The fast-posterior superior insula (Fast-PSI)

A neuronavigation-free targeting method for noninvasive neuromodulation

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The posterior-superior insula (PSI) is a safe and potentially useful target for non-invasive neuromodulation in the treatment of patients with peripheral neuropathic pain [1]. However, its identification requires costly and time-consuming brain imaging and neuronavigation [2].

Attempts to standardize stimulation TMS targets with neuronavigation using coordinate-atlases were done, however, only superficial cortical areas are available in these atlases [3]. A big step made was the standardization of the insular location and subdivisions as proposed by Faillenot et al. (2017), who located the insula gyri into MNI152 coordinates intervals, allowing it to be used as regions of interest in different studies [4]. Improvements in methods to facilitate the identification of deep cortical structures based on EEG landmarks have become available, but the need to use the 10–20 system, the different intra-individual cranial proportions and lack of validation for non-invasive neuromodulation are main limitations that fueled new neuronavigationless approaches [5]. One successful example is the detection of the dorsolateral prefrontal cortex, which was developed by Beam et al. (2009), using scalp and diameters distances combined. This neuronavigation-free method is already validated and accepted worldwide [6].

Intracranial structure proportions are generally constant, as demonstrated in human skull [7] and brain studies [8]. Based on these data, and taking into account cranial shapes differences between individuals, and with the hypothesis that intracranial distances proportions between craniometric landmarks and the orthogonal scalp projection of the PSI (sPSI) are similar between people, we proposed the "Fast-PSI": a novel method to identify the sPSI based on craniometry and intracranial Euclidian distances proportions comparisons between four scalp points. After giving written informed consent to participate in the protocol (Ethics Review Board#28659714.1.0000.0068), eleven healthy participants (four females, 31.5 ± 9.5 years) had their sPSI and cranial landmarks MNI152 coordinates identified by neuronavigation.

The stereotactic based Euclidean distances between nasion and sPSI (N-sPSI), nasion and inion (N–I), vertex and sPSI (Cz-sPSI) and vertex and tragus (Cz-T) were calculated with the formula $\sqrt{[(X1-X2)^2+(Y1-Y2)^2+(Z1-Z2)^2]}$ [9]. Then, the craniometricbased Euclidean distances between sPSI and the same landmarks were measured with a pachymeter. To differentiate them from the stereotactic based Euclidian distances names, they were called as: a) nasion-sPSI; b) nasion-inion; c) vertex-sPSI; and d) vertex-tragus distances.

Assuming that both stereotactic based and craniometric based Euclidean distances had similar proportions of: i. nasion-sPSI to nasion-inion distances and ii. vertex-sPSI to vertex-tragus distances, these proportions were compared. This was performed using paired two-tailed Student's *t*-test with Bonferroni correction for multiple analyses. Statistical significance was set at $p < 0.05$, and values were considered as similar if $p > 0.20$.

Since the proportions were similar, two correction factors could be developed: the "correction factor 1", the proportion inside nasion-inion distance that corresponded to nasion-sPSI distance; and the "correction factor 2", the proportion inside vertex-tragus distance that corresponded to vertex-sPSI distance (either calculated or measured Euclidian distances).

1. The Fast-PSI formula

a. Identification of the vertex (the point where the nasion-inion and tragus-tragus scalp distances intersect).
b. Identification of the Nasion–sPSI line: result from nasion-inion Euclidian distance x correction factor 1;
c. Identification of the vertex-sPSI line: result from vertex-tragus Euclidian distance x correction factor 2.
d. Fast-PSI is the intersection point between nasion-sPSI and vertex-sPSI lines (Fig. 1).

After identifying the vertex, nasion-inion and vertex-tragus Euclidian distances should be traced with a pachymeter, being the two only distances the examiner need to measure. They should be inserted in the software in millimeters, resulting in two output measures: "nasion-sPSI line" and "vertex-sPSI line". The point of intersection of these lines is the orthogonal scalp projection of the PSI identified without the need of neuronavigation: the "Fast-PSI" (Fig. 1).

