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Left in the middle? Reliability of "bilateral" hemispheric language dominance.

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Käbi Van Den Hoeck
Student number: 02006192

Supervisor(s). Dr. Robin Gerrits, Prof. Dr. Guy Vingerhoets

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Preface

First of all, I would like to thank my promotor, Robin Gerrits, for all the support, feedback and patience during the making of this study. My curiosity was stirred to explore the area of language dominance and noninvasive neuroimaging methods due to the expertise you provided, which made the process of creating this thesis interesting and educating. I could not have imagined better guidance. Furthermore, I would like to thank friends and family for their interest and motivation throughout the entire process.

Abstract

Language processing in the human brain exhibits a common pattern of lateralization, with the left hemisphere playing a dominant role for the majority of individuals. However, a small proportion of individuals show right hemispheric dominance, and a question arises regarding the existence of a third group characterized by “bilateral” language lateralization, in which neither hemisphere has a clear dominance over the other. Previous research has used non-invasive neuroimaging techniques to explore brain activity during language tasks in individuals with minimal left-right differences in hemispheric activation. However, there remains disagreement in how to categorize these individuals, and studies on the test-retest reliability in individuals with bilateral language dominance are limited. This master thesis aims to examine the prevalence of bilateral hemispheric language dominance and evaluate the reliability of classifying individuals as bilateral in terms of language processing. Functional transcranial Doppler sonography, a non-invasive hemodynamic neurophysiological technique, was employed to measure brain activity during a word generation task. Participants classified as ‘bilateral’ as well as clearly left language dominant controls were invited to repeat the task during another session. The total research sample consists of 176 participants, of whom 18 bilateral participants and 8 left-dominant individuals participated in the retest session. The findings of this study support the prevailing notion of left hemispheric dominance for language processing in both right-handers and left-handers. Importantly, a significant proportion of left-handed individuals demonstrate bilateral language dominance, in line with previous studies. The test-retest reliability analysis reveals moderate reliability in classifying individuals with bilateral hemispheric language dominance (ICC = 0.54) and a good reliability for the left-dominant group (ICC= 0.70). Furthermore, the split-half reliability analysis demonstrates a higher correlation in the inconsistent bilateral group compared to the consistent bilateral group, indicating variability in language lateralization within individuals over time. Finally, sign flips, representing changes in language lateralization between subsequent test sessions, are rare in the study sample. The findings are used to formulate methodological recommendations for classifying language dominance, particularly when the difference in brain activity is small. This thesis provides valuable insights into the test-retest reliability and classification of bilateral language dominance, shedding light on the limitations and underscoring the need for further research in this area.

Nederlandse samenvatting

Taalverwerking in de hersenen vertoont een veelvoorkomend patroon van lateraliteit, waarbij de linkerhersenhelft een dominante rol speelt bij de meerderheid van individuen. Er is echter een kleine groep individuen die rechts-hemisferische dominantie vertoont. De vraag rijst naar het bestaan van een derde groep gekenmerkt door "bilaterale" taallateralisatie, waarbij geen van beide hemisferen duidelijk dominant is ten opzichte van de andere. Eerdere onderzoeken hebben gebruik gemaakt van niet-invasieve neurobeeldvormingstechnieken om de hersenactiviteit tijdens taaltaken te onderzoeken bij individuen met minimale links-rechts verschillen in hemisferische activatie. Er blijft echter onenigheid bestaan over hoe deze individuen geclassificeerd moeten worden, en onderzoeken naar de test-hertest betrouwbaarheid zijn beperkt. Dit onderzoek heeft als doel de prevalentie van bilaterale hemisferische taaldominantie te onderzoeken en de betrouwbaarheid van het classificeren van individuen als bilateraal te evalueren. Functionele transcraniële Doppler-echografie, een niet-invasieve hemodynamische neurofysiologische techniek, werd gebruikt om de hersenactiviteit te meten tijdens een woordgeneratietaak. Deelnemers die werden geclassificeerd als 'bilateraal' en duidelijk links-dominante controles werden uitgenodigd om de taak te herhalen tijdens een tweede sessie. De totale dataset bestaat uit 176 deelnemers, waarvan 18 bilaterale en 8 links-dominante individuen deelnamen aan de hertestsessie. De bevindingen van dit onderzoek ondersteunen het idee dat voornamelijk links-hemisferische taaldominantie aanwezig is bij zowel rechtshandigen als linkshandigen. Belangrijk is dat een aanzienlijk aantal linkshandige individuen bilaterale taaldominantie vertoont, in overeenstemming met eerdere studies. De analyse van de test-hertest betrouwbaarheid vertoont een matige betrouwbaarheid bij het classificeren van individuen met bilaterale hemisferische taaldominantie (ICC = 0,54) en een goede betrouwbaarheid voor de links-dominante groep (ICC = 0,70). Verder toont de analyse voor split-half betrouwbaarheid een hogere correlatie aan in de inconsistente bilaterale groep in vergelijking met de consistente bilaterale groep, wat wijst op variabiliteit in taallateralisatie bij individuen in de loop van de tijd. Ten slotte zijn veranderingen in taallateralisatie tussen opeenvolgende testsessies zeldzaam in de onderzoekspopulatie. De bevindingen worden gebruikt om methodologische aanbevelingen te formuleren voor het classificeren van taaldominantie, met name wanneer het verschil in hersenactiviteit klein is. Dit onderzoek biedt inzichten in de test-hertest betrouwbaarheid en classificatie van bilaterale taaldominantie, beschrijft de beperkingen en benadrukt de noodzaak van verder onderzoek op dit gebied.

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Introduction

The human brain is one of the largest and most vital organs in the human body, as well as one of the most complicated ones, with billions of nerves controlling all our bodily functions (Goetz, 2007). The brain is divided into three main parts: the cerebrum, the brainstem, and the cerebellum. The cerebrum is the largest part of the brain and is further divided into two halves, called the left and the right hemispheres. (Guy-Evans, 2021). The two hemispheres each control and regulate the opposite part of the body, with the left hemisphere controlling the right side of the body, and the right hemisphere controlling the left side of the body. The two hemispheres are connected by a bundle of nerves called the corpus callosum, which allows them to communicate with each other. (Guy-Evans, 2021). Even though the brain is divided into two halves, they are not perfectly mirror copies of one another (Wan et al., 2022). Each has a unique neural network that is skilled at managing different types of information, processing sensory inputs in various ways, and controlling different sorts of movement (Rogers, 2021). This is known as "brain lateralization" and implies that certain abilities and functions are more controlled by one hemisphere over the other. While both hemispheres are typically active, one side often dominates for specific cognitive functions (Rogers, 2021).

There is a common pattern in the lateralization of cognitive functions across the human population (Rogers, 2021), with language being a well-documented example. In the general population, language relies mainly on the left hemisphere of the brain, while only a small proportion relies on the right hemisphere (Vingerhoets, 2019). The question arises whether there is a third group in which there is bilateral “lateralization,” meaning that both hemispheres are equally dominant (Bernal & Ardila, 2014). This would be a surprising finding, given the benefits of lateralization, which will be described later. Even though it would be surprising, evidence for the existence of a bilateral language system is already found in individuals with epilepsy (Bernal & Ardila, 2014). Data was also collected in healthy individuals to investigate whether bilateral linguistic lateralization occurs in the same way. Although bilateral activation has been observed, the occurrence is rather rare; 5% in right-handers and 10-15% in left-handers (Székely et al., 2005; Li et al., 2020; Carey & Karlsson, 2019).

Various non-invasive neuroimaging methods have been used in prior research to examine brain activity during language tasks in healthy individuals (Jansen et al., 2006; Bethmann et al., 2007; Wilke & Lidzba, 2007). These studies have identified a subset of individuals who exhibit minimal left-right differences in hemispheric activation during linguistic tasks. However, there is considerable heterogeneity in how these individuals are categorized, with no consensus and a wide variety on a specific definition.

The last sentence addresses the actual issue of the lack of test-retest reliability in bilateral language dominance. Only if individuals consistently show a minor left-right difference across multiple assessments, it would be justified to classify them as bilateral. Many non-invasive neuroimaging studies have moderate to high reproducibility when it comes to linguistic lateralization (Johnstone et al., 2020; Nettekoven et al., 2018; Rutten et al., 2002; Stroobant & Vingerhoets, 2001; Wilson et al., 2017), but they mostly include clearly left-dominant individuals and are therefore less informative about the reliability of weakly lateralized individuals. Other studies have small sample sizes (Johnstone et al., 2020) and yet others combine right language dominance with bilateral dominance (Stroobant & Vingerhoets, 2001). In summary, there are few data available to assess the reproducibility of bilateral dominance.

In this thesis, I will focus on the reliability of 'bilateral' hemispheric language dominance. The literature overview will cover lateralization in general, the methods used to investigate lateralization, and the findings regarding language dominance.

Literature Review

2.1 What is lateralization?

Language, memory, spatial attention, and other cognitive brain functions have been extensively studied in terms of 'hemispheric lateralization'. The study of this lateralization has therapeutic and theoretical implications. For example, people with unilateral brain injury may have difficulties with language functions, but the degree of the problems partly depend on how lateralized the language is. (Knecht et al., 2002).

2.1.1 Lateralization defined

Brain lateralization, also known as hemispheric lateralization, refers to the phenomenon wherein one hemisphere of the brain exhibits a greater degree of responsibility or complete control over a specific function when compared to the other hemisphere (Noggle & Hall, 2011). Hemispheric specialization is the ability of each hemisphere of the brain to mediate different elements of behavior. With few exceptions, both hemispheres can process most types of information, so this specialization is relative. However, both do so in different ways, each with its own strengths and difficulties (Mendoza, 2011). The left and right hemispheres have different activation patterns in response to different cognitive activities. A hemisphere is said to be dominant if it is more activated or involved in a particular function (Bear, Connors, & Paradiso, 2006). A function is lateralized if it is preferred or more activated in one hemisphere. The lateralization pattern that occurs across the population is referred to as typical functional brain segregation.

Two types of lateralization can be distinguished (Rogers, 2021). The first is individual lateralization, which refers to the degree to which an individual's cognitive functions and behaviors are predominantly associated with one hemisphere of the brain over the other. The second form is directed lateralization, also known as population lateralization. This refers to the fact that the direction and strength of this lateralization is prototypical throughout the population. In other words, a function that is performed by the right hemisphere in a given individual is generally performed by the right hemisphere in other individuals. There are exceptions, for example, where there is no distinction between the two hemispheres of the brain for particular functions, or groups where the lateralization is reversed, but population lateralization refers to the generality described above (Rogers, 2021). The most obvious example of population lateralization in humans is hand preference: the majority of the population is right-handed, with a smaller proportion being left-handed (Papadatou-Pastou et al., 2020).

2.1.2 Left and right hemisphere

According to the left-right brain dominance theory, each brain part has been assigned for distinct functions. In general, the left hemisphere controls the right half of the body, while the right hemisphere controls the left part. Related to that, each brain side receives information from the opposite visual field (Corballis, 2014). As stated by Vingerhoets (2019), the left hemisphere is responsible for language, praxis, and calculation dominance, whereas the right hemisphere supports spatial attention, facial recognition, and prosody of speech. This aligns with the previously mentioned population lateralization.

Different functions are assigned to each halve of the brain, however both hemispheres do not work independently, but as a whole. The corpus callosum connects the left and right sides. It is a dense network of nerve fibers that ensures that both hemispheres of the brain can interact and transmit information to each other (Trobe, 2010). In contrast to the left-right brain dominance theory, some researchers believe in the left brain/right brain dichotomy, which can be described as our entire brain working all the time, but certain areas are more active than others (Dawson, 2020).

In addition to the assumption that both hemispheres of the brain work together, there is evidence that when one side of the brain is damaged, the other side can take over some functions, which can be explained as functional plasticity. This is the brain's ability to shift functions from one damaged area to other, non-damaged areas after trauma (Grafman, 2000).

