Carotid Artery Reactivity Measurement among Healthy Young People towards Early Detection of Alzheimer Disease

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Abstract: - Alzheimer's disease (AD) mostly occurred in elderly is a progressive neurodegenerative disorder associated with disruption of neuronal function. A lot of effective methods have been invented to detect AD in the early stage. However, the developed methods have either high risk (using positron emission tomography (PET) and computed tomography (CT) scanning), high cost and long scanning duration (magnetic resonance imaging [MRI]) or not accurate enough (electroencephalography [EEG]). Fortunately, previous studies found that AD could be caused by the dysfunction of carotid artery which stimulates synaptoxic B-amyloid (AB) accumulation in the brain. Carotid artery condition could be evaluated through characterization method using reactivity feature (dilation capability) with its blood flow velocity as the parameter. Ultrasound machine is the ultimate modality analyzing the carotid artery structure since this modality has been used safely, accurately, cost effectively and quickly in detecting carotid artery blood flow velocity. Hence, the Doppler imaging technique using ultrasound machine in evaluating healthy young people carotid artery reactivity is implemented in this study in order to find its normal reactivity value. This normal value could be used to differentiate between healthy people and Alzheimer patient. All 30 subjects whose are less than 30 years old have been scanned with ultrasound machine using Doppler technique before and after having exercise to achieve 85% of their Maximal Heart Rate (MHR). Readings of carotid artery blood flow velocity before exercise (rest) and after exercise (stimulated) are taken to be compared to obtain its percentage increment value (reactivity). Based on the result, the normal carotid artery reactivity value is 143.6% for male and 103.3% for female.

Key-Words: - Alzheimer disease, ultrasound Doppler imaging, carotid artery reactivity (CAR), carotid artery blood flow velocity

1 Introduction

Alzheimer's disease (AD) is a progressive neurodegenerative disorder associated with disruption of neuronal function which is the most common cause of dementia in the elderly [2]. Early detection among potential individuals to get AD is very essential in order to reduce the risk of AD where it has affected 24.3 million people worldwide in 2010 with increment around 4.6 million yearly [3]. Treatment in the early stage is very efficient in treating AD especially before any clinical symptoms shown [4]. For the sake of detecting AD at early stage, structural and functional brain has to be evaluated first. Fundamentally, single photon emission tomography (SPECT) and positron emission tomography (PET) are used for brain functional imaging while computed tomography (CT) and magnetic resonance imaging (MRI) are used for brain structural imaging. SPECT and PET will show reduced neuronal function in human brain such as altered cerebral glucose and altered cerebral blood flow while CT and MRI will show tissue atrophy due to loss of synapses and neurons because of AD process [5].

It has been proven before that AD could be accurately detected by analyzing carotid artery structure. This is due to vascular abnormalities have the great potential to lead to vascular dysfunction which able to stimulate synaptoxic B-amyloid (AB) accumulation in the brain considered as the central process for AD formation [6]. Thus, a lot of new techniques have been explored to study vascular function in term of cerebral blood flow (CBF) including diffusion weighted imaging (DWI), diffusion tensor imaging (DTI), arterial spin labeling (ASL) and blood oxygenated level dependent (BOLD) [7]. However, doppler imaging technique using ultrasound machine is the most suitable one compared to other method since this modality has been used safely, accurately, cost effectively and quickly in measuring carotid artery blood flow velocity [1]. Hence, it is very important to assess carotid artery structure and its condition using ultrasound machine. This could be done through analyzing of carotid artery reactivity (CAR) in term of its blood flow velocity as previous studies found that AD could be accurately detected by analyzing of cerebral vessel reactivity (CVR) [6]. CAR indicates the capacity of blood vessels to dilate when being stimulated by several particular stimuli where the bigger the dilation, the better the condition of carotid artery (CA) [8].

