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Étude des bases neurales de l'asymétrie d'appui

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Année 2020

NEURAL CORRELATES OF WEIGHT BEARING ASYMMETRY

THÈSE
PRÉSENTÉE POUR L'OBTENTION DU TITRE DE DOCTEUR EN MÉDECINE
DIPLÔME D'ÉTAT

Adélie CHRISTIAENS

[Données à caractère personnel]

THÈSE SOUTENUE PUBLIQUEMENT À LA FACULTÉ DE MÉDECINE DE GRENOBLE

Le : 20/10/2020

DEVANT LE JURY COMPOSÉ DE

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Résumé

Objectif. L'asymétrie d'appui est un comportement postural fréquent et possiblement sévère après un accident vasculaire cérébral (AVC). Elle est liée au déficit de la commande motrice volontaire, à la négligence spatiale, à la représentation spatiale et à la verticalité. Les corrélats neuro-anatomiques de l'asymétrie d'appui n'ont cependant jamais été étudiés à ce jour. L'objectif de cette étude est donc de déterminer, pour la première fois, les structures impliquées dans l'asymétrie d'appui.

Méthode. Il s'agit d'une cohorte de 72 patients (43 ayant une lésion droite et 29 une lésion gauche), ayant eu à la fois une IRM cérébrale et un enregistrement posturographique à la phase subaigüe après un premier AVC hémisphérique. Les corrélations anatomo-cliniques ont été réalisées en utilisant la méthode Voxel Lesion Symptom Mapping (VLSM) avec le logiciel SVLRSMGui (Zhang et al., 2014) pour la substance grise. La substance blanche a été analysée en utilisant le module Tractotron de BCBToolkit (Foulon et al., 2018).

Résultats. L'analyse VLSM a révélé une forte association entre l'asymétrie d'appui et des structures corticales : cortex pariétal postérieur et insula postérieure, mais aussi sous corticales : thalamus postéro-latéral et putamen. Aucun lien statistique n'a été retrouvé entre l'asymétrie d'appui et les faisceaux de substance blanche. Néanmoins, le faisceau cortico-spinal et le faisceau longitudinal supérieur semblent impliqués.

Conclusion. Il s'agit de la première étude visant à déterminer les bases neurales de l'asymétrie d'appui en position debout, sur une série de 72 patients évalués à la phase subaigüe après un premier AVC hémisphérique. Concernant la substance grise, le cortex pariétal, l'insula postérieure, le putamen et le thalamus postéro-latéral sont liés à l'asymétrie d'appui et construisent ensemble le schéma corporel et les représentations spatiales de façon générale. Concernant la substance blanche, nous devons analyser plus spécifiquement le rôle du faisceau cortico spinal et du faisceau longitudinal supérieur.

Mots clés : Troubles de la posture, asymétrie d'appui, bases neurales, Voxel Localised Symptom Mapping, BCB Toolkit

Abstract

Objective. Weight Bearing Asymmetry (WBA) occurs frequently after a stroke and can be severe. It is a complex postural behaviour, linked to muscle weakness, Unilateral spatial neglect (USN), spatial representation and verticality. The neural determinants of WBA have never been studied. This study is a first attempt to determine the neural bases of WBA.

Methods. This is a cohort study of 72 inpatients (43 patients with right-sided and 29 patients with left-sided lesions) with both MRI and posturographic assessment (obtained with a two-force platform) in the subacute stage after a first hemispheric stroke. Anatomico-correlation was achieved using the Voxel Lesion Symptom Mapping (VLSM) method with the SVLRSMGui software (Zhang et al., 2014) to analyse grey matter, and using tractotron on BCBToolkit to analyse white matter (Foulon et al., 2018).

Results. VLSM analysis reveals a strong association between WBA and cortical structures (posterior parietal cortex, posterior insula) and subcortical structures (postero-lateral thalamus and putamen). Regarding white matter tracts, the cortico-spinal tract (CST) and superior longitudinal fasciculus (SLF) seem to be involved, but the correlation is not statistically significant.

Conclusion. This is the first study to investigate and identify the neural bases of weight-bearing control in standing position, using a series of 72 individuals tested at the subacute stage after a first hemispheric stroke. Concerning grey matter, the parietal cortex, posterior insula, putamen, and posterior-lateral thalamus are related to weight bearing asymmetry. Together these contribute to construct spatial representations in order to stand upright. Concerning white matter, the involvement of the SLF and the CST should be specifically analysed in further studies.

Key words: Postural disorders, Weight bearing asymmetry, neural bases, Voxel Localised symptom mapping, BcBToolkit

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I. Introduction

Humans in standing position prefer to bear more weight on one of their feet, called their postural foot, rather than being strictly symmetrical. The other foot (known as the preferred foot) supports less weight and is used for ability tasks (such as kicking a ball) (Chapman et al., 1987; Hatta et al., 2005). In some conditions (as in unilateral lower limb amputation or unilateral neurological deficits) this support asymmetry may increase, become pathologic and is also called Weight Bearing Asymmetry (WBA). Most dramatic WBA are observed after stroke, with some patients bearing less than 30% of their weight on their paretic leg (Genthoon, Rougier, et al., 2008; Rougier & Genthoon, 2009; Sackley & Lincoln, 1991). This stability disorder is frequent after stroke. Indeed, about 1/3 of patients stand asymmetrically in the subacute stroke stage, and this behaviour remains present in the chronic stage. (Jamal et al., 2019). After stroke, WBA can be severe, contributing to major balance (Chauvin, 2020; Mansfield et al., 2013) and gait (Guillebastre et al., 2012) disorders, and exposing patients to autonomy loss and a high risk of falling (Mackintosh et al., 2006). The challenge is therefore to understand clinical and neurological determinants of WBA, regarding brain structures.

1. WBA diagnosis

Definition

The threshold for diagnosing pathological WBA is not well determined. From studies of healthy participants or studies comparing stroke patients with a control group, it seems that a threshold of 41% of body weight spontaneously supported by the affected lower limb is the most appropriate cut-off to diagnose WBA (Guillebastre et al., 2012; Jeanson et al. in preparation; Sackley and Lincoln, 1991). Above this threshold, the distribution of body weight on both lower limbs seems in the normality ranges. In this study we use this 41% threshold to determine a pathological asymmetry, called WBA.

In patients with WBA, postural instability is commonly found and associated, with important oscillations, needing an increased energy expenditure to stand upright (de Haart et al., 2004; N. Genthoon & Rougier, 2005; D. Pérennou, 2005; Rougier, 2007).

Evaluation

WBA is evaluated using posturography, which is a measurement of positions and displacements of the center of pressure (CP), together with vertical forces applied to the ground by each lower limb, in a calm standing position. Indeed, the CP is the application point of the resultant upward force exerted by the support surface on the feet in reaction to gravity. Balance is ensured when the CP is projected well within the base of support provided by the two feet (Pérennou & Bronstein, 2005).

Posturography requires one or two force platforms:

- Two force platforms measure the percentage of total body weight leading under each foot, and therefore direct information about the symmetry of weight bearing.
- A single force platform gives information about position and displacements of the CP and indicates the rhythmic aspects of postural sways (Gasq et al., 2014). It provides a measure (in mm) corresponding to the distance between the standard CP (between the two heels) and the patient's CP. This measure can be converted using the following formula:

$$\%WBA = 50/[50/(D/2+55)*CPR_{es}]$$
 (CPR_{es} = center of pressure mean position in lateral axis, D= distance between the two heels in mm) (Genthon, Gissot, et al., 2008).

Two examples of postural drawing are represented figure 1.

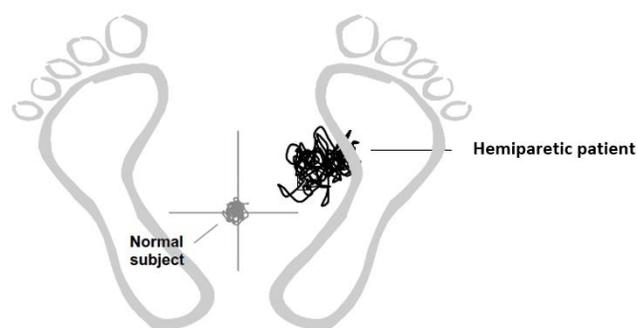


Figure 1: Posturographic drawing of a healthy subject and a left hemiparetic patient, presenting oscillations and right deviation of center of pressure.

