

Celebrating 50 years  
of Independence of  
Bangladesh

**SPECIAL ISSUE  
PUBLICATION**

# Special Issue

## Section - III

**Research on  
Neuro and  
Rehabilitation  
Science Topics**

## Commemorating 50<sup>th</sup> year of Independence of Bangladesh - Scholarly Research Investigations

With utmost respect from the core of our hearts, we intend to commemorate the 50th year of Independence of the Great Nation of the People's Republic of Bangladesh by acknowledging the ground-breaking research calibre of the Bangladeshi Research Scientists and Scholars, who kept on delivering with outstandingly innovative experimentations throughout the world. We conceived this special issue to provide a platform to disseminate outcomes of multidimensional research investigations, which have been conducted mostly in universities and research institutes in Bangladesh and neighbouring nations. These highly skilled research scientists of Bangladesh have employed cutting-edge technologies to investigate the complex and yet unexplored aspects associated with diverse areas of life ranging from medical and health issues, cognitive neuroscience, rehabilitation sciences, issues pertaining to motor control, enhancement in sports performance, motor skill limitations influencing overall development among Specially Able Children and factors associated with management of health risk as well.

In this Special issue in Section I, we have included the meta-analytic systematic review studies. These studies have examined impacts of lifestyle on PCO; effectiveness of proprioceptive training on OA limitations; efficacy of differential coordination training regimes on motor deficiencies; and benefits of VMBR and Biofeedback techniques on the performance of athletic skills. Here, the noteworthy fact is that all those meta-analytic investigations have been conducted including almost every of the previously carried out valid and authentic RCTs following rigorous methodology.

Health Science topics in Section - II have encompassed extensive research on exclusively vital current issues associated with the awareness and behavioural manifestations pertaining to the outbreak of COVID19 from a Bangladeshi perspective. Further to that, studies on the impacts of exercise interventions in enhancing health status as well as cognitive functions as the precursor for effective management of Type 2 DM among Bangladeshi individuals and cost-effectiveness of those interventions, are breakthrough investigations that are already universally acknowledged as apex research outcomes. Section III, however, has included studies on cognitive neuroscience aspects associated with neural processing of auditory attention characteristics in dyslexic children, and visual attention and language processing investigated among pregnant women. These studies have been carried out incorporating sophisticated gazettes for the assessment of topographic cortical activation based on ERP and fMRI evaluations. In this section experiments on the rehabilitation sciences are also disseminated. While one case study has reported on the utilization of unique techniques for prosthetic rehabilitation, the other study has been conducted introducing EMG biofeedback and modified isokinetic intervention techniques following rigorous methodology to minimize feelings of pain and perceived stiffness among elderly osteoarthritic patients. Finally, Section - IV has been considered to include investigations on the effectiveness of VMBR and Biofeedback intervention techniques on athletic performance excellence; the impact of motor skill training on complex reaction ability in young-adult individuals having partial dyspraxia. Apart from all those, this section has also included outcomes of an extensive study on Specially Able Children, in which facilitative impact of young athlete (motor skill-oriented) training on tandem walking ability has been thoroughly investigated.

We have critically reviewed (double-blind review) and evaluated all the manuscripts submitted for publication in this issue. The final reviewer has adequately ensured that as per the suggestions of the reviewers, original research submissions have been optimally modified. Thereafter, all the Section Guest-editors of this issue, upholding the core academic and research integrity, have endeavoured to leave no stone unturned to warrant the quality and validity of the research documents accepted for publication. In every section content of the articles are linked with the cited references, which may provide optimal opportunity to the learned researchers. Apart from that, we have also provided back-and-forth links of cited documents, so that the readers can easily check the citations in the list of references and can promptly go back to the area of discussion.

We can vouchsafe that we have aspired only to invigorate the academic and research milieu of Bangladesh. This country on the brink of achieving hard-earned independence was proclaimed as the “bottomless basket”. I am sure I am not the only one who strives hard to showcase the development of the Nation of Bangladesh, the country having full of enthusiasm. Here I am being the Lead Guest-Editor would like to acknowledge the dedication of all the Guest-Editors and Reviewers for their sincere contributions. I would most sincerely like to thank all of them, who relentlessly took care of their responsibilities to ensure the validity of the research articles and the high academic standard of this issue.

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## ***SECTION III – Research on Neuro and Rehabilitation Science Topics***

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Manuscript No.	Title	Authors	Page no.
<a href="#"><u>MS-BD50-Res-Exp. Neuro-Rehab Sc-1</u></a>	AUDITORY ATTENTION AMONG CHILDREN WITH DYSLEXIA: TOPOGRAPHIC MAPPING AND BRAIN FUNCTIONAL CONNECTIVITY ANALYSIS USING P300 COMPONENT	Siti Atiyah Ali, Tahamina Begum, Faruque Reza, Nor Asyikin Fadzil, Faiz Mustafar	1 - 5
<a href="#"><u>MS-BD50-Res-Exp. Neuro-Rehab Sc-2</u></a>	MULTIFACTORIAL CONTRIBUTION OF STIFFNESS AND BODYWEIGHT ON FEELINGS OF PAIN AMONG KNEE OSTEOARTHRITIC PATIENTS	Soumendra Saha, Srilekha Saha, Amran Bin Shokri, Faria Sultana, Maruf Ahmed, Naresh Bhaskar Raj	6 - 12
<a href="#"><u>MS-BD50-Res-Exp. Neuro-Rehab Sc-3</u></a>	VISUAL SENSORY PROCESSING AND ATTENTION DURING VISUAL ODDBALL TASK IN PREGNANT WOMEN: N100 ERP COMPONENT ANALYSIS AND TOPOGRAPHIC MAP DISTRIBUTION	Devi Ananth, Tahamina Begum, Faruque Reza	13 - 16
<a href="#"><u>MS-BD50-Res-Exp. Neuro-Rehab Sc-4</u></a>	SYNTACTIC MALAY LANGUAGE PROCESSING IN PREGNANT WOMEN: ANALYSIS OF THE N400 COMPONENT	Nurul Nazihah Zaidil, Tahamina Begum, Faruque Reza, Jong Hui Ying, Rozaida Abdul Rauf	17 - 22
<a href="#"><u>MS-BD50-Res-Exp. Neuro-Rehab Sc-5</u></a>	PROSTHETIC REHABILITATION OF AN OCULAR DEFECT – A CASE REPORT	Md Minhaz Ul Islam Nizami, Ahmed Mushfiqur Rahman, Nafij Bin Jamayet, Zuryati Ab-Ghani, Adam Husein	23 - 25
<b>Process of Acceptance for SECTION III articles (Articles on Neuro and Rehabilitation Science)</b> <a href="#"><u>Information on Reviewers and Section Guest Editors</u></a>			