Determining the CAR value could be done with measuring the carotid artery blood flow [9] which automatically increase the carotid blood flow (CBF) [10]. In order to confirm that carotid artery reactivity can be used to detect AD in early stage, characterization of carotid artery blood flow in healthy people need to be obtained first so that it can be compared and analyzed with Alzheimer patient later. All the subjects have undergone adequate exercise to stimulate carotid artery reactivity under hypertension condition. In this study, a significant value has been acquired for normal carotid artery reactivity among young healthy people. With this value, someone can use it as a reference value to categorize either he or she has Alzheimer disease or not. Currently, most of the studies related to diagnosing AD are always use cerebral vessel as the main indicator and drug or CO2 as the stimulator. However, cerebral vessel study needs expert personnel to handle the expensive transcranial Doppler ultrasound to obtain good and accurate result. According to Kolb B. et al, carotid artery blood flow could replace the cerebral blood flow [11]. Hence, carotid blood flow will be the main indicator in this study which allows utilization of conventional Doppler ultrasound and easy to handle in obtaining accurate and good result.

2 Material and Methods

2.1 Subjects/Data collections

In this study, 10 subjects of male and female each are selected to be participated for data collection. They are invited to have free scanning on the carotid artery using Doppler ultrasound imaging technique. The subjects are below than 30 years old, non smoker, free from any vascular disease and have normal blood pressure. Before start data collection, their details such as name, ic no, age, weight, height, blood pressure and oxygen concentration are taken. Personal interview between the subject and the researcher also done to ensure the subjects are really fit and suitable to participate in this study. Table 1 shows the average value for subject details.

Table 1
Details of subjects

Characteristics	Average Value
Mean age	22.5 ± 3.3
Mean weight	70 kg ± 8.5
Mean height	165.7cm ± 5.4
Mean blood pressure	125/83 mm Hg ± 8.4/6.2
Mean oxygen concentration	99% ± 1.5

2.2 Measurement

For the measurement, there are some steps to be done to get the data acquired. Figure 1 shows the data acquired which is image of Doppler ultrasound carotid artery.

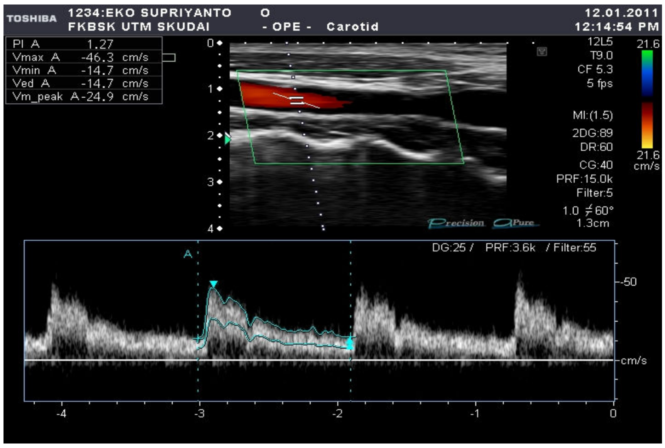

Fig. 1: Doppler ultrasound carotid artery image

Meanwhile figure 2 show the flow chart of carotid artery characterization process in human.

