic movements do not show a stable phase relation, oscillating at different periods. The base oscillations change in amplitude and period after the start of a discrete movement: the periods get slower, and the amplitudes get larger (Sternad et al., 2007).

In summary, when starting a secondary rhythmic movement against the backdrop of another rhythmic movement, healthy participants exhibited strong spatiotemporal coupling (Sternad et al. 2007). Phase entrainment was visible at the point of movement initiation, proving coupling existed prior to the secondary movement's preparation. When a discrete movement was started, there was no coupling in healthy adults. The acallosal patients, by contrast, did not exhibit this phase entrainment at movement initiation for either discrete or rhythmic secondary movements. Furthermore, during the bimanual phase of the rhythmic task, the acallosal patients showed attenuated coupling, although the degree of this uncoupling varied between the three patients.

On the one hand, the perturbation effect was reduced for healthy participants when the secondary task was rhythmic, in a way that the movements of the two arms could be integrated into a unified coordination pattern (Sternad et al. 2007). On the other hand, for acallosal patients, the perturbation effect was independent of whether the secondary movement was discrete or rhythmic. This finding is consistent with the hypothesis that for the acallosal patients, the movement patterns associated with each hand are independent (Sternad et al. 2007).

2.4 Results: Sternad et al. (2007) study

According to Sternad et al. (2007), the findings from the control and acallosal groups suggest that the spatiotemporal constraints observed during bimanual rhythmic movements are highly dependent on communication across the CC. Although the findings have pointed to a cortical location for these interactions, the necessary neural regions remain unknown. Interestingly, neuroimaging studies of bimanual interlimb coupling have revealed premotor and posterior parietal cortex activation during rhythmic movements (Wenderoth et al. 2004, 2005). Similarly, interference that occurs during the planning and execution of spatially conflicting discrete reaching movements activates the parietal cortex's posterior areas. In addition, in a patient undergoing a two-stage callosotomy procedure, spatial uncoupling was not apparent until the second, more posterior resection, was performed (Eliassen et al. 1999, 2000). Hence, Sternad et al. have hypothesized that intermanual constraints in symmetric actions are caused by activation and transcallosal interactions supported by the parietal lobes.

The lack of coupling between the two limbs when the secondary movement involved a discrete movement in both the healthy controls and the acallosal patients, has suggested that the control signals for rhythmic and discrete movements have little confluence. Neuroimaging studies indicating differential engagement of cortical and subcortical areas for these two classes of movements have provided additional support for this hypothesis (Sternad et al., 2007).

It is important to highlight the difference in rhythmic and discrete movements between individuals lacking a CC because of agenesis or because of callosotomy. As mentioned before, continuous bimanual coupling was severely damaged in the callosotomy patients. That said, the performance of patients with callosal agenesis was different from what was seen in the other participants (Sternad et al., 2007). The patient with callosal agenesis did not use different frequencies for the two rhythmic movements, unlike the split-brain patients. These findings show that temporal coupling during continuous movements can develop in people who have never had a CC. This coupling could occur if, for example, a single hemisphere controls bimanual actions or if an expanded anterior commissure is functionally recruited (Sternad et al., 2007).

It is important to note, however, that the performance of the patients with callosal agenesis differs significantly from that of the healthy controls, both in terms of the onset of the rhythmic movement and the adopted phase. Thus, while split-brain patients and individuals with callosal agenesis both experience challenges in interhemispheric coupling and bimanual rhythmic movements, there are differences between these groups. Split-brain patients exhibit compromised bimanual coupling, while individuals with callosal agenesis can establish some temporal coordination. Nevertheless, both groups demonstrate limitations compared to healthy controls, emphasizing the crucial role of the CC in facilitating efficient communication and coordination between the hemispheres during bimanual movements (Sternad et al., 2007).