To this day, posturographic assessment has not yet been standardised, although some criteria seem to be defined. However, we know that at least three sessions (Lafond et al., 2004; Pinsault & Vuillerme, 2009), lasting at least 30 seconds (Carpenter et al., 2001; Pinsault & Vuillerme, 2009) are required. Patients have to stand barefoot (Jeanson et al., n.d.), feet spaced as comfortably as possible; around 17 cm apart (Boumer et al., 2018; McIlroy & Maki, 1997) and without technical aids. Instructions given to the subject influence the outcome of posturography and should be standardized (Nardone & Schieppati, 2010). Currently, stroke patients with severe deficits are not able to do posturographic recording. The conditions of posturographic recording will have to be adapted for these patients. Moreover, beyond the clinical necessity, the assessment of the most severe asymmetric patients should allow a better understanding of mechanisms underlying WBA.

2. Determinants of the WBA

Although a major target in stroke rehabilitation, WBA is still poorly understood. WBA seems to result from a compromise in the control of an impaired body orientation with respect to gravity and the control of an impaired body stabilisation with respect to the base of support (Chauvin, 2020; Pérennou, 2006). This assumption is based on the fact that WBA seems to be both the direct consequences of some deficits such as weakness and spatial neglect (Chauvin, 2020) which prevent the affected lower limb from fully contributing to postural stabilisation, and also a strategy to compensate for a contralesional lateropulsion induced by a wrong internal model of verticality. In the following paragraphs we will attempt to describe what is known today about the effects of each deficit on the post-stroke WBA.

Weakness

Several studies suggest a strong involvement of weakness, asymmetric muscular tone and motor control in WBA (Chauvin, 2020; Genthon, Rougier, et al., 2008; Marsden et al., 2005; Pérennou, 2005). The assumption is that less weight is borne on the paretic leg due to weakness and in order to prevent destabilisation and falls. DOBRAS_IP (a recent study conducted in our neurological rehabilitation unit)

showed that weakness is the major factor related to WBA (Chauvin, 2020). Nevertheless, weakness alone cannot explain WBA. Postural control and spatial cognition appear to be involved too (Genthon et al., 2008).

Unilateral spatial neglect

Unilateral spatial neglect (USN) is one of the most disabling deficits after stroke. It is defined as the inability to take stimuli from the contralesional hemispace into account. « Patients fail to orient, respond to, and report sensory events occurring in the contralateral sides of space and of the body, to explore these portions of space through movements by action effectors (eye, limbs), and to move the contralateral limbs. » (Vallar & Calzolari, 2018). In clinical practice, spatial neglect is often separated into two entities: body and non-body neglect. Its processing is complex and involves sensory modalities, cognitive and attentional processes (Corbetta et al., 2005), spatial representations and coordinate systems (Halligan et al., 2003).

Relationship between WBA and spatial neglect has often been reported (Pérennou, 2006). Neglect seems to participate in WBA through its attentional component (less use of the paretic leg caused by attentional deficit) and its representational component (less use of the paretic leg caused by deficits in representation and body schema). Furthermore, neglect patients are more unstable and present WBA more frequently than non-neglect patients (Chauvin, 2020).

Spatial representations bias

To stand upright and interact with his environment, man must constantly gather representations of the parts of his body relating to each other and to the environment, thus constructing spatial references. The representations consist in multisensorial (visual, vestibular, somesthetic) integration in different frames of spatial reference, which can be distorted and cause postural disorders. Two main groups of spatial referential are described: egocentric and allocentric. Their misperception could result in disruption of the coordinates used to stand upright and symmetric.

Neural correlates of Weight Bearing asymmetry

The relation between distortion of spatial representation and WBA was first suggested by Rode et al., 1997. They observed a predominance of both postural imbalance and displacements of the CP in left hemiparetic patients. The right hemisphere, known to be the hemisphere of spatial cognition (Halligan et al., 2003), seemed to be involved in WBA. They also suggested that WBA could be due to a displacement of the postural sagittal reference toward the lesion's side. The sagittal reference is an egocentric reference, measured using the Subjective Straight Ahead (SSA) (Rousseaux et al., 2014): subject is asked to point “straight ahead” with or without vision. SSA is represented in figure 2. Egocentric references are characterised by multisensorial integration referring to the subject (Colombo et al., 2017). However, no study was able to confirm this supposed causal relationship between the lateral translation of the midsagittal plane and the WBA (Jamal et al., 2018).

In contrast, an association between WBA and a rotation in the representation of the Longitudinal Body Axis (LBA) has been demonstrated (Barra et al., 2007, 2009) and then confirmed (Hugues et al., 2015). The assessment of the LBA representation has been proposed Barra et al., 2007. The subject is in supine position in the dark and is asked to indicate verbally how a luminous rod should be adjusted in the frontal plane to align it with their LBA. Similarly to SSA, LBA is an egocentric frame of reference. They are both illustrated in figure 2. A contralesional deviation of LBA is frequently observed in hemiparetic patients (Barra et al., 2007).

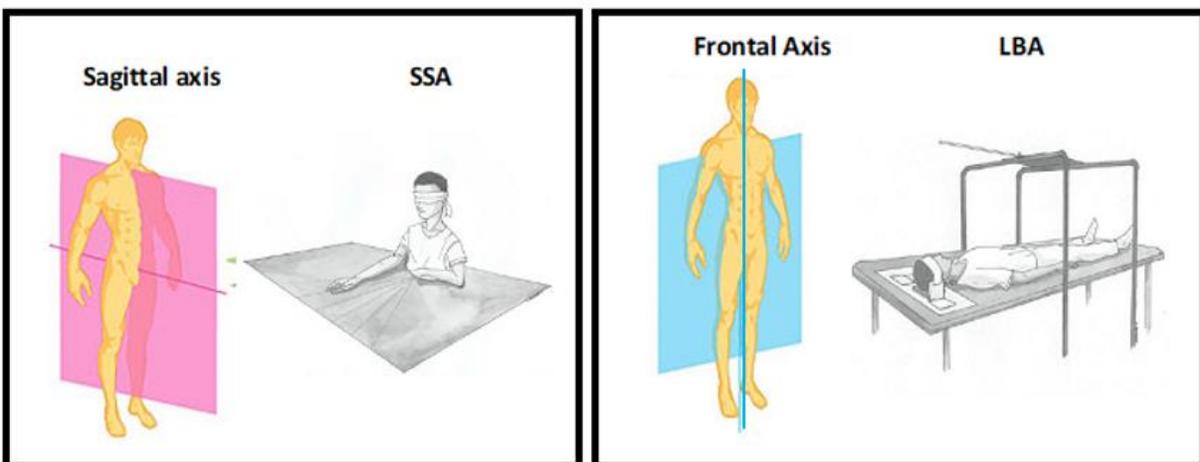


Figure 2: A. Measurement of SSA, which is a spatial representation egocentric reference in the sagittal axis. B. Measurement of LBA, which is a spatial representation of egocentric reference in the frontal axis.

A third hypothesis was then formulated about links between verticality and WBA. The sense of verticality constitutes a fundamental allocentric spatial reference (distinguished by multisensory integration of objects without taking into account the subjects' position (Colombo et al., 2017)) for perception and action. It allows to determine the position of body relative to the direction of gravity and participates in postural control. Vertical representation in frontal axis is evaluated by Visual Vertical (VV) and Postural Vertical (PV) (Pérennou et al., 2008; Piscicelli & Pérennou, 2017). They are both represented in figure 3. After a stroke, they are frequently rotated to the contralesional side particularly in case of right lesions (Pérennou et al., 2008). This pathologic deviation of the sense of verticality causes postural disorders, due to a wrong body orientation with respect to gravity, inducing a postural behaviour called lateropulsion (Pérennou et al., 2008). Patients with lateropulsion should mechanically bear more weight on the side of the body tilt (also the side of the contralesional bias in verticality perception), therefore the paretic side. This is not the case in most patients who seem to avoid overloading the paretic lower limb to keep standing and avoid falling on the side of the lateropulsion (Barra et al 2010, Chauvin et al 2020). This finding supports the view defended by many authors that the post-Stroke WBA is partly a compensatory strategy developed by patients to remain standing (et al., 2010; Chauvin, 2020; Pérennou, 2005).

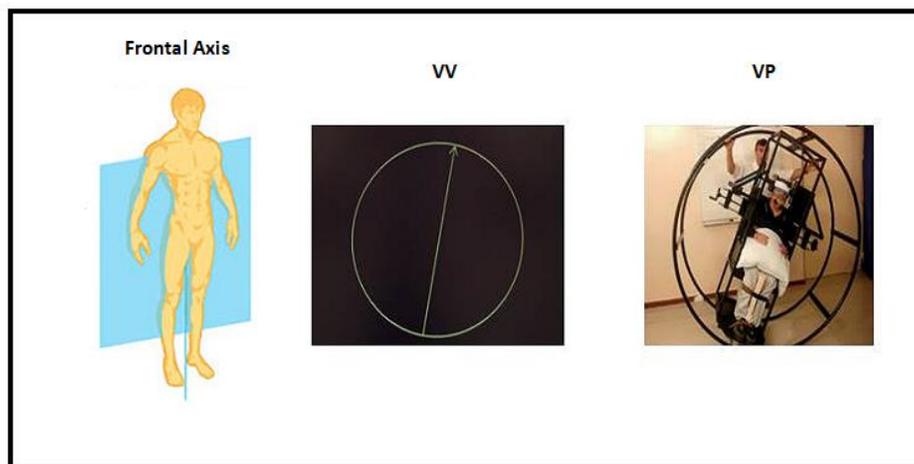


Figure 3: Measurement of VV and PV, which are allocentric spatial representation in frontal axis.