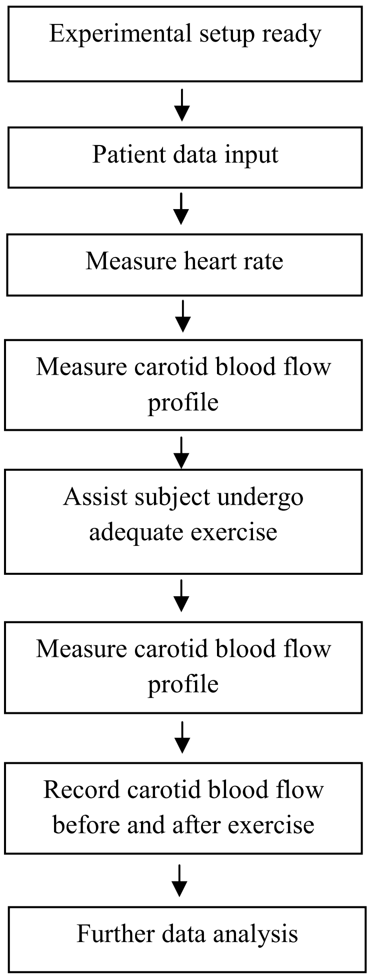

Fig. 2: Flow chart of carotid artery characterization

This measurement is done with two different parts which are under rest condition (normal) and under

ISBN: 978-1-61804-041-1

exercise condition (stimulated). After being explained by the researcher, the subject started the process of the experiment. The heart rate and carotid artery blood flow under rest condition are taken simultaneously. Heart rate reading is taken using patient monitor while ultrasound machine with Doppler imaging technique have been utilized to record the carotid artery blood flow. Heart rate and carotid artery blood are recorded in beat per minute and centimeter per second respectively. When all the required data are taken, subject asked to have adequate exercise on the treadmill. The period of the exercise and the speed of the treadmill are not fix as long as the heart rate of the subject achieve 85% of maximal heart rate. Subjects asked to warm up their body first to avoid any injury during the exercise period. The subject heart rate is being observed during all the time of exercise and once the subject achieves the target heart rate, he or she will be scanned immediately using ultrasound machine to record his or her carotid artery blood flow. This is because to avoid decline of the subject heart rate in order to remain the target heart rate during the recording process of carotid artery blood flow. Subjects are asked to have rest first and being ensured they are in good condition before leaving examination room.

2.3 Hypertension Method

Adequate exercise has been used as the stimulator to create carotid artery reactivity. The reactivity state could be achieved when the subject heart rate reach 85% of its maximal heart rate after having adequate exercise [13]. Maximal heart rate (MHR) is calculated in beat per minute (bt/m) and determined with specific formula [12]. The formulas are shown as followed:

Male MHR : 220 – age [1]

Female MHR : 200 – age [2]

2.4 Data Analysis

The condition of the carotid artery is being assessed in this study. The assessment is based on its reactivity. The reactivity of carotid artery could be determined through the blood flow velocity passed it. The faster the blood flow, the more the carotid artery reacted. The more the carotid artery reacted, the better the condition of the carotid artery. In this study, unharmed exercise method has been selected as the stimulator for the carotid artery to react or dilate as big as possible. Hence, the carotid artery blood flow velocity before and after having exercise will be compared and analyzed to find the increment percentage and at the same time find the normal carotid reactivity among young healthy people. This normal value could be used to compare with the value belong to Alzheimer patient so that it could be used as the main indication to categorize healthy people and Alzheimer patient. The normal carotid reactivity value could be obtained through below formula:

Percentage increment =

$$\frac{\text{Stimulated CA velocity- Normal CA velocity}}{\text{CA velocity}} \times 100 \qquad [3]$$

Increment value =

Stimulated CA velocity – Normal CA velocity [4]

3 Result and Analysis

3.1 Test Result

All results from this study are shown in this section. It includes the readings of carotid artery blood flow velocity and subject heart rate which are taken during rest and exercise state.

Table 2
CA blood flow velocity changes of male subject

n^{th} subject	Rest (normal)(cm/s)	Exercise (stimulated)(cm/s)
1	51.5	99.9
2	60.5	130
3	47.4	106.7
4	70.9	169.7
5	60.8	151.3
6	49.9	124.2
7	54.5	139.7
8	51.8	138.8
9	45.5	123
10	44.8	121.5
Average value	53.76	130.48

Table 2 shows the result for 10 male subjects. The results show the reading carotid artery blood flow velocity (cm/s) during rest (normal) and exercise (stimulated) condition. From the result, the lowest velocity for rest condition is 44.8 meanwhile the highest one is 70.9. The average velocity for rest condition is 53.76 cm/s. On the other hand, the lowest velocity for stimulated condition is 99.9 meanwhile the highest one is 169.7. The average velocity for stimulated condition is 130.48 cm/s.

