



Are tilted writing and drawing after stroke related to a biased perception of the vertical?

Flora Diaine

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Année 2019

**L'INCLINAISON DE L'ECRITURE ET DU DESSIN APRES UN AVC EST-ELLE UNE MANIFESTATION
D'UN BIAIS DE PERCEPTION DE LA VERTICALE ?**

**ARE TILTED WRITING AND DRAWING AFTER STROKE RELATED TO A BIASED
PERCEPTION OF THE VERTICAL?**

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

Flora DIAINE

[Données à caractère personnel]

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RÉSUMÉ

Titre : L'inclinaison de l'écriture et du dessin après un AVC est-elle une manifestation d'un biais de perception de la verticale ?

La dysgraphie spatiale, survenant parfois après un accident vasculaire hémisphérique droit (AVCD), est partiellement expliquée par l'héminégligence. Nous avons étudié la responsabilité d'un biais de représentation de la verticale dans l'inclinaison antihoraire de l'écriture et du dessin, et cherché à proposer des critères valides pour diagnostiquer une inclinaison de l'écriture et du dessin après AVCD.

Cette étude observationnelle portait sur 61 patients droitiers testés 30 jours après un AVCD et 44 sujets sains appariés en âge et sexe. Tous devaient écrire et dessiner un matériel standardisé. Nous mesurions l'inclinaison de la marge et des lignes sur un test d'écriture, ainsi que l'inclinaison des arbres et des lignes de base sur une copie de dessin. L'héminégligence et les verticales posturale (VP) et visuelle (VV) étaient évaluées chez les patients. Les statistiques étaient non paramétriques et les normes définies par le 95^{ème} percentile des données des sujets sains. Un signe négatif indiquait une inclinaison antihoraire.

Les normes pour diagnostiquer une inclinaison du matériel étaient de $-6,9^\circ$ pour la marge, $-4,9^\circ$ pour les lignes et $-5,5^\circ$ pour les arbres. Les sujets sains écrivaient et dessinaient avec une inclinaison antihoraire. Vingt-trois patients (38%) avaient au moins 1 critère anormal. Comparés aux autres ils étaient plus sévèrement atteints concernant la latéropulsion ($p=0,001$), le biais de VP ($p=0,018$) et VV ($p=0,001$), la négligence extrapersonnelle et l'hémianopsie.

Cette étude donne des critères valides pour diagnostiquer une inclinaison antihoraire de l'écriture et du dessin, que présentaient 38% des patients. Ces derniers avaient un plus grand biais de perception de la verticale. Les sujets sains écrivaient et dessinaient de façon inclinée.

MOTS CLÉS : AVC, hémisphère droit, cognition spatiale, représentation de la verticale, dysgraphie spatiale, écriture inclinée.

ABSTRACT

Title: Are tilted writing and drawing after stroke related to a biased perception of the vertical?

Spatial dysgraphia showed after a right hemispheric stroke (RHS) is partially explained by spatial neglect. This study aimed to test the hypothesis that the counterclockwise tilt of the handwriting and drawing is due to a counterclockwise tilt in representing the vertical, transposed to the sheet of paper. It also aimed to propose valid and reliable criteria with cutoff values to routinely diagnose a counterclockwise tilt of the writing or the drawing in victims of RHS.

This is an observational study on 61 right-handed patients tested 30 days after a RHS and 44 aged and sex matched healthy subjects. All were asked to write and draw by hand standardized material. We measured the inclination of the margin and lines of a writing test, the inclination of the trees and base lines of a drawing copy test. Spatial neglect, postural vertical (PV) and visual vertical (VV) were assessed in patients. Statistics were non-parametric and normality was defined as the 95th percentile of normal data. Negative signs indicated counterclockwise tilts.

The cutoff to diagnose a tilted material was -6.9° for the left margin, -4.9° for the lines written and -5.5° for the trees. Healthy subjects had a significant counterclockwise writing and drawing tilt. At least one criterion presented a counterclockwise tilt in 23 patients (38%). Compared to others, these patients showed greater lateropulsion ($p=0.001$), bias in PV ($p=0.018$) and VV ($p=0.001$), non body neglect and more hemianopia.

This study gives valid and reliable criteria to diagnose a counterclockwise tilt of the writing or drawing, found in 38% of the patients. These latter showed a greater bias in perception of verticality. Healthy subjects wrote and drew with a counterclockwise tilt.

KEY WORDS: Right hemispheric stroke, spatial cognition, verticality representation, spatial dysgraphia, tilted writing.

Introduction

Handwriting and drawing require motor, sensitive and cognitive skills, involving both hemispheres. In right handers the left hemisphere controls the motor component [1,2] whereas the right hemisphere controls the spatial organization [3].

Spatial dysgraphia observed after right hemispheric stroke (RHS) corresponds to a spectrum of signs bearing on the spatial layout of the written language [4]: writing exclusively in the right half of the paper, overwriting or compressing some words, omitting, repeating or substituting letters or graphemes, but also slopping writing lines and a progressive increase of the left margin. Most of these signs are secondary to spatial neglect (NSU), found in about 50% of victims of a RHS [5,6].

Recently Jolly et al [7] have reported a case suggesting that the counterclockwise tilt of the handwriting and drawing is due to a counterclockwise tilt in representing the vertical, transposed to the sheet of paper referring to top and bottom. This paper appeals confirmation in a series of consecutive individuals tested at a subacute stage after a RHS. This was the main objective of the present study.

Our second objective was to implement a feasible methodology to assess writing and drawing orientation, and propose valid and reliable criteria with cutoff values to routinely diagnose a counterclockwise tilt of the writing or the drawing in individuals undergoing rehabilitation after a RHS.

Material and method

Participants

Data of 105 individuals were analyzed for this study: 61 with a hemispheric stroke compared to 44 healthy participants.

Individuals with a stroke were part of the DOBRAS-R cohort (ClinicalTrial.gov NCT03203109), which followed 228 individuals aged from 18 to 80, victims of a first unilateral hemispheric stroke documented by an MRI and admitted in our neurorehabilitation department from January 2012 to November 2018. Motor, sensitive, functional and cognitive data were systematically collected by trained professionals at 30 ± 2 days (D-30), 60 ± 2 days (D-60), and 90 ± 2 days (D-90) post-stroke. Because spatial dysgraphia is much more frequent after right hemisphere lesions [4,8,9], we selected observations of individuals with a RHS. The left hemisphere being dominant for language in most individuals, they had intact language skills. We also selected observations of right-handers (Edinburgh ≥ 0.6), to test writing and drawing abilities of individuals using their strong right upper limb. For each observation we selected data of the first assessment completed as regards of relevant variables for this study: writing and drawing, spatial neglect, and verticality perception, among systematic assessments performed at D-30, D-60, or D-90 post-stroke (Flow chart in [Figure 1](#)).