In conclusion, WBA is clearly a complex postural behaviour, resulting from weakness, USN, spatial representation and compensatory mechanisms. While there are many behavioural arguments in favour of the involvement of these different histopathological mechanisms in WBA, can neuro-anatomical arguments also be found?

3. What might be the WBA neural bases?

No study to this day has analysed the neural bases of the WBA. We assume that the neural bases of each determinant detailed above should contribute to build a neural network devoted to the control of the weight bearing in standing position. The following paragraphs summarize the neural bases of weakness, USN, the representation of the body (postural body schema) and of the verticality perception.

Neural bases of weakness

Several cerebral structures are implicated in motor control, especially the motor cortex and the corticospinal tract (CST) which is the principal motor pathway for voluntary movements (Welniarz et al., 2017).

Neural bases of unilateral spatial neglect

Several studies have explored the neural bases of USN, which seems supported by a large neural network involving both grey and white matter. Cortical grey matter structures mainly involve the superior temporal and inferior parietal cortex (Karnath et al., 2001; Lunven et al., 2019; Lunven & Bartolomeo, 2017; Suchan & Karnath, 2011). However, white matter tracts involve mainly the intrahemispheric tracts, especially branch 2 of the Superior Longitudinal Fasciculus (SLF) (Lunven & Bartolomeo, 2017; Thiebaut de Schotten et al., 2005), which connects the anterior intraparietal sulcus and the angular gyrus to the inferior frontal gyrus (Lunven & Bartolomeo, 2017; Wiesen et al., 2019). It has also been recently shown

Neural correlates of Weight Bearing asymmetry

that interhemispheric connections play a role, in particular via the corpus callosum (Lunven et al., 2019; Lunven & Bartolomeo, 2017).

Neural bases of body and spatial representations

Postural control and spatial representations require the integration of sensory and motor information, which is accomplished by parietal cortex, especially the retro-rolandic cortex (Baier et al., 2012; Ferber & Karnath, 1999; Rousseaux et al., 2014). Posterior insula is also known to be involved in spatial representation (Mazzola et al., 2014).

Neural bases of verticality

Several brain areas are known to be implicated in balance and verticality perception. The role of the vestibular cortex (Lopez et al., 2012), with the posterior insula (Brandt et al., 1994), more precisely, the insular posterior long gyrus (Baier et al., 2012; Mazzola et al., 2014), and the temporo-parietal junction have been demonstrated. Subcortical structures have also been identified as the postero-lateral thalamus (Barra et al., 2010; Karnath et al., 2000), the putamen and the caudate nucleus (Baier et al., 2012).

4. Hypotheses

Localizing brain-behavior relationships remains a key goal in cognitive neuroscience and in clinical neurology. Knowledge of the neural bases is necessary to a better understanding of the deficits' physiopathology, allowing improvement of rehabilitation methods. Thus far, no study has yet investigated the brain structures involved in WBA. The multiple relationships, previously described, between WBA and weakness, USN, spatial representation and verticality perception suggest a partly common physiopathology and the implication of the same neuroanatomical network.

Neural correlates of Weight Bearing asymmetry

The aim of our study was therefore to identify brain structures involved in WBA in patients after hemispheric stroke. To that purpose, we explored anatomo-clinical correlations between lesions and WBA in patients after stroke in grey but also white matter. Indeed, lesion symptom analysis (grey matter analysis) traditionally assumes that visible and directly damaged areas are responsible for a patient's symptoms. Following this logic, the areas that are the most frequently damaged by the lesion are considered as the neuronal substrate for the function. However, the dysfunction of distant areas that are connected to the damaged tissue has also been reported. The networks are disrupted even by distant lesions through disconnection and diaschisis mechanisms. In this perspective, we first performed a Voxel Lesion Symptom Mapping (VLSM), a modern method allowing grey matter analysis by revealing voxels statistically damaged in case of WBA. Then, we used the Brain Connection and Behaviour (BCB) Toolkit software (Foulon et al., 2018) to analyse white matter tract disconnection. Stroke lesions are well suited for these analyses because they go along with structural imaging data which reflect the area of infarcted and irretrievably lost neural tissue. Their behavioural consequences can be directly linked to the original function of the impaired part of the brain (Karnath et al., 2019).

Our assumption was that the control of the weight bearing in erect stance relies on several brain areas involved in the motor command (motor cortex, CST), spatial attention and representation referred to the gradient right/left (temporal and parietal cortex, SLF and corpus callosum), body representation (parietal cortex, posterior insula), and verticality representation (vestibular cortex, postero-lateral thalamus, putamen and caudate nucleus).

The aim of this study was to address, for the first time, the question of the existence of neural bases for the control of weight bearing in erect stance, and to test the hypothesis that these neural bases would involve the grey and white structures listed above. We tested this hypothesis in a cross-sectional study of a series of consecutive patients admitted in our neurorehabilitation ward after a first hemisphere stroke, who had a posturography and an anatomical MRI about 2 months after the stroke. Neuroanatomical correlates were investigated by the VLSM approach for grey matter analysis and the tractotron method in BCBToolkit for white matter analysis.

II. Methods

1. Study Design

This was a monocentric observational study using the data of the DOBRAS Cohort (Determinants of Balance Recovery After Stroke; ClinicalTrials.gov NCT03203109). Participants were comprehensively assessed in routine care, initially in the first weeks after being admitted in rehabilitation ward of Grenoble-Alpes University hospital. Assessments of sensory, motor, and cognitive deficits were performed at due time by trained and multidisciplinary examiners, with blinding to other data and study hypotheses. Patients were included between 2012 and 2019. Among patients included in DOBRAS Cohort, some had a posturographic registration in the frame of the ancillary study DOBRAS_Initial_Posturography (DOBRAS-IP).

2. Ethical considerations

DOBRAS study was performed in accordance with Helsinki Declaration and was registered at the National Committee for Informatics and Freedom (Commission nationale informatique et liberté; CNIL No2014874-v1). According to French law, observational studies do not require approval by ethic committee, provided participants have been informed of the specific research and are not opposed. Here all eligible individuals were informed of the DOBRAS study (orally and by written documents) and those who did not want to participate signed an opposition form. It was the case for only 10 patients between 2012 and 2019.

3. Participants

Among patients included in the DOBRAS Cohort after a first hemispheric stroke, 95 had a posturography and were included in the ancillary study DOBRAS-IP. Here we present data of patients of the DOBRAS-IP Study who had a controlled MRI about 2 months after stroke.

Neural correlates of Weight Bearing asymmetry

Inclusion criteria for DOBRAS Cohort were:

- Age \geq 18 years and \leq 80 years
- First unilateral hemispheric stroke, right or left

Exclusion criteria for DOBRAS Cohort were:

- History of stroke
- History of vertigo or loss of balance
- Cognitive disorders prior to stroke
- Psychiatric disorders
- Severe verbal comprehension difficulties
- Patient opposition
- Unstable medical conditions

For the present study, specific eligibility criteria were applied.

Inclusion criteria for this specific study were:

- Inclusion in DOBRAS_IP study (i.e. patients being part of the DOBRAS cohort and having been assessed by posturography)
- MRI realised at subacute stage

Exclusion criteria for this study were:

- Bilateral brain damage detected after careful reading of MRI
- Multiple brain damage detected after careful reading of MRI
- Subarachnoid haemorrhage stage IV (Fisher classification) detected after careful reading of MRI
- Hydrocephalus with cognitive disorders
- Cerebral oedema with cerebral herniation
- Posturographic registration assessed more than three months after stroke

Anatomo-clinical correlation and particularly VLSM method does not provide a theoretical number of participants. However, it seems reasonable to include more than 30 patients by referring to relevant scientific literature (Karnath et al., 2019).