In conclusion, interhemispheric coupling, and the role of the CC in a complex asymmetric bimanual task were investigated further by Sternad et al. (2007) and important findings were reported. In their experiment it was possible to affirm that secondary movement initiation is mediated by callosal connections and that individuals without the CC would show spatiotemporal independence of the two hands. Furthermore, perturbations exerted by secondary movement appear to be mediated by subcortical structures. In addition, spatiotemporal coupling in bimanual rhythmic movements is significantly impaired in the absence of the CC and the differences between tasks with discrete and rhythmic components in healthy controls are consistent with the hypothesis that discrete and rhythmic movements are two distinct movement types.

2.5 The contribution of posterior CC to interhemispheric tactile transfer: insights from neuropsychological assessment

The results of the first intermanual transfer study (Sternad et al., 2007) highlighted the importance in the contribution of the anterior part of the CC in the transfer of information between the two cerebral hemispheres. Nevertheless, it is also important to highlight the importance of the posterior part of the CC. One study that focused on this part of the CC was done by Fabri et al. (2005) to explore the contribution of the posterior CC to the interhemispheric transfer of tactile information. Fabri et al. examined the performance of six patients with varying degrees of callosal resection on three neuropsychological tests designed to assess the interhemispheric transfer of tactile information.

It's important to highlight that the anterior fibers that connect the frontal lobes transfer motor information, whereas the posterior fibers that connect the temporal, parietal, and occipital lobes transfer somatosensory (posterior midbody), auditory (isthmus), and visual (splenium) information (Fabri et al. 2005). As a result, patients who have lesions in different areas and of varying sizes within the CC are expected to display different signs/symptoms of disconnection. These signs/symptoms will depend on the specific callosal region that has been damaged.

According to Fabri et al. (2005), a previous functional MRI (fMRI) study (Fabri et al. 1999), on split-brain patients revealed somatosensory cortical activation by unilateral tactile stimulation of a hand only in the contralateral hemisphere of patients with resections including the posterior part of the callosal body. Patients with an intact posterior callosal body (PCB), by contrast, showed activation of somatosensory areas in both hemispheres, just like healthy control participants. Among the patients from the previous functional MRI study, who took the Tactile Naming Test (TNT; see below), those with an intact PCB performed exceptionally well. All these findings have suggested that both ipsilateral hemispheric activation and good TNT scores require the integrity of the interhemispheric fibers conveying tactile information. These fibers run through the posterior part of the PCB (Fabri et al. 2005).

To validate and supplement these findings with information on interhemispheric tactile transfer, Fabri et al. (2005) administered three specific neuropsychological tests to six patients who had been studied with fMRI by Fabri et al. (1999). The extent of the callosal resection and, more importantly, the fMRI cortical activation, evoked in the parietal operculum (PO) and the post-central gyrus (PCG) by ipsilateral hand tactile stimulation, were correlated with the performance of the patients. These three specific neuropsychological tests were done 4-6 years after split-brain and were conducted in a quiet room, with the patients seated, while blindfolded, in front of the experimenter. Objects were presented out of sight and on a soft board to avoid possible noise cross-cueing. The number of stimulus alternatives was used to calculate chance-level performance (Fabri et al. 2005).

The three specific neuropsychological tests to evaluate the interhemispheric transfer of somatosensory information were (Fabri et al., 2005):

1. *The Tactile Naming Test (TNT).* This test assesses the ability to name tactile stimuli that are only presented to the right hemisphere (left hand). Fifteen common and easily manipulable objects that had never been shown to the patients before were used. Each object was shown twice in random order, once to the left and once to the right hand. The researchers considered successful performance as achieving more than 80% correct answers. This high accuracy indicated evidence of interhemispheric transfer in the tactile modality, suggesting that tactile information is effectively transferred from the right hemisphere to the left hemisphere, which is typically responsible for language processing and expression. Poor performance, by contrast, was interpreted as evidence for impaired information transfer.
2. *The Same–Different Recognition Test.* This test determines whether the patient can compare tactile stimuli presented to each hemisphere separately. Patients were asked to manually explore two common objects held in each hand at the same time and to say whether these objects were identical or different. This task necessitates the