Healthy subjects were recruited in our immediate environment and hospital employees in order to establish norms for writing and drawing data. They had no history of neurological disorders and were right handed. They were matched for sex and age and blind from the study hypothesis.

Ethical considerations

The Study was performed in accordance with the Helsinki Declaration. It was registered at the National Committee for Informatics and Freedom (Commission Nationale Informatique et Liberté; No. 2014874 v1), and in a WHO study register (NCT03203109 ClinicalTrial.gov; Determinants of Balance Recovery After Stroke [DOBRAS]). All participants provided written informed consent. According to French law, this observational study did not require approval by an ethics committee for patients. For healthy controls the study was approved by the Ethical Review Board of Grenoble-Alpes University (CERGA-2019-04-09-1). The reporting of this paper follows STROBE statement (additional material).

Tasks and criteria

The writing orientation was analyzed from the writing test of the *Batterie d'évaluation de la négligence* (BEN) [10]. Individuals had to manually write on three lines their name and surname, address, and profession (Figure 2). We used a blank sheet of paper (portrait), put flat on a table, centered on the trunk of participants, with the inferior border parallel to the table's edge. No instruction was given on writing orientation and speed. Each production was carefully scanned, with apparent right edge, giving a vertical reference for analysis. Four measures were done by one operator (FD) blinded regarding tests of verticality perception and spatial neglect: *the left margin tilt* with respect to vertical (Figure 2a); *the tilt of the three first lines* with respect to horizontal (Figure 2b). We planned a priori to average the inclination of the three lines and to check the validity of this approach by comparing the inclination of these lines both in individuals with a stroke and in controls. These latter measures were performed with a software specially designed (Angle Calculator [11], details given in additional material). By convention [12,13], a negative sign indicated a counterclockwise tilt.

To estimate the reliability of these measurements we correlated measures obtained by Angle Calculator to those obtained with a protractor, on 15 patterns of writing tilted from 0 to 50° (15 margins and 45 lines). This was performed by an operator (FD) who always started with the protactor, then applied Angle Calculator. We then analyzed the inter-rater reliability of the measures performed with Angle Calculator. Thirty writing materials obtained in individuals with a RHS were analyzed by two independent operators (FD and AV or FD and LD).

The drawing orientation was analyzed from Gainotti's drawing test [14]. The figure was displayed on a landscape format paper, put flat on a table and parallel to its edge, and centered on the body axis. Participants were instructed to copy the figure on the underlying blank space. Each production was scanned to allow measurements made by one operator (FD) who used Angle Calculator. Two types of criteria were measured: the tilt with respect to the vertical of each of the four trees, and the tilt with respect to the horizontal of each of the two baselines of the drawing (Figure 3). Methodological details are given in additional material. We planned a priori to average the inclination of the three right-most trees and to leave apart the left-most tree (supposed to be omitted in case of spatial neglect) and to check the validity of this approach by comparing the inclination of these trees both in individuals with a stroke and in controls. We also planned to average the inclination of the two lines after comparing their inclination. FD was blinded regarding tests of verticality perception and spatial neglect.

We then analyzed the inter-rater reliability of measurements with Angle Calculator in individuals with a RHS. Thirty drawing materials were analyzed by two independent operators (FD and AV or FD and LD). By convention [12,13], a negative sign indicated a counterclockwise tilt. We chose not to analyze the inclination of the house's walls because the house is drawn in perspective and its copy implies complex cognitive tasks that may interfere with verticality representation.

Ranges of normality beyond which a counterclockwise tilt could be diagnosed in patients were calculated from the data of the 44 healthy participants, for all indices of writing and drawing orientation. A criterion was abnormal if inferior to the value corresponding to the 95th percentile.

Verticality perception was explored by VV and PV. For VV, subjects sat in a dark room and adjusted a luminous rod to the vertical position [15,16] (Figure 4). The difference between patients' adjustments and vertical were calculated. For PV, subjects sat in complete darkness in a wheel [17] equipped with an inclinometer (Figure 5). The examiner inclined the wheel to the left or right. The patient gave an estimate of her/his PV by signaling the point of feeling upright. A negative sign indicated a counterclockwise tilt for VV and PV (norms from -2.5° to +2.5°)[15].

Body and non-body neglect were assessed each by 4 tests. Non-body neglect was assessed with the bells test [18], reading test [19], overlapping figure test [20], and the 4 non-body items of the Bergego scale [21]. **Body neglect** was assessed with 4 tests: the comb and razor [22], Bisiach [23], and fluff tests [24], and the 4 body items of Bergego scale [21]. From the results to these tests with respect to their ranges, we built composite scores assessing non-body and body neglect from 0 to 100 (see additional material).

The disability and deficits of individuals with stroke were also assessed by trained therapist. For the disability, the Functional Independence Measure (FIM) [25] was used. Gait disorders were assessed by the mFMA gait score [26]. The contralesional lateropulsion was evaluated by the Scale for Contraversive Pushing (SCP) [27]. Lateropulsion was defined by $SCP \geq 0.75$ and Pusher Syndrome (PS) for $SCP \geq 3$ and ≥ 1 for each subdomain (body tilt, pushing behavior, resistance to corrections). Apraxia was assessed by the Apraxic screen of Tulia [28] (<9). The presence or absence of hemianopia was manually evaluated.

Statistics

We firstly tested the normal ranges of writing and drawing orientations among 44 age-matched healthy controls. We considered the cutoff of score inferior to the 95th percentile as abnormal for each test.

A Kruskal Wallis was applied to detect the difference of inclinations of the three right trees (drawing) or first three lines (writing). Then we investigated the inter-rater reliability of ad hoc Angle Calculator for writing and drawing orientations. Inter-rater reliability (examiners A1 versus B1) was determined by calculating the interclass correlation coefficient (ICC). Absolute reliability was assessed with the Bland-Altman method with 95% confidence intervals, and with the SE of measurement ($SEM = SD_x \times \sqrt{1 - ICC}$). SEM was then used to estimate the minimal detectable change ($MDC_{95} = 1.96 \times SEM \times \sqrt{2}$) for 95% degree of confidence on writing and drawing orientations.