Ninety-five patients had posturography recording in the subacute stage and were included in DOBRAS_IP study. Twelve patients included in DOBRAS-IP were excluded from our study because they have no MRI or because their MRI were acquired too late (over 3 months) or only in the acute stage (<14 days post-stroke). After careful reading of the MRI by experts, seven patients with severe brain damage (mainly bilateral or complicated lesions) were excluded. Four other patients were excluded because they had atypical and unexplained postural behaviour. Their paretic leg supported more weight than their non paretic leg. This WBA is not common, complex to understand and probably underpinned by a different mechanism from that involves in the usual WBA studied in this research. For these reasons, we decided to exclude these 4 patients, who will be separately studied. We therefore analysed 72 patients in our study. Figure 4 represents the flow chart.

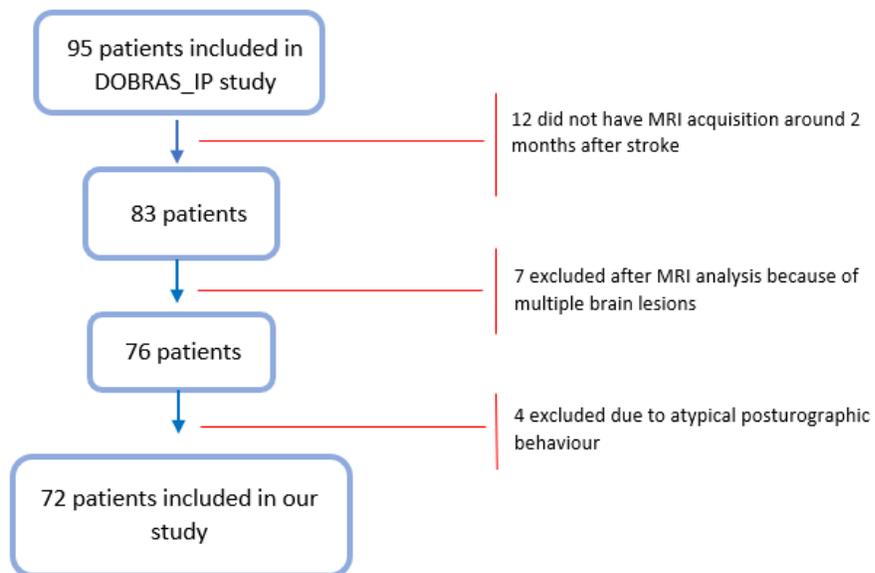


Figure 4: Flow Chart

4. Measuring WBA with posturography

Procedure

Posturography was performed if possible, at the day-30 session of the DOBRAS study assessments (30 days after stroke) by a trained examiner (physiotherapist or medical doctor) blinded of study hypothesis. Patients who were not able to stand by their own on D30 were assessed later, always before three months. Body weight distribution was measured in bipodal stance using the commercial two-force platform Feetest6 (Techno Concept©) fixed to the ground in a quiet room dedicated to this activity. Patients stood barefoot, one foot on each of the two platforms, heels separated by 14 cm, both feet perfectly parallel. This standardization allowed a reliably measure of vertical forces (% of body weight) distributed under each lower limb. For security reasons, participants stood within a handrail shaped behind and besides the plate-forms (figure 5), with a chair behind them. They were helped to stand-up from this chair and sit down for a rest, at any time, if needed. The examiner checked feet positions on the plate-forms before each trial, then stood at the paretic side to prevent fall during trials. In patients with severe deficits, trials requiring help (handrail grip, human assistance) were considered aborted and then repeated.

Instructions and conditions

Participants were instructed to remain upright as still as possible, with arms hanging alongside their trunk, without talking, looking at straight ahead. Three trials of 30 seconds were recorded. Participants were instructed to look at a visual target (small colour ball of 3 cm diameter) positioned at gaze level on a white wall distant from 1.8 m. This limited visual information was considered sufficient to optimize the use of vision to orientate and stabilize the body, without biasing the task (no clue about the direction of the vertical). The visual fixation aimed at limiting eyes and body movements exploring the surroundings, which would affect the results in the lateral plane.

Data analysis

We collected three main postural indices during this assessment:

- Percentage of body weight loading under each foot (%)
- CP position in sagittal and frontal axis (mm)
- Variations of CP position in sagittal and frontal axis (mm)

Analyses were performed using the Percentage of body weight under the feet, directly given by the two-force platform. The results were expressed as the percentage of the total body weight loading controlateral side (paretic side) and corresponded to the average of the 3 trials. This variable was named Weight Bearing on the paretic leg (WB_{paretic}).



Figure 5: Illustration of posturographic registration

5. Brain imaging

Acquisition

T2 FLAIR images performed two months after stroke either with 1.5T Magnetom Vision Plus MRI (Siemens, Erlangen, Germany) or 1.5T Achieva MRI (Philips, Amsterdam, The Netherlands) were used for lesion identification.

Lesion mapping plots were carefully examined for vascular lesions apart from the stroke area or brain oedema which might distort the lesion mapping. None of participants included showed atrophy cortical or substantial oedema. Presence of white matter hyperintensities (WMH) was reported and classified according Fazekas score (De Guio et al., 2016) as illustrated in Figure 6. Patients with high Fazekas score were not excluded (n= 6).

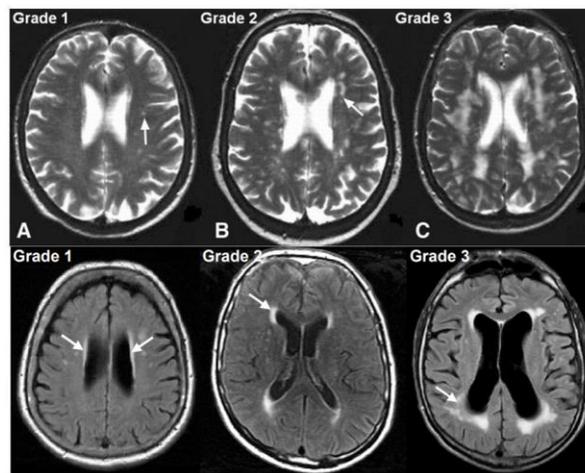


Figure 6: MRI with WMH and Fazekas score. (from Pr Dider Dormont, www.sfrnet.org)

The acquisition of imaging data in the subacute stroke phase (vs chronic stage), two months post-stroke, are well suited for lesion-behaviour mapping analyses because they clearly reflect the area of infarcted and irretrievably lost neural tissue as well as clear behavioural consequences that can be directly linked to the original function of the impaired part of the brain. The brain has not yet had time to functionally reorganise (Karnath et al. 2019).

Normalisation

Lesions were manually reconstructed by using MRICron (Rorden & Brett, 2000) from MRI axial slices (axial AC-PC, T2 flair, 4-mm thickness). Lesions were drawn manually by a first trained operator on axial slices of a T1-weighted MRI template from the Montreal Neurological Institute (www.bic.mni.mcgill.ca/cgi/icbm_view) normalized to Talairach's space and controlled by a second trained operator. Both operators were blinded to clinical measurements and study hypothesis. Disagreements were resolved by consensus.

We did not use automatic segmentation and normalisation algorithms on these MRI, performed in clinical setting, manual reconstruction is more reliable (Kimberg et al., 2007). This is particularly true for lesion analysis of older subjects ; their cerebral architecture being frequently modified (mostly ventricular dilatation or cerebral atrophy) (Rorden et al., 2007).

Analysis

Grey matter analysis

Lesion-deficit correlation studies are conducted with millimeter-scale precision, named VLSM. It consists to analyse each voxel and to separate them into two groups: healthy and injured voxels. Then, continuous behavioural scores of these two groups are compared by a t-test for parametric continuous variables and by binomial test for dichotomic variables (Baldo et al., 2012). VLSM produces a statistical map showing the strength of the relationship between damage at any given voxel and performance on a behavioural measure of interest (Bates et al., 2003), with MNI coordinates (w, y, z). This method presents two main advantages. First, continuous behavioural variables are analysed without threshold. Secondly, lesional data are treated without location prediction (Bates et al., 2003; Kimberg et al., 2007; Rorden et al., 2007; Rorden & Karnath, 2004).

For this analysis, we used SVLRSMGui software package (Zhang et al., 2014) available in the MATLAB toolbox. Correction for multiple comparisons was achieved by employing non-parametric permutation test, as recommended for medium-sized samples. Data were permuted 1000 times with each permutation

resulting in a calculated cut-off t -value with $\alpha = 0.05$. The same analysis was realised with a fixed $\alpha = 0.01$. Voxels injured in less than 5% of patients were not analysed. Lesion volume is an important confounding variable in lesion-symptom mapping analyses because larger lesions tend to cause more severe deficits regardless of location. Lesion volume was also regressed out of both behavioural and lesion data. Lesion volume is expressed in voxels, given by MRICron software. This approach is nearly equivalent to a regular partial correlation, ANCOVA model (Bates et al., 2003)

All lesions were analysed on the same cerebral side, to increase statistical power. Firstly, all lesions were analysed in the right side. It means that the lesion reconstructions of the 29 left strokes were reversed (flipped) to be combined with those of right strokes. Secondly, all lesions were analysed in the left side (the 43 right lesions flipped to the left side). This technic is common in literature. In addition, we controlled this methodology by performing the analysis on both sides to compare them and ensure that there was no side effect. No differences were revealed between these two analyses, so only analysis with right lesions (right lesions + left lesions to the right side) are presented in results.