## AUDITORY ATTENTION AMONG CHILDREN WITH DYSLEXIA: TOPOGRAPHIC MAPPING AND BRAIN FUNCTIONAL CONNECTIVITY ANALYSIS USING P300 COMPONENT

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dyslexia; EEG coherence; ERP; mismatch negativity (MMN); P300; topography.

### ABSTRACT

**Background:** Learning disabilities are very much related to attention. Attention domain is one of the major constituents of the cognitive processing. The dyslexic children sometimes undergo with auditory attention deficits, which leads to difficulties in reading, spelling, and writing.

**Aim:** Due to a wide gap in the auditory cognitive processing among dyslexia, we investigated auditory cognitive function (attention), topographic mapping, and brain functional connectivity analysis in children with dyslexia using the Event-Related Potential (ERP) technique.

**Method:** Twenty-four Malay children were recruited as dyslexic (n=12) and control (n=12) groups. A 128-electrode ERP sensor net was used with auditory oddball stimuli that required subjects to count mentally the target tones while ignoring the standard tones. Amplitudes and latencies of the P300 component were analysed at 19 electrode channels in a 10-20 system. Mean differences between target and standard stimuli in amplitudes and latencies of the P300 component were collected.

**Results:** P300 amplitudes were significantly higher in the dyslexic group as compared to the control group at C3 and Cz locations. Significantly longer and significantly shorter latencies were found at FP2, Fz, and T3, T5, respectively in the dyslexic group comparing with the control group. Results of topographic scalp distribution revealed that, during target stimuli, the dyslexic group showed P300 distributions to the left parieto-occipital areas and during standard stimuli, the distribution was at left parietal and central areas. Also, more interconnected regions were found in the dyslexic group.

**Conclusion:** Our present results concluded higher attention in dyslexia that proved a compensatory strategy mechanism for unspecified auditory cognitive impairment with a left-lateralized hemispheric scalp distribution.

## 1. INTRODUCTION

The reading process requires complex neural activities in maintaining attention towards sensory stimulations, for instance, while processing the visual orthographic structures and auditory phonemic sound association<sup>1</sup>. Failure in giving attention to stimulations may lead to learning problems as seen in autism, attention-deficit hyperactivity disorder (ADHD), and even dyslexia. Studies have been done in revealing impaired cognitive skills in autism<sup>2</sup>, ADHD, and learning disabilities<sup>3</sup>. Unfortunately, a lack of information exists related to the assessment of cognitive function on the learning difficulty in dyslexia, specifically in the study of auditory cognitive function. In dyslexia, the learning difficulties related to reading, spelling, and writing mainly associated with the auditory phonological deficit have a causal link to the impairment of auditory perception processing<sup>4</sup>. Auditory cognitive function interrelated to sensory system processing is required in the process of phonological processing in learning and language development.

ERP is an electrophysiological method that is used in capturing small, evoked voltages of neuronal activity using any stimulus or event<sup>5</sup>. It is a non-invasive method and safe for all ages. Neuronal activity is highly fast occurring brain activity and signified as a

summation of the joint firing rate of populated neurons. In the current study, we particularly have an interest in the understanding of auditory attention cognitive skills that are suggested to be reflected in ERP parameters of the P300 ERP component<sup>6</sup>. P300 component is usually used to assess attention during the learning task<sup>7</sup>. Decreased amplitudes and delayed latency of N1, P2, and P300 ERP components indicated poor auditory processing onset, diminished auditory perception, and attention, respectively<sup>8</sup>. Reduced P300 amplitudes suggested weak capacity of mental workload<sup>9</sup>. P300 component can be used in clinical diagnosis for certain disorders such as epilepsy<sup>10</sup>, autism spectrum disorder (ASD)<sup>11</sup>, and Alzheimer's Disease<sup>6</sup>, but not for learning difficulties such as dyslexia as many types of research are still progressing and confined to different modalities of studies. No significant difference was found in P300 amplitudes, but significantly different right hemispheric dominance of the P300 component was found in dyslexics suggesting compensatory development on visual stimulations<sup>12</sup>. So far, auditory attention assessment with topographic scalp mapping of evoked potential in dyslexia still lacks in findings. Therefore, scalp mapping distribution might provide additional insights into hemispheric dominance and lateralization in

revealing a possibility of an auditory compensatory mechanism in dyslexia.

The possibility of a compensatory mechanism in dyslexia has been represented by the resting state of quantitative electroencephalography (qEEG)<sup>13</sup>. Significantly higher delta and theta activities were asymmetrically found in dyslexics at left-hemispheric parieto-occipital areas<sup>13</sup>, suggesting immature neuronal electrical activity<sup>14</sup>. No hemispheric dominance but similar gamma neural oscillations were found in both hemispheres in dyslexics suggestive of primary cortical disruption in phonological development<sup>15</sup>. Dyslexia had weaker EEG synchronization in the language region of the left hemisphere, and no significant neuronal connectivity (EEG coherence) was created<sup>16</sup>. Therefore, in the present study, we investigated auditory attention by analysing amplitudes and latencies of the P300 component, neuronal scalp mapping distributions, and EEG coherence during auditory oddball stimuli in children with dyslexia. Therefore, the current study aimed to investigate the auditory cognitive function, the scalp mapping distribution, and functional connectivity using Phase Locking Value (PLV) and EEG coherence in children with dyslexia using Event-Related Potential (ERP) study. The findings of this study may help in revealing the neuronal network processing and functional flaws in dyslexia, assisting in the early detection and intervention for those affected.