Since most our data for post-stroke individuals followed non-Gaussian distribution, the continuous data were presented as medians with interquartile ranges (IQR). Dichotomized data were presented as numbers and proportions. The relation of vertical orientation between manual measurements with a protactor and Angle Calculator measurements was tested by a Pearson correlation. According to the 3 criteria cutoffs, we dichotomized all individuals into two groups: tilted writing or drawing (WD, at least one abnormal score among three tests) and upright WD groups. We compared the differences between the two groups using Mann Whitney test or Chi-square test (including Fisher exact test). Effect sizes between groups were calculated manually by using Z values of the Mann-Whitney test $r = Z/\sqrt{n}$, and X^2 or FET of Chi-square test $v = \sqrt{X^2/n \cdot df}$. Effect sizes ≥ 0.1 , 0.3, or 0.5 represent a small, medium, or large effect, respectively. All variables found significant ($p < 0.05$) within two groups comparisons were then included in a step-wise multivariate regression model (binary logistic regression). Odds ratios (ORs) were estimated with 95% confidence intervals (95% CIs). Significance level was set at $p < 0.05$. Statistical analysis was performed with SPSS 20.0. Without any other indication, data are given in the form: median (1st quartile; 3rd quartile), 95th percentile, or mean (Standard deviation). The agreement between the existence of a tilt in the writing (lines) and in the drawing (trees) was analyzed by the kappa statistics.

Results

Participants

We analyzed 61 complete observations of individuals tested after a RHS, 47 on D-30 (77%), 10 on D-60 (16%), and 4 on D-90 (7%). Their median age was 66 years (53;71); 36 were males (59%). The stroke type was ischemic (n=55, 90%), hemorrhagic (n=6, 10%). At the time of the assessment, their disability was moderate, with a median FIM score of 101.5 (74.2;114), and a median mFMA gait score of 5 (2;6) indicating that half was able to walk without technical aid. A left hemianopia was found in 19 individuals (31%). No apraxia was found.

The 44 healthy participants tested were comparable in age (median 62 [58;70]; $p=0.751$) and sex ratio (24 males, 54%; $p=0.648$) to participants with a RHS.

Validity of the measures

There was a strong correlation between angular measures obtained with a protactor and those given by Angle Calculator ($r=0.998$; $p<0.001$), indicating that measures performed by Angle Calculator were valid.

Determining criteria from the feasibility in patients

As for the writing, 60 individuals with stroke had followed the instructions and wrote 3 lines (or more). Only one individual had written less than 3 lines (2 lines). In addition no difference was found between the three lines in patients ($p=0.622$). Consequently, we decided to average the orientation of the 2 or 3 first lines available to determine the criteria ***left margin tilt*** and ***lines' tilt***. So determined, these criteria could be obtained in all patients which made highly feasible our assessments of the writing tilt.

As for the drawing orientation, 55 individuals (90%) had drawn the 4 trees, 5 (8%) had only drawn the 2 most rightward trees (omitting those leftward), and 1 individual (2%) had drawn only the most rightward tree, neglecting the 3 others. We found no difference in the orientation of the 2 or 3 most rightward trees when available (98% of cases; $p=0.141$).

Therefore to determine the criterion ***trees' orientation*** we decided to average the orientation of the 3 or 2 available trees, otherwise we kept the orientation of the only tree

drawn. So determined, this criterion could be obtained in all patients. This was not the case for the baselines of the drawing, missing in 7 individuals (11%), and only drawn on the right part in 6 others. Because of the modest feasibility for this criterion, we decided to discard it for further analyses.

To sum up it was highly feasible to obtain three criteria: the *left margin tilt* and the *lines' tilt* for the writing, *trees's tilt* for the drawing (mean of the 3 or 2 most rightward tree, otherwise the one the most rightward).

Reliability of selected criteria in patients

As for the writing, the inter-rater reliability was high both for the margin (ICC=0.999, with 95% CI [0.998-1]; $p<0,001$) and the lines (ICC = 0.988 with 95% CI [0.975-0.994]; $p<0,001$) tilts, with measurement error acceptable for the margin tilt (SEM=1.6°, MDC=4.5°), and satisfactory for the lines tilt (SEM=0.94°, MDC=2.6°).

As for the drawing, the inter-rater reliability was high for the trees tilt (ICC=0.927 with 95% CI [0.852-0.964]; $p<0,001$), with acceptable measurement error (SEM=2.6°, MDC=7.1°).

Ranges of normality for the selected criteria

Interestingly, the writing and the drawing material were not perfectly upright in normals. If no difference from the vertical was found for the margin ($p=0.265$), likely because of the great dispersion of data (median -1.8° [-5.3;3.6], both the orientations of lines (median -1.2° [-2.3;-0.3]) and trees (median -1° [-2.5;0.5]) were subjected to a counterclockwise tilt with respect to the horizontal ($p<0.001$) and the vertical ($p=0.003$), respectively. The cutoff values (95th percentile) determined from the data in normals and beyond which a counterclockwise tilt could be diagnosed in patients were -16.9° for the margin, -4.9° for the lines, (writing) -5.5° for the trees (drawing).

There was no influence of the age on the orientations of the margin ($p=0.853$), the lines ($p=0.404$) or the trees ($p=0.554$). There was no influence of the sex on the orientation of the margin ($p=0.897$), the lines ($p=0.322$) or the trees ($p=0.494$).

Writing and drawing orientations in patients

In all individuals with a stroke, the median *margin tilt* was -1.9° (-9.8;2.6), the median *lines' tilt* was -2° (-3.9;-0.4) and the median *trees' orientation* was -0.53° (-3.8;1.7). At least one

criteria was counterclockwise tilted in 23 patients (38%): 10 (16%) showing a counterclockwise margin tilt, 11 (18%) showing a counterclockwise lines' tilt, and 8 (13%) showing a counterclockwise trees' tilt. Four individual (7%) showed a counterclockwise tilt bearing on 2 criteria, and 1 (2%) bearing on the 3 criteria. [Table 1](#) compares the three criteria of writing and drawing orientation found in these 23 patients to those found in the 38 others with a normal writing or drawing orientation (no abnormal tilt on any criteria), and also to controls. Patients with an upright writing and drawing (upright WD) had criteria similar to normals. Patients with a tilting writing or drawing (tilted WD) showed greater tilts than normals and other patients, for the margin tilt, the lines' tilt, but not for the trees' tilt. The effect sizes were large as far as the lines' tilt is concerned. They were medium for the margin tilt. In all individuals with a stroke, there was a small concordance between the lines' tilt and the trees' tilt ($\kappa=0.32$; $p=0.02$).