The resulting maps were analysed using MRICrogl, which is a software for visualisation of 2D lesion slices and renderings of brain imaging data. The *automated anatomical labelling atlas (aal)* (Tzourio-Mazoyer et al., 2002) was superimposed to the statistical map resulting from VLSM analysis, to precisely identify damaged brain structures.

White matter analysis

White matter tracts disconnection was analysed using the BcBToolKit software (Foulon et al., 2018). Each patient's lesion was compared with an atlas of white matter tracts indicating, for each tract, the proportion of disconnection in the MNI152 coordinate system. We considered a tract to be involved when its affected proportion was estimated above 50% (Thiebaut de Schotten et al., 2014). This method is freely available as *tractotron* in *BCBtoolkit* (Foulon et al., 2018) (Figure 7). Mann-Whitney comparisons were performed subsequently and for each tract, to compare WB_{paretic} between both preserved and disconnected patients.

Neural correlates of Weight Bearing asymmetry

We focused on the CST, the three branches of the SLF and the corpus callosum because of their implication in weakness and spatial cognition.

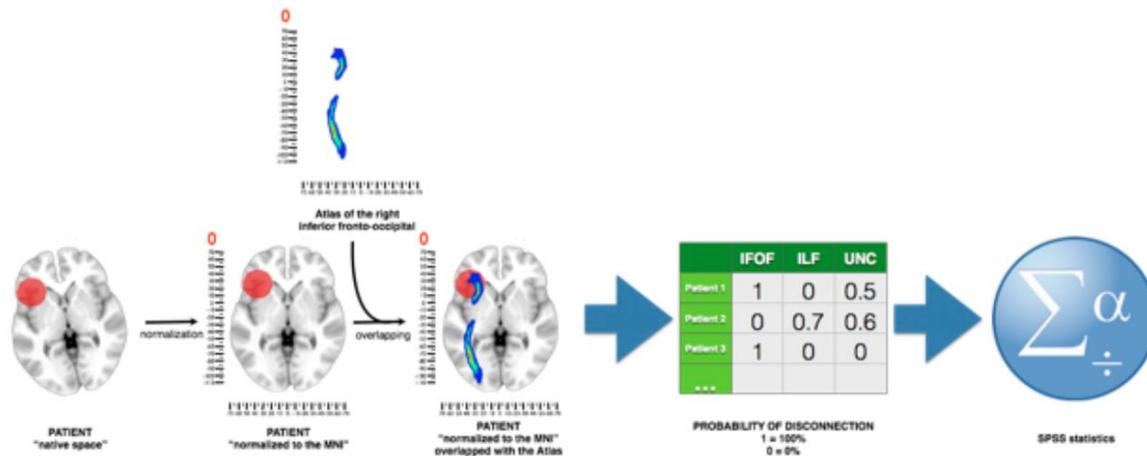


Figure 7: Tractotron step by step (<http://www.bcblab.com/BCB/Tractotron.html>)

6. Other clinical assessments

Other clinical data were also carefully assessed and were collected for this study.

Handedness laterality was assessed with the Edinburgh inventory (Oldfield, 1971). Patients were considered right-handed with a score > 0.6 .

Deficits

Data on spatial neglect were assessed by Catherine Bergego Scale (CBS) (Azouvi et al., 2003), the most sensitive assessment of neglect than conventional paper and pencil tasks (at the same time body, non-body, and ecological). CBS is a behavioural scale consisting of 10 four-point scale items related to neglect in everyday life.

Motor weakness was assessed by a standardized examination of muscle strength using Held and Pierrot-Deseilligny classification (Lacôte et al., 1996). Eight muscle groups of both the upper and lower limb were tested and rated on a six-point scale. The final score expressing the motor function of the paretic lower limb was then adjusted to range from 0 to 40 (normal motor command) (Ashworth, 1964).

Hypoesthesia was manually tested on both contralesional upper and lower limbs by trained physicians who manually assessed pressure sensitivity using Monofilament Test (score increases with the hypoesthesia) (Valk et al., 1997).

The severity of contralesional lateropulsion was estimated using the Scale for Contraversive Pushing (SCP) (Karnath et al., 2000) ranging from 0 to 6 (severe lateropulsion and pushing).

All assessments are described in details in the study of Daï et al. (Daï et al., in press).

Balance and gait disorders, and disabilities

Postural abilities were evaluated using the Postural Assessment Scale for Stroke (PASS) (Benaim et al., 1999), ranging from 0 to 36 (good postural control). Gait independence was measured using a motor assessment scale (Lindmark & Hamrin, 1988) ranging from 0 to 6 (independent gait). Disability was assessed by Functional Independency Measure (FIM) with a total score ranging from 18 to 126 (functional autonomy) (Granger et al., 1986)

6. Statistics

Statistical analyses were realised using R software (3.6.0 version, 2019). Descriptive statistics were generated for each variable. Distribution normality was verified with Shapiro-Wilk test. Data are expressed as mean (Standard Deviation) or median [Q1; Q3] as appropriate (Gaussian distribution or not). Only the following variables *percent body weight loading paretic side* and *Height* had gaussian distribution. Group comparisons (between patients with WBA and patients without WBA) were performed using t-test for *Height* and Wilcoxon-Mann-Whitney test for the other continuous variables. Categorical

variables were compared using Chi-square test (Fisher's exact test if required). The correlation between WB_{paretic} and lesion size was analysed using Kendall test. Unless specified otherwise, the significance level was fixed at $p=0.05$. P Exact values under 10^{-3} are not indicated.

III. Results

1. Participants features

Characteristics of participants are reported in table 1. They were 65 [58; 74] years old, 49 (68%) males. Forty-three patients had a right hemisphere lesion (60%) and 29 a left one (40%). Characteristics of participants correspond to the features of post stroke population in the subacute stage described in the literature, with moderate severity, more right lesions with spatial disorders. The posturography was performed with a median delay after stroke of 34 [29; 63] days.

Weight Bearing asymmetry

The distribution of WB_{paretic} followed a normal distribution ($p=0.060$), as shown in figure 8. Mean and median were 44.4 (7.75) % and 44.9 [40.2; 49.9] % respectively.

WB_{paretic} was comparable for right and left strokes ($p=0.114$), which allowed flipping lesions for the VLSM analysis.

We constituted two groups of patients according to the threshold recommended by previous studies (Guillebastre et al., 2012; Jeanson et al. in preparation; Mansfield et al., 2013; Sackley and Lincoln, 1991). Twenty-two (30%) patients were considered showing an abnormal WBA with a $WB_{\text{paretic}} < 41\%$ of body weight. Their averaged WB_{paretic} was 36.6 (5.2) % of body weight. The others ($n=50$, 70%) were considered without WBA. Their mean WB_{paretic} was 48.4 (4.5) % of body weight.

Neural correlates of Weight Bearing asymmetry

Table 1: Clinical description of all patients and group comparison (patients with and without WBA).

