Comparison of changes in mean flow velocity in anterior cerebral artery before and during cognitive stimulation between non-stroke and post-stroke people

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Abstract. Transcranial Doppler (TCD) is a tool that has been used widely to measure cerebral blood flow and changes in the cerebral autoregulatory mechanism that can be observed during cognitive stimulation task as changes in mean flow velocity (MFV). This cross-sectional study was to compare the anterior cerebral arteries (ACA) MFV changes during cognitive stimulation using TCD in post-stroke and control group in Neurology Department Adam Malik General Hospital. From August to December 2016, all subject underwent TCD examination to assess baseline characteristic both side of ACA; then the patients were stimulated using Stroop Task. During stimulation, we measured changes in MFV that were correlated with cerebral autoregulation in total 13 pairs of post-stroke and control recruited. Paired t-test was used to evaluate the difference in baseline and during stimulation for each post stroke and control group while independent t-test was used to determine the MFV changes difference between both groups. There were significant differences for MFV changes in each artery for control [R-ACA (p=0.001), L-ACA (p=0.001)] and post-stroke [R-ACA (p=0.001), L-ACA (p=0.001)]. Meanwhile, there was no significant difference for MFV elevation for arteries compared between groups [R-ACA (p=0.374) and L-ACA (0.272)].

1. Introduction
The first introduction of TCD started on 1979 when Satomura and Kaneko introduced pulsed doppler shift sonography to study cerebral hemodynamics, while three years later Rune Aaslid presenting the single–gated TCD that helped the clinician to measure vascular flow non invasively.[1] TCD nowadays is a popular diagnostic tool with 2 MHz pulsation transducer equipped with manual handling for measuring cerebral blood flow velocity on the circle of Willis and vertebrobasilar system through temporal calvaria region, orbital either foramen magnum.[2] Cognitive stimulation could be as amplification or extension of core capacity of neurobehavioural through improvement or augmentation of internal and external information processing system. The process involves information perception, attention selection, representation and information retaining while all of these are for creating a proper executive value of behavioral motoric output.[3] The example of this is Stroop Task, a simulation where the subject read aloud colors of the words that don’t elaborate with the colors word written (e.g., word “RED” written with yellow ink). This incompatible information will create interference and conflict response resulting increment in an executive effort to reduce mistakes.[4]
Conflict-control model already informs us that there is monitoring from the anterior cingulate cortex (ACC) that interact with the dorsolateral of the prefrontal cortex (DL-PFC), both have functional connectivity and activated when a conflict of executive function and attentive perceptual selection detected.[5] In this process, the foremost superior control area includes DL-PFC which have supplied from other tertiary center and making dynamics filtering mechanism that controls some interference patterns on either cortical or subcortical layer activated with executive reasoning.[6] It is the reason patient with frontal lobes lesions will have disruptive behavior system, one of them are the difficulty of deciding and making choices, which can test through Stroop Task.[7] These areas are supplied by an anterior cerebral artery (ACA) as one of its major vasculatures.[8]

Previous research has illustrated a potential correlation of TCD examination with specific cognitive activities, where Kelley et al. show that there was a 1.6-10.6% of increment of mean flow velocity on 70 subjects through selective regional CBF increment on the cortical system and specific cerebral metabolism modulation. This increment was believed to be the results of reduction of resistance that allow flow velocity to increase from dilation of the vascular precapillary bed which was a physiological consequence from carbon dioxide (CO₂) pooling as cerebral metabolites from the cognitive activity.[9] Post-stroke was a condition after stroke when cerebral plasticity reorganization had taken place usually start on a 1st month to 3rd month after stroke onset. It has been known that stroke impact on cerebral autoregulation and inhibition, also on executive function and complex daily activity after three months of stroke onset, hypothetically will differ from non-stroke individuals.[10,11] Aoi et al. also stated that after stroke condition, especially chronic infarct, there would be cerebral autoregulation disruption that can affect the functionality of the patients.[12] Research conducted by Chen et al. also confirmed that moderate to severe stenotic vascular disease as it degree would directly affect the brain autoregulation system.[13] This study aimed to compare the changes in MFV of anterior cerebral arteries (ACA) during cognitive stimulation in normal and post-stroke people as measured by TCD.

2. Materials and Methods
After receiving ethical approval from Health Research Ethical Committee, Medical School of University Sumatera Utara, Medan-Indonesia, we conducted a series of examination from August 2016 through December 2016 on 13 subject post-stroke patients and 13 control of normal subject on Integrated Diagnostic Installation of Adam Malik General Hospital. Inclusion criteria for the subject were patients with minimum three months previous history of stroke and already confirmed by standardized non-contrast Head CT, while inclusion criteria for control were people without a previous history of stroke and transient ischemic attack (TIA). Exclusion criteria for both groups were subjects or controls with a decreased level of consciousness, significant heart disease, color-blinded and total-blinded, word-blinded and/or dyslexia, motoric and/or sensory aphasia, having difficulties on comprehending and/or coordinating with cognitive stimulation’s instruction. Having Alzheimer and/or vascular dementia or any significant perceptual, neurocognitive or psychiatric liability were also exclusion criteria.

Informed consent was asked from all of the subjects and controls onsite. The MFV of bilateral ACA were measured using TCD Sonara Tek Version 04, Processor Celeron M.13 GHz and the baseline values were recorded. The insonation was done on carotid sites on post-stroke subjects and matched the same depth of each correlating artery on the same subjects for ACA sample volume (transtemporal window, away flow, depth 60-75 mm).[14] However, at the same depth ranges, we couldn’t apply the exact depth for every subject due to vascular anatomical variation. After measuring baselines MFV, the subjects were asked to read aloud and finished four subsets of Stroop Task-Victoria version as a cognitive stimulation tools while we measure the MFV changes from the initial value. The data were collected and calculated using IBM SPSS 24 and shown through descriptive and statistical analysis. Meaning differences using Chi-Square Test or Fisher’s Exact Test, while we measure the difference between baseline and during stimulation MFV of ACA on both groups using
paired student t-test, while independent t-test was used to compare MFV changes between both groups.