We then comparatively analyzed the clinical characteristics of the 23 patients with a tilted WD to the 38 other patients with an upright WD ([table 2](#)). Age, sex, and stroke type were comparable, as well as their level of independence, and degree of apraxia. Patients with a tilted-WD presented a clear clinical profile. They showed a greater lateropulsion secondary to a bias in the representation of the vertical (biased PV and VV), a spatial neglect specifically bearing on the non-body domain, and a hemianopia. The association with deficits in representing the vertical was especially strong, but not systematic. However a transmodal bias of verticality (both VV and PV) was found in 12/23 (52%) patients with a tilted-WD and only in 7/38 patients with upright-WD (18.4%, $p=0.006$). Conversely in the 19 patients who showed a transmodal bias of verticality representation (both VV and PV), 12 (63%) had a tilted-WD. A lateropulsion was found in 15/23 (65%) individuals with tilted-WD versus 6/38 (16%) individuals with upright WD ($p<0.001$). All the effect sizes were medium.

We then further analyzed the determinants of the line's tilt which was the most relevant criterion to quantify the orientation of the written or drawn material. We conducted a step-wise logistic regression on the classification tilted versus upright WD, finally 3 types of variables significant in the univariate analysis entered into the model ([table 2](#)): the existence of a lateropulsion, the existence of a hemianopia, and the composite score of non-body neglect. The existence of a lateropulsion was the main determinant of the tilted lines (odd ratio = 6.4; 95% CI [1.4-29.7]; $p=0.019$), whereas the influence of the non-body neglect (odd ratio = 1; 95% CI [0.97-1.05]; $p=0.675$), and of the hemianopia (odd ratio = 1.6; 95% CI [0.36-7.05]; $p=0.54$) was

not independently significant. This finding shows that the tilted writing is mainly related to a biased verticality representation.

Discussion

This is the first study investigating the orientation of writing and drawing material on a series of individuals tested about 30 days after a first RHS (n=61), and compared to 44 controls matched in age and sex. After having implemented valid and reliable criteria to quantify the orientation of the writing and the drawing, we show that a tilted WD is frequent (38% of patients in this series) and that this misorientation is mainly due to a tilted representation of the vertical.

Criteria and methodology for measuring tilted WD after a stroke

We tested 2 types of material: instructed handwriting (identity, address, profession on 3 successive lines), and hand drawing of a model (Gainotti figure). Each material was conceived to give 1 criterion of orientation with respect to the vertical (margin, trees) and 1 criterion of orientation with respect to the horizontal (lines). These 4 criteria were measured with Angle Calculator [11], a software we implemented in order to use it in clinical practice. The best criterion was the mean orientation of the 3 lines written (lines' tilt). The comprehensibility and the feasibility were excellent since 104/105 individuals wrote 3 lines on which measurement were always easy from the operating mode we defined. In 1/105 individual, the criterion was obtained from 2 lines written. This tool has an excellent criterion validity with a perfect correlation with the gold standard (protactor). This criterion was also highly reliable with interobserver ICC almost reaching 1 with a reasonable minimum detectable change (2.6°). Its discriminative validity was excellent with differences between groups of individuals (healthy controls, patients with upright writing and drawing, and patients with a tilted writing or drawing) highly significant with large effect sizes. All these properties made the task of writing three lines under very simple instructions, the way to measure their orientation with respect to the horizontal and the final criterion obtained by averaging the orientation of the three lines a very interesting novel tool and criterion for assessing the writing orientation of the individuals with a RHS in clinical practice. The 3 other criteria had much less satisfactory properties and may be discarded for further studies and clinical practice.

Why did healthy subjects have tilted writing and drawing

A recent pilot study [7] has revealed that normal subjects ($n=12$) instructed to write by hand on a blank sheet of paper centered with respect to their trunk and head do not write horizontally but with a systematic slight counterclockwise tilt (mean -1.8° ; $SD=1^\circ$). They also drew with a similar counterclockwise tilt of the baselines to be copied (-1.5° ; $SD=0.6$). The current study confirms these findings with similar magnitudes for the lines' tilt (median -1.2° [$-2.3;-0.3$]) and extends it to the vertical with trees drawn tilted (-1° [$-2.5;0.5$]). This is not an imprecision of the action to write or to draw, because the tilt was systematic. Also the representation of the vertical was not assessed in these healthy subjects, one may assume that it was normal because the representation of the vertical and the horizontal have been repetitively found normal in healthy subjects [15–17]. Therefore we do not think that this normal counterclockwise tilt in writing and drawing is due to a spatial bias. Instead we think that this bias might be due to the kinematic of the shoulder. This hypothesis could be tested by comparing the orientation of the writing and drawing in left and right handers, the native language of whom being associated to writing from left to right or right to left.

Importance of writing and drawing tilt after a RHS

We observed that the writing and drawing are frequently tilted in individuals with a RHS, with a prevalence comparable to that known for spatial neglect [6,29] and a bias in the representation of the vertical [17] (about 40%). Magnitudes of this tilt were pronounced, reaching a maximum of 51° . If the present study was not design to check the persistence of an orthogonality between bias in the representation of the vertical and of the horizontal, this orthogonality was interestingly preserved in the patient JW experimentally investigated recently [7].

Determinant of the tilted WD after a RHS

Our multivariate analysis showed that the unique determinant of tilted lines was the existence of lateropulsion, known to express a counterclockwise tilt in the representation of the vertical in RHS. So our series confirms findings suggested by our case study [7]. These patients who showed a lateropulsion due to a bias in verticality representation also often present a spatial neglect which explains the association found with spatial neglect. It was also noteworthy

that this association was important for the non body neglect (visual neglect), vision being crucial to guide the writing.

Perspectives and clinical implications

It is easy to detect and quantify a tilted writing in neurorehabilitation. Our study strongly suggests to do it systematically. This may alert of the existence of a bias in verticality perception, which should be further analyzed to guide the rehabilitation. Conversely, the writing tilt could be modulated by appropriate rehabilitation techniques, as shown by Jolly et al [7]. This remains to be tested in large series of patients with the idea that training patients to write and draw upright could help to recalibrate the internal model of verticality and facilitates balance and gait recovery.