VARIABLES	ALL PATIENTS (N=72)	PATIENTS WITH WBA (N=22)	PATIENTS WHITHOUT WBA (N=50)	
AGE (Years)	65 [58 ; 74]	68 [62 ; 74]	67 [54 ; 73]	P=0.185
GENDER (Males)	49 (68%)	10 (45%)	39 (78%)	P=0.006
WEIGHT (kg)	72.2 [65.0 ; 83.0]	67.4 [58.4 ; 79.6]	75.0 [68.0 ; 83.0]	P=0.074
HEIGHT (cm)	170 (10)	171 (11)	167 (9)	P=0.125
LATERALITY (Edinburgh score)	0.9 [0.8 ; 1]	1 [0.8 ; 1]	0.9 [0.7 ; 1]	P=0.361
COMPLETION DATE (Days)	34 [29 ; 63]	60 [30 ; 74]	33 [28 ; 54]	P=0.122
STROKE SIDE (Right, Left)	R=43 (60%) L=29 (40%)	R=16 (73) L=6 (27%)	R=27 (54%) L=23 (46%)	P=0.136
STROKE MECHANISM (Haemorrhagic, Ischemic)	H=15 (21%) I=57 (79%)	H=8 (36%) I=14 (64%)	H=7 (14%) I=43 (86%)	P=0.056
STROKE SIZE (Voxels)	3072 [912 ; 10772]	3672 [1315 ; 9065]	2397 [834 ; 15539]	P=0.709
WMH (Fazekas score)	1 [1 ; 2]	2 [1 ; 2]	1 [0.25 ; 2]	P=0.072
WEAKNESS (/40)	32 [22 ; 38]	22 [18 ; 30]	35 [28 ; 39]	P<10⁻³
HYPOESTHESIA (Monofilament)	4.3 [4 ; 4.7]	4.5 [4.2 ; 5.3]	4.2 [3.8 ; 4.7]	P=0.190
NEGLECT (CBS D30)	6.0 [1.0 ; 12.5]	9.0 [5.5 ; 17.0]	4.5 [0.0 ; 8.5]	P=0.018
LATEROPULSION (SCP D30)	0.25 [0.00 ; 1.75]	1.63 [0.06 ; 2.69]	0.00 [0.00 ; 1.25]	P=0.004
BALANCE (PASS D30)	32.0 [23 ; 35]	25.5 [20 ; 29]	33.0 [29 ; 36]	P<10⁻⁴
GAIT D30	5.00 [2 ; 6]	2.00 [0.25 ; 2.75]	5 [3 ; 6]	P<10⁻⁴
FUNCTIONAL AUTONOMY (FIM D30)	93 [68 ; 113]	69 [63 ; 87]	105 [82 ; 116]	P<10⁻⁴

White Matter HyperIntensities, CBS: Catherine Bergego Scale, SCP: Scale for Contraversive Pushing, PASS: Postural Assessment Score for Stroke, FIM: Functional Independence Measure

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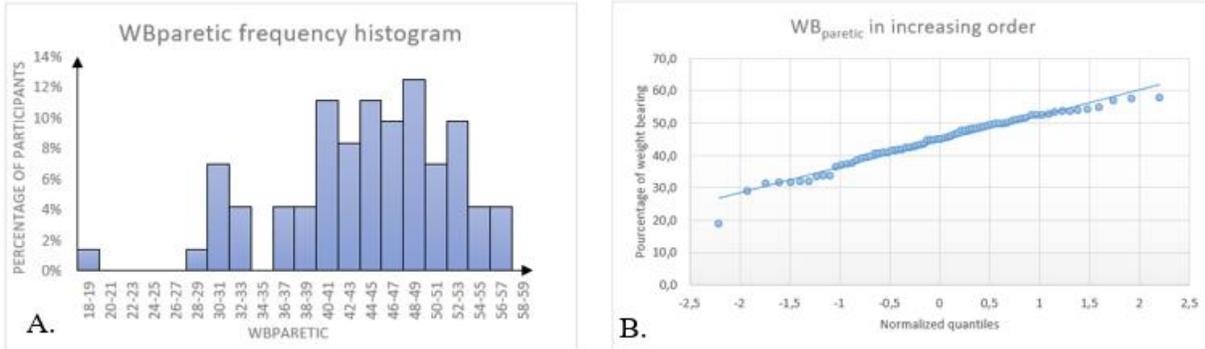


Figure 8: A. Frequency histogram of $WB_{paretic}$. B. Henry's curve for $WB_{paretic}$ variable.

As for demographic characteristics, both groups were comparable concerning age, weight, height, and hand laterality. The delay between stroke and posturography was not different between the two groups. Contrariwise, there were more males in the group without WBA (78%) than in the WBA group (45%). This gender effect was likely due to the fact that females were older than males: 70 [66 ; 76] years vs 67 [54 ; 73] ($p=0.046$), with greater weakness: 30/40 [18 ; 32] vs 35/40 [25 ; 39] ($p=0.017$).

As for stroke's characteristics, both groups were fully comparable. Indeed, lesion side, lesion size, stroke mechanism and presence of WMH were not significantly different between groups. Note that right lesions were not found more frequently in WBA patients ($p=0.136$) than in patients without WBA. $WB_{paretic}$ was comparable for right and left strokes ($p=0.114$), which allowed flipping lesions for the VLSM analysis.

As expected, patients with abnormal WBA had greater weakness, lateropulsion and spatial neglect and showed lesser balance and gait abilities.

Lesion size

The median size of all patients' lesions was 3072 [912; 10772] voxels. The median lesion size did not differ between patients with WBA and patients without WBA (3672 [1315; 9065] vs. 2397 [834; 15539] voxels, $p=0,709$). Moreover, lesion size was not correlated with $WB_{paretic}$ ($r=-0.072$, $p=0.374$).

2. Brain imaging

Overlap

Overlay of lesion plots mapping of right and left lesions are shown in Figure 9.

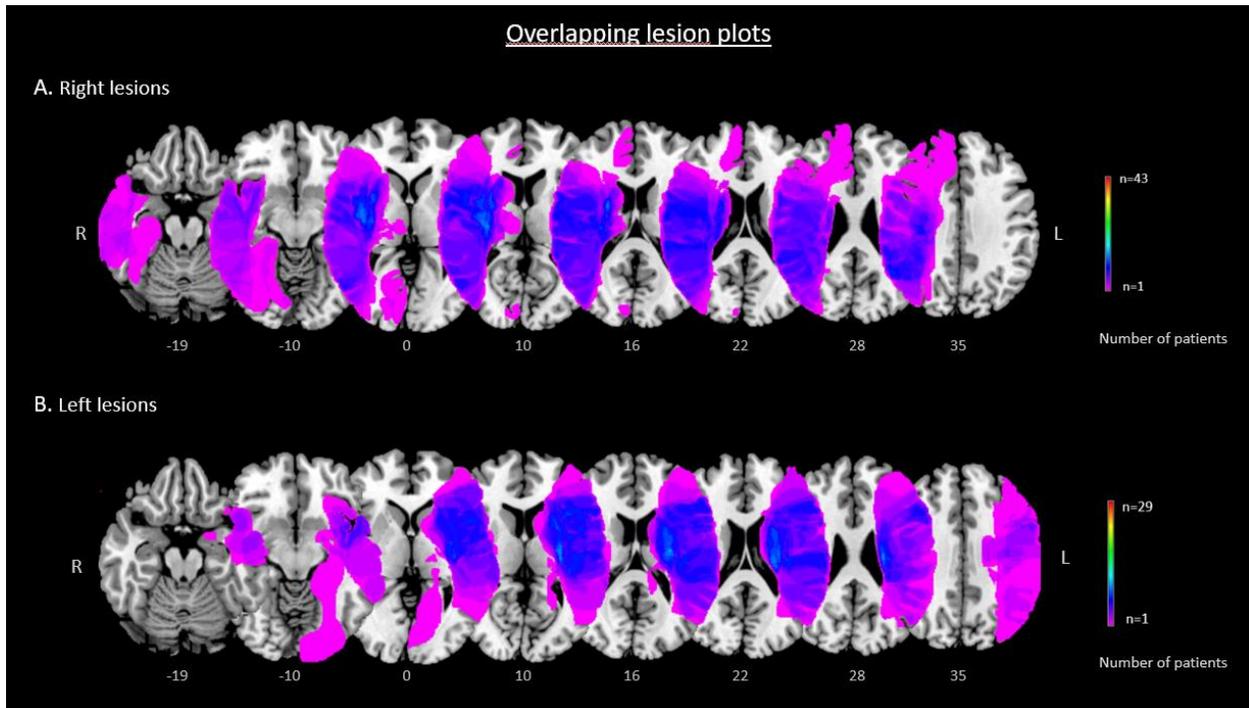


Figure 9: Overlay of lesion plots. A. for 43 participants with right-brain damage. B. for 29 participants with left-brain damage. The number of overlapping lesions is illustrated by a colour code ranging from from violet ($n=1$) to red ($n=43$ for right lesions and $n=29$ for left lesions)

Grey matter analysis

Figure 10 illustrates the results of the VLSM analysis, performed on all lesions represented on the right hemisphere. Key damaged areas involved in abnormal WBA were the posterior insula (35, -21, 6), the posterior parietal cortex especially the supramarginal gyrus (60, -38, 34), the caudal putamen (30, -16, 9) and the postero-lateral thalamus (21, -17, 9).