Table 3
CA blood flow velocity changes of male subject

n^{th} subject	Rest (normal)(cm/s)	Exercise (stimulated)(cm/s)
1	110.5	163.2
2	67.2	104.1
3	60.2	102.3
4	59	117.2
5	51.5	111.2
6	53.7	120.8
7	50.6	115.7
8	50	124.6
9	47	127.3
10	42.5	117.2
Average value	59.2	120.4

Table 3 shows the result for 10 female subjects. The results show the reading carotid artery blood flow velocity (cm/s) during rest (normal) and exercise (stimulated) condition. From the result, the lowest velocity for rest condition is 42.5 meanwhile the highest one is 110.5. The average velocity for rest condition is 59.2 cm/s. On the other hand, the lowest velocity for stimulated condition is 102.3 meanwhile the highest one is 163.2. The average velocity for stimulated condition is 120.4 cm/s.

3.2 Analysis carotid artery blood flow velocity and heart rate increment

The increment value and the target data which is normal carotid artery reactivity percentage are shown in these following tables.

Table 4
Carotid Artery blood flow velocity increment in male

n^{th} subject	Increment value(cm/s)	Increment percentage (%)
1	48.4	94
2	69.5	114.8
3	59.3	125.1
4	98.8	139.3
5	90.5	148.8
6	74.3	148.9
7	85.2	156.3
8	87	167.9
9	77.5	170.3
10	76.7	171.2
Average value	76.7	143.6

Table 4 shows the lowest increment value among male subjects is 48.4 cm/s while the highest one is 76.7 cm/s. The average increment value is 76.7 cm/s. On the other hand, the lowest carotid artery blood flow velocity increment percentage is 94% while the highest one is 171%. The average for this increment percentage is 143.6%.

Table 5
Carotid Artery blood flow velocity increment in male

n^{th} subject	Increment value (cm/s)	Increment percentage (%)
1	52.7	47.6
2	36.9	54.9
3	42.1	69.9
4	58.2	98.6
5	59.7	115.9
6	67.1	124.9
7	65.1	128.6
8	74.6	149.2
9	80.3	170.8
10	74.7	175.8
Average value	61.2	103.3

Table 5 shows the lowest increment value among female subjects is 52.7 cm/s while the highest one is 74.7 cm/s. The average increment value is 61.2 cm/s. Apart from that, the lowest carotid artery blood flow increment percentage is 47.6% while the highest one is 175%. The average for this increment percentage is 103.3%.

Table 6
Heart rate increment in male subject

n^{th} subject	Increment value (bt/m)	Increment percentage (%)
1	59	79
2	77	88
3	71	102
4	82	127
5	87	128
6	83	139
7	90	139
8	99	140
9	82	149
10	111	179
Average value	82	127

Table 6 shows the lowest heart rate increment value among male subjects is 59 while the highest one is 111. The average increment value is 82 bt/m. On the other hand, the lowest heart rate increment percentage is 79% while the highest one is 179%. The average for this increment percentage is 127%.

Table 7
Heart rate increment of female subject

n^{th} subject	Increment value (cm/s)	Increment percentage (%)
1	58	70
2	61	71
3	60	75
4	63	77
5	69	78
6	66	79
7	70	88
8	65	105
9	85	119
10	84	121
Average value	69	88

Table 7 shows the lowest heart rate increment value among female subjects is 58 while the highest one is 85. The average increment value is 69 bt/m. On the other hand, the lowest heart rate increment percentage is 70% while the highest one is 121%. The average for this increment percentage is 88%.