For example, Grafman (2000) studied an adolescent who had suffered a right hemisphere injury as an infant. The adolescent's left parietal lobe took over some visuospatial functions normally performed by the right side. However, the math skills that were taught in school after his injury were normally stored in the left hemisphere. This made learning math difficult because there was little room left in the left hemisphere, which had already taken over the visuospatial skills of the right hemisphere. However, neuroimaging studies showed that mathematics activated the left hemisphere, suggesting that the left hemisphere was still genetically programmed to process it, even though it was now more focused on spatial processing (Grafman, 2000).

2.1.3 Why is our brain lateralized?

Lateralization is found not only in humans but also in a variety of animals, suggesting that it has certain advantages (MacNeilage et al., 2009). The reason why the human brain is lateralized does not seem to have a single, universal cause, but rather a number of contributing variables. Evolutionary theories suggest that millions of years ago, the brain was only one- third the size of today's human brains, and as the brain grew over the years, duplication of functions across both hemispheres no longer made sense since it would have been an inefficient allocation of resources (Levy, 1977). The brain is an energy-intensive organ, and duplicating functions across hemispheres would have required an excessive amount of energy and resources, diverting them away from other critical biological processes. From an evolutionary perspective, specialization of each hemisphere to handle distinct functions would have been a more effective strategy, as it would allow for improved information processing and efficient allocation of resources (Isler & Van Schaik, 2009; Rogers, 2021). Therefore, functions began to be distributed, freeing one hemisphere to perform other functions (Levy, 1977).

More recent studies describe the contemporary advantages of lateralized brains. One of these is that lateralization maximizes the neuronal capacity of the brain. This is because when one hemisphere is engaged in a particular activity, the other hemisphere still has room for other additional tasks. This means that tasks are not duplicated on both sides, saving space. (Vallortigara, 2006). Second, the brain is able to process multiple functions simultaneously when both hemispheres are performing different tasks (Rogers et al., 2004).

Numerous studies have been conducted to determine the cause of brain lateralization and the benefits associated with it. However, this does not explain why the majority of the population is lateralized in the same direction and for the same functions. Rogers et al., (2013) linked this to social behavior. When one interacts with the other, one can broadly expect how the other will respond because of parallel lateralization, e.g., handshaking, which is mostly done with the right hand. Most of the evidence concerning the downsides of brain lateralization comes from animal studies. When a predator approaches a vertebrate from the non-dominant side, the vertebrate does not perceive it as quickly as when it approaches from the dominant side (Vallortigara, 2006). The downsides of lateralization in humans seems to be a less studied topic.

2.2 Research methods

The role of the right and left hemispheres in the control of various cognitive tasks, has been studied in various ways over the decades since the idea of lateralization had been conceptualized (Bradshaw, Bishop & Woodhead, 2017). Methods for studying brain lateralization range from less common methods such as post-mortem examinations to safe, mostly noninvasive technologies. Several methods will be described, with particular emphasis on those relevant to this thesis.

2.2.1 Invasive methodologies

2.2.1.1 Postmortem examination

The study of brain lesions (e.g., aphasia) and their consequences is a possible technique for studying the brain and its laterality. One way this can be done is by postmortem examination (Tanner, 2009). This technique, which has long been the only one available for investigating the lateralization of the brain, has already significantly advanced our understanding of the lateralization of cognitive functions (such as Broca's and Wernicke's language regions). Paul Broca, a prominent French physician, and anatomist, observed that patients with language disorders or aphasia, characterized by difficulties in speaking or understanding language, had damage to a specific region of the left hemisphere of the brain (Finger, 2004). One of Broca's most famous patients, "Tan," could only produce the single word "tan" despite his ability to understand language. Upon examining Tan's brain after his death, Broca discovered a lesion in the left hemisphere of the brain in the area that now bears his name. This led him to conclude that damage to this specific region of the brain was the cause of the patient's language impairment (Finger, 2004). In subsequent years, Broca identified multiple patients who had difficulties with producing articulate speech, as a result of damage to the left frontal lobe of the brain, which he later called "Broca's area." The resulting speech disorder, characterized by difficulties with speech production, was termed "Broca's aphasia" (Finger, 2004). Today's research consistently confirms the existence of Broca's area, found with postmortem examination. For example, a study by Meinzer et al. (2012) used transcranial magnetic stimulation (TMS) to show that stimulation of Broca's area improved language performance in patients with aphasia, supporting the idea that Broca's area plays a causal role in language production.

Brain lesions can be used to map brain functions and examine differences from normally functioning brains (Tanner, 2009). However, brain damage is rarely focal, meaning that other interactions and cofactors also play a role in the damage. Thus, the absence of or difficulty with a particular brain function is not always due to damage to that one particular area. Moreover, the assumption that a damaged brain functions like a healthy brain except for the damaged part can be problematic (Tanner, 2009).

2.2.1.2 Split-brain studies

Split-brain studies were a second way to learn about lateralization. In this approach, the carpus callosum, a thick bundle of nerves that connects the two hemispheres of the brain, is severed, or cut (Rosen, 2018). This procedure was initially performed to cure epilepsy and not to study the lateralization of the brain. Nevertheless, it has provided us with important insights into the fields of cognitive psychology by teaching us about hemisphere lateralization, language processing, cognitive functions, and so on (Rosen, 2018). It is an invasive approach, which is why it cannot be performed in healthy people and is even rarely used nowadays.

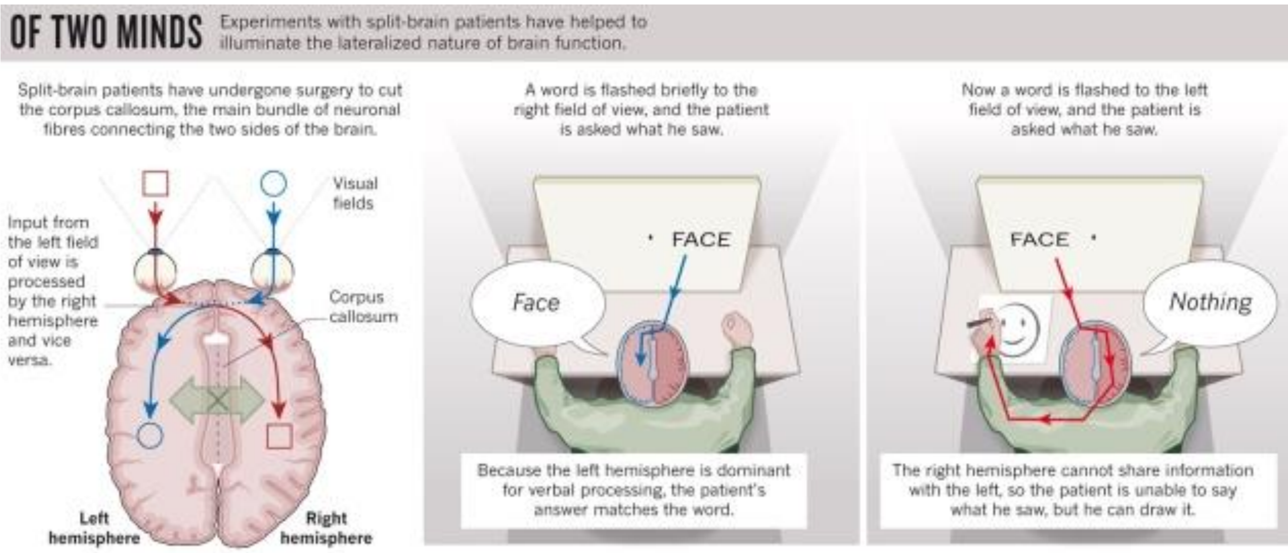
Split-brain research aims to better understand how the two hemispheres of the brain process and respond to different stimuli. When the corpus callosum is severed or cut, the two hemispheres of the brain become separated from one another and unable to interact. This separation allows one hemisphere to be stimulated to see how it responds without being distracted by the other hemisphere (Gazzaniga, 2000).

One example of a split-brain study is the experiment conducted by Roger Sperry and Michael Gazzaniga in the 1960s (Sperry, 1968). The study consisted of 11 participants, all of whom had undergone commissurotomies (the severing of the corpus callosum) for severe epilepsy (Sperry, 1968). The method involved presenting visual stimuli to each hemisphere of the brain. More specifically, they presented an image of a word either to the left visual field (which is processed by the right hemisphere), or to the right visual field (which is processed by the left hemisphere) (Pinto et al., 2017). Participants were then asked to identify what they saw, see Figure 1 (Wolman, 2012).

The results showed that participants were able to correctly identify the word presented to the right visual field (which was processed by the left hemisphere, responsible for language processing) by verbally naming it. However, when asked to identify the word presented to the left visual field (which was processed by the right hemisphere), participants were unable to verbally name it, but they were able to use their left hand (controlled by the right hemisphere) to indicate what the word was by pointing to it (Sperry, 1986). These findings provided insight into the lateralization of brain function, demonstrating that the left and right hemispheres of the brain have different specializations: both hemispheres are able to recognize written words, but only the left hemisphere can produce speech (Sperry, 1968).

Figure 1.

'The split brain: A representation of the divided hemispheres'



Note. Adapted from "The split brain: A tale of two halves" by D. Wolman, 2012, Nature, 483(7389), p. 260. Copyright 2012 by Nature Publishing Group

2.2.1.3 Wada-testing

Another invasive procedure, called the Wada test, was originally performed prior to ablative surgery for epilepsy or tumor resection (Loring, 1997; Kundu et al., 2019). The test helps to determine which hemisphere of the brain is responsible for certain cognitive functions, especially language and memory, aiding in surgical planning and decision-making. By temporarily inhibiting one hemisphere at a time through the injection of a sedative in one of the carotid arteries, the Wada test allows clinicians to evaluate the functional capacities of the contralateral hemisphere. This information is valuable for identifying the dominant hemisphere and assessing the potential risks and benefits of surgical procedures that may impact cognitive abilities. Additionally, the Wada test can provide insights into the prognosis of seizure outcomes following specific surgical interventions, helping guide treatment strategies and improve patient care (Loring, 1997; Kundu et al., 2019).

Wada and Rasmussen (1960) observed a temporary loss of function, i.a. in language functions, following the injection of the dominant hemisphere. In contrast, the injection of the nondominant hemisphere resulted in either no language loss or significantly diminished impairment. These findings led the authors to propose that the Wada test could serve as a valuable tool for determining hemispheric language dominance. Subsequently, this procedure has been widely employed in individuals with severe epilepsy (Bernal and Ardila, 2014). Patients were sometimes found to have no or equal loss of language regardless of which hemisphere was injected. This is the first indication of the possible existence of “bilateral” dominance. The downside of Wada testing is that the sedative is only effective for a brief period of time, thus there aren't many observations per person to assess dominance. Another drawback is that, due to its invasiveness, the Wada test is limited to individuals with certain neurological conditions who would benefit from it (e.g., epilepsy patients) (Szaflarski, 2020). In addition, epilepsy itself is a neurological condition characterized by abnormal brain activity, and the presence of epilepsy may influence the organization and functioning of language-related regions in the brain. Therefore, the patterns of language lateralization observed in epileptic patients may not necessarily reflect the typical organization seen in the general population (Chauhan et al., 2022). Furthermore, Wada testing is not without risks. In a study by Loddenkemper, Morris & Möddel (2008), complications occurred in nearly 11% of 677 patients during testing, and 0.6% still had neurological deficits 3 months afterward. Therefore, noninvasive methods are preferred for lateralization testing in healthy subjects.