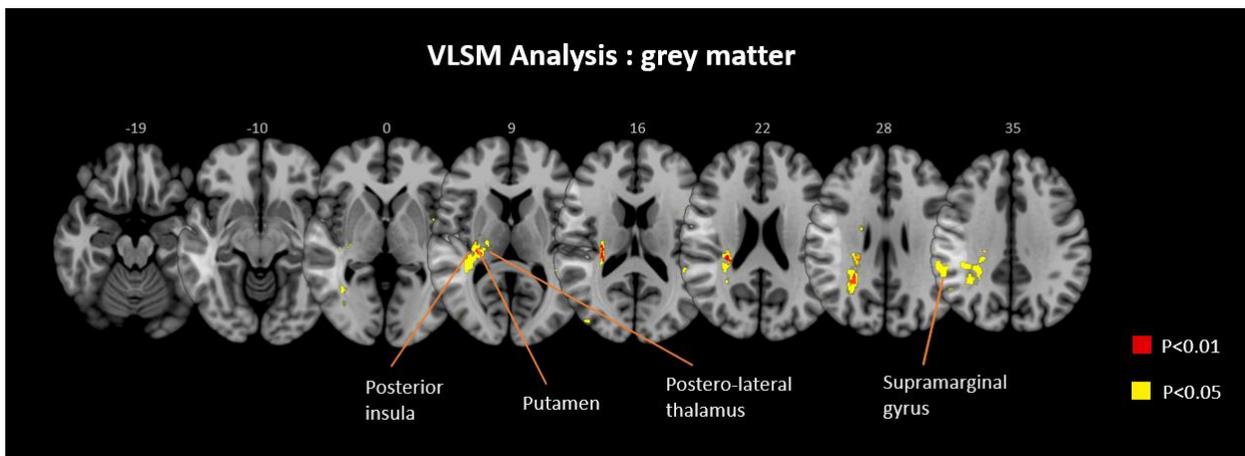
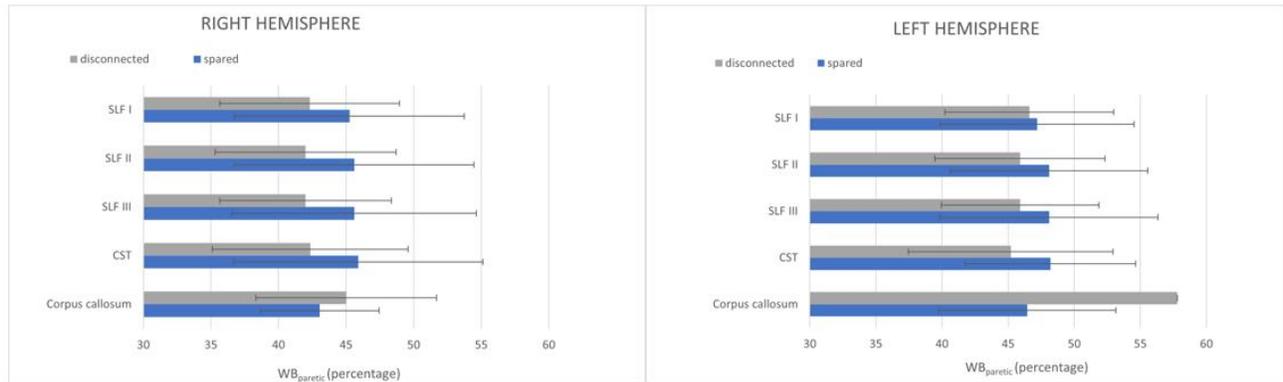


Figure 10: Voxel-based symptom-lesion mapping (VLSM) of WBA for 72 individuals with right- and left-brain damage after stroke, all lesion analysed in the right side (right lesions and left lesions flipped to the right side). VLSM results are represented by a colour code: yellow for $p < 0.05$, red for $p < 0.01$.

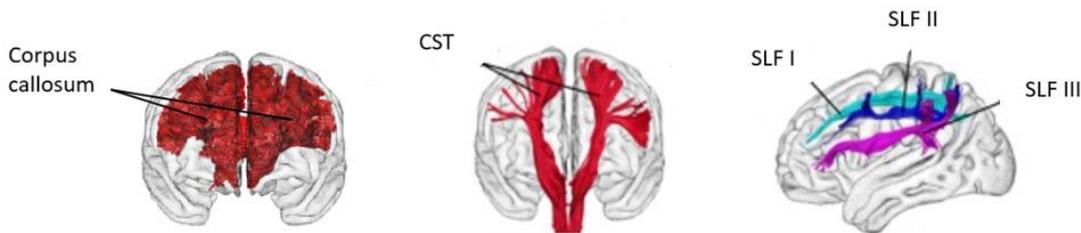
White matter analysis

Figure 11 shows the results of white matter analysis using Tractotron-BCBToolkit, performed for each hemisphere. There was no significant WB_{paretic} difference between spared and disconnected fasciculi, for each of the five tracts of interest. However, we can see that the WBA was smaller when the CST and the SLF are disconnected, which is not the case of the corpus callosum.

Neural correlates of Weight Bearing asymmetry



A



B

Figure 11: A. WB_{paretic} for patient with (grey) or without (blue) tract disconnection. SLF I: Superior longitudinal Fasciculus tract 1, SLF II: Superior longitudinal fasciculus tract 2, SFL III: superior longitudinal fasciculus tract 3, CST: corticospinal tract. B. Illustration of tracts of interest (Rojkova et al., 2016).

IV. Discussion

The present study is the first to investigate the neural bases of the weight bearing control in erect posture. WBA was carefully quantified by a posturography performed about 30 days post-stroke in a series of 72 consecutive patients admitted in a rehabilitation ward after a first hemispheric stroke. Neuroanatomical correlates were analysed on anatomical MRI performed about 2 months post-stroke, with a statistical lesion analysis approach (VLSM), controlling for lesion size (Bates et al., 2003). Key brain structures involved in pathological WBA were the posterior insula, the parietal cortex, the putamen and the posterolateral thalamus. Using *tractotron* on BCBToolKit, no white matter tract was statistically associated with WBA.

To have high quality brain images we choose to analyse only imagery with MRI performed about 2 months after stroke. At this time, patients are medically more stable, and in case of haemorrhagic stroke, the core of the damaged brain appears clear and is also easier to delineate. This period of time is recommended to increase the reliability of brain imaging analyses, especially neuroanatomical correlates (Nagaraja et al., 2020). Lesions were manually drawn to prevent aberrations from automatic software, and also to be more accurate. To ensure the quality of our procedure, the delineation was controlled by a second operator and disagreements were resolved by consensus. Concerning grey matter, the Voxel-based Lesion Symptom Mapping (VLSM) method is to date the one recommended for studies searching neuroanatomical correlates (Karnath et al., 2019). In our study, we used the VLRSMgui package, a recommended toolbox implemented in Matlab (Zhang et al., 2014). Appropriate corrections were applied, and the effect of lesion size was controlled by adding it as a covariate. Concerning white matter, analyses were realised using *tractotron* on BCBToolKit, which is a recent and modern software able to study functional brain networks.

Regarding the descriptive statistics, the characteristics of participants corresponded to the features of post stroke population, in the subacute stage, described in the literature (Béjot et al., 2009). The two groups constituted (with and without WBA) were comparable concerning age, weight, height, and hand laterality, but differed in gender. Indeed, in this study, females were older and presented more important weakness than men. Knowing that WBA increases with age (Sackley & Lincoln, 1991) and weakness (Nicolas Genthon, Rougier, et al., 2008; Marsden et al., 2005; D. Pérennou et al., 2005), these differences could also explain why WBA was more frequent in females than in men in our study. The deficits were more important for patients with WBA, who had greater weakness, lateropulsion and NSU and showed lesser balance and gait abilities. These results are totally consistent with the literature (Guillebastre et al., 2012; Mansfield et al., 2013; Dominic Pérennou, 2006).

This study revealed the implication of several grey matter structures in WBA. Two cortical structures were associated with WBA: the posterior insula and the postero-superior parietal cortex, more precisely the supramarginal gyrus. Two subcortical structures were associated too, the posterolateral thalamus and the putamen, specifically in its caudal part. We made the hypothesis that neural bases of WBA involve those of weakness, NSU and spatial representation. All the four brain areas identified in our study are involved in spatial representation. Indeed, the thalamus is a main cerebral structure for multi-integration, which is

known to be involved in the representation of verticality (Barra et al., 2010; Karnath et al., 2000). Postero-lateral thalamus contains neurons that process and relay vestibular, proprioceptive and visual signals to the vestibular cortex, and is also identified as a relay structure (Christophe Lopez & Blanke, 2011). The putamen is known to be implicated in movement control (Alexander et al., 1990), spatial representation (Kunimatsu et al., 2019) and verticality perception (Baier et al., 2012). The posterior and superior parietal cortex is an heteromodal and multisensorial area (Baier et al., 2012; Pérennou et al., 2014), involved in spatial cognition. Finally, posterior insula is known to be involved in spatial cognition and specifically in verticality perception (Baier et al., 2012; Brandt et al., 1994; Mazzola et al., 2014). This study also showed the involvement in WBA of neural bases of spatial representation and verticality. The parietal cortex is implicated in NSU, especially its inferior part (Karnath et al., 2001; Lunven et al., 2019; Lunven & Bartolomeo, 2017; Suchan & Karnath, 2011). The involvement in WBA of neural bases of NSU needs to be further studied and detailed. These results strengthen the idea of the complexity of WBA and allow to better understand its mechanisms and neural determinants. Regarding these results, WBA, as a frequent and severe postural disorder, must be evaluated in clinical routine after stroke.