3.3 Correlation between carotid artery blood flow and heart rate

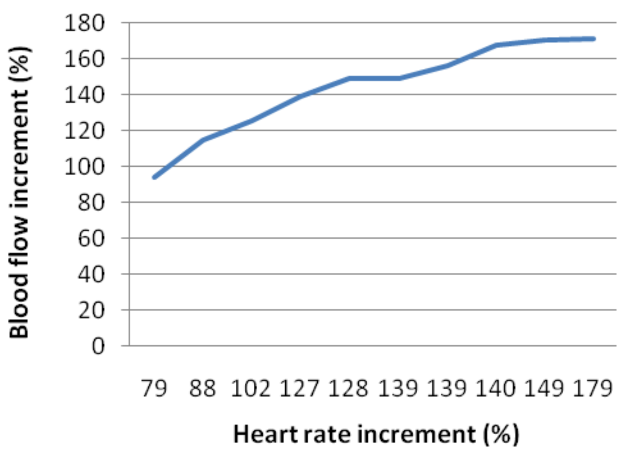

Fig. 3: Correlation between heart rate and blood flow velocity in male subjects

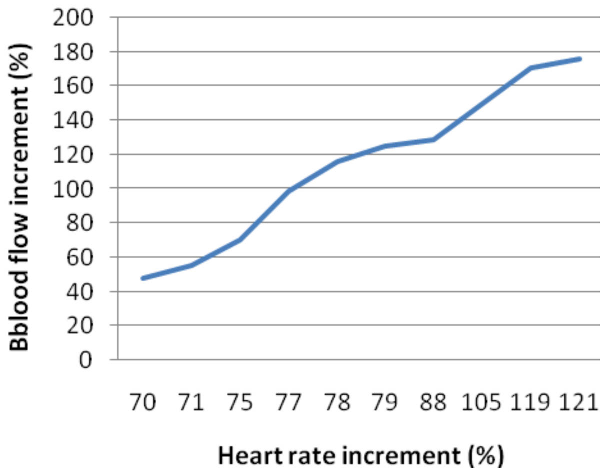

Fig. 4: Correlation between heart rate and blood flow velocity in female subjects

Figure 3 and 4 represent the correlation between heart rate and carotid artery blood flow velocity for male and female respectively. Both figures show that the carotid artery blood flow velocity is directly proportional to heart rate. The faster the blood flow, the higher the heart rate will be.

3.4 Comparison between male and female on carotid artery characterization

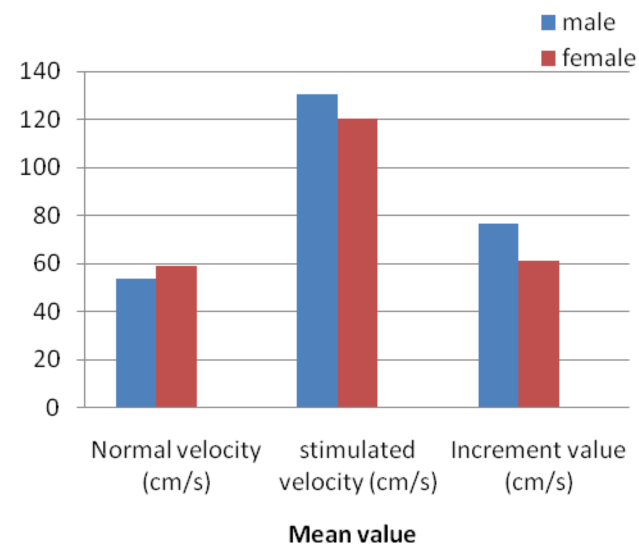

Fig. 5: Overall comparison between male and female carotid artery characterization.

Figure 5 shows that male will have higher value than female in two parameter which are stimulated carotid artery velocity and carotid artery blood flow increment value. Meanwhile, female will have higher value in the normal carotid artery velocity might because of female subjects are not really active in sport that make they are less fit than males subjects.