## 2. MATERIALS AND METHODS

### 2.1. Study design, Ethics, Study location, and Participants consent

This study is a quantitative, cross-sectional, and non-interventional study that utilized a group of children with dyslexia and normal healthy participants. We gained human ethical approval from the ethical committee of Universiti Sains Malaysia (USM) (USM/JEPeM18030177). The study procedure was mentioned in our previous studies<sup>17,18,19</sup>. To set the agreement for the experiment especially on children with dyslexia, we collected consent from the Ministry of Health Malaysia and the school authorities of both control and children with dyslexia. The ERP study was done in MEG/ERP room at Hospital Universiti Sains Malaysia (HUSM) and both parents and children gave their written informed consent before the experiment was conducted.

### 2.2. Subjects

A total of 24 Malay primary school children ranging from 7 to 11 years were recruited in this study and were equally divided into dyslexics and controls. The sample of dyslexic and control groups was recruited based on the convenience sampling method that screened the potential primary school children before recruitment. The children with dyslexia were screened and recruited based on the medical reports (provided and granted by school authorities) and also based on the scores of *Instrumen Senarai Semak Dyslexia Kementerian Pelajaran Malaysia* (Dyslexia Screening Instrument (DSI) by the Ministry of Education) that was assessed by their school teacher<sup>20</sup>. Meanwhile, for the control group, children were recruited based on the normal scores of DSI, with no major diseases, and having proper age skills in learning, reading, and writing.

All children in both groups had no behavioural issues as was assessed by a psychiatrist. All the recruited dyslexic subjects were clinically diagnosed as dyslexia by paediatrician (based on medical reports) with an undetermined level of severity as the determination of severity is subjective<sup>21</sup> and unclear cut of diagnostic category<sup>22</sup> in the clinical evaluation as no precise instrument could be used to diagnose the severity of dyslexia empirically. This

is because dyslexic individuals may have variations of difficulties, with some having difficulty in word reading, writing, spelling, or word comprehension, which is not practically separated from the diagnosis processes and still not well defined medically. All the recruited children with dyslexia underwent a learning rehabilitation, which they may eventually habituate and adapt to learning strategy, and therefore, severity level is not practically applicable for this cognitive study. Moreover, they did not receive any specific audio-visual training to discriminate the phonetic features of voice.

### 2.3. ERP procedures

An auditory oddball paradigm was used for the ERP experiment. E-Prime v 2.0 software (Psychology Software Tools, Inc, Sharpsburg, Pennsylvania, USA) was used for the presentation of stimuli. All participants sat in a dimly lit room with headphones placed on both ears while wearing a 128-electrode ERP sensor net on their heads. Standard and target tones were presented as a part of the auditory oddball paradigm. Standard tones were 60 dB sound pressure level (SPL), with high-frequency presentations (80%), and low pitched (1KHz) and target tones were 60 dB SPL, with a low frequency of presentations (20%), and high pitch (2KHz). The subjects were asked to count silently the target tones and ignore the standard tones. The duration of tone was 100 ms with a rise/fall time of 10ms. Data was recorded with Net-Station Software (Electrical Geodesic, Inc, Eugene OR USA). The mean values of standard and target tone stimuli were collected for amplitudes and latencies of the P300 ERP component which were analysed further at 19 electrode sites using a 10-20 system.

### 2.4. Data analysis

The raw data was filtered with 0.3 to 50 Hz of the band-pass filter with a 0.5 Hz stimulus rate. The sampling rate was 250 Hz. The impedance of the electrode was ensured to be below 50 KΩ. Segmentation was done from 100 ms before stimulus presentation to 800 ms after stimulus<sup>17,18,19</sup>. Artefacts such as eye movements, eye blinks, and body movements were removed by using artefacts detection tools in Net-station software. The baseline correction was made 100 ms before the stimulus. The values of mean differences of standard and target tone stimuli were collected for amplitudes and latencies of the P300 component. To see significance between groups, we used an independent t-test provided by Statistical Package for the Social Sciences Software (SPSS 24), with the significant level set as  $\leq 0.05$ .

Mapping of topographic distribution was done using a toolbox, EEGLAB, runs with MATLAB environment<sup>23</sup>, and functional connectivity measurement using PLV and EEG Coherence among recorded ERP signals was performed in control and dyslexic groups using MATLAB based HERMES<sup>24</sup> signal synchronization processing toolbox. Statistical configurations were Wilcoxon test, alpha = 0.05, FDR<sub>q</sub> = 0.1, FDR type = 2, max distance = 1.5, and number of clusters and number of permutation being 10 and 100, respectively.

## 3. RESULTS

### 3.1. Demographic information

The mean age (SD) of the control group was 10.75 (1.14) years (n=12) and that of the dyslexic group was 10.83 (1.16) years (n=12). The values of mean differences of standard and target stimuli are shown for the P300 ERP component at 19 electrode sites in a 10-20 EEG system (Table 1).

### 3.2. Results in amplitudes and latencies of the P300 ERP component

Two electrode sites showed a significant difference between the groups. Dyslexic groups evoked significantly higher amplitudes at C3 (4.52 (3.15)  $\mu$ V,  $p=0.045$ ) and Cz (3.26 (3.14)  $\mu$ V,  $p=0.009$ ) compared to the control group (2.07 (3.21)  $\mu$ V and 0.19

(3.00)  $\mu$ V, respectively) (Table 1). Besides, significantly prolonged P300 latencies were observed in the dyslexic group at two locations of FP2 (598.33  $\pm$  87.71 ms) and Fz (625.33  $\pm$  74.23 ms) and significantly shorter P300 latencies were at T3 (465.67  $\pm$  98.64 ms) and T5 (429.00  $\pm$  66.81 ms) areas comparing with the control group (Table 1).