Regarding white matter analysis, we did not find tract disconnection correlated with WBA. As a result of this first level of assessment, it would be easy to conclude that there is no brain network involved in WBA. Such a conclusion would be premature and erroneous. On one hand, it should be remembered that the analysis of white matter tracts disconnection using *Tractotron* in BCBToolkit (Foulon et al., 2018) compares each patient's lesion with an atlas of white matter tracts indicating for each voxel, the probability of finding a white matter tract in the MNI152 coordinate system. The calculated proportion of disconnection expresses the severity of disconnection, but it is probably not a good severity index for the disconnection because a small lesion can disconnect the entire tract. So these first results must be considered with the utmost caution, and complementary analyses are required. In this perspective, we intend to investigate the existence of a structural connectivity network between the cortical and subcortical areas identified by VLSM analysis by using *AnaCOM2*, also available within the BCBtoolkit (Foulon et al., 2018). This second level of assessment should allow us to identify clusters of brain lesions that are associated with WBA, that is, connections that are critical for this given function (Kinkingnéhun et al., 2007). In the context of this medical thesis, this analysis could not be conducted but we plan to do so in the near future. On the other hand, it is unlikely that the specific brain areas identified as key structures

for WBA separately operates. It is now clearly demonstrated that cerebral networks have a major role in cerebral functioning (Duffau & Duchatelet, 2016). Based on the literature, we focused on white matter fasciculus of interest, known to be involved in the determinants of WBA (CST, SFL and corpus callosum). The cortical and subcortical structures identified in this study have structural connections, such as the thalamo-insular projections, which link thalamus and insula (Barra et al 2010). The several brain areas identified in this study would therefore work together in a large network. The extension of this network would explain why WBA is so frequent after stroke. It might support many possibilities of brain plasticity and recovery. These elements argue the necessity of further and more precise analyses of white matter with AnaCOM2.

We can see on the figure 11 that WB_{paretic} is smaller in case of disconnected SLF and CST than in spared. This tendency is more present in the right hemisphere but is however not statistically significant. The implication of these two fasciculi would be consistent with data from the literature. The **CST** is a white matter fasciculus which connects the motor cortex to the effector muscular system. It also controls voluntary movements. Its implication in WBA would be totally coherent with clinical knowledge that shows higher weakness in asymmetric patients ($p < 10^{-3}$). The role of weakness in postural disorders and WBA is mainly reported in the literature (Genthon, et al., 2008; Marsden et al., 2005; Pérennou, 2005). The **SLF** is known to be involved in executives functions (Urger et al., 2015) and in neglect, specifically with its second branch (Lunven & Bartolomeo, 2017). Its involvement in spatial cognition was also studying in the literature. Some studies have indeed demonstrated its implication in the processing of visuo-spatial information, especially in the right hemisphere (Thiebaut de Schotten et al., 2011). Its implication in WBA would also be coherent with our clinical data, which revealed more severe neglect and lateropulsion in WBA patients. On contraries, **corpus callosum** damages seem not to be involved in WBA. Nevertheless, it is considered disconnected in only four patients in our study.

Regarding our descriptive statistics, WBA did not seem to be lateralized: the side of lesion was not different between groups ($p=0.136$). We can see that lesions tend to be more lateralised in the right side for patients with WBA (73%) than for those without (54%), but this tendency is not statistically significant in our study. A right lateralisation of WBA, as the other postural disorders, would be coherent with knowledge. Indeed, right hemisphere is strongly involved in spatial cognition and representation (Halligan

et al., 2003). After right lesion, WBA is more severe and more frequent in the chronic stage (Jamal et al., 2019). Moreover, relation between LBA deviation and WBA is more important in the event of right brain damage (Barra et al., 2009; Jamal et al., 2018, 2019). We cannot conclude about a brain lateralisation of WBA in this study and it will be evaluated in further study with a larger sample to increase power.

Study limitations

VLSM analyses required a minimum of 30 observations (Karnath et al., 2019). Despite a much higher sample size (72 participants), we had to flip lesions to get clear results. This procedure seemed robust because of the non-lateralization of WBA, and because results were similar when lesions were flipped on the right and on the left side. Another limitation is that our method to assess WBA requires patients able to stand upright for 30 seconds. In the subacute stage, severe patients were unable to do that and were therefore not included. With such selection criteria, patients with severe WBA were excluded of this study. But we wanted to perform this study in the subacute stage, to analyse structures directly involved in WBA. In the chronic stage, WBA appears rather to be a compensatory strategy to prevent contralesionally falling and is also more attributable to new mechanical constraints caused by WBA itself (Genthoen et al., 2008; Pérennou et al., 2005). A difference of WBA between males and females was found, but was in fact due to confounders, as described above.

V. Conclusion

This is the first study to investigate and identify the neural bases of weight-bearing control in standing position, using a series of 72 individuals tested at the subacute stage after a first hemispheric stroke. Concerning grey matter, the parietal cortex, posterior insula, putamen, and posterior-lateral thalamus are related to weight bearing asymmetry. Together these contribute to construct spatial representations in order to stand upright. Concerning white matter, the involvement of the SLF and the CST should be specifically analysed in further studies.

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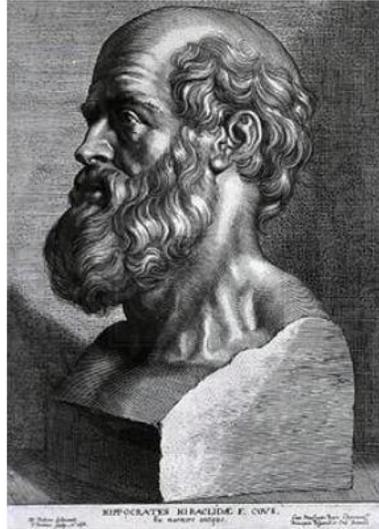
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SERMENT D'HIPPOCRATE

En présence des Maîtres de cette Faculté, de mes chers condisciples et devant l'effigie d'HIPPOCRATE,

Je promets et je jure d'être fidèle aux lois de l'honneur et de la probité dans l'exercice de la Médecine.

Je donnerai mes soins gratuitement à l'indigent et n'exigerai jamais un salaire au dessus de mon travail. Je ne participerai à aucun partage clandestin d'honoraires.

Admis dans l'intimité des maisons, mes yeux n'y verront pas ce qui s'y passe ; ma langue taira les secrets qui me seront confiés et mon état ne servira pas à corrompre les mœurs, ni à favoriser le crime.

Je ne permettrai pas que des considérations de religion, de nation, de race, de parti ou de classe sociale viennent s'interposer entre mon devoir et mon patient.

Je garderai le respect absolu de la vie humaine.

Même sous la menace, je n'admettrai pas de faire usage de mes connaissances médicales contre les lois de l'humanité.

Respectueux et reconnaissant envers mes Maîtres, je rendrai à leurs enfants l'instruction que j'ai reçue de leurs pères.

Que les hommes m'accordent leur estime si je suis fidèle à mes promesses.

Que je sois couvert d'opprobre et méprisé de mes confrères si j'y manque.

THÈSE SOUTENUE PAR : CHRISTIAENS Adélie

TITRE :

NEURAL CORRELATES OF WEIGHT BEARING ASYMMETRY

CONCLUSION :

This is the first study that investigates and identifies neural bases of weight bearing asymmetry from a series of 72 individuals tested at the subacute stage after a first hemisphere stroke. Concerning grey matter, these neural bases gather the parietal cortex, the posterior insula, the putamen, and the postero-lateral thalamus. Concerning white matter, we did not find a specific network as we expected. It suggests that any cerebral network is devoted to weight bearing asymmetry, which seems to be underpinned by several brain areas implicated in different functions. These brain areas convey together the motor command, built up and update the sense of the upright, the body schema, and more generally spatial representations. The extension of this network explains why WBA is so frequent after stroke. It might also support much possibilities of brain plasticity and recovery.

VU ET PERMIS D'IMPRIMER

Grenoble, le : 7/10/20

LE DOYEN

Pour le Président
et par délégation

Le Doyen de Médecine
Pr. Patrice MORAND

Pr. Patrice MORAND



LE PRÉSIDENT DE LA THÈSE



Pr. PERENNOU Dominic