Study limitations

The main limitation was the retrospective analysis of data of the writing and the drawing collected in routine in patient. We cannot exclude that the sheet of paper was not always perfectly centered even if neuropsychologists carefully checked that point. Some degrees of misalignment may have occurred during the session in patients especially in patient seated in their wheelchair.

The constitution of groups of individuals was not optimal, because the group with tilted writing and drawing included individuals with lines considered upright. Given the relatively small sample of this series, it was not possible to constitute a group limited to individuals with tilted lines.

Conclusion

In this study, we investigated 61 individuals tested about 30 days after a RHS and 44 healthy subjects. Among the criteria tested to analyze the tilted writing and drawing, three were found reliable: the mean lines' tilt, which was the most solid criterion, the left margin tilt (writing) and the mean inclination of the right most trees (drawing). At least one criterion was tilted in 23 patients (38%), who showed a greater bias in perception of verticality. The lateropulsion was the main determinant for the mean lines' tilt. This association was strong but not systematic, suggesting that a biased internal model of verticality is not the only mechanism underling these manifestations. This is corroborated by the fact that healthy subjects also have a tilted writing and drawing, despite a precise perception of verticality. These criteria could be used as an alert for the need of evaluating the perception of verticality by more specific tests, in order to begin an appropriated rehabilitation.

This study opens the field for larger cohort studies exploring the link between the mean lines' tilt and verticality perception.

THÈSE SOUTENUE PAR : Flora DIAINE

TITRE :

L'INCLINAISON DE L'ÉCRITURE ET DU DESSIN APRES UN AVC EST ELLE UNE MANIFESTATION D'UN BIAIS DE PERCEPTION DE LA VERTICALE ?

CONCLUSION :

Dans cette étude nous avons investigué le matériel de 61 patients victimes d'un AVC droit et de 44 sujets sains. Parmi les critères testés pour analyser l'inclinaison de l'écriture et du dessin 3 étaient fiables : l'inclinaison moyenne des lignes, de la marge (écriture) et l'inclinaison moyenne des 3 arbres de droite (dessin). Au moins un critère était incliné chez 23 patients (38%), qui avaient un plus grand biais de perception de la verticale, surtout dans sa composante visuelle. Cette association était forte mais non systématique, suggérant qu'un biais du modèle interne de verticalité n'est pas le seul mécanisme sous-tendant ces manifestations. Ceci est corroboré par le fait que les sujets sains écrivent et dessinent également inclinés malgré une perception précise de la verticalité. La négligence et l'hémianopsie semblent également impliquées. Ces trois critères pourraient être utilisés comme alerte, indiquant la nécessité de l'évaluation de la perception de la verticalité par des tests plus spécifiques dans le but d'entreprendre une rééducation adaptée.

VU ET PERMIS D'IMPRIMER
Grenoble, le : 09/09/2019

LE DOYEN

Pour le Président
et par délégation

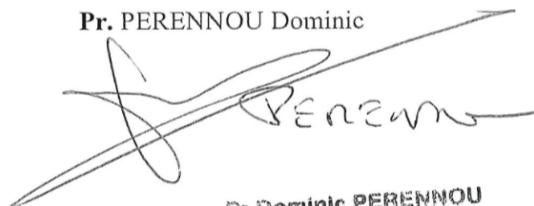
Le Doyen de Médecine
Pr. Patrice MORAND

Pr. Patrice MORAND



LE PRÉSIDENT DE LA THÈSE

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Tables and figures

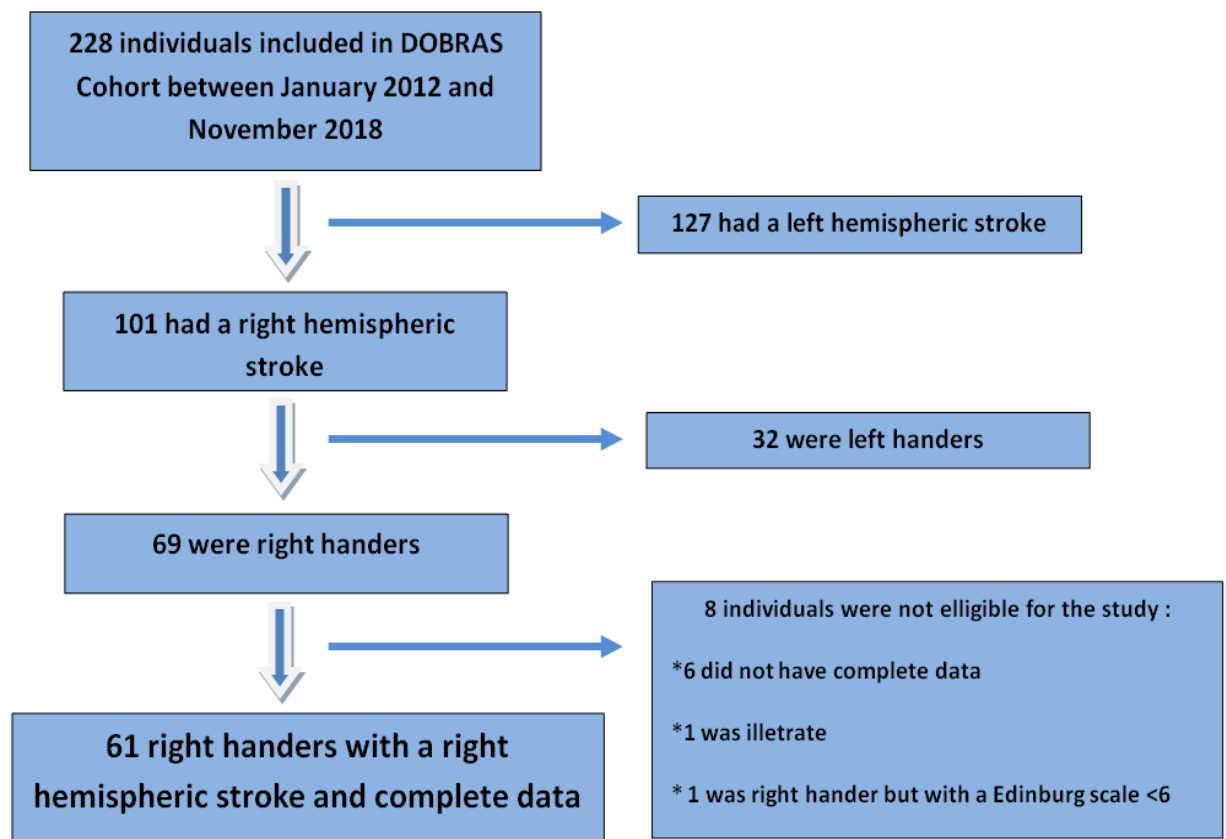
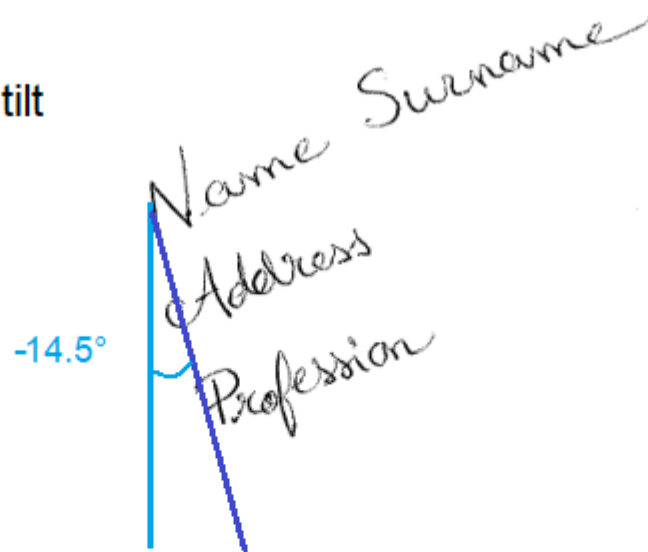