**Table 1: Mean ( $\pm$ SD) differences of standard and target stimuli were displayed for the amplitudes and latencies of the P300 ERP component between control and dyslexic groups.**

Areas	Control group	Dyslexic group	Control group	Dyslexic group	Amplitude $p$ -value: P300	Latency $p$ -value: P300
	Amplitudes of P300 (in $\mu$ V) (mean $\pm$ SD)		Latencies of P300 (in ms) (mean $\pm$ SD)			
Fp1	10.70 $\pm$ 7.41	11.36 $\pm$ 7.64	528.33 $\pm$ 124.53	578.00 $\pm$ 113.94	0.421	0.174
F3	5.92 $\pm$ 4.42	6.57 $\pm$ 4.25	499.67 $\pm$ 127.74	529.67 $\pm$ 120.78	0.368	0.292
F7	6.43 $\pm$ 3.20	8.68 $\pm$ 5.02	514.67 $\pm$ 99.50	518.00 $\pm$ 110.32	0.119	0.471
Fp2	10.37 $\pm$ 7.11	12.15 $\pm$ 6.57	513.33 $\pm$ 104.86	598.33 $\pm$ 87.71	0.278	0.027*
F4	4.96 $\pm$ 4.53	7.31 $\pm$ 5.65	532.67 $\pm$ 116.42	563.33 $\pm$ 121.21	0.153	0.28
F8	6.82 $\pm$ 3.40	6.33 $\pm$ 5.20	502.33 $\pm$ 92.97	483.00 $\pm$ 83.16	0.400	0.309
C3	2.07 $\pm$ 3.21	4.52 $\pm$ 3.15	480.00 $\pm$ 113.61	498.67 $\pm$ 124.79	0.045*	0.362
C4	2.68 $\pm$ 2.90	5.18 $\pm$ 4.17	462.00 $\pm$ 122.68	489.33 $\pm$ 104.93	0.063	0.293
T3	5.64 $\pm$ 3.24	6.86 $\pm$ 6.26	571.67 $\pm$ 102.98	465.67 $\pm$ 98.64	0.292	0.012*
T4	6.69 $\pm$ 3.97	7.70 $\pm$ 4.37	519.33 $\pm$ 103.21	485.33 $\pm$ 78.86	0.294	0.201
P3	3.32 $\pm$ 2.86	3.70 $\pm$ 3.67	527.33 $\pm$ 129.91	479.33 $\pm$ 121.91	0.397	0.195
T5	4.79 $\pm$ 4.31	4.04 $\pm$ 3.74	577.33 $\pm$ 102.55	429.00 $\pm$ 66.81	0.335	0.000***
P4	4.27 $\pm$ 5.90	4.95 $\pm$ 4.42	429.67 $\pm$ 91.05	442.33 $\pm$ 87.52	0.382	0.374
T6	7.98 $\pm$ 10.63	2.83 $\pm$ 7.69	505.00 $\pm$ 115.64	467.33 $\pm$ 83.55	0.106	0.199
O1	6.58 $\pm$ 9.75	4.63 $\pm$ 3.52	543.33 $\pm$ 115.28	471.33 $\pm$ 118.78	0.270	0.086
O2	5.12 $\pm$ 7.43	3.69 $\pm$ 7.43	447.00 $\pm$ 113.44	496.67 $\pm$ 96.62	0.331	0.144
Fz	7.56 $\pm$ 4.59	7.60 $\pm$ 5.79	529.67 $\pm$ 136.89	625.33 $\pm$ 74.23	0.492	0.028*
Cz	0.19 $\pm$ 3.00	3.26 $\pm$ 3.14	434.33 $\pm$ 122.23	520.33 $\pm$ 132.75	0.009*	0.068
Pz	4.04 $\pm$ 7.02	4.33 $\pm$ 6.85	456.00 $\pm$ 127.77	458.33 $\pm$ 107.67	0.462	0.482

\*Note: significant =  $p \leq 0.05$

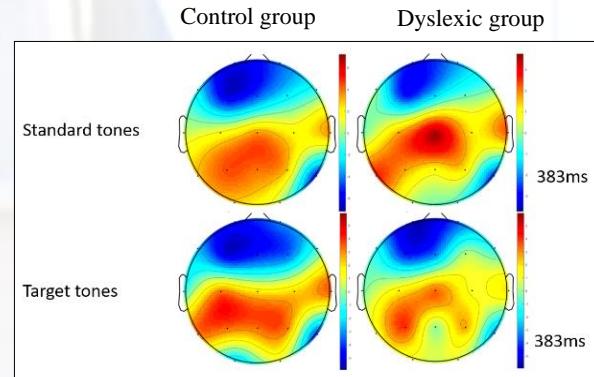
### 3.3. Results of Topographic scalp distribution of P300 component

The topographic scalp mapping distribution for P300 amplitudes is shown in Figure 1. During standard stimuli, P300 distribution in both groups was similar in left parietal, and central areas. However, dyslexics had slightly higher voltage neuronal activity in the central area compared to controls. Target stimuli evoked higher P300 voltage at left parieto-occipital areas in control and low P300 voltage activity at same areas in the dyslexic group (Figure 1).