In a second experiment, two blinded raters assessed the Fast-PSI test-retest, intra- and inter-rater reliability coefficients in other five

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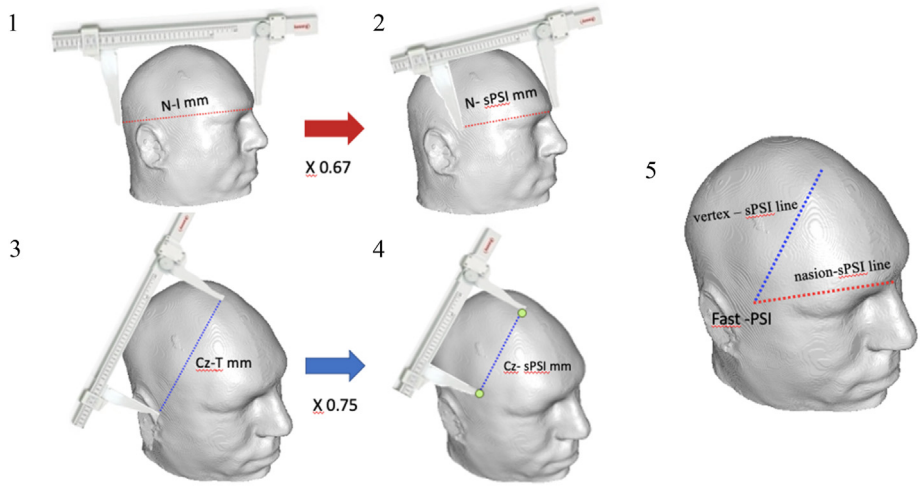

Fig. 1. Demonstration on how to perform the "Fast-PSI".
1: Euclidian distance between nasion and inion.
arm 1 (fixed): at nasion; arm 2: at inion.
2: Euclidian distance between nasion and orthogonal scalp projection of the PSI (sPSI), using correction factor 1.
arm 1 (fixed): at nasion; arm 2: at sPSI vertical compass line.
3: Euclidian distance between vertex and tragus.
arm 1 (fixed): at vertex; arm 2: at tragus.
4: Euclidian distance between vertex and orthogonal scalp projection of the PSI, using correction factor 2.
arm 1 (fixed): at vertex; arm 2: at sPSI horizontal compass line.
5: Fast-PSI = point of intersection of nasion-sPSI horizontal line and vertex-sPSI vertical line.
§ All distances are in millimeters.
§§ All distances are measured with a pachymeter.
§§§ Correction factor 1 = 0.67; Correction factor 2 = 0.75.
Figure from a 3D-brain image model and exported as NIfTI files using Mango brain visualization software (http://ric.uthscsa.edu/mango/).

different healthy volunteers (four women, 31.0 ± 4.0 years), resulting in ten hemispheres measurements. Then, they were compared with the neuronavigated method. The mean time to perform the fast-PSI and the standard neuronavigation technique were measured by a third researcher and them compared.

The stereotactic based mean distances' proportions were: (N-sPSI)/(N–I) = 0.67 ± 0.01 and (Cz-sPSI)/(Cz-T) = 0.75 ± 0.02. The craniometric based mean distances' proportions were: (a/b) = 0.67 ± 0.00 and (c/d) = 0.75 ± 0.02. There were no statistic differences between them p = 0.635 and = 0.236 respectively. These data resulted in the *correction factor 1 = 0.67; and the correction factor 2 = 0.75.*

2. The Fast-PSI formula

Nasion-sPSI line = nasion-inion Euclidian distance x 0.67 (correction factor 1) and vertex-sPSI line = vertex-tragus Euclidian distance x 0.75 (correction factor 2).

Fast-PSI = intersection point between nasion-sPSI and vertex-sPSI lines (Fig. 1).

3. The Fast-PSI web-based version

A Fast-PSI electronic version was developed in Rstudio IDE, with the Shiny version 1.4.0 package, and published with a video demonstration on Rstudio Shiny Server [10]: available at https://juliocesar9999apps.shinyapps.io/fast_psi_app/

There was no statistical difference between the intra-rater and inter-rater measurements, or between Fast-PSI and neuronavigated coordinates. Cronbach's alpha was 0.91.

4. Fast-PSI x neuronavigation method realization time

The mean time to identify the PSI by neuronavigation was 41.2 ± 2.59 minutes, without the time to undergo MRI. The mean time for the "Fast-PSI" determination was 1.33 ± 0.04 minutes (for more details please refer to appendix).

Here, the development and validation of the "Fast-PSI" method is presented to identify the orthogonal scalp projection of the PSI without the need of neuronavigation. Using craniometric landmarks and distances between them, one can identify the PSI using a pachymeter. The technique was compared to the neuronavigated location method, showing a very high precision. Not only it was a fast and accurate procedure, but it showed high intra- and inter-rater reliability.

Our results support the reliability and accuracy of the Fast-PSI approach to perform PSI rTMS. Future studies comparing usefulness of this framework in clinical trials and in everyday practice will help determine its usefulness.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.brs.2022.08.009.

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