Figure 1: Study flow chart

a/ Margin tilt



b/ Lines' tilt

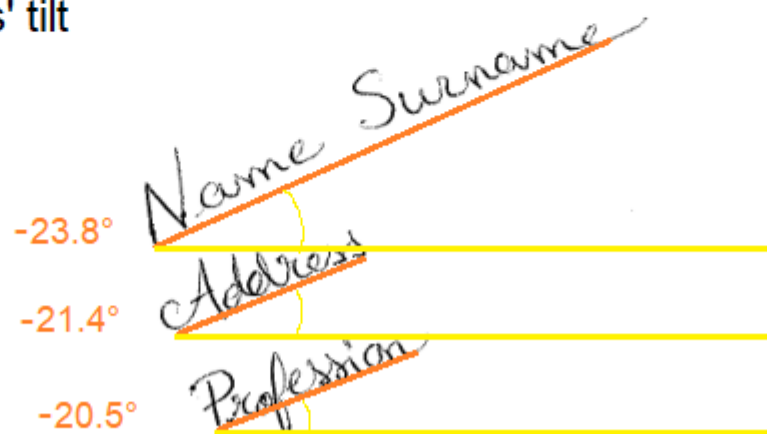


Figure 2: Schematic view of the way to compute criteria of the writing orientation

Tilt of the left margin with respect to the vertical and tilt of the 3 lines with respect to the horizontal.