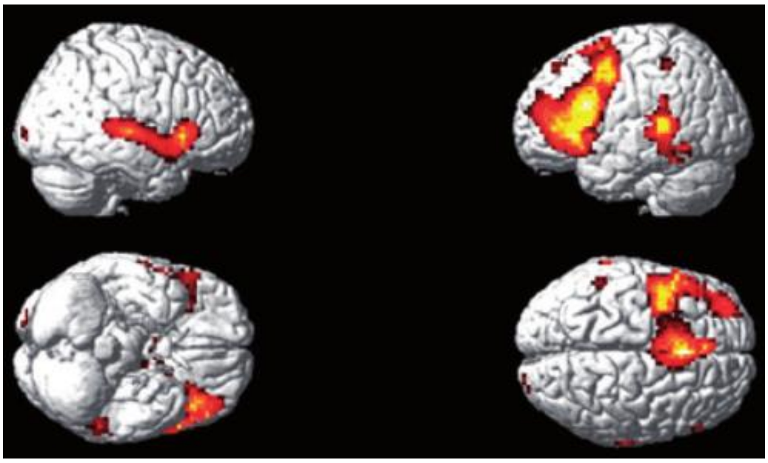
2.2.2 Non-invasive methods

2.2.2.1 Functional Magnetic Resonance Imaging (fMRI) & Lateralization Index (LI)

For a long time, only invasive procedures, such as those mentioned above, could provide an accurate assessment of hemispheric dominance (Jansen et al., 2006). In the late 1980s, regional cerebral blood flow was found to increase near regions of neuronal activation (Raichle, 1998). Not much later, functional magnetic resonance imaging (fMRI) was developed. This non-invasive brain imaging device identifies brain activity by detecting fluctuations in blood flow. fMRI can determine which parts of the brain are less or more active during different actions, such as moving your legs or thinking about certain words (Maziero et al., 2020). One hemisphere of the brain is considered dominant if it exhibits higher activity than the other hemisphere, characterized by increased neuronal impulses and blood flow. To visualize and analyze this brain activity, researchers utilize imaging techniques such as BOLD imaging (blood oxygen level dependent imaging), which converts these neuronal impulses into a three-dimensional image. BOLD imaging provides a colored map of the brain, highlighting the regions with the highest activity (Kim & Bandettini, 2011) see Figure 2 (Pahs et al., 2013)

Figure 2.

'*Functional fMRI map of language activation'*



Note. Adapted from *"Asymmetry of planum temporal constrains interhemispheric language plasticity in children with focal epilepsy" by Pahs et al. (2013), Brain, 136(10), p. 3163–3175. Copyright 2013 by the Oxford University Press. Adapted with permission.*

In the context of fMRI studies examining lateralization, researchers often employ a metric known as "LI" (lateralization index). LI is a quantitative measure derived from BOLD imaging that assesses the difference in brain activity between specific areas of the left and right hemispheres. It is used to quantify the extent of lateralization observed in the brain (Kim & Bandettini, 2011) by describing the direction (left, right) and the strength (how strongly left or right) of lateralization (Binder et al., 1995).

The calculation of the LI (lateralization index) depends on the specific formulation used. Generally, the LI is computed as the difference in brain activity between the left and right hemispheres divided by the sum of their activations; $LI=(L-R)/(L+R)$. This calculation yields an index ranging from -1 to +1. A score of +1 indicates complete left lateralization, while -1 represents complete right lateralization; scores close to 0 indicate a bilateral pattern (Ruff et al., 2008). For example, consider a language task where the activation levels in the left hemisphere (L) are 0.9 and in the right hemisphere (R) are 0.1. When using the LI formula: $LI = (0.9-0.1)/(0.9+0.1) = 0.8/1.0 = 0.8$. In this example, the LI value is 0.8, which is close to +1 and which indicates a strong left lateralization or left dominance.

Participants with large LIs can be easily classified as left- or right-dominant, while participants with small LI's indicating that activity was more or less symmetrical are more difficult to classify (Mazoyer et al., 2014). Some authors consider small LIs to reflect measurement error and propose to exclude them, while others simply assign them to the right or left dominant hemisphere, and still others assign them to a separate "bilateral" category claiming that their language system lacks hemispheric specialization, for example comparable to the bilateral patterns occasionally observed during Wada testing (Carey & Karlsson, 2019; Vingerhoets, 2019) Although typically less than 10% of the participants in a given sample are considered to have a small LI, deciding how to classify them lacks consistency which presents a major issue in laterality research. The variability in strategies for dealing with small LIs makes it difficult to compare rates of left, bilateral and right dominance in different studies and populations (Vingerhoets, 2019).

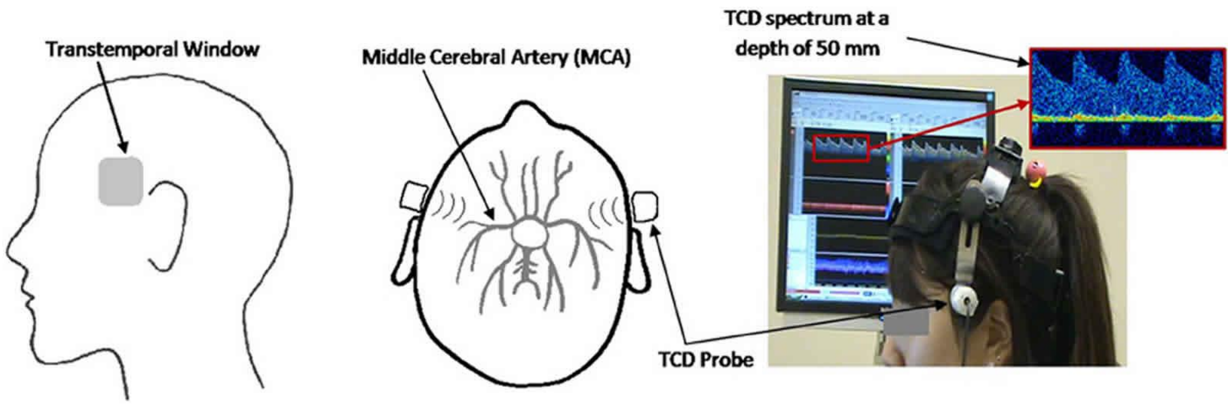
Lastly, the utilization of fMRI is not without its drawbacks. One prominent limitation of fMRI is its high cost, which often leads to restricted sample sizes in research studies. Additionally, the requirement for participants to remain still during the scanning process poses a challenge, as movement can activate certain brain regions. Moreover, head motion can disrupt the magnetic resonance signal, significantly diminishing the quality of the scan and necessitating the exclusion of affected data (Hausman et al., 2022). In terms of cost, another technique called functional transcranial Doppler sonography (fTCDS), may be a better choice.

2.2.2.2 Functional Transcranial Doppler Sonography (fTCDS)

Functional Transcranial Doppler Sonography (fTCDS) is a technique closely related to fMRI but much cheaper to administer, see Figure 3 (Lu et al., 2014). Practically, probes are put on the scalp to send ultrasound into the brain's arteries and measure the reflected sound. The probes are placed at one of the 'ultrasonic windows' to measure the blood flow. This is a place on the scalp where the skull bone is thin enough to allow ultrasound to pass. Almost all previous studies have used the 'transorbital window', which is positioned around the cheekbone (zygomatic arch), 1-5 cm in front of the ear (Duschek & Schandry, 2003). As the transorbital window can also be used to detect other cerebral arteries, it is important to identify the correct artery. The most important criteria for vessel identification are the depth of insonation, the direction of blood flow, and the position of the probe in the ultrasound window (Duschek & Schandry, 2003). Although blood flow can be measured trough several arteries, the middle cerebral artery (MCA) is the most commonly used one due to its location and size. This artery is responsible for collecting approximately 60-70% of the blood flow from the internal carotid artery (ICA), thereby serving as an adequate representation of the total blood flow to one hemisphere (D'Andrea et al., 2016), see Figure 4 (Ashish, 2023). However, other arteries such as the anterior cerebral artery (ACA), posterior cerebral artery (PCA), and basilar artery (BA) can also be chosen (D'Andrea et al., 2016). After identifying a specific artery and obtaining signals of sufficient quality, the probe can be fixated to the head with a tight headband (Duschek & Schandry, 2003). After these preparations are done, ultrasound will be sent into the artery and changes in the blood flow velocity (BFV) can be measured (Stroobant & Vingerhoets, 2001). In detail, the technique is based on a 'frequency shift' caused by the relative motion of vibrations when ultrasound signals are reflected on red cells in the bloodstream of an artery. The size of this frequency shift depends on the speed of blood flow, so increased blood flow corresponds to an increase in brain activity, similar to the BOLD response in fMRI (Duschek & Schandy, 2003).

Figure 3.

'View of the ultrasound probe set at the transtemporal insonation window, directed toward the MCA.'

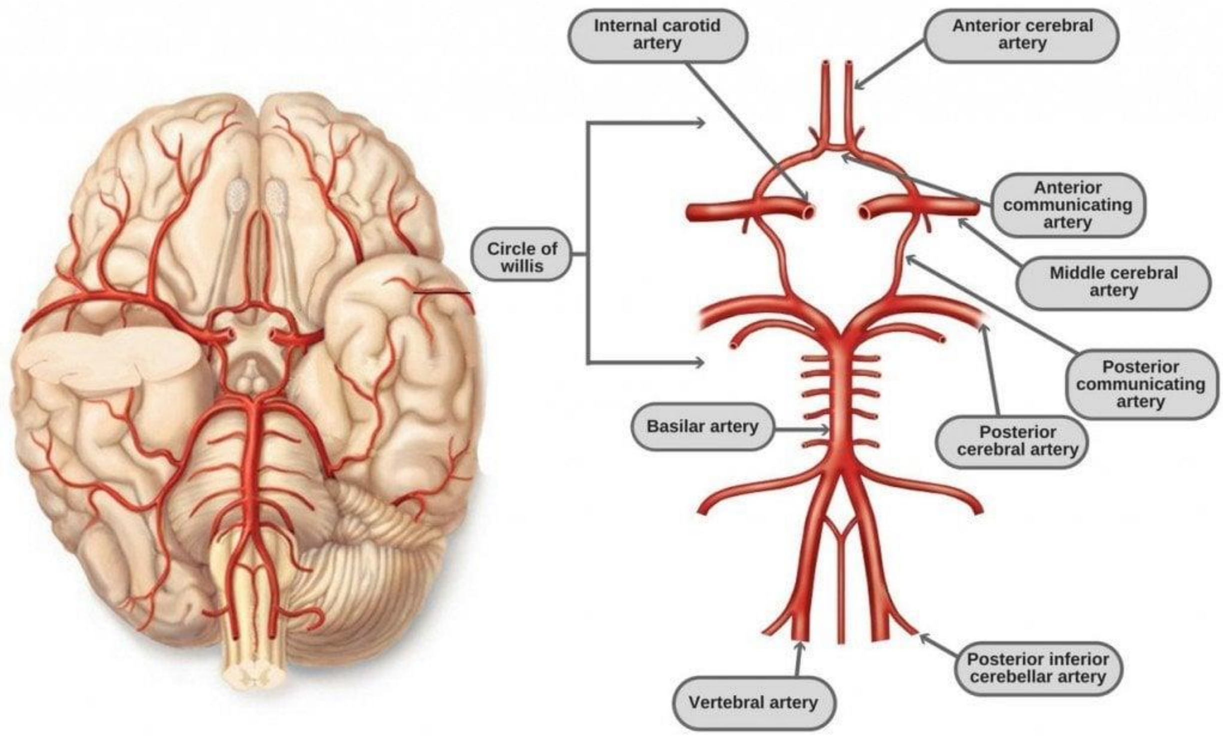


Note. Adapted from *Lu, J., Mamun, K. a. A., & Chau, T. (2014). Online transcranial Doppler ultrasonographic control of an onscreen keyboard. Frontiers in Human Neuroscience, 8.*

Given the mobility of the technique and its ease of use, fTCDS seems to be a valuable method. Since participants do not have to lay still in a device as with fMRI, Doppler sonography appears to be suitable for a wide range of participants, including children or people with physical limitations (which can make it difficult to lay still for several minutes) (Stroobant, et al., 2009; Stroobant et al., 2011). Doppler sonography provides high temporal resolution, which means that blood flow can be recorded continuously and accurately under a variety of stimulating situations. This allows researchers to assess the strength of the response and record the temporal dynamics that result from responses to stimuli. fMRI can offer similar advantages, but other neuroimaging methods are often unable to record blood flow continuously, so the temporal dynamics cannot be detected (Duschek & Schandry, 2003).

