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PATIENT FACING SYSTEMS

How Reliable Is the Pinaya Method for Assessing Cognitive Lateralization with Functional Transcranial Doppler Ultrasound?

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Dear Sir:

Pinaya and colleagues [1] propose an alternative processing method for the laterality index (LI), and compared it with established methods for handling functional Transcranial Doppler (fTCD) data. The authors conclude that the results were highly comparable across methods when using fTCD for a motor task, with their method having the advantage of being computationally simpler. In this letter we report our evaluation of the Pinaya method (henceforth 'Pinaya') when analyzing fTCD data from the Word Generation task, commonly used to study cerebral lateralization for language production. We focus on reliability, as it is critical when researching human cognition with fTCD, but may be even more important when evaluating cerebral lateralization in patients.

The processing method proposed by [1] includes only independent normalization of the left and right channels and then calculation of the LI, differing from established methods [2, 3] in two important ways: no data cleaning is performed and no transformation is carried out to reduce rhythmic modulations of the blood flow velocity (BFV) as a result of the heart cycle. In addition, in [1] the LI is calculated as the difference between mean BFV during the baseline and mean BFV during the period of interest, whereas others [2, 3] have used the mean BFV difference in a 2 s window centered on the peak difference value during the period of interest.

Here we report the reliability of three processing methods ('Pinaya', 'Deppe', and 'Deppe+'; we do not report on the 'Knecht' method mentioned in [1] as it preceded 'Deppe' as is no longer used) using the standard Word Generation task consisting of: a brief auditory tone and 'Clear mind' presented on the screen (5 s), a single letter cueing silent word generation (15 s), a brief tone and 'Say' cueing verbal report of generated words (5 s), and 'Relax' (40 s). All 26 letters of the alphabet were used, resulting in 26 epochs. Participants were 17 Macquarie University students (mean age = 22.2, min = 17, max =53, 11 female) completing experiments for course credit [Ethics approval: 5,201,500,074]. Relative to letter onset, baseline was set at −15 to −5 s and the period of interest was 5 to 15 s. The Deppe method was as stipulated in [1], that is, without the recommended removal of epochs with extreme values [2]. The Pinaya method, originally conducted on a single epoch [1], was calculated as the average across all epochs, as with the other methods. The Deppe + method [described in 2 and implemented in 3] included the removal of epochs with (i) BFV ± 50 of the mean activation and (ii) with an absolute left-right activation separation of five times the inter-quartile range of the individual's activation separation distribution, resulting in a minimally lower average number of trials included in the analysis per participant (Pinaya and Deppe $M = 25.94$, Deppe + $M = 24.29$).

LI values for each method are presented in Fig. 1, panel a. Using 95 % confidence interval comparisons to zeros, all methods indicate left-lateralization at the group level. At the individual level, the majority of participants are also left-lateralized: Pinaya =10, Deppe =12, Deppe + = 13 (the remaining participants were not lateralized). However, using Deppe or Deppe + an additional 2 or 3 individuals, respectively, were identified as left-lateralized. These individuals were categorized as not lateralized when using Pinaya. The internal reliability of the methods was determined by correlating the

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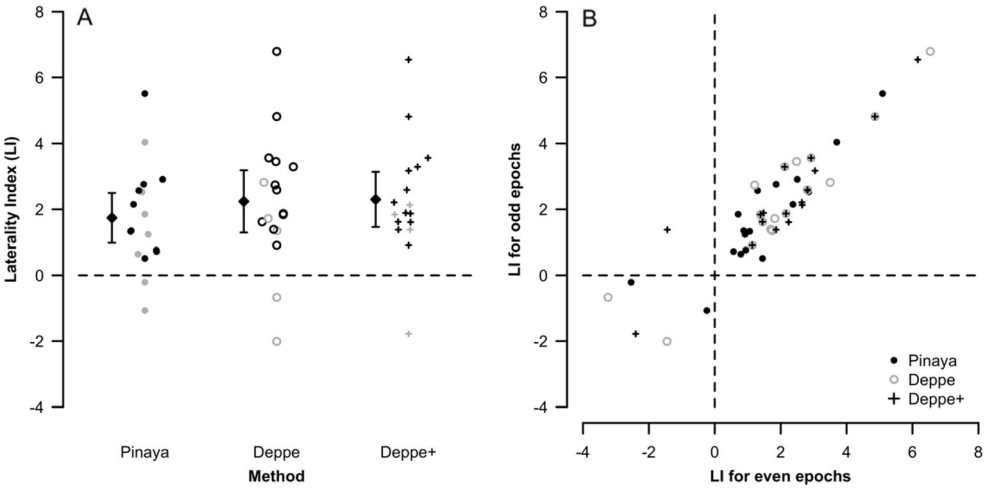

Fig. 1 Panel **a**: Individual and group (95 % confidence intervals) laterality indices (LIs) for each processing method (*black* indicates individuals left-lateralised for language; *gray*, not lateralized). Panel **b**: Scatter plot of LIs for odd and even epochs for each calculation method

LIs calculated for the odd and even epochs (i.e., split-half reliability) – only possible with multiple epochs, not with the methods employed in [1]. These values are presented in Fig. 1, panel b. Spearman's ρ was used to minimize the effect of extreme values. The methods showed medium to high reliability: Pinaya =0.63 [95 % confidence intervals: 0.14 0.92], Deppe =0.55 [0.03 0.93], and Deppe + = 0.82 [0.48 0.97]; and very strong correspondence with each other: Pinaya-Deppe = 0.97 [0.84, 1], Pinaya-Deppe+ = 0.89 [0.67, 1], Deppe-Deppe + = 0.89 [0.65, 1]. There was no statistical difference (Z-transformation comparison) between the reliability coefficients for the different methods (all p-values > .3).

In conclusion, the Pinaya method shows medium reliability; however, in order to maximize reliability of fTCD when studying lateralization of cognitive functions, we recommend using previously established methods. The Pinaya method may have benefits in other applications (e.g., brain computer interfaces) but this is yet to be demonstrated.

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