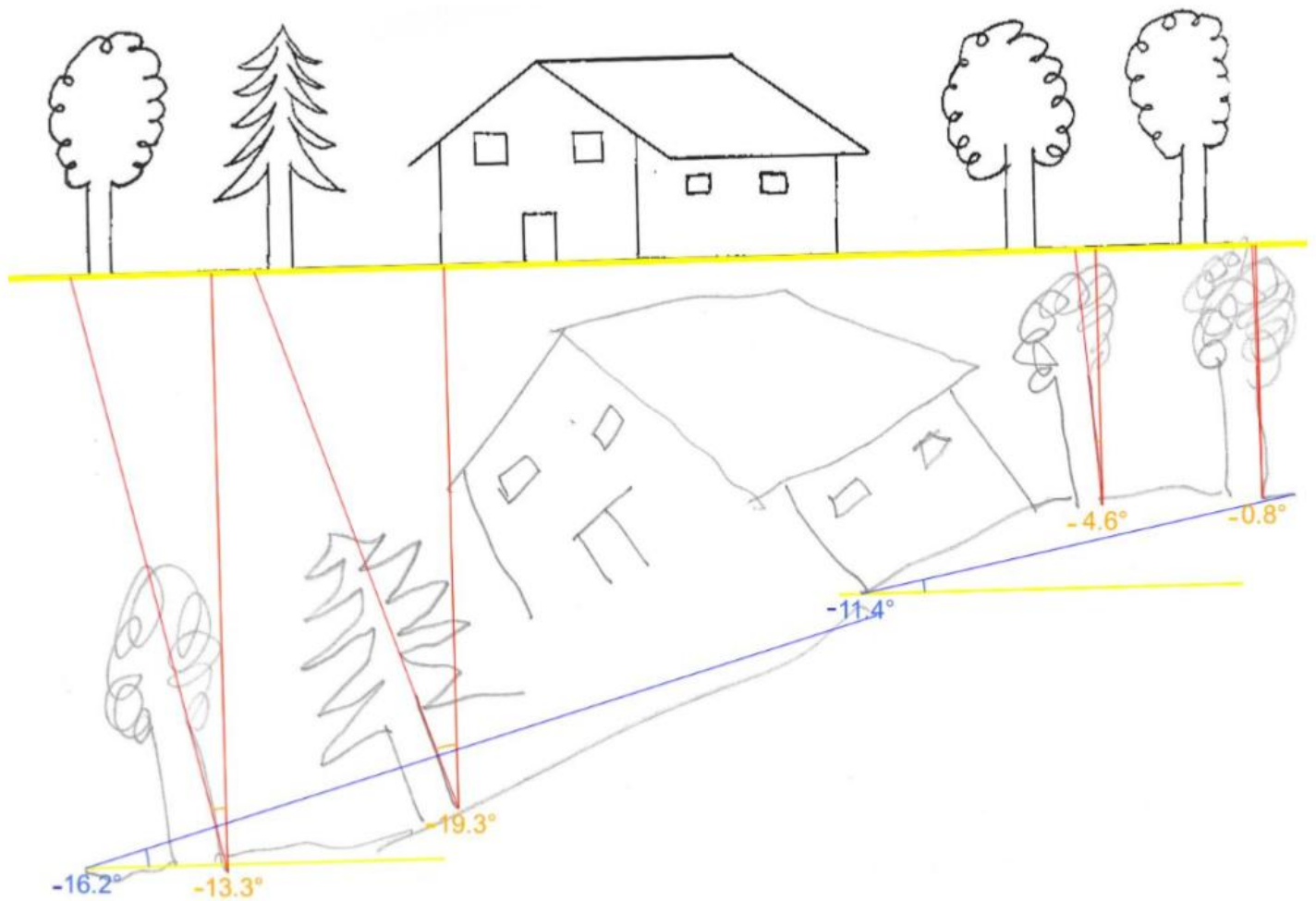
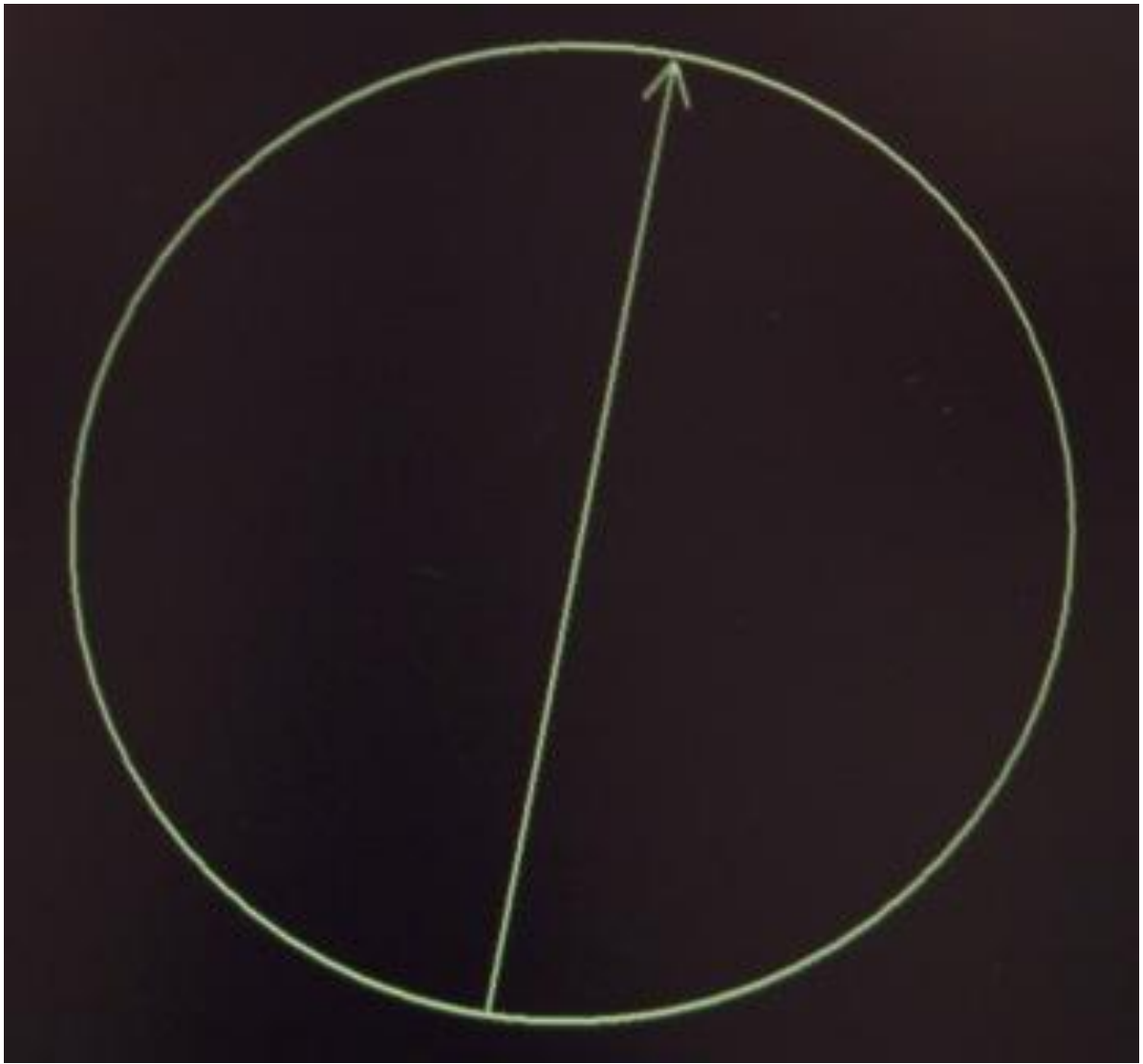


Figure 3: Schematic view of the way to compute criteria of the drawing orientation

Inclination of the left and right baseline with respect to the horizontal, and inclination of the four trees with respect to the vertical.



[Figure 4: Measuring Visual Vertical : luminous rod](#)



[Figure 5: Measuring postural vertical with the wheel paradigm](#)

Table 1: Comparison between patients and healthy subjects for writing and drawing measurements

Data are presented in the form median (Q1;Q3) ; Effect sizes ≥ 0.1 , 0.3, and 0.5 represent a small, medium, and large effect, respectively

Criteria	Healthy Control n=44	Patients with RHS and upright WD n=38 (62%)	Patients with RHS and tilted WD n=23 (38%)	Healthy controls vs patients with upright WD	Healthy controls vs patients with tilted WD	Patients with tilted WD vs patients with upright WD
Margin tilt (°)	-1.8 (-5.3 ; 3.6)	-0.6 (-4.7 ; 5.2)	-9.7 (-39 ; -0.9)	p=0.36	p=0.003 r=0.37	p=0.001 r=0.42
Lines' tilt (°)	-1.2 (-2.3 ; -0.3)	-1.4 (-2.5 ; -0.1)	-4.7 (-11.1 ; -2.3)	p=0.798	p<0.001 r=0.5	p<0.001 r=0.55
Trees' tilt (°)	-1 (-2.5 ; 0.5)	-0.4 (-2.7 ; 2.1)	-1 (-6 ; 1.4)	p=0.193	p=0.57	p=0.147

Here large effect size were found for the criterion lines' tilt, both for the comparison of healthy controls with individuals with a tilted WD and for the comparison of individuals with and without a tilted WD.

Table 2: Comparison between patients with tilted WD and patients with upright WD

Data are presented in the form median (Q1;Q3) or number of observations (%) ;
 Effect sizes ≥ 0.1 , 0.3, and 0.5 represent a small, medium, and large effect, respectively.