Figure 4.

'Circle of Willis.'



Note. Adapted from Ashish. (2023). *"Circle Of Willis: Anatomy, Diagram And Functions." Science ABC. Retrieved from https://www.scienceabc.com/humans/circle-of-willis-anatomy-diagram-and-functions.html.*

In terms of validity and reliability, fTCDS appears to correlate well with fMRI and other methods. In a study by Schmidt et al. (1999) that looked at hemispheric response differences, both fMRI and fTCDS found a clear dominance of the right hemisphere for visuospatial tasks and a consistent gender-specific reaction. In another study of linguistic dominance, the results of the Wada test and fTCDS were compared and found to be equivalent (Knecht et al., 1998). In a third study, Deppe et al. (2000) assessed fMRI and fTCDS data from 13 participants based on their lateralization index (LI). The LI results of both methods were concordant with a linear relation of 0.95 (=r) in each of the 13 subjects, indicating that both approaches correlate in the direction of lateralization and in strength.

Although fTCDS has the advantage of providing high temporal resolution, it does not provide high spatial resolution, meaning that brain activity can not be localized precisely to the brain areas that produced this activity (Duschek & Schandry, 2003). The fact that fTCDS measures brain activity through specific arteries, which supply blood to large parts of the brain, such as the MCA that supplies blood to 60 a 70% of the cortex, has implications (e.g., for the design of tasks). Considering that the MCA supplies blood to a large portion of the cortex, rather than a specific brain region, any changes in blood flow velocity in the MCA may represent a more general response to the task, rather than a specific activation of a particular brain area (Duschek & Schandry, 2003). As a result, tasks that are more likely to activate specific brain regions may not be as suitable for fTCDS studies, as the results may not be as specific to those regions. Instead, tasks that are more likely to produce a general response throughout the cortex may be more appropriate for fTCDS studies.

In addition, other imaging techniques can detect blood flow changes in smaller arteriolar branches, whereas fTCDS cannot (Duschek & Schandry, 2003). Furthermore, issues with the ultrasonic window could occur. In the study by Deppe et al. (2000), the ultrasound window was absent or too weak in 5% of the participants. In the older population, it can reach 10% or more (Duschek & Schandry, 2003). The thicker bone structure makes it more difficult to insonate blood flow. Thicker bone structure can reduce the ultrasound signal in fTCDS because the bone absorbs and scatters ultrasound waves (Kwon et al., 2006). The attenuation of ultrasound waves in the skull bone occurs due to multiple mechanisms (Pinton et al., 2011). Firstly, the bone has a higher density and stiffness than soft tissue, which makes it a stronger absorber of ultrasound waves. Secondly, the bone contains air pockets which can scatter and reflect the ultrasound waves. As the ultrasound waves pass through the skull bone, their intensity decreases due to these attenuation mechanisms, which leads to a reduction in the depth of penetration and signal intensity. This can result in a lower signal-to-noise ratio and decreased sensitivity to changes in blood flow velocity (Pinton et al., 2011).

Despite the few limitations highlighted, the benefits of fTCDS makes it an attractive tool for large-scale testing.

2.3. Lateralization and language

Language is the cognitive function that has received the greatest attention in lateralization research. In the 1860s, French physician Paul Broca evaluated a patient with language limitations; in particular, his speech was limited to two words. A postmortem examination revealed damage to the left frontal cortex. Other people who had similar language problems appeared to have the same left frontal brain damage (Nishitani et al., 2005). This revelation was intriguing because it led to the conclusion that speech and language are controlled by the left hemisphere. Later, he retracted his statement, adding that the left hemisphere of the brain is specialized for language in the majority of the population, but not all, as some people with right hemisphere dysfunction suffered from aphasia. Carl Wernicke's studies in the 1870s supported the data indicating left hemisphere specialization for language in the majority population. Wernicke's patients, unlike Broca's, could speak but had difficulty interpreting language. Postmortem examination revealed damage to the higher temporal lobe in the left hemisphere (Nishitani et al., 2005). Both brain areas are now referred to as Broca's and Wernicke's areas and are the regions most associated with language. Nevertheless, both areas also perform other cognitive functions, and language is not limited to these two regions but also depends on other areas. (Tremblay & Dick, 2016).

2.3.1 Left, right or bilateral language dominance?

Considering Broca's and Wernicke's findings, language is localized in the left hemisphere, with a few cases it being localized in the right hemisphere. Multiple studies examined the brain activity of healthy individuals during language tasks. They all reported that in some people, there was little difference between the left and right hemispheres' levels of activity (Bethmann et al., 2007; Jansen et al., 2006; Ocklenburg, Hugdahl & Westerhausen, 2013; Wilke & Lidzba, 2007). Not only did recent research report this finding, the possible existence of bilateral language dominance dates back as far as the results from Wada-testing in 1964 by Branch et al. (Kundu et al., 2019). The question arises as to the reliability of this discovery. If they maintain a small LI across multiple test-retest trials, this could be considered a possible third group with bilateral hemispheric language dominance. Not just the reliability of this, but also whether these people have a qualitatively different form of language dominance than people who have significant lateralization, might be called into question.

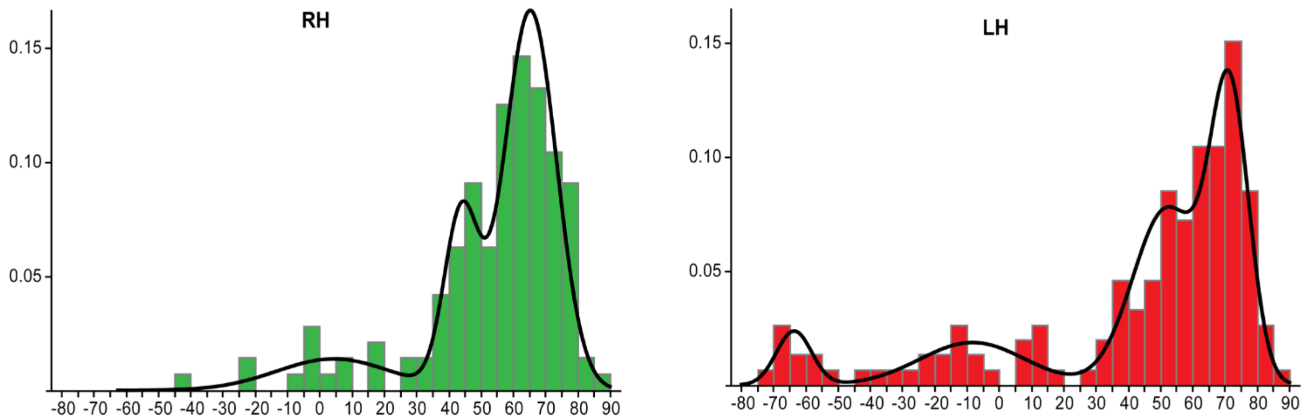
2.3.1.1 Language dominance in left- and right handers

The graphics below (Figure 5), originally from Mazoyer et al. (2014), provide a summary of the distribution of language in right- and left-handers. The hemispheric dominance for language was assessed using fMRI during a language task. Specifically, a covert sentence generation task (SENT) compared with a covert word list recitation (LIST). As described by Mazoyer et al. (2014), during the SENT task, study participants were asked to create sentences with the same structure. Each sentence had to start with a subject (such as "The little boy" or "The gentleman") and a complement (such as "with his satchel" or "in shorts"), followed by a verb describing an action and ending with another complement of place (like "in the street" or "on the beach") or manner (like "with happiness" or "nastily"). While creating the sentences, the participants had to focus on a white-cross in the center of the screen and press a button when they had finished forming the sentence in their head. In the LIST task, participants had to silently recite a list of months in order and press the button when they had completed the task (Mazoyer et al., 2014).

They applied Gaussian mixture modeling, a probabilistic method for modeling real-world datasets (Halari et al., 2005). The green bars represent the LI's of right-handed people, while the red bars represent the LI's of left-handed people. The right side of the graphic represents left-hemispheric language dominance (LLD) and is referred to as 'typical language lateralization'. The left side of the graphic shows right-hemispheric language dominance (RLD) and is referred to as 'atypical language lateralization'. The third group, those with a small LI or 'bilateral' language dominance (BLR), is also shown, this time around 0 on the x-axis. BLR is also referred to as 'atypical language lateralization (Mazoyer et al., 2014). In a review by Vingerhoets (2019), a problem with the distinction between typical and atypical language lateralization is highlighted. He mentions that there is no general cut off point, making it difficult to separate BLR from LLD or RLD.

Figure 5.

'Distribution of language in left- and right-handers.'



Note. Adapted from *Mazoyer et al. (2014), Figure 4, with permission from the authors and published in PLoS ONE, under the Creative Commons Attribution License.*

As can be seen in the diagrams, left hemisphere dominance is most prevalent and is almost evenly distributed between left and right handers. Around the middle, both hand preferences show multiple forms of 'bilateral dominance'. Strikingly, right-hand dominance occurs almost exclusively in left-handers. Therefore, Vingerhoets (2019) recommends that the term 'atypical language dominance', as we have previously used it for RLD and BLR, should be used with caution as an overarching term. Since there is an obvious difference between the two groups, a differentiation should be made. Based on the graphs, he asked whether there is a relationship between atypical linguistic dominance (BLR and RLD considered together) and left-handedness. His answer was yes, but only in individuals who rely on the right hemisphere for language, not in bilateral individuals.

Based on neuroimaging methods, 90% of the population relies on the left hemisphere for language functions (Mazoyer et al.,2014). However, the 90% does not appear to be evenly distributed between right- and left-handers. Slightly more than 90% of right-handers have LLD, while the rate drops to 70-75% for left-handers. A relationship between hand and language dominance may be suspected (Vingerhoets, 2019). However, Mazoyer et al. (2014) suggested that the difference between left- and right-handers is not evidence of a relationship between hand and language dominance. As a result, it means that the perceived difference depends almost exclusively on the group of left-handers who have right hemisphere dominance, and that there is otherwise no relationship. Explained in a little more detail, atypical language dominance is a combination of RLD and BLR, and the atypical dominance in right-handers seems to consist almost exclusively of BLR (10-15 %, the same as in left-handers). The atypical form in left-handers also includes a small group with RLD (6.5%) (Mazoyer et al., 2014). In summary, except for the small group left-handers with RLD, there are almost no differences between the groups. Thus, according to Mazoyer et al. (2014), there is a relationship between atypical language dominance and left-handedness, but only among those with RLD, not among those with BLR (because an equal proportion is found in the left- and right handers). Either way, this evidence can be questioned. Several studies have shown that left-handed people are more likely to have bilateral language dominance than right-handed people based on fMRI, fTCDS and Wada testing (Bernal & Ardila, 2014; Kundu et al., 2019)

2.3.1.2 Data on bilateral language lateralization

Bilateral representation of language has been observed during Wada testing in patients with intractable epilepsy (Bernal & Ardila, 2014). In the Wada procedure, as described previously, brain function in one hemisphere is temporarily interrupted by an intracarotid injection of a sedative. In 5 large publications with a total of 1799 epilepsy patients, the resulting language impairments were usually clearly lateralized. Approximately 10% of right-handers and 27% of non-right-handers (left and ambidextrous) showed a bilateral pattern instead in which either no language deficits were noted ("bilateral-independent") or in which language was impaired to a similar degree regardless of the sedated hemisphere ("bilateral-dependent") (Gates & Fangman,1997; Kurthen et al., 1994; Möddel et al., 2009; Rasmussen & Milner, 1977; Risse, Loring et al., 1999). Modern neuroimaging studies such as fMRI have also found bilateral representation of language in epileptics, confirming the results of the Wada test (Adcock et al., 2003; Springer et al., 1999). However, it should be considered that part of the bilateral representation in epileptics may be due to an atypical development trajectory or possibly due to brain plasticity that has reorganized their language circuitry (Bernal & Ardila, 2014). In addition, it should be taken into consideration that bilateral patterns obtained in Wada testing, not always are reproduced by fMRI testing and vice versa (Janecek et al., 2013). This begs the questions whether those results are reliable and whether they represent an actual underlying bilateral dominance. Janecek et al. (2013) conducted a study on 229 epilepsy patients to examine the discordance rates between Wada and fMRI tests on the language laterality index (LI). They found that 14% of the patients had discordant results, with the highest discordance in patients classified as having bilateral language by either one test. The fMRI LI was the strongest predictor of discordance, with a lower fMRI LI resulting in a larger difference between the Wada and fMRI LIs. The authors speculated that fMRI may be more sensitive to right hemisphere language processing than Wada. In some cases, the right hemisphere may not be able to sustain even minimal performance when the left hemisphere is anesthetized, leading to the patient appearing entirely left-lateralized on the Wada test. Despite the discordance rate, Janecek et al. (2013) concluded that Wada and fMRI results are more similar than they are different, based on their study of epilepsy patients.