ISBN: 978-1-61804-041-1

4 Conclusion

As conclusion, this study is successfully in assessing the reactivity of human carotid artery. It is able to measure the carotid artery blood flow velocity changes due to the reaction from the carotid artery or the dilation effect of the carotid artery. This is because the carotid artery responded towards the hypertension condition realized by adequate exercise. This study found that the normal carotid reactivity value among young healthy people is 143.6% for male and 103.3% for female. This normal carotid artery reactivity value can be used as an indicator to evaluate the risk to get AD. Apart from that, this study also found that carotid artery blood velocity is directly proportional to heart rate. Hence, carotid artery reactivity measurement method can be projected as a new approach to contribute in early detection of Alzheimer disease.

References:

[1] E. Supriyanto, M. A. Jamlos, N. Humaimi, and L. K. Kheung, " Segmentation of Carotid Artery Wall towards Early Detection of Alzheimer Disease" in Proceedings of the 15th WSEAS International Conference on Circuits, Corfu Island, Greece, July 14-16, 2011, pp. 201-206.

[2] Prince S. E., Woo S., Doraiswamy P. M., Petrella J. R., "Functional MRI in the early diagnosis of Alzheimer's disease: is it time to refocus?", Expert Rev. *Neurotherapeutics* (2008) 8 (2), 169-175

[3] Wierenga C. E., Bondi M. W., "Use of Functional Magnetic Resonance Imaging in the Early Identification of Alzheimer's Disease", *Neuropsychol Rev* (2007) 17: 127-143

[4] Morris J. C., Storandt M., Miller P., McKeel D. W., Price J. L., Rubin E. H., Berg L., "Mild Cognitive Impairment Represents Early-Stage Alzheimer Disease", *Arch Neurol*. (2001) 58:397-405

[5] Mueller S. G., Weiner M. W., Thal L. J., Petersen R. C., Jack C. R., Jagust W., Trojanowski J. Q., Toga A. W., Beckett L., "Ways toward an early diagnosis in Alzheimer's disease: The Alzheimer's Disease Neuroimaging Initiative (ADNI)", *Alzheimer's & Dementia 1* (2005) 55–66

[6] Yeshuvath U. S., Uh J., Cheng Y., Cook K. M., Weiner M., Arrastia R. D., Osch M. V., Lu H., "Forebrain-dominant deficit in cerebrovascular reactivity in Alzheimer's disease", *Neurobiology of Aging* (2010) 02.005

[7] Tarawneh R., Holtzman D. M., "Biomarkers in translational research of Alzheimer's Disease", Neuropharmacology 59 (2010) 310-322

[8] Scwertfeger N., Neu P., Schlattmann P., Lemke H., Heuser I., Bajbouj M., "Cerebrovascular reactivity over time course in healthy subjects", Journal of the Neurological Sciences 249 (2006) 135-139

[9] Wierenga C. E. and Bondi M. W., "Use of Functional Magnetic Resonance Imaging in the Early Identification of Alzheimer's Disease", Neuropsychol Rev (2007) 17: 127-143

[10] Yeshuvath U. S., Amezcua K. L., Varghese R., Xiao G., "On the assessment of cerebrovascular reactivity using hypercapnia BOLD MRI", NMR Biomed. (2009) 22 (7): 779-786

[11] Kolb B., Diane L., Rotella, Stauss H. M., "Frequency response characteristic of cerebral blood flow autoregulation in rats", Am J Physiol Heart Circ Physiol (2007) 292: H432-H438.

[12] Tanaka H., Monahan K. D., Seals D. R., "Age-Predicted Maximal Heart Rate Revisited", Journal of the American College of Cardiology (2001) Vol. 37, No. 1.

[13] Nishime E. O., Cole C. R., Blackstone E. H., Pashkow F. J., Lauer M. S., "Heart Rate Recovery and Treadmill Exercise Score as Predictors of Mortality in Patients Referred for Exercise ECG", JAMA. (2000)284:1392-1398.