Criteria	Tilted WD N=23 (38%)	Upright WD N=38 (62%)	p values	Effect sizes
Age (years)	68 (64 ; 73.5)	65 (53 ; 68)	0.062	-
Sex (male)	12 (52%)	24 (63.2%)	0.398	-
Stroke type (ischemic)	21 (91%)	34 (89%)	1	-
FIM (18-126)	99.5 (74 ; 117)	102 (79 ; 114)	0.962	-
mFMA gait score (0-6)	2 (0 ; 5)	5 (2 ; 6)	0.007	r=0.35
SCP (0-6)	1.75 (0.2 ; 5.5)	0 (0 ; 0.4)	0.001	r=0.44
PV (°)	-4 (-8.1 ; -1)	-1.4 (-3.4 ; -0,6)	0.018	r=0.3
VV (°)	-6.4 (-10.6 ; -2.3)	-1.2 (-4 ; 0.2)	0.001	r=0.41
Body Neglect	11.1 (6.4 ; 20.3)	12.9 (6.4 ; 22.4)	0.503	-
Non Body Neglect	10.3 (7.4 ; 17.2)	2.9 (0.8 ; 8.4)	<0.001	r=0.45
Hemianopia	12 (52.2%)	7 (18.4%)	0.006	V=0.35
Apraxia	12 (9.5 ; 12)	12 (12 ; 12)	0.672	-

Additional material

STROBE Statement—Checklist of items that should be included in reports of cohort studies

	Item No	Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (b) For matched studies, give matching criteria and number of exposed and unexposed
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) If applicable, explain how loss to follow-up was addressed (e) Describe any sensitivity analyses
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)
Outcome data	15*	Report numbers of outcome events or summary measures over time
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which

		confounders were adjusted for and why they were included
		(b) Report category boundaries when continuous variables were categorized
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at <http://www.strobe-statement.org>.

Operating mode for Angle Calculator

1/ Criteria used on BEN writing test :

The first step was to define the objective vertical by clicking on two distant points on the right edge of the paper.

For *the margin tilt* the operator had to click on the most left-most point on each line. The application calculated a regression line with these three points, and the angle between this line and the objective vertical.

For *the inclination of the three lines* the operator had to click on the lowest point of the first and last letter with no descender, to define an inclination line. The application calculated the angle between this line and the perpendicular to the objective vertical.

2/ Criteria used on the drawing test (Gainotti figure) :

The first step was to define the objective horizontal by clicking on two distant points of the model figure baseline.

Then the operator defined on the individual production the inclination line of each tree by clicking on the lowest and highest point of the right edge of each trunk. *The inclination of each tree* was defined by the angle between this line and the perpendicular to the objective horizontal. We chose to use the right edge of each tree because we supposed several patients would have an object centered neglect.

To determine *the inclination angle of the left baseline* the operator had to click on the left extremity of the baseline and on the intersection point between the baseline and the house's second wall (i.e. the middle of the figure).

For *the inclination angle of the right half line* the operator had to click on the intersection point between the baseline and the house's second wall and on the right extremity of the baseline. The application calculated the angle between these half lines and the objective horizontal.

Selection of items from Catherine Bergego Scale :

Body neglect :

- 1/ Forgets to groom or shave the left part of his/her face
- 2/ Experiences difficulty in adjusting his/her left sleeve or slipper
- 3/ Forgets to clean the left side of his/her mouth after eating
- 4/ Forgets about the left part of his/her body (exemple : forgets to put his/her upperlimb on the armrest ; or his/her left foot on the wheelchair rest ; or forgets to use his/her left arm when he/she needs to)

Non body neglect :

- 1/ Forgets to eat food on the left part of his/her plate
- 2/ Has difficulty in paying attention to noise or people addressing to him/her from the left
- 3/ Experiences difficulty in finding his/her way towards the left when traveling in familiar places or in the rehabilitation unit
- 4/ Experiences difficulty in finding his/her personal belongings in the room or bathroom when they are on the left side

Cotation :

0=no neglect 1=mild neglect
2=moderate neglect 3=severe neglect

Total : (Total score/number of valid items) x 8 = .../24

Non specific items which we did not use :

- 1/ Experiences difficulty in looking towards the left
- 2/ Collides with people or objects on the left side, such as doors or furniture (either while walking or driving a wheelchair)

Composite scores for neglect

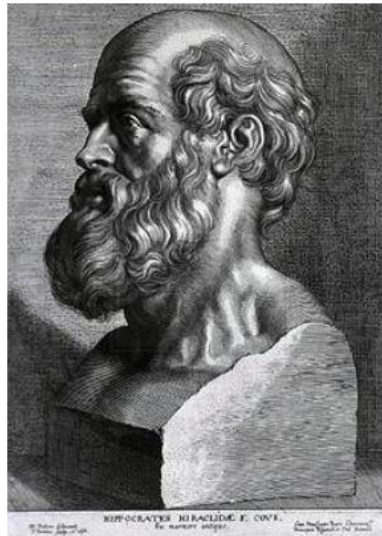
Composite Score for extracorporal neglect :

Test	Rating	Formula	Left USN if
1/ Bells test	R_1 =Number of omissions (0 to 35)	$S_1=(R_1/35) \times 100$	$> 6/35$ (17.14%)
2/ Overlapping figures	R_2 =Number of omissions (0 to 20)	$S_2=(R_2/20) \times 100$	$> 1/20$ (5%)
3/ Reading test	R_3 =Number of omissions (0 to 116)	$S_3=(R_3/116) \times 100$	$> 1/116$ (0.86%)
4/ Extracorporal items of Begergo Scale	R_4 =(Score/number of valid items) x 4 (0 to 12)	$S_4=(R_4/12) \times 100$	$> 1/12$ (8.33%)
Extracorporal neglect composite Score/100	/	$S_T=(S_1+ S_2+ S_3+ S_4)/4$	$> 7.83\%$

$S_1(\%)$ =Score at test 1 ; $S_T(\%)$ = Total score

Composite Score for corporal neglect :

Test	Rating	Formula	Left USN if
5/ Bisiach test	R_5 =Score eyes open + score eyes closed (0 to 6)	$S_5=(R_5/6) \times 100$	$> 1/6$ (16.67%)
6/ Fluff test	R_6 =Number of omissions	$S_6=(R_6/15) \times 100$	$> 3/15$ (20%)
7/ Comb and razor test	R_7 =(Right shot-left shot) / (right shot + left shot + ambiguous) x 100	$S_7=R_7$	$> 11\%$
8/ Corporal items of Bergego Scale	R_8 =(Score/number of valid items) x 4 (0 to 12)	$S_8=(R_8/18) \times 100$	$> 1/12$ (8.33%)
Corporal neglect composite score/100	/	$S_{T2}=(S_5+ S_6+G+ S_8)/4$	$> 14\%$



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.