One may wonder whether the “bilateral-dependent” and “bilateral-independent” patterns observed during Wada testing and FMRI in epileptic patients, also occur naturally as a developmental variant of brain organization in the general population (Gerrits, 2022). Findings on this seem to be less consistent and data on test-retest reliability is less available.

In healthy humans, fMRI is commonly used to measure task-related brain activity and estimate a laterality index (LI) that indicates the difference in activity between hemispheres. The challenge is to collect a large number of people with low LIs in order to gather data on bilateral language dominance. Previous studies found their prevalence to be around 5% in right-handers and 10% to 15% in left-handers, depending on the study (Carey & Karlsson, 2019; Li et al., 2020; Székely et al., 2005). If across test-retest sessions, the direction of laterality is replicated but not the degree, it may be preferable to classify individuals as left- or right-language dominant. Exclusion of small LIs is warranted when neither direction nor degree are repeatable (Vingerhoets, 2019). Test-retest studies do show that fMRI-derived LIs are generally moderately to highly repeatable (Johnstone et al., 2020; Nettekoven et al., 2018; Rutten et al., 2002), but they are largely composed of left-dominants and thus provide little information about the reliability of weakly lateralized cases. Only one fMRI study clearly reports low inter-session reproducibility of bilaterality, but it involved only 10 subjects and did not report how many of them were classified as bilateral (Jansen et al., 2006). Reanalysis of a recent split-half reliability study suggests that bilaterality may not be well reproducible across two fMRI runs (Johnstone et al., 2020). While traditional fMRI LI-based categorization does not allow for subdivision of bilateral language dominance, another study was able to do so using an algorithm (Zago et al., 2017). They used a machine learning algorithm to learn the fMRI activity patterns associated with the language dominant and non-dominant hemispheres in their study, and then categorized the subjects' hemispheres as dominant or non-dominant. Most had one dominant and one nondominant hemisphere, indicating that they were lateralized. However, about 5% of subjects had two dominant hemispheres ("co-dominant") and 3% had two nondominant hemispheres ("co-non-dominant"), which corresponds to the "bilateral-independent" and "bilateral-dependent" categories identified by the Wada test. Part of the problem with classifying LIs is that there is no agreement on whether a deviation in activation is small enough to be considered symmetrical. For this reason, many different criteria for defining bilateral dominance have been proposed in the literature, ranging from LI <5% to LI <60%, with LI <20% being the most common (Bradshaw et al., 2017).

Like fMRI, fTCDS yields very consistent results (Stroobant & Vingerhoets, 2001; Woodhead et al., 2019). The word generation task (WG) is a popular task in this approach, in which participants must randomly recall words beginning with a specific letter. Small sample studies using fTCDS and the WG task were found to be highly replicable with respect to the LI (Knecht et al., 1998). Several studies using the WG task have found consistent left hemisphere lateralization in right-handers (Buchinger et al., 2000; Knecht et al., 1996, 2001; Rosch, Bishop, & Badcock, 2012), making this technique a promising tool for testing language laterality with fTCDS. However, there are few fTCDS test-retest studies of bilaterality in language laterality. One study did indicate strong replicability for a subset of nine "atypical" participants (Hodgson & Hudson, 2017); however, this subset included both bilateral and right-language dominants and was conducted on individuals with DCD. In summary, fTCDS is a promising tool for studying language lateralization in healthy individuals, but there is limited evidence for reliability, particularly for bilateral dominance.

2.3.2 Sex differences in language lateralization

Sex differences in brain lateralization have been a subject of interest in several studies. However, when it comes to language lateralization, the findings have been inconsistent. Hirnstein et al. (2019) conducted a comprehensive review of studies on sex differences in hemispheric asymmetry and concluded that there are indeed sex differences, with males showing greater lateralization. Nevertheless, they acknowledged that the effect size is relatively small and can only be reliably demonstrated through large-scale studies. In another study, Clements et al. (2016) found that females exhibited more bilateral activation in the inferior frontal gyrus during a language task, while males showed a greater left lateralization. However, it is important to note that other studies (Frost et al., 1999; Unterrainer et al., 2000; Weiss et al., 2003) did not find significant sex differences in language lateralization.

Overall, the research on sex differences in hemispheric lateralization presents conflicting results, ranging from males being more lateralized to no discernible sex differences. If there are indeed sex differences in language lateralization, indicating greater lateralization in males, the effect size appears to be relatively small and requires further investigation through large-scale studies.

2.4 Modulating factors in language activation

When studying the lateralization of speech using noninvasive methods, the reproducibility of results may be affected by several modulating variables. Because there are situational effects, bilateral linguistic activation (as measured by fMRI/Doppler) may not (always) be reproducible.

2.4.1 Physiological factors

Physiological factors such as heart rate and respiration are spontaneous cardiovascular variations in flow velocity (Diehl et al., 1991). In addition, consumption of substances such as alcohol, caffeine, or cigarettes can also affect the cardiovascular system (Stroobant & Vingerhoets, 2000). To limit these possible variations, candidates may be asked to abstain from these substances the day before the test. However, since these factors affect both hemispheres of the brain, there should actually be no fluctuations when the lateralization index is measured between the two sides (Knecht et al., 1998).

Other, more general factors such as emotions, fatigue, concentration etc., may also play a role (Stroobant & Vingerhoets, 2000). Concentration and fatigue can be counteracted by covering many different tasks so that habitual behavior does not develop.

2.4.1.1 Practice effects

The outcomes of functional transcranial Doppler sonography evaluations may be impacted when the same language task is repeated several times. This is due to the possibility that performing the task repeatedly might make it easier for the brain, affecting the cerebral blood flow velocity (CBFV) during the testing process (Knecht et al., 1998). However, a study by Knecht et al. (1998) with 10 participants who were tested twice and one participant who was tested 10 times, showed that there was no change in the relative side-to-side CBFV increase during word generation. Knecht et al. (1998) questioned if the repetition of the task affects the amount of mental effort needed to complete the task. If so, the consistency of the language laterality index (LI) shown in the test-retest findings may be since increases in blood flow to the brain have already reached their maximum level, and variations in effort between moderate and maximal strength would not alter this local impact. Changes in the language LI would only occur if the size or interhemispheric distribution of brain regions exhibiting enhanced blood flow were to take place (Knecht et al., 1998).

2.4.1.2 Menstrual cycle in woman

The women's menstrual cycle, which may impact hemispheric lateralization, is another physiological aspect that might be addressed. A study by Helmstaedter et al. (2015) tended to research the test-retest reliability of fTCDS on language dominance. Over an interval of 4-5 weeks, the expressive language dominance of 11 males and 11 females with epilepsy was evaluated. Helmstaedter et al. (2015) noticed great variability in women’s lateralization indices which led to lack of reliability. Because of these findings, the menstrual cycles of the women were taken into account, despite it not being the main purpose of the study, which also kept them from making an in-depth analysis of the menstrual cycle's effect. However, they observed a significant change from left hemisphere dominance towards bilaterality around the onset of menstruation, followed by a significant reversal afterwards. In contrast, previous studies (Fernandez et al., 2013; Hausmann et al., 2000) reported the opposite, with bilaterality being more prevalent in the luteal phase than the menstruation phase. The studies varied in that they were all on contraceptives in Helmstaedter et al.'s (2015) study, which may have contributed to the different results.

Helmstaedter et al. (2015) reported a case of a 28-year-old female with epilepsy, which raised questions about the accuracy and reliability of imaging methods (fMRI; fTCDS) in comparison to deactivating methods (IAT; also known as Wada test). The imaging data indicated left hemispheric language dominance, but an IAT test, taken 3 months later, showed atypical patterns with the probable participation of the right hemisphere. To clarify this discrepancy, fMRI and fTCDS tests took place again the next 2 days. Surprisingly, both tests showed bilateral language dominance. It was questioned what the IAT would have shown during the first imaging examinations, when both imaging techniques revealed left language dominance. The evaluations (fMRI, fTCDS and IAT) were thus performed at the same point in the menstrual cycle as the initial assessments. The imaging results consistently suggested left dominance, while the IAT once more revealed right hemisphere engagement. The menstrual cycle is a significant consideration when employing fTCDS for language dominance since the case offers preliminary evidence of a potential distinction between functional imaging and deactivation approaches in doing so (Helmstaedter et al., 2015).

2.4.2 Age

In addition, the lateralization of language seems to depend on age. In a study with a large sample (Hirnstein et al., 2013), participants were divided into age categories: Children (< 10 yrs), young adolescents (10-15 yrs.), young adults (16-50 yrs.), and older adults (> 50 yrs.). In young adults, males appeared to be more lateralized than females, but in young adolescents it was the opposite, with females being more lateralized. The stronger lateralization is most likely due to the earlier puberty of female teenagers and the associated brain maturation. In summary, lateralization of language appears to vary with age; it increases from early childhood through adolescence and peaks in young adulthood (Hirnstein et al., 2013). The HAROLD model also suggests that hemispheric asymmetry decreases in older adults and with age, which is evident in cognitive tasks (Cabeza, 2002). Greater bilateral lateralization could reflect compensatory processes. In contrast, one study did not support the HAROLD model. In fact, they found that left language lateralization decreases with age, but only in male right-handers and only in the temporal cortical area (Nenert et al., 2017). It should be considered if the HAROLD model is reliable for language since the model was originally designed for memory.

Present study

Many research questions about the lateralization of language seem to remain unanswered. Specifically, little data is available to judge the reliability of bilateral speech (language) representation. The goal of this study is to fill this gap by examining the test-retest reproducibility of bilateral speech representation. Achieving this requires to first overcome the practical hurdle of finding a sizeable group of participants with small LI’s. Previous studies estimate their incidence to be 5% of right-handers and 10-15% of left-handers (Basic et al., 2004; Li et al., 2020; Székely et al., 2005; Zago et al., 2017;). Consequently, investigating small LI’s implies large groups need to be tested. Using fMRI for this would not only be time-consuming, but also expensive. In an attempt to study bilateral LI's in a cost-efficient manner, we will use a technique closely related to, but much cheaper than fMRI called functional transcranial doppler sonography (fTCDS). Although fTCDS, in contrast to fMRI, cannot precisely localize brain activity, it costs next to nothing to use and is fast. Moreover, it agrees well with other methods for determining hemispheric language dominance, fMRI included (Deppe et al., 2000).

These features make fTCDS an attractive tool for large-scale testing. In addition to using fTCDS to allow inclusion of a large sample size, we will also increase the chance of detecting volunteers with bilateral speech representation by over-sampling left-handers. We will tackle two specific research questions: The first one is 'What is the test-retest reliability of bilateral speech dominance?' and the second one is 'How often does someone change hemisphere dominance across sessions?'. This is because a common procedure is to classify participants dichotomously with LI = 0, but research is lacking that shows how often this gives rise to inconsistent classification across sessions (especially with bilateral individuals or when the LI difference is small).