transfer of tactile information across the cerebral hemispheres. Twenty physically identical or different objects were randomly presented to the participants. Also, in this case, good performance indicated transfer and poor performance did not. Chance level performance was interpreted to mean that the inputs from the two hands went to different hemispheres and that there was no communication between the hemispheres. In other words, when the participants were only able to guess correctly between the two stimulus alternatives (same or different), it indicated that the inputs from the two hands were processed in different hemispheres, with no effective communication between them. (50% of correct answers: two stimulus alternatives, i.e., same, or different).

3. *The Tactile Finger Localization Test.* This test evaluates the person’s capacity to localize tactile stimuli on the proximal or distal phalanx of one hand's fingers and to transfer that knowledge to the other hand. The examiner lightly stimulated one of eight randomly chosen points on each hand (proximal or distal volar surface of fingers 2–5, three stimulations per point, 24 random trials per hand). The person was instructed to press each stimulated point with the thumb of the same hand (intramanual task) or the thumb of the opposing hand on the corresponding point (intermanual task). In the intramanual task, the person uses the same hand that received the stimulation to locate and press the corresponding point. In the intermanual task, the person uses the thumb of the opposing hand to press the corresponding point.

The study included six patients (Figure 11), aged 24-38 years, who had undergone complete or partial CC resection for drug-resistant epilepsy (Fabri et al. 2005). Complete CC resection was performed on three patients (D.D.C., D.D.V., and R.N.). The entire splenium was intact in three other patients (A.P., P.M., and L.P.). In one of them (L.P), the PCB was spared as well (Fabri et al. 2005).

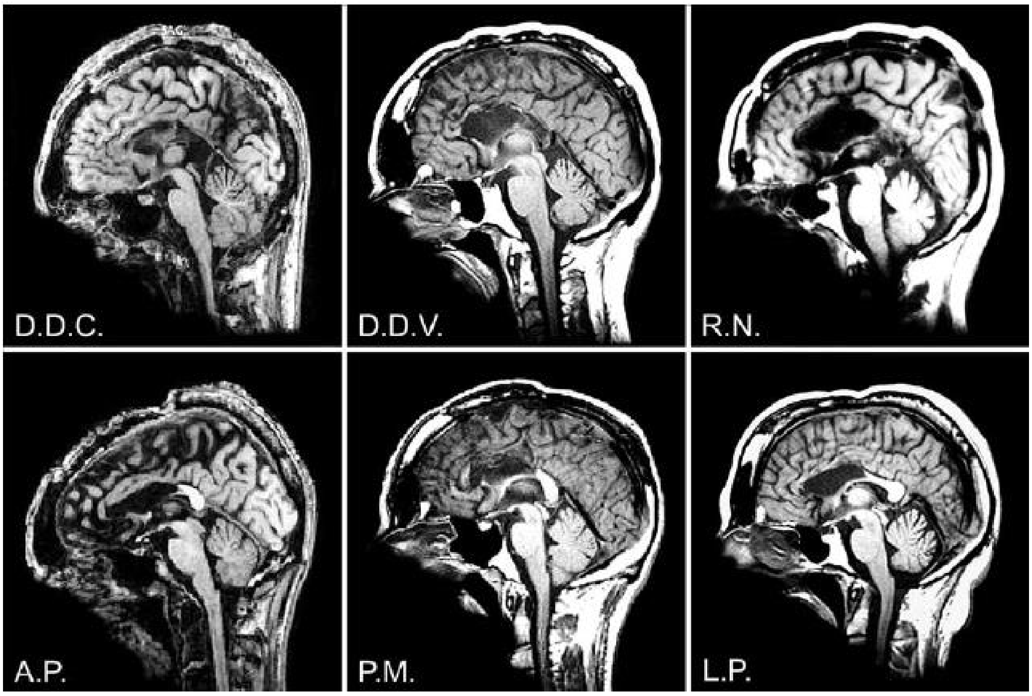

Figure 11. *MR images of midsagittal brain slices obtained from T1-weighted spin-echo sequences showing the extent of callosal resection in 6 patients (Fabri et al. 2005).*