**Figure 1: P300 topographic scalp distribution was shown between control and dyslexic groups in standard and target stimuli. Note: Red colour indicated positive and blue colour indicated negative voltages.**

### 3.4. Results on functional connectivity of P300 ERP component

Statistical analysis of coherence did not show any significant result from the P300 epoched EEG signals. Topographic visualization of EEG coherence results is depicted in Figure 2a, with no significant inter-dependencies in control and dyslexic

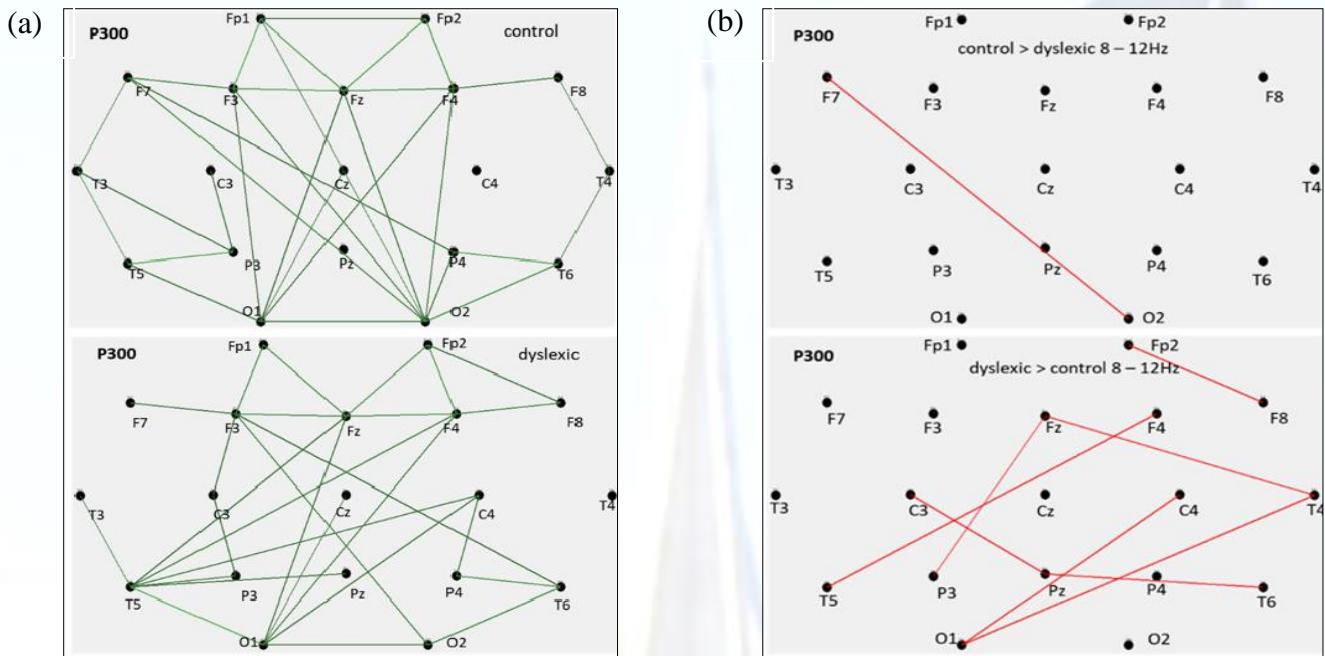


**Figure 1**

groups in the frequency domain (power spectra). Topographic visualization of PLV from the P300 epoched signal at 8-12 Hz frequency band between control and dyslexic groups is shown in Figure 2b. More interconnected EEG nodes were observed in dyslexic as compared to non-dyslexic control groups (Figure 2).

The present study evaluated the auditory attention in children with dyslexia by analysing the amplitudes and latencies of the P300 ERP component using the auditory oddball paradigm. Additionally,

scalp mapping topography and functional connectivity were compared between groups. Significantly higher P300 amplitudes were found at C3 and Cz areas in dyslexics than in the control group.



**Figure 2:** Brain connectivity of P300 ERP component was shown among different electrode positions between control and dyslexic groups. Frequency, threshold, and min distance were 10.7 Hz, 0.4, and 0.5, respectively (Figure 2a). For EEG coherence, phase-locking values (PLV) were shown for the P300 component between the group at 8-12 Hz frequency band (Figure 2b).

Significantly longer (FP2, Fz) and significantly shorter (T3, T5) P300 latencies were found at four areas in the dyslexic group. P300 topographic distribution demonstrated that standard tone elicited the left parietal and central areas for both groups, but dyslexics had higher P300 activation. Left parieto-occipital areas were activated during target stimuli for both groups with comparatively less activation in the dyslexic group. Additionally, more interconnected regions were found in dyslexics.

#### 4.1. P300 ERP component and Topographic scalp mapping

P300 ERP component signifies the ability in concentrating or giving attention to any given task or stimulus<sup>2</sup>. Higher amplitudes and shorter latencies of the P300 component reflect higher attention in cognitive processing<sup>8</sup>. We discovered significantly higher P300 amplitudes at two areas and shorter latencies at two areas in children with dyslexia compared with control children (Table 1) which suggested greater auditory attention in children with dyslexia in contrast with some previous studies involving subjects with learning disabilities<sup>9,12</sup>. A significantly lower P300 component was found in dyslexics during speech oddball stimuli, agreeing with the deficit theory in auditory processing disorder<sup>25</sup>. We assumed that our children with dyslexia had intact explicit pattern learning that required mental task response (counting) to target tones<sup>26</sup>. Another explanation of the contrasting findings, higher attention in dyslexics, can be elucidated by the compensation on deficit sensory processing in dyslexics, by giving extra attention to the target tones. Beidas et al., (2013) suggested that to achieve accurate decoding in the stage of grapheme-phonemic conversion in reading, most of the attentional resources were invested in dyslexics, hence, indicating that attentional demand and investment is higher in dyslexia than the control<sup>27</sup>. The scalp mapping voltage distribution area for P300 amplitudes in standard tones was similar between groups at left parietal, and central areas but higher activity was observed in the case of the dyslexic group (Figure 1). Compared to target tones, P300 amplitudes scalp mapping distributions in dyslexics conferred a little

lower activity at left parieto-occipital areas, while control readers had a higher scalp voltage activity (Figure 1). Based on the scalp mapping distribution in standard tone, structural left hemisphere lateralization of P300 amplitudes in dyslexics was slightly prominent than the control readers indicating that the dyslexics exerted extra attentional effort towards standard tone, justifying the significant trend of higher P300 amplitudes in dyslexics<sup>9,12</sup>. Compensatory factor in the learning process of children was a recent finding discovered by neuroscientists, whereby a study showed the left hemisphere lateralization of the dyslexic brain in response to speech sound<sup>28</sup>.