Methods and materials

4.1 Participants

Meeting the goal of this study was complicated by the fact that bilateral activation during speech tasks is rather uncommon and it is not known a priori which participants will show this pattern. This means that speech dominance had to be determined in a large number of volunteers just to gather a reasonably sized subgroup of participants with small LI's. That is why we first identified people with a small speech LI from others fTCDS studies that we run concurrently and invited those - as well as clearly left speech dominant controls - to participate in a follow-up session scheduled one to eight weeks later, during which they completed the same fTCDS speech task a second time. Other participants were recruited through various methods, including Psychology credit students from the Faculty of Psychology and Educational Sciences at Ghent University, volunteers who were compensated for their participation, and through the Ghent University Sona web service. To increase the chances of detecting individuals with bilateral language representation and to allow for a larger sample size, we oversampled left-handers,

We strived to collect useable retest data of minimally 47 participants with initial bilateral speech dominance and an equal number of controls with initial left speech dominance. The maximum sample size was 70 participants per subgroup. The exclusion criteria for all participants were: no reported history of neurological disease, diagnosed mental problem or neurodevelopmental disorder. In order to be eligible to be invited to participate in the retest session, participants must meet following criteria in a) age between 18-40 years b) native Dutch speaking c) normal or corrected-to-normal vision d) agreed to be contacted for participation in follow-up studies as indicated on the informed consent filled out during the first test session e) for the bilateral speech dominant subgroup: classified as bilateral based on the word generation task performed during the first test session f) for the clearly left speech dominant subgroup: classified as left dominant based on the word generation task performed during the first test session and matching in terms of age (difference of at most 3 years), handedness and biological sex to an already re-tested participant in the bilateral speech dominant group, regardless of whether that participant also was classified as “bilateral” during the retest session. Description of the dataset can be found under point 5.1 Demographics.

4.2 Data collection procedures

Following approval by the ethics committee of the Faculty of Psychology and Pedagogical Sciences of UGent, participants were subject to a standard procedure during the study. Participants were scheduled for a 90-minute time slot which consisted of a briefing, the test session, and relevant data collection. Prior to the test session, participants were informed about the study's objective, the tasks, and the Doppler technique. Informed consent was obtained before proceeding with the test session. Next, two ultrasound probes were placed bilaterally over the temporal bone window in order to target the middle cerebral artery (MCA), which supplies blood to core language regions within the frontal and temporal lobe. The procedure to determine the temporal window and place the probes on each participant took approximately 30 minutes. Once the probes were in place, participants were asked to complete three tasks. After the tasks, relevant demographic data was collected, including information about siblings, handedness, education, native language, birth time, etc.

4.2.1 Tasks

My master thesis is part of a broader research that implements fTCDS. During the testing session, participants completed three separate tasks: 1) word generation task 2) line bisection task 3) tool pantomiming task. Only the first one is relevant to my thesis, which is why the other two tasks will not be described further. All participants performed the three tasks while functional transcranial doppler sonography (fTCDS) data was recorded to measure brain activation asymmetries evoked by these tasks, which are designed to determine dominance for speech (word generation), manual praxis (tool pantomime) and spatial attention (line bisection judgement).

Every task consisted of one practice block and 16 experimental blocks, each of which lasted 38s and had an identical structure. Each block started with the message "Maak je hoofd leeg" ("clear your mind") displayed on the screen for 3s to inform the participant the task will soon start. The task itself then started, and lasted for 20s, after which a fixation cross was shown for 15s to indicate a rest period. Participants were asked to try to keep a clear mind during this rest phase. Each experiment also started with a 12s rest period.

The task in order to determine hemispheric language dominance, is called the 'word generation task'. Generating words is among the most commonly used tasks to determine hemispheric dominance for speech and elicits clearly left lateralized responses in most people, in line with the well-established population-wide leftward asymmetry of language production (Knecht et al., 2001). During this task, participants were asked to covertly say as many words as possible starting with a visually displayed letter. All letters were displayed on a gray background for 20s and they correspond to the most common beginning letters in Dutch: S, B, K, V, P, A, O, T, G, R, M, D, H, L, W, Z. Each letter appeared only once during the experiment and was presented pseudo-randomly.

4.3 Data Processing

4.3.1 fTCDS data

The fTCDS data was preprocessed in a semi-automated fashion using a modified R script based on Woodhead et al., 2021 (Royal Society Open Science), which had been uploaded to https://osf.io/chmk5/. The raw CBVF was first down sampled from 100 to 25Hz and then segmented into epochs of 38s (10s before task onset until 28s post-onset). Next, the data was inspected for spikes and dropouts (points outside of the 0.0001–0.9999 quantiles of the CBFV data). If there was only a single artefact within an epoch, it is replaced with the mean for that epoch. If more outlier data points were identified, the epoch were excluded. Each epoch of the raw data was visually inspected for artefacts and were rejected if the user observed an artefact within the baseline period and/or period-of-interest. Subsequently, the data was normalized by dividing the CBF by the mean and multiplying by 100. This ensured that the CBFV values beame independent of the diameter of the MCA and of the angle of insonation of the Doppler probe, since the velocity of blood flow depends on the angle of insonation. If the angle of insonation changes, the reported blood flow velocity may also change (Stroobant & Vingerhoets; 2000). Heart cycle integration was performed next, after which epochs are baseline corrected using the interval between block onset and the ten seconds prior to the onset. Finally, epochs containing values below 60% or above 140% of the mean normalized CBFV were marked as artefacts and removed.

For each fTCDS task, an LI was calculated as the average difference, across all retained epochs, in CBVF between the left and right MCA in a period of interest of 20s, starting from 3s post-task onset until the end of the task period. In addition, two more LI's were calculated using only odd and even trials. Finally, a participant-specific standard error of the LI of whole task is calculated from the left-right CBFV difference across trials. This standard error serves to compute a confidence interval used to classify participants in a data-driven way based on their speech dominance. A participant is bilateral speech dominant if the 95% confidence interval around the LI includes 0 and is left or right speech dominant if if the 95% confidence interval around the LI does not include 0 and is negative or positive respectively.

In order to ensure data quality, fTCD Epochs were excluded if the normalized CBFV is lower than 60% or higher than 140% of that participant's mean CBFV. If a participant has fewer than 10 remaining epochs in their word generation fTCD data of either test session, they were excluded from the analysis.

4.3.2 Statistical analysis

All data was analyzed in R 4.0.4 in conjunction with RStudio 2023.03.0+386. Several packages and methods were used to analyze the results.

First, the test-retest reliability of hemispheric language dominance was assessed using the intraclass correlation coefficient (ICC) method. The ICC, chosen as the statistical analysis method, provides a measure of both correlation and agreement between measurements, and its interpretation is straightforward (Koo & Li, 2016). The ICC ranges from 0 to 1, where values below 0.5 indicate poor reliability, 0.5 to 0.75 indicate moderate reliability, 0.75 to 0.9 indicate good reliability, and values above 0.9 indicate excellent reliability (Bobak et al., 2018). There are various forms of ICC, each with distinct assumptions in their calculation, leading to different interpretations (Koo & Li, 2016). For this analysis, we utilized ICC2, which employs a two-way mixed model with absolute agreement and a single rater, as our goal was to assess the reliability of a single measurement moment (Koo & Li, 2016). ICC2 was calculated separately for participants classified as bilateral in session 1 and for the control group of left-dominants. To perform the analysis, we first selected the relevant data for session 1 and session 2 using the 'subset()' function. Subsequently, the subsets were merged based on their 'Retest_ID' using the 'merge()' function. To compute the ICC, an input matrix was constructed using the 'matrix()' function, containing the measurements from session 1 and session 2. Finally, the 'ICC()' function was employed to calculate the correlation coefficient. This approach allows us to assess the test-retest reliability of hemispheric language dominance for both the bilateral group and the left-dominant control group.

Second, in order to assess the consistency of dichotomous classification of hemispheric dominance, the following steps were taken. First, the lateralization category ("left-bilateral" or "right-bilateral") was assigned based on the sign of the LI values using the 'ifelse()' function.

Subsequently, the subsets were merged based on the 'Retest_ID' using the 'merge()' function. Finally, the 'sum()' function was used to compare the lateralization categories between session 1 and session 2, counting the number of sign changes. This analysis provides insights into the consistency of hemispheric dominance classifications over time.

Lastly, a split-half reliability analysis was conducted to evaluate the consistency between even and odd items for participants with consistent bilateral laterality. The Spearman-Brown correlation method, which is the most appropriate reliability statistic for a two-item scale, was used along with the standardized coefficient alpha (Eisinga et al., 2013). The correlation coefficients range from -1 to 1, where -1 represents a perfect negative correlation, 0 represents no correlation, and 1 represents a perfect positive correlation. To perform the analysis, the relevant data for both sessions was selected using the 'subset()' function. Then, the even trials and odd trials from both sessions were combined using the 'c()' function. Finally, the Spearman correlation between the combined even trials and combined odd trials was calculated using the 'cor()' function with the argument 'method = spearman'.

Results

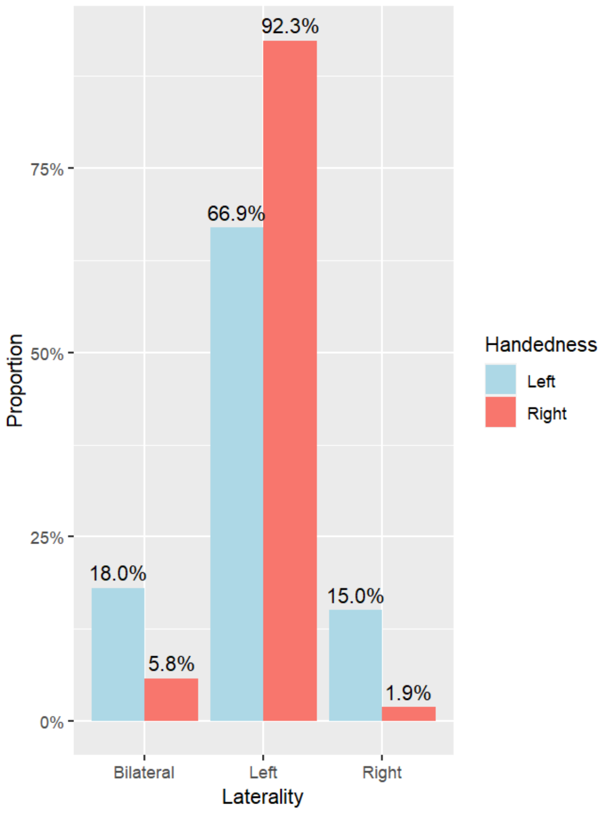
5.1 Demographics

The initial dataset comprised 193 participants. Nonetheless, the exclusion criteria led to the removal of 8 participants due to the absence of signal in the MCA, 7 participants due to the presence of a neurodevelopment disorder, and 2 participants due to insufficient remaining epochs in their word generation fTCD data (less than 10). Consequently, the final sample size consisted of 176 participants, comprising 32 males (18.2%) and 144 females (81.8%), with an average age of 21 years (SD = 3.7). Regarding handedness, out of the total sample, 125 participants were left-handers (71%), and 51 participants were right-handers (29%). Among the right-handers, 76.5% were female and 23.5% were male, while among the left-handers, 84% were female and 16% were male. It is worth noting that the research is still ongoing, and the final dataset will include additional participants.