According to Fabri et al. (2005), because preoperative MR scans were not available, the extent of the intact surface was calculated by comparing the area of spared midsagittal callosal surface, in each patient, to the area of spared midsagittal callosal surface measured in the MR scans of 20 healthy control patients (unpublished data). Furthermore, as determined by the Edinburgh handedness inventory (Oldfield RC. 1971), all patients were right-handed.

2.6 Results: Fabri et al. 2005 Study

The results of Fabbri et al. (2005) were:

- On the TNT, the patients with complete split-brain (i.e., D.D.C., D.D.V., and R.N.) performed well with their right hand (mean: 93% correct responses vs. 99% control group), but poorly with their left (mean: 30% correct responses vs. 99% control group). It is important to point out, that the left-hand performances of patients with complete split-brain differed significantly from that of patients with partial split-brain and that of the healthy control group. By contrast, the right-hand performance did not differ among the three groups. The partial split-brain patients (A.P., L.P. and P.M.) performed well with both hands (mean: 93% correct answers for the right hand, 95% correct responses for the left; control score: 99% with both hands).
- On the Same–Different Recognition Test, the performance of the complete split-brain patients was highly variable, with correct responses ranging from 50% to 100%. Two of the three patients with complete split-brain (D.D.V. and R.N.) received scores at the chance level (55% and 50% correct, respectively, compared to 99% correct in the healthy control group) and failed the TNT with the left hand. Surprisingly, despite his complete split-brain, the third patient (D.D.C.) performed well on this test. The partial split-brain patients gave 95-100% correct answers (mean score of controls: 99%), showing an intact exchange of interhemispheric tactile information.
- On the Tactile Finger Localization Test, the complete split-brain patients, in the intramanual task, gave 100% correct answers with both hands (control's score 100%). In the intermanual task, correct responses were 78-93% with the right hand and 67-90% with the left (95% and 96% correct, respectively, of the control group. Interestingly, among the complete split-brain patients, the proportion of correct responses to right hand stimulation (resulting in a left-hand response) was generally higher, with a mean of 84%, compared to the correct responses to left hand stimulation

(resulting in a right-hand response), which had a mean of 76%. This suggested that the transfer of sensory information from the left hemisphere to the right hemisphere was more effective than in the opposite direction. On the other hand, the partial split-brain patients performed well with both hands in both the intramanual and intermanual tests. Their individual correct answers ranged from 77% to 100%, which were comparable to the mean values of the control group (100% for intramanual, 96% for intermanual right hand, and 95% for intermanual left hand stimulation).

In conclusion, these tests confirm that the PCB is the "tactual" channel and provides additional proof that interhemispheric transfer in the tactile modality is likely mediated by the fibers running in the posterior part of the CC body (Fabri et al. 2005).

2.7 Interhemispheric transfer of implicit memory in acallosal individuals: insights from perceptual priming and visuoperceptual skill learning

Finally, another important study was conducted by Forget et al. (2009) to investigate interhemispheric transfer in individuals with callosal agenesis. More precisely, the researchers aimed to investigate whether perceptual priming, a form of implicit memory, can be transferred across the hemispheres in individuals with acallosal brains. Perceptual priming refers to a phenomenon in which prior exposure to a stimulus enhances the processing and recognition of that stimulus when encountered again. It is a form of implicit memory, meaning that it operates unconsciously and without deliberate effort.