#### 4.2. EEG coherence

Children with dyslexia did not show any significant EEG coherence compared to control children in the current study (Figure 2), which is consistent with another study<sup>29</sup>. More interconnected phase synchrony was found in children with dyslexia compared to control at 8 to 12 Hz of alpha-band indicating that an increased number of brain regions are engaged to compensate a certain level of attention processing related to the auditory task demand. On the contrary, the non-dyslexic control group allocated a fewer number of brain areas to the equal amount of task demand to maintain the attention level compared to dyslexic<sup>30,31</sup>.

A compensatory mechanism is an alternate neural pathway that bypasses the left hemisphere of the brain that is functionally and structurally essential for reading and language learning, which alters the white matter pathway<sup>32</sup>. Nevertheless, a compensatory mechanism might be changed along with the reading experience, pedagogies or rehabilitation, age development<sup>33</sup>, and even in different task stimuli setting<sup>36</sup>. Due to that, the manifestation of a compensatory mechanism in dyslexics is varying across studies. The lack of study in digging the neural processing in dyslexia has limited our current knowledge on the real causes of why dyslexics were more affected in reading, writing, and spelling, instead of other learning skills. It might happen because of different functional and structural brain regions in children with dyslexia compared to

normal children, and different processing might interfere in the way they perceive and process sensory stimuli, which need to be further investigated using proper neuroimaging and localizing techniques such as fMRI and MEG.

## 5. CONCLUSION

This ERP study of non-speech-related auditory oddball stimuli revealed the auditory attention among children with dyslexia, their scalp mapping distributions, and functional connectivity by EEG coherence and PLV. P300 ERP findings suggest that children with dyslexia showed better auditory attention but by the dint of exploiting several brain areas compared to control as a compensating mechanism. Also, the left lateralization of scalp mapping distribution on the left-brain hemisphere in dyslexics approved our ERP findings. The current findings are essentials in understanding the neural mechanism of dyslexic's brain response towards non-speech auditory stimulations. Hence, these results might help children with dyslexia to have better intervention strategies to improve their quality of life. To elucidate further, the use of speech (e.g. da/ba, true words, and pseudo words) related to auditory ERP studies in dyslexia are required.

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## 7. AUTHORS CONTRIBUTION

**Conceived and designed the experiments:** FR, SAA, TB

**Collected data and performed the experiments:** SAA, TB

**Contributed with materials/analysis tools:** FR, TB

**Analysed the data:** SAA, TB

**Wrote the manuscript:** SAA, TB

**Checked and edited the format:** FR, TB

**Final approval:** SAA, TB, FR, NAF, FM

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## MULTIFACTORIAL CONTRIBUTION OF STIFFNESS AND BODYWEIGHT ON FEELINGS OF PAIN AMONG KNEE OSTEOARTHRITIS PATIENTS

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Pain, Stiffness, Bodyweight, Osteoarthritis, EMG, Isokinetic, Physiotherapy, Biofeedback

### ABSTRACT

**Background:** Osteoarthritis of knee is a common degenerative joint disorder that affects the weight bearing joints. Many types of the intervention have been used in the treatment, while interventions such as isokinetic training, biofeedback has not been extensively used in the rehabilitation.

**Aim:** This experiment intended to investigate relationships between pain, stiffness, and functional disability among the knee OA patients in relation to the differential interventions.

**Method:** The Department of Orthopaedics, Hospital Univ. Sains Malaysia, selected 45 subjects (both male and female, aged between 50 to 63 years) who were diagnosed with OA of the knee of Grade II and III (Kellgren-Lawrence criteria) severity. They were subjected to assessment of proprioception by employing isokinetic device BIODEX 4 System Pro, rectus femoris muscle electrical muscle potentiality (Mega ME 6000 Biomonitor EMG), and gait and force distribution by Qualisys 3D motion analyser and Bertec force distribution analyser, respectively. Apart from that, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) self-report survey was used to assess subjective experiences of pain, stiffness, and physical difficulties associated with OA. Following the baseline evaluation, participants were categorised into three equal sample size groups at random (Viz. Gr. A, Gr. B, and Gr. C). Gr. A participants received training of Conventional Physiotherapy exercises, such as strengthening, stretching, and range of motion exercises. Modified Isokinetic Training at 90° and 150°/second was imparted to Gr. B subjects. Participants in Group C, on the other hand, received Electromyography Biofeedback = EMG-BF intervention training. All of the interventions were carried out following same protocol (25-30 minutes per session; 2 sessions per week for 10 weeks), totalling 20 sessions. Mid-term evaluation was carried out after 5 weeks of training following similar protocol, while after 10 weeks post-intervention analyses were conducted. Further to that, in order to ascertain the question of sustainability, post-follow-up evaluations were carried out in two phases (follow-up 1 and 2 respectively).

**Results:** Sustainable reduction in perceived pain was evident only among participants of EMG-BF group, while for the isokinetic group no such improvement was noticed.

**Conclusions:** Multiple linear regression analyses and structural equation model revealed stiffness, weight and height of the OA participants emerged as significant predictors for the level of pain perceived by the participants.

## 1. INTRODUCTION

Osteoarthritis of knee being one of the most severe degenerative complication, which is aetiologically well-documented as resultant of prolong performance of weight-bearing activities in obese individuals<sup>1</sup>. Even though it has been well propagated by the clinicians, physiotherapists, health professional that middle-aged and elderly individuals should refrain from weight-bearing activities, and even if they are exercise enthusiasts, they should be following alternative or modified forms of exercise schedules<sup>2</sup>, which are not supposed to aggravate osteoarthritic complications<sup>3</sup>, middle-aged and elderly individuals in course of their day-to-day chores usually come across unavoidable situations, wherein they inevitably put awkward pressure on their weight-bearing joints<sup>4</sup>. Since the introduction of isokinetics into modern rehabilitation protocols, researchers and clinicians have faced many difficulties concerning the effects and outcome of such protocols. The issues of protocol structure, such as dose, length or load, are still not settled. Despite these uncertainties, it is clear that the isokinetic

conditioning programs have great advantage over other conditioning and rehabilitation methods<sup>5,6,7</sup>.