3. Results
From a total of 13 post-stroke subjects as cases, there were ten men (76.92%) and three women (23.08%) and 13 non-stroke subjects as controls there were nine men (69.23%) and four women (30.77%), with overall mean age 37.85 ± 15.44. We have concluded mean differences of each artery insonation on table 1 using Fisher’s Exact Test.

Table 1. Mean differences between non-stroke and post-stroke people (cm/sec).

| Vascular Sample Volume | Total     | Non Stroke | Post Stroke | p value |
|------------------------|-----------|------------|-------------|---------|
| R-ACA                  | Baseline  | 42.40 ± 11.37 | 54.67 ± 9.67 | 39.13 ± 12.36 | 0.11* |
|                        | Stim      | 50.37 ± 13.36 | 54.65 ± 11.39 | 46.10 ± 14.24 | 0.48* |
|                        | Delta     | 8.09 ± 4.99  | 8.98 ± 4.00  | 7.20 ± 5.84  | 0.41* |
| L-ACA                  | Baseline  | 34.14 ± 9.79  | 36.72 ± 6.37  | 31.56 ± 12.03 | 0.34* |
|                        | Stim      | 45.99 ± 13.14 | 51.35 ± 8.88  | 40.62 ± 14.78 | 0.48* |
|                        | Delta     | 11.08 ± 9.22  | 13.10 ± 10.52 | 9.05 ± 7.59  | 0.68* |

*aFisher’s Exact Test

Paired t-test was used to compare baseline MFV and during stimulation for either non-stroke and post-stroke group and independent student t-test to determine changes of MFV between groups. Using 95% Confidence Interval (CI 95%), we found significant differences for MFV changes in each artery for normal group [R-ACA (p=0.001) and L-ACA (p=0.001)] and post-stroke group [R-ACA (p=0.001) and L-ACA (p=0.001)] (Table 2). While these results look favorable, we did not find any significant difference for MFV elevation compared between groups [R-ACA (p=0.374) and L-ACA (0.272)] (Table 3).

Table 2. Mean differences between baseline and stimulation in both groups (cm/sec).

| Vascular sample volume | Non Stroke | p       | Post Stroke | p       |
|------------------------|------------|---------|-------------|---------|
| R-ACA                  | Baseline   | 45.67 ± 9.67 | 0.001 | 39.13 ± 12.36 | 0.001 |
|                        | Stimulation| 54.65 ± 11.39 |       | 46.10 ± 14.24 |       |
| L-ACA                  | Baseline   | 36.72 ± 6.37 | 0.001 | 31.56 ± 12.03 | 0.001 |
|                        | Stimulation| 51.35 ± 8.88 |       | 40.62 ± 14.78 |       |

independent t-test

Table 3. Mean differences of MFV elevation in non-stroke and post-stroke people (cm/sec).

|                  | Non Stroke | Post Stroke | p       |
|------------------|------------|-------------|---------|
| Delta R-ACA      | 8.98 ± 4.00 | 7.20 ± 5.84 | 0.374   |
| Delta L-ACA      | 13.10 ± 10.52 | 9.05 ± 7.59 | 0.272   |

To be compared to control subjects, MFV elevation also happened in stroke subjects but rather with lower values (Figure 1 and Figure 2).
4. Discussion
The results of TCD examinations on both groups show that there was significant elevation on both groups on stimulations using Stroop Task in the normal group [R-ACA (p=0.001) and L-ACA (p=0.001)] and post-stroke group [R-ACA (p=0.001) and L-ACA (p=0.001)]. After dividing the MFV into two different categorized groups, we also found the highest MFV elevation for ACA was at L-ACA also at the non-stroke group (13.10 ± 10.52 cm/sec). As like in our research, a study done by Kelley et al. showed that cognitive stimulation using video games increased all MFV either on ACA and also on middle cerebral artery (MCA). While the highest increment on Kelley et al study was on R-MCA (59 ± 12 to 66 ± 14 cm/sec).[9] This differences may be caused by the different modalities of cognitive stimulation on Kelley et al. research compared to our study (video games compared to Stroop task). From Dahl et al. presumed in their research, any increment in MFV per percent velocity measured with TCD would correlate with cerebral blood flow (CBF) in milliliters per 100 gram per minutes also with its vasoreactivity.[15] It explains to us why MFV in the post-stroke group, while increased, were lower compared to controls group. However, there’s some limitations of this study. First, we were not excluding one with nootropics drugs which from a pharmacological point of view, some nootropics might increase cerebral blood flow and confound cognitive ability on subjects comprehension on Stroop Task.[16,17] Second, we also see that there were imbalances for stroke risk factor such hypertension, diabetes, dyslipidemia and smoking that was rarely in controls group. Lastly, subjects characteristic variable such as age range and level of education may be confounding factor for any baseline MFV.

5. Conclusions
Cognitive stimulation would increase MFV on both post-stroke subjects and stroke subjects. On the control side, L-ACA shows prominent elevations compared with R-ACA. Hypothetically due to cerebrovascular autoregulation disturbances, this does not happen on post-stroke subjects. There are significant differences between baseline and during stimulation MFV changes in each artery, yet there are no significant differences in MFV changes compared to normal patients and post-stroke patients groups. More studies ahead on these subjects with more samples are encouraged to support these findings.

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