According to Forget et al. (2009), individuals with callosal agenesis and early operated split-brain patients do not show disconnection signs in tasks requiring explicit or declarative responses. They can accurately compare stimuli in each hand and perform well on lateralized recognition tasks. Nevertheless, they exhibit impairments on tasks involving interdependent motor control, bilateral motor coordination, and the transfer of visuomotor learning tasks (Forget et al. 2009).

It has been suggested that the limited compensation observed in these cases may be due to the restricted interhemispheric transfer of implicit or unconscious processes, with subcortical transfer of information likely limited to explicit knowledge. This dissociation between implicit and explicit memory in split-brain and callosal agenesis individuals requires further investigation. According to Forget et al. (2009), different memory processes, such as declarative and nondeclarative memory, involve distinct neuronal networks. Declarative memory relies on processing in the posterior neocortex and frontal neocortex, while nondeclarative memory, including procedural memory and priming, operates through independent systems.

Furthermore, the fragmented picture task, developed by Snodgrass et al. (1987; as cited by Forget et al., 2009), allows for the assessment of two types of implicit memory processes: perceptual priming and visuoperceptual skill learning. These tasks measure the learning of the physical configuration of stimuli (perceptual priming) and the improved performance on the task itself through practice (visuoperceptual skill learning).

The study of Forget et al. (2009) aimed to test Berlucchi's hypothesis (Berlucchi et al. 1995), suggesting that interhemispheric transmission of implicit information may be absent in cases of callosal agenesis. To do so, interhemispheric transfer was assessed in two distinct nondeclarative tasks: visuoperceptual skill learning and perceptual priming, in patients who had early disruptions or congenital absence of interhemispheric communication.

These patients provide an opportunity to explore the contribution of cortical systems involved in these forms of implicit memory (Forget et al. 2009). It is important to mention that a modified version of the fragmented pictures task was used, excluding verbal responses to avoid bilateral explicit conscious awareness and potential facilitation of transfer. Manual responses were employed, except for one acallosal patient who responded verbally, allowing for observations on the impact of verbal labeling on transfer.

On the basis of previous findings, it was expected that early split-brain and acallosal patients would show perceptual priming and visuoperceptual skill learning in one hemisphere. By contrast, these patients would show difficulties in transferring this learning to the other hemisphere. Furthermore, by considering the significant role of the right hemisphere in visuoperceptual abilities, the presence of hemispheric asymmetry in these processes was also evaluated (Forget et al. 2009).

The procedure was as follows: participants sat in a quiet room, facing the computer screen and were given instructions to fixate their gaze on a central point while the stimuli were presented, with each presentation lasting no more than 15 seconds (Figure 12). The presentation started with the most fragmented form of the picture. If a participant couldn't correctly identify the object or animal in the highly degraded form, they pressed the right key, and the computer moved on to the next level of fragmentation, which was slightly less fragmented or more complete. This process continued until the participant correctly recognized the image or until the image was presented in its unfragmented form.

Once the participant identified the item, the computer recorded the identification threshold for that particular picture. If an item was completely unrecognized, it was recorded as level 9. Stimulus identification was assessed in two modalities: manual versus verbal. In the manual modality, participants pressed the left key to indicate recognition without verbalizing the identification. In the verbal modality, participants had to correctly name the fragmented picture before pressing the left key.