In contrast to weight training, maximal torque can be achieved through the whole range of motion when isokinetic training principles are applied, which may explain their larger training effect. A significant decrease in maximum voluntary isometric contraction (MVIC) of the quadriceps muscles in patients with knee OA that can be improved by voluntary muscle activation<sup>8,9</sup>. One of the treatment methods that can be easily used for elderly patients with knee OA is isometric exercise, the application of which has been associated with significant improvement in the MVIC of the quadriceps muscles. The EMGBF device has been intended to turn the action potential of the muscle into visual or aural feedback signals, which can alter the subject's voluntary activity, in order to improve the patient's active participation in treatment with isometric exercises<sup>10,11</sup>. When EMGBF is included in an exercise programme, it has been demonstrated that subject compliance and motivation rise significantly<sup>12</sup>. Physical therapy can help reduce knee osteoarthritis pain, oedema, and stiffness while also improving knee joint function.

Walking, bending, kneeling, squatting, and sitting can all be made simpler. In fact, a 2000 study found that a combination of manual physical therapy and supervised exercise has functional benefits for patients with knee osteoarthritis and may delay or prevent the need for surgery<sup>13</sup>. This study was designed to determine the relationship between pain, stiffness, physical characteristics, and functional limitation related to the interventional training viz. isokinetic training, EMG-BF and conventional physiotherapy.

## 2. METHODOLOGY

This study was conducted with intention to investigate the impacts of isokinetic training and electromyography biofeedback intervention training, besides introduction of conventional physiotherapeutic intervention in reduction of pain perceived by the participants suffering from osteoarthritis (OA) of knee. 45 participants (both male and female) in the age range of 50-63 years, diagnosed as suffering from OA of knee of Grade II & III (Kellgren-Lawrence criteria) level of severity were recruited from the Department of Orthopedics, Hospital Universiti Sains Malaysia. All of them were subjected to pre-intervention assessment at the laboratory of Exercise and Sports science program and the laboratory of School of Medical Sciences, Universiti Sains Malaysia. Extent of proprioception was assessed employing the isokinetic device BIODEX 4 System Pro, and specific electrical muscle potentiality, maximum voluntary contraction and fatigability was evaluated incorporating the Mega ME 6000 Biomonitor EMG evaluation system. Further to that, Qualisys 3D motion analyser and Bertec force distribution analyser was used to analyse gait and force distribution across the knee joint, respectively. Besides all those aforementioned objective evaluations, subjective feelings of pain, stiffness, and physical dysfunction were also assessed by employing the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) self-report inventory. WOMAC osteoarthritis index was used to record and analyse the subjective feelings (subjective self-report scores)<sup>14</sup> on perceived

pain, stiffness, and difficulty in performing day-to-day activities, which are commonly associated with osteoarthritis of knee joint. WOMAC Osteoarthritis index relies on the participant's feeling about their health status with osteoarthritis. WOMAC Osteoarthritis index is a reliable tool<sup>15</sup>.

After the baseline assessment, participants were randomly categorized into three equal sample size groups (Viz. Gr. A, Gr. B, and Gr. C), each group consisting of 15 participants. Gr. A participants were subjected to training of Conventional Physiotherapy exercises consisting of strengthening exercises, stretching exercises and range of motion exercises. Gr. B participants received Modified Isokinetic Training at velocities of 90° and 150°/second. Gr. C participants, on the other hand were exposed to training of Electromyography Biofeedback intervention. All the interventions were carried out following similar protocols (viz., 25 - 30 minutes/session; 2 sessions/week for 10 weeks), which altogether accounted for 20 sessions. Detailed information on the intervention techniques, protocols, frequency, and duration of differential exercise regimes are available in the following links. Conventional physiotherapy intervention protocol, for instance is available at: <http://dx.doi.org/10.13140/RG.2.2.21874.43205>. Similarly, the protocols for Modified Isokinetic Training (please see the details at: <http://dx.doi.org/10.13140/RG.2.2.31206.75840>) and for the protocols for the EMG Biofeedback intervention techniques, are available at: (<http://dx.doi.org/10.13140/RG.2.2.18165.09448>). Following these intervention regimes, intervention sessions were being conducted, and after 5 weeks of intervention, following the baseline assessment protocol, mid-term assessment was conducted, and followed by that post intervention assessment was carried out after the accomplishment of 10<sup>th</sup> week of intervention. After the completion of intervention sessions, participants were instructed not to attend the training sessions, and not to get engaged in any sort of physical training, exercise, or sport programme for the next 8 weeks. Thereafter post-follow-up assessments on all of the variables were conducted to investigate the issue of sustainability, which was verified by the post-follow-up assessments 1 and 2 following identical assessment protocols after completion of 14<sup>th</sup> and 18<sup>th</sup> week.