The dataset can be separated into two subsets: the first one comprising the initial test session wherein all the recruited participants participated, and the second one involving the participants who underwent both the initial test session and a subsequent retest session (N = 26). The individuals who showed bilateral language lateralization in the initial test session were invited to partake in the retest session (N = 18), along with a few participants who showed strong left hemispheric dominance in the initial test session (N = 8), as a control group. The distribution of hemispheric lateralization thus was categorized into three groups: bilateral, left dominant, and right dominant. The analysis revealed that among right-handers, 5.9% exhibited bilateral language lateralization, whereas among left-handers, this proportion was 16%. Moreover, 92.2% of right-handers displayed left hemispheric language dominance, whereas 68.8% of left-handers showed the same pattern. Notably, only one right-handed individual exhibited right hemispheric dominance, whereas this pattern was observed in 15.2% of left-handed participants. The raw distribution of hemispheric language dominance by handedness is presented in Figure 1. In terms of sex differences in language lateralization, among male participants, 75% were classified as left dominant, 15.6% as right dominant, and 9.4% as bilateral. For female participants, 75.7% exhibited left dominance, 10.4% right dominance, and 13.9% demonstrated bilateral language dominance.

Figure 1.

Distribution of hemispheric language dominance by handedness in session 1.



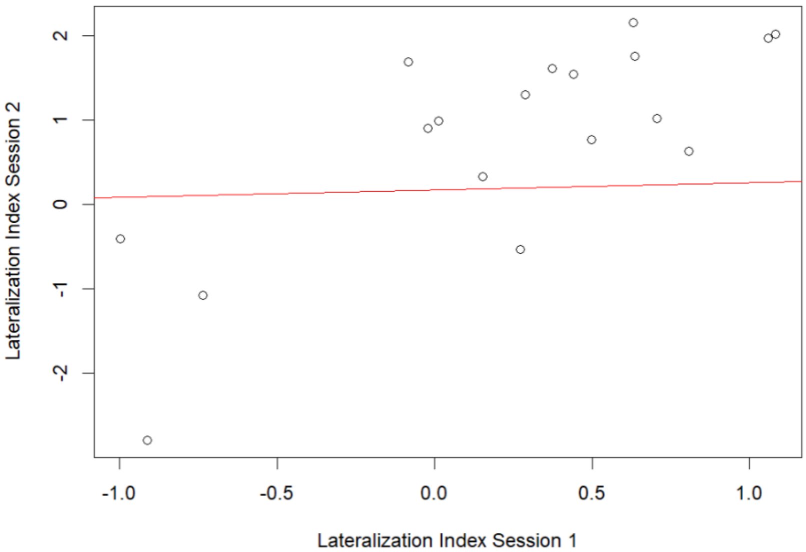
5.2 Test-retest reliability

To assess the test-retest reliability of the hemispheric language dominance classification for participants identified as bilateral in the initial test session, a second test session was conducted. In total, 23 participants were initially classified as bilateral, out of which 18 took part in the retest session (experimental group), along with 8 control participants who were classified as left-dominant in the first session (control group). All participants underwent the same procedure as in the initial session. Among the 18 bilateral participants who completed the retest session, 9 participants (50%) maintained their bilateral classification for hemispheric language dominance. Meanwhile, 8 participants (44.4%) were now classified as left-dominant, and one participant (5.6%) was now classified as right-dominant. Notably, all control participants who were classified as left-dominant in the first session remained classified as left-dominant in the second session. The demographic characteristics of bilateral participants and left-dominant participants can be found in Table 1 and Table 2, respectively, presented in section 5.3.

The test-retest reliability of the bilateral classification for hemispheric language dominance was evaluated using the interclass correlation coefficient (ICC). The analysis was based on the two test sessions. The ICC was calculated using a single random rater model, resulting in an ICC value of 0.54, which falls within the range of moderate reliability. This ICC was statistically significant ($F = 4.01$, $p = 0.003$, 95% CI = 0.11;0.80), meaning that the level of agreement observed between the two test sessions is unlikely to have occurred by chance. For a visual representation of the correlation between the LIs across two test sessions, see Figure 4.

Figure 4.

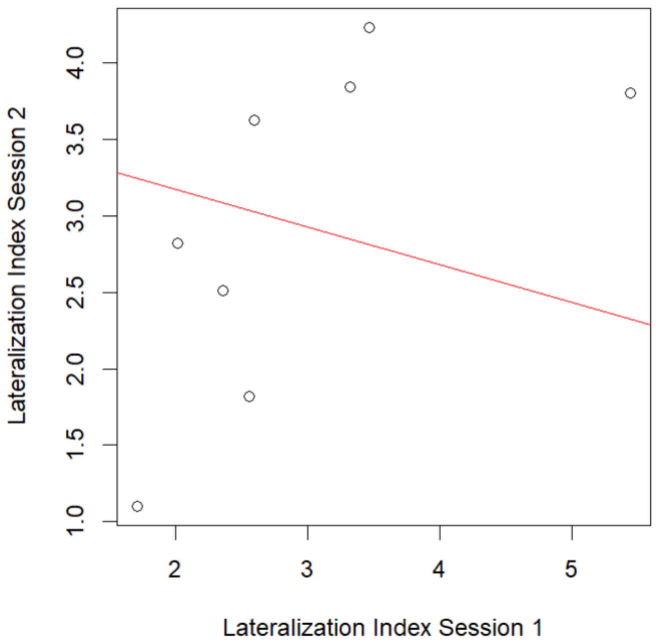
Correlation of the LIs across two test sessions for participants classified as bilateral in session 1.



The test-retest reliability was also evaluated for the control group consisting of individuals with left hemispheric dominance. The ICC value, using the single random rater model, was 0.70, indicating a good level of agreement between the two test sessions. This ICC value was found to be statistically significant ($F = 5.6$, $p = 0.019$, 95% CI = 0.101;0.93), suggesting that the observed agreement between the two test sessions is unlikely to have happened by chance. For a visual representation of the correlation between the LIs across two test sessions, see Figure 5.

Figure 5.

Correlation of the LIs across two test sessions for participants classified as left dominant in session 1.



5.3 Consistency of dichotomous classification of hemisphere dominance

Based on the analysis of the language lateralization indices, sign flips were examined to evaluate the consistency of the dichotomous classification of hemispheric dominance (left or right dominant). A negative LI indicates right-bilateral hemispheric lateralization, while a positive LI indicates left-bilateral lateralization. Comparing both test sessions, the data showed that out of the total participants, three underwent sign changes, see Table 1. Specifically, one participant changed from left-bilateral to right-bilateral (BLD13), one participant changed from right-bilateral to left-bilateral (BLD15), and one participant changed from right-bilateral to left-dominant (BLD18).

In contrast, when the same analysis was performed on the control group, consisting of participants who were classified as left-dominant, there were no sign flips observed (Table 2).

Table 1.

'*Lateralization indices over the two test sessions, for participants classified as bilateral in session 1.*'

Classified as (Left/Right) Bilateral in session 1							
	LI session 1	*Classification*	*LI session 2*	*Classification*	*Handedness*	*Sex*	*Age*
BLD01	0.013	Left Bilateral	0.983	Left Bilateral	Left	Male	19
BLD02	0.498	Left Bilateral	0.767	Left Bilateral	Left	Female	18
BLD03	0.629	Left Bilateral	2.151	Left Dominant	Left	Female	18
BLD04	0.635	Left Bilateral	1.751	Left Dominant	Left	Female	18
BLD05	-0.735	Right Bilateral	-1.082	Right Bilateral	Left	Female	19
BLD06	1.059	Left Bilateral	1.971	Left Dominant	Left	Female	21
BLD07	0.705	Left Bilateral	1.016	Left Bilateral	Left	Female	30
BLD08	0.807	Left Bilateral	0.624	Left Bilateral	Left	Female	19
BLD09	-0.997	Right Bilateral	-0.412	Right Bilateral	Left	Female	33
BLD10	1.082	Left Bilateral	2.019	Left Dominant	Left	Female	18
BLD11	0.373	Left Bilateral	1.612	Left Dominant	Left	Female	18
BLD12	-0.913	Right Bilateral	-2.797	Right Dominant	Left	Female	21
BLD13	**0.273**	**Left Bilateral**	**-0.537**	**Right Bilateral**	Left	Male	22
BLD14	0.152	Left Bilateral	0.331	Left Bilateral	Left	Female	21
BLD15	**-0.021**	**Right Bilateral**	**0.904**	**Left Bilateral**	Left	Female	19
BLD16	0.287	Left Bilateral	1.296	Left Dominant	Left	Female	20
BLD17	0.441	Left Bilateral	1.544	Left Dominant	Left	Female	19
BLD18	**-0.083**	**Right Bilateral**	**1.687**	**Left Dominant**	Left	Female	20
					Left-handed=100% Right-handed=0%	*Female = 88.9% Male = 11.1%*	*M= 20.7 SD = 4.14*

Table 2.

'Lateralization indices over the two test sessions, for participants classified as left dominant in session 1.'

Classified as Left Dominant in session 1					
	LI session 1	*LI session 2*	*Handedness*	*Sex*	*Age*
LLD01	2.596	3.623	Right	Male	20
LLD02	5.442	3.799	Left	Female	18
LLD03	2.557	1.817	Left	Female	21
LLD04	2.011	2.817	Left	Male	19
LLD05	3.319	3.837	Left	Female	18
LLD06	3.466	4.231	Left	Female	18
LLD07	2.358	2.510	Left	Female	20
LLD08	1.709	1.104	Left	Female	18
			Left-handed=87.5% Right-handed=12.5%	*Female=75% Male=25%*	*M=19 SD=1.95*

5.4 Split-half reliability

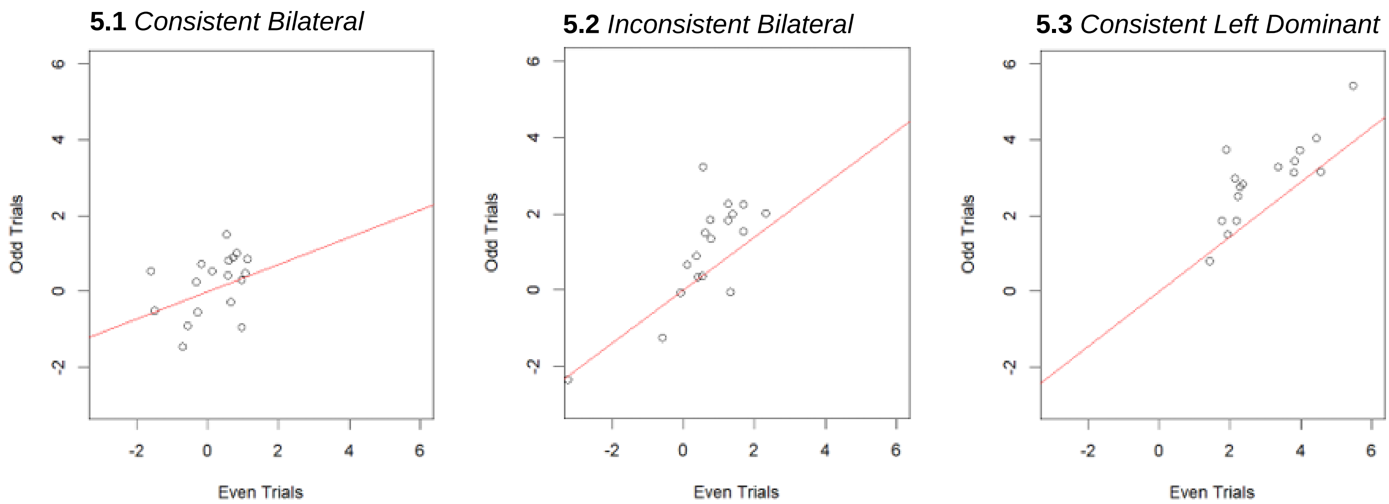
The split-half reliability analysis was conducted to assess the consistency between even and odd items for participants exhibiting consistent bilateral laterality. The obtained correlation coefficient was 0.36, indicating a moderate positive correlation between even and odd trials for consistent bilateral participants. See figure 5.1 for a visualization of the correlation.