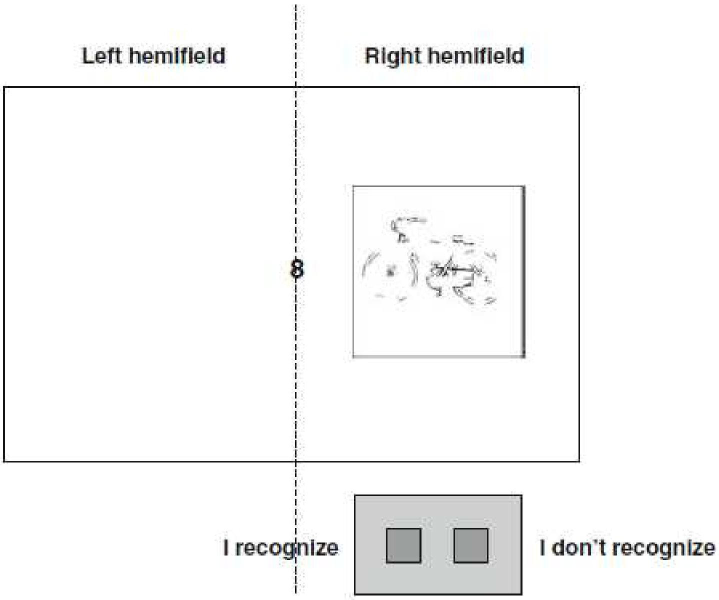

Figure 12. *Schematic representation of procedures (Forget et al. 2009)*

After a brief familiarization period with four stimulus presentations, the test consisted of two phases. In the first phase, participants completed five training sessions for one hemisphere, with each session consisting of 32 fragmented pictures. Following a 15-minute break, participants were presented with 32 old, fragmented pictures from the training phase, mixed randomly with an equal number of new pictures. These old (primed) pictures and new pictures were equally distributed between the trained and untrained hemispheres. The data collected provided two separate measures: visuoperceptual skill learning, determined by a decrease in identification thresholds over the five training sessions, and perceptual priming, indicated by a decrease in thresholds between the old and new picture sets presented to each hemisphere in the final phase (Forget et al. 2009).

Transfer of skill learning was evaluated by comparing the average identification thresholds from the last training block to the average identification threshold of the new picture set presented to the untrained hemisphere. The difference in thresholds obtained by the untrained hemisphere for old and new pictures during the second part of the testing served as a measure of priming transfer. Additionally, a separate explicit recognition test was conducted on paper for complete pictures. Participants were asked to circle any pictures they had not seen during the sessions from a set of 260 images.

2.8 Results: Forget et al. (2009) study

Several key findings regarding acallosal patients were reported in the study:

1. Lack of transfer: Acallosal and early split-brain participants did not show any transfer of priming from the trained to the untrained hemisphere. The priming effect was limited to the trained hemisphere only, unlike neurologically intact participants who exhibited priming in both hemispheres.
2. Limited compensation: Acallosal participants with an intact anterior commissure showed the same pattern of results as a participant with agenesis of the anterior commissure. This suggests that the alternative secondary interhemispheric pathway and subcortical commissures, hypothesized to be involved in compensatory mechanisms, cannot facilitate interhemispheric transfer of perceptual priming in acallosal individuals.
3. Implicit processing deficits: Acallosal patients showed deficits primarily in the implicit component of the task. There were no significant differences between acallosal and control groups in the declarative recognition of stimuli, suggesting that the impairments in acallosal participants are limited to tasks involving implicit processing.
4. Preservation of declarative recognition: Despite the deficits in implicit processing, acallosal patients performed normally in the declarative recognition of stimuli. This may be attributed to the involvement of anterior regions and the use of compensatory mechanisms, such as subcortical pathways, during declarative recognition tasks.

Overall, the results reported by Forget et al. (2009) have suggested that acallosal individuals have limitations in interhemispheric transfer of perceptual priming and show deficits in implicit processing, while declarative processing remains relatively intact. These findings support the dissociation between declarative and nondeclarative memory in acallosal participants.

CHAPTER 3:

CONCLUSIONS

3.1 General conclusions

This thesis aimed to highlight some important findings made by studies on the intermanual transfer effect. The results, for example, reported by Caillé et al. (2005), indicated that a deficit in motor coordination was observed in patients with more posteriorly located lesions, whereas a deficit in motor planning was observed in patients with more rostrally located lesions. The most posterior section of the sample, including the anterior portion of the body of the CC, abolished interhemispheric transfer of simple somesthetic information (touch perception) but not tactile discrimination (intermanual shape comparisons). Caillé et al. (2005) hypothesized that more complex somesthetic information is transmitted via the caudal region of the CC's body, which was spared in all patients.

This suggests that specific deficits in interhemispheric integration in the motor and somesthetic modalities are produced by sectioning different portions of the anterior CC (genu and anterior body). These deficiencies are in line with the anterior callosal fibers' anteroposterior topography, which defines five vertical callosal segments based on specific arithmetic fractions of the maximum anterior–posterior extent. The contribution of these specific disconnection deficits found by Caillé et al. (2005) may inform neurosurgeons about the effects of anterior callosotomy and enable the implementation of corrective measures if needed to mitigate potential deficits in interhemispheric communication and functioning.

Understanding these deficits allows neurosurgeons to anticipate and evaluate the potential effects of anterior callosotomy on patients' motor and somesthetic functions. It helps them make more informed decisions when considering this surgical intervention as a treatment option. Furthermore, if the deficits are deemed, significantly and adversely impacting the patient's overall well-being, neurosurgeons can explore strategies to mitigate or compensate for these effects. This may involve developing rehabilitation or compensatory techniques to enhance interhemispheric communication or exploring alternative surgical approaches that minimize potential deficits.

Sternad et al. (2007) investigated interhemispheric coupling and the role of the CC in a complex asymmetric bimanual task and reported significant findings. Sternad et al. were able to confirm that callosal connections mediate secondary movement initiation and that individuals lacking the CC would exhibit spatiotemporal independence of the two hands. Secondary movement perturbations appear to be mediated by subcortical structures (e.g., the thalamus, the basal nuclei, the amygdala, etc.). In addition, in the absence of the CC, spatiotemporal coupling in bimanual rhythmic movements is significantly impaired, and the differences on tasks with discrete and rhythmic components, in healthy controls support the hypothesis that discrete and rhythmic movements are two distinct movement types.

The special contribution of the study by Sternad et al. (2007) was that, over the last two decades, a substantial body of literature has accumulated mostly about the significance of the spatiotemporal constraints between the two limbs during bimanual movements. Nevertheless, even though bimanual movements with distinct task demands for the two hands are more common in daily behavior, little attention has been paid to this topic. Sternad et al. (2007) highlighted these bimanual movements, particularly in acallosal patients. The comparison of Sternad et al. (2007) among healthy participants and acallosal patients has provided insights into how direct interhemispheric communication across the CC contributes to spatiotemporal constraints, which occur when one arm initiates a new movement while the other limb produces an ongoing rhythmic movement.

Fabri et al. (2005) evaluated interhemispheric transfer of tactile information. The differences between the two split-brain groups (i.e., complete vs. partial), as well as those between the complete split-brain patients and healthy controls, were significant. The partial split-brain group performed similarly to the healthy control group. Thus, the neuropsychological results have supported previous functional findings, showing that the interhemispheric tactile transfer dependents on posterior CC integrity. Fabri et al. provided additional evidence that interhemispheric transfer in the tactile modality is likely mediated by fibers running in the PCB, confirming the callosal localization of the tactual channel.

The study from Forget et al. (2009), finally, made a unique contribution by examining how acallosal individuals, who typically do not show signs of disconnection in tasks requiring explicit responses, perform in tasks involving implicit processes. Specifically, the study investigated visuoperceptual skill learning and perceptual priming, without any motor involvement. The findings revealed that acallosal participants did not exhibit implicit learning of visuoperceptual skills and had limited interhemispheric transfer of the priming effect compared to neurologically intact participants. These results suggest that the compensatory pathways, potentially made by subcortical commissures, are insufficient for facilitating interhemispheric transfer of perceptual priming when the CC is absent. The findings of Forget et al. have supported the presence of a dissociation between declarative and nondeclarative memory in individuals with callosal agenesis, as previously proposed. Furthermore, the implications of these findings are discussed within the framework of neurobiological theories of memory systems.