Additionally, the split-half reliability analysis was performed on participants who exhibited inconsistent bilateral laterality (bilateral in session 1, left/right dominant in session 2). The obtained correlation coefficient was 0.69, indicating a stronger positive correlation between even and odd trials for inconsistent bilateral participants. See figure 5.2 for a visualization of the correlation.

Lastly, the split-half reliability was computed for participants showing consistent left dominance. The correlation coefficient between even and odd trials in this subgroup was 0.72, indicating strong positive relationship. See figure 5.3 for a visualization of the correlation.

Figure 5.

Correlation of the LIs in even and odd trials across two test sessions.



Discussion

The primary objective of this study was to examine the test-retest reliability of bilateral language dominance and the frequency of changes in hemisphere dominance across multiple testing sessions. To investigate this, participants completed a word generation task while their hemispheric dominance was assessed using transcranial doppler sonography.

6.1 Theoretical Implications

The assessment of test-retest reliability for the bilateral classification of hemispheric language dominance was conducted using the intraclass correlation coefficient (ICC). A comparison between the ICC results of the control group (left-dominant) and the experimental group (bilateral) revealed that the control group exhibited a higher ICC value of 0.70, indicating good test-retest reliability for the left-dominant classification. Meanwhile, the experimental group yielded an ICC value of 0.54, suggesting a moderate level of test-retest reliability for the bilateral classification. It is important to approach the interpretation of the bilateral classification with caution due to the moderate ICC value observed. The available test-retest data for individuals with bilateral language classification is limited, making it challenging to directly compare our findings with existing research. Nevertheless, the ICC obtained from the control group aligns with previous studies utilizing fMRI and fTCDS, which have reported moderate to highly reproducible laterality indices for individuals clearly classified as left-dominant (Johnstone et al., 2020; Nettekoven et al., 2018; Rutten et al., 2002; Stroobant & Vingerhoets, 2001; Wilson et al., 2017). In terms of bilateral language reproducibility, the findings are less definitive, with some fMRI studies reporting poor inter-session reproducibility, albeit with small sample sizes (Jansen et al., 2006; Johnstone et al., 2020). Our study's moderate level of reproducibility aligns more closely with a fTCDS study that demonstrated good reproducibility in nine atypical participants, although this subsample (Hodgson & Hudson, 2017) comprised both bilateral and right-dominant individuals. It is possible that (clearly) right-dominant individuals exhibit greater reproducibility, potentially contributing to the higher reliability index observed in that study. Notably, our study boasts the largest sample size for test-retest reliability assessment of bilateral individuals to date.

Another reliability factor that was measured, was the split-half reliability of LIs between even and odd trials over two test-sessions. Surprisingly, we found that the inconsistent bilateral group exhibited a higher correlation (0.69) compared to the consistent bilateral group (0.36). This unexpected finding suggests that the participants in the inconsistent bilateral group experienced relatively fewer fluctuations in their language lateralization over time and that individuals with a consistently bilateral classification may have experienced some variability or fluctuations between the two test sessions, leading to a lower degree of correlation. Specifically, the consistent bilateral group contains more people with irregular odds and even LIs in at least one of the two sessions. However, it is worth noting that if there is no or only a slight difference between the two hemispheres, it is not uncommon for slight variations in activation to occur during and over the tasks, leading to alternating dominance between hemispheres. These fluctuations may contribute to the observed variability in language lateralization. The split-half reliability was the highest for the consistent left-dominants with a correlation of 0.72. The literature available for spit-half reliability allows for the assessment of reliability within a single test session rather than across multiple sessions (Bruckert et al., 2021). This restricts our ability to directly compare our findings with other studies that have reported split-half reliability over multiple sessions.

Furthermore, in evaluating the consistency of the dichotomous classification of hemispheric dominance (left or right dominant), sign flips between test sessions were examined as a measure of change in the direction of language lateralization. The occurrence of sign flips was found to be seldom in this study. Specifically, no sign changes were observed in the left-dominant control group, and among individuals with a relatively small asymmetry difference (bilateral group), only 3 individuals (17%) demonstrated a sign flip. To assess the impact of these sign flips, an analysis was conducted to estimate the potential error in classification. It was determined that approximately 2.7% of left-handed individuals had an incorrect classification as bilateral due to the sign flips. This estimation was derived by multiplying the proportion of left-handers classified as bilateral in the first session (16%) by the percentage of participants with a sign flip (17%), resulting in an approximate error rate of 2.7%. When maintaining a dichotomous classification, a key consideration arises regarding the exclusion of individuals with a bilateral classification. In this sample, 16% of left-handers were classified as bilateral. Therefore, the decision to accept a 3% error rate would imply retaining these individuals, even if a small amount was incorrectly classified due to the sign flips. This raises the question of whether accepting a 3% error in classification is justifiable in order to avoid excluding 16% of bilateral left-handed individuals. It calls for a careful examination of the trade-off between maintaining a dichotomous classification, the costs in terms of time and finances of excluding participants and the potential misclassification of a small percentage of participants.

Lastly, regarding the rate of (a)typical language dominance, the observed distribution of hemispheric lateralization in our first test-session-sample is in line with previous research, indicating that our study captured a representative sample. The results demonstrate a predominance of left hemispheric language dominance, with 92.2% of right-handers and 68.8% of left-handers displaying this pattern. These proportions are consistent with previous studies reporting percentages of approximately 70-75% in left-handed individuals and slightly over 90% in right-handed individuals (Vingerhoets, 2019). These findings support the notion that, in the general population, regardless of sex or handedness, language relies mainly on the left hemisphere of the brain (Vingerhoets, 2019). Furthermore, right hemispheric dominance was observed in 15.2% of left-handers and only in one right-handed individual, which is consistent with earlier research indicating a prevalence of right hemispheric dominance ranging from 6% to 20% in left-handers and from 0% to 10% in right-handers (Knecht et al., 2000; Szaflarski et al., 2017; Vingerhoets, 2019). The prevalence of bilateral language dominance aligns with reported rates of approximately 5% in right-handers and 10-15% in left-handers (Carey & Karlsson, 2019; Li et al., 2020; Székely et al., 2005) corroborating the validity of our findings with 5.9% in right-handers and 16% in left-handers. Considering the earlier mentioned study conducted by Mazoyer et al. (2014), they proposed that there was no association between left-handedness and atypical language dominance, except for a small subset of left-handers who exhibited right-hemispheric dominance. They observed that an approximately equal proportion of bilateral dominance was found among left-handed and right-handed individuals. However, this statement has been challenged by several studies employing fMRI, fTCDS, and Wada testing, which have demonstrated that left-handed individuals are more likely to exhibit bilateral language dominance compared to right-handed individuals (Kundu et al., 2019; Bernal & Ardila, 2014). In line with these findings, our study also does not support the statement that there is no relationship between left-handedness and atypical language dominance. Instead, our results align with the conclusions drawn by Kundu et al. (2019) and Bernal & Ardila (2014), as we observed nearly three times the prevalence of bilateral dominance among left-handers compared to right-handers. However, it is essential to interpret this finding cautiously since our study deliberately included an oversampling of left-handed participants, which increases the likelihood of detecting bilaterality in this subgroup. A similar cautious approach should be taken when considering the distribution of laterality by sex. In our study, females appear to exhibit bilateral activation more often (13.9%) compared to males (9.4%), which is partly consistent with the findings of Clements et al. (2016). They reported that females demonstrated increased bilateral activation in the inferior frontal gyrus during a language task, while males showed a stronger left lateralization. However, it is important to consider the uneven distribution of males (N = 32) and females (N = 144) in our sample, as this may have influenced the detection of bilateral dominance. It should be noted that the majority of participants were recruited from the Faculty of Psychology and Educational Sciences at Ghent University, where female students constitute a larger proportion of the student population. Moreover, men in our sample did not show stronger left lateralization than women. This could be explained by the finding that more men than women showed right hemispheric dominance.

6.2 Methodological Recommendations

When combining our findings regarding bilateral language dominance, we observed a moderate test-retest reliability (0.54), a moderate split-half reliability (0.36), and a small error rate (3%) within a dichotomous classification. Based on these results, the choice between a dichotomous or trichotomous classification depends on the specific objectives and context of the study or clinical application.

A dichotomous classification offers a simplified approach to interpreting and analyzing the distribution of language dominance. By categorizing individuals into clear left or right dominant groups, this classification method enhances the comparability of findings with existing literature and clinical practices that predominantly utilize a binary classification system (Bradshaw et al., 2017). Importantly, a dichotomous classification remains defensible, even with small LIs, given the low number of sign flips observed. While employing a dichotomous classification necessitates considering the small percentage of error associated with this approach, it offers the advantage of yielding a larger sample size for subsequent research investigations and provides a broader basis for generalization of findings.

On the other hand, a trichotomous classification acknowledges the existence of individuals with bilateral dominance, potentially capturing the complexity of language lateralization more accurately. This classification allows for a more nuanced understanding of the distribution of language dominance and recognizes the presence of individuals with shared language processing between both hemispheres, in line with the “bilaterals” occasionally found during Wada testing. However, it is worth noting that half of the individuals classified as “bilateral” based on the usual classification method (the Z-test method used in our study) were not reproducible, impacting the defensibility of a trichotomous classification. Researchers specifically interested in investigating “bilateral” language dominance as a phenomenon might benefit from testing their participants multiple times to identify the ‘true’ or ‘consistent’ bilaterals.

In summary, in the context of a research environment, adopting a dichotomous classification may be practical for the purpose of facilitating comparisons. Researchers specifically interested in investigating bilateral language dominance may benefit from multiple retest sessions to identify consistent bilaterals. However, in a clinical setting, such as during surgical interventions, the focus is on individual cases rather than population averages. Therefore, the identification and detection of anomalous cases, even if they occur infrequently, hold significant importance (Tailby et al., 2017).

6.3 Limitations

Finally, several limitations of this study can be addressed. First, we strived to collect usable retest data of 47 bilateral participants an equal number of controls with initial left speech dominance but managed to gather only a bit more than one third of the bilateral participants (N=18), and approximately one sixth of the left-dominant participants (N=8). Next, we only did one retest-session. Using a single retest session may not fully capture the temporal stability of language lateralization, as it does not account for potential fluctuations or variability in language dominance over longer periods. Multiple retest sessions conducted over an extended duration would provide a more comprehensive evaluation of the stability and reliability of the classification. Additionally, a larger number of retest sessions would enable us to examine the biological variability and the consistency of language dominance over time and investigate potential patterns or trends in the classification. Therefore, the generalizability of our findings to long-term language lateralization stability may be limited due to the use of a single retest session. Furthermore, it is worth noting that our sample primarily consisted of young participants. Due to ethical considerations, we did not collect information regarding the menstrual cycle, which prevented us from incorporating this factor into the interpretation of our results. Finally, it is important to consider a methodological adjustment made in our study when comparing the results to other studies. Specifically, we excluded the overt component of the word generation task, where participants typically generate words internally and then verbalize them. This decision was made to minimize the potential influence of short-term memory on the calculation of the lateralization index and to minimize signal interferences. While this adjustment is not a limitation in itself, it should be taken into account when interpreting and comparing our findings with those of other studies that include the overt component in the word generation task.

6.4 Suggestions for future research

Subsequent investigations may explore potential differences between the consistently bilateral group and consistent (left) highly lateralized individuals in various aspects, such as language performance and organization of the language system. These investigations can utilize fMRI to examine regional brain activity. Additionally, it is worth considering whether individuals classified as bilateral for word production, also exhibit bilateral activation in other domains of language processing, including language comprehension, syntax, and other related aspects.

Conclusion

In conclusion, the present study provides valuable insights into the test-retest reliability and classification of bilateral language dominance. The findings indicate a moderate level of test-retest reliability for the bilateral classification, moderate split-half reliability, and a small error rate within a dichotomous classification. The decision to adopt a dichotomous or trichotomous classification depends on the specific objectives and context of the study or clinical application.

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