3.2 Main limitations

The main limitations of the aforementioned studies are the relatively small sample sizes and the limited data access, as full split-brain surgery is becoming increasingly rare. Furthermore, most of the disconnection deficits following split-brain are not visible to the untrained observer and can only be identified under specialized, tightly controlled experimental circumstances. Another limitation, concerning only the Fabri et al. (2005) study is that performance was measured solely in terms of response accuracy, with no regard for response times.

As mentioned before, experimental paradigms that are limited to measuring response accuracy may miss more subtle performance decrements that become apparent only when response speed is considered. In addition, regarding again all the studies reported in Chapter 2, any attempt to link specific callosal areas to behavioral functions must consider individual differences in brain organization and fiber distribution. Therefore, to find the answers to these questions, further studies are required.

As a result of the abovementioned findings, there are several knowledge gaps regarding the intermanual transfer effect that could be filled by additional research. For instance, these days, complete split-brain surgeries are uncommon. It is crucial, hence, that we attempt to provide answers to the fundamental questions while these patients are still available for research. Therefore, it would be beneficial for future research to administer the same tests to as many of the available patients as possible, in order to examine the variations among patients. In addition, it is necessary to employ tasks that are sensitive enough to detect the intermanual transfer effect and focus more both on sensory functions (somesthetic or visual) and motor functions.

3.3 Harnessing intermanual transfer effects in rehabilitation: insights and applications

In conclusion, in the present thesis, we have attempted at highlighting the importance of understanding the underlying mechanisms of intermanual transfer effects. Future studies should further investigate the neural pathways that are involved in intermanual transfer, as well as the factors that influence the strength and duration of these effects. In terms of clinical implications, the findings suggest that intermanual transfer effects could be utilized in rehabilitation programs for individuals with brain injuries or disorders. For example, after elaborating on this, here are some possible ways in which these findings could be applied in rehabilitation:

1. Cross-training: intermanual transfer effects indicate that training one hand can lead to improvements in the other hand's performance. Rehabilitation programs could utilize this knowledge by implementing cross-training exercises. For example, if a patient has motor deficits in their dominant hand, the rehabilitation program could involve training the non-dominant hand as well, expecting that the improvements in the non-dominant hand could transfer to some extent to the affected hand.
2. Bilateral training: intermanual transfer effects suggest that bilateral training, involving both hands simultaneously, may have benefits for motor recovery. Rehabilitation programs could incorporate activities that require coordinated movements of both hands. This approach may promote interhemispheric communication and enhance motor function in individuals with brain injuries or disorders.
3. Sensory stimulation: intermanual transfer effects also suggest that tactile or sensory stimulation in one hand can result in improvements in the other hand's sensory processing. Rehabilitation programs could involve sensory stimulation techniques, such as touch or proprioceptive exercises, that target the unaffected hand. The goal

would be to enhance sensory processing and potentially facilitate improvements in the affected hand's sensory function.

4. Cognitive interventions: in addition to motor interventions, the findings of intermanual transfer effects may have implications for cognitive rehabilitation. Training cognitive tasks, such as attention or memory exercises, with one hand may lead to improvements in cognitive function in the other hand. Rehabilitation programs could incorporate cognitive interventions involving manual tasks to promote cognitive improvement.
5. Neuroplasticity facilitation: the utilization of intermanual transfer effects in rehabilitation programs aims to harness the brain's neuroplasticity, its ability to reorganize and adapt after injury or disorder. By engaging both hands and promoting communication between the hemispheres, rehabilitation programs can potentially facilitate neuroplastic changes and optimize recovery outcomes.

Overall, the study of intermanual transfer effects in split-brain and acallosal patients provides valuable insights into the functioning of the human brain and has important implications for both basic and applied research. Further exploration of this phenomenon could lead to a better understanding of brain plasticity and the development of more effective therapies for brain-related conditions.

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