## 3. RESULT

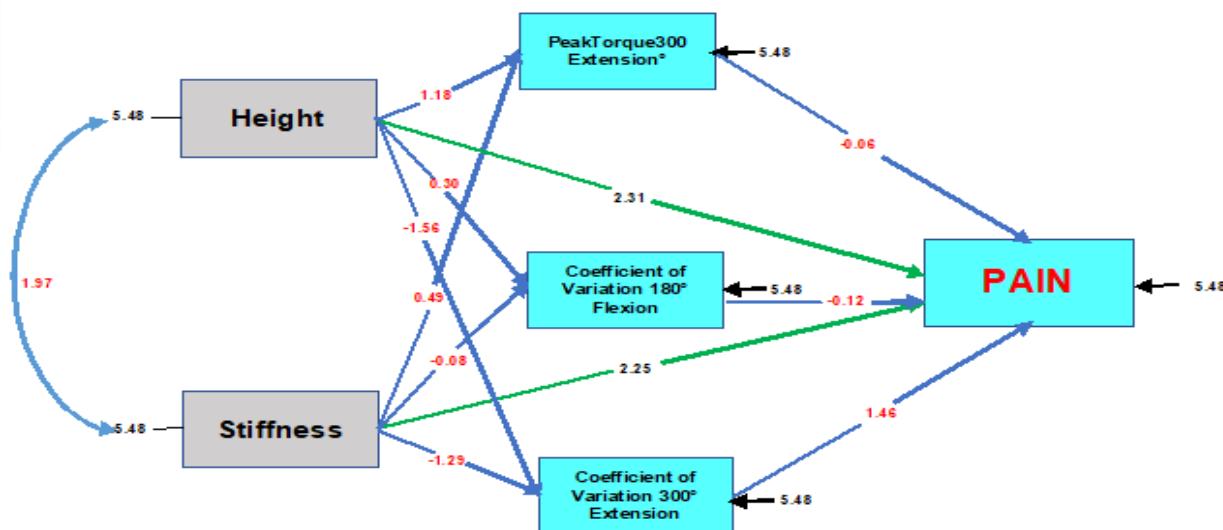
**Table 1 - Descriptive Statistics on WOMAC Scores Across the Different Interventions and Five Measurements**

Groups	Number of Measurements	Pain		Stiffness		Difficulty	
		Mean	SD	Mean	SD	Mean	SD
Conventional Physiotherapy Intervention	Pre-intervention	6.47	2.33	2.79	1.53	22.86	11.62
	Mid-intervention	3.73	1.58	1.43	1.28	15.07	12.41
	Post-intervention	2.27	1.28	1.00	1.36	12.57	11.92
	Post-Follow-up 1	1.47	1.13	1.36	1.60	11.86	10.07
	Post-Follow-up 2	0.80	0.86	0.86	0.95	9.93	7.24
Isokinetic Training Intervention	Pre-intervention	6.31	3.14	3.13	1.19	20.00	7.81
	Mid-intervention	4.81	3.73	2.27	0.80	13.47	7.19
	Post-intervention	4.25	2.74	1.20	1.01	9.87	7.79
	Post-Follow-up 1	3.44	2.53	0.67	0.82	5.87	4.67
	Post-Follow-up 2	2.81	2.81	0.60	0.63	3.73	3.71
EMG Biofeedback Intervention	Pre-intervention	5.71	3.34	2.38	1.02	20.63	10.20
	Mid-intervention	2.86	3.03	2.63	1.50	15.63	11.24
	Post-intervention	1.43	1.40	1.88	1.15	15.25	10.40
	Post-Follow-up 1	1.79	2.42	0.88	0.81	11.13	10.14
	Post-Follow-up 2	1.07	0.83	1.06	1.24	9.75	9.43

Table 1 represented outcomes of descriptive statistics on WOMAC subjective self-report analysis scores. Since, the basic assumptions of statistical analysis (normality data and homogeneity variance), were completed prior to the primary analysis, normality of data was established using Kolmogorov-Smirnov test and Shapiro-Wilk test. The Kolmogorov-Smirnov test and Shapiro-Wilk test was used to evaluate whether the probability distribution differs from a hypothesized distribution. As per the results obtained from the Kolmogorov-Smirnov Test

and Shapiro-Wilk test, satisfactory level of normality of data in the selected parameters was reported. Under the purview of this experiment although pairwise comparison on stiffness and difficulty parameters were not analysed, overall phase wise data evident amongst different groups, however, clarified that outcomes indicated reduction in both levels of stiffness and difficulty perceived by the participants. As no baseline differences were not evident, these modifications could be attributed to the intervention techniques, which were introduced to the participants.

Structural Equation Model explaining interrelationships between physical characteristics of OA participants and muscle strength factors aggravating feelings of pain



Chi - Square = 4.82, df = 3, P-value = 0.42030, RMSEA = 0.000

This SEM was conceived to explain interrelationships between differential dispositional and existing features of all of the participants, who were suffering from OA of knee, and their functional limitations on their pre-intervention level of perceived pain. Outcomes of this SEM are presented herewith (Chi-Square = 4.82, df = 3, P-value = 0.42030; Chi Square/df = 4.82/3.00 = 1.606; RMSEA: 0.000; Standardized RMR: 0.0465; Non-Normed Fit Index (NNFI): 1.289; Comparative Fit Index (CFI): 1.000; Root Mean Square Residual (RMR): 0.0465; Incremental Fit Index (IFI): 1.012; Goodness of Fit Index (GFI): 0.984) which, however, revealed validity of this SEM.

Based on the outcomes it could be interpreted that besides the additive or intervening effects of other force-motion (isokinetic) parameters, height of the participants and pre-existing level of perceived stiffness, strongly contributed behind the pain perceived by the participants. Precisely this SEM confirmed that, even if the participants had differential extents of force-motion abilities, their height, and the level of stiffness in knee perceived at the pre-intervention condition, determined the extent of pain perceived by these knee OA participants. Thus, the SEM implied that, irrespective of additive and mediating effects of force-motion abilities, taller individuals who perceived higher level of stiffness felt higher extent of pain.

### Outcomes of linear, multiple linear and non-linear regression equations

Table - 2 - Table of Multiple Linear Regression Analysis for explanation on Pre-Intervention level Perceived Pain (Conceived for all of the OA participants)

Model a: Dep. Variable: Perceived Pain at Pre-intervention phase	Unstandardized Coefficients			Standardized Coefficients		Correlations			Collinearity Statistics	
	B	Std. Error	Beta	t	Sig.	Zero-order	Partial	Part	Tolerance	VIF
(Constant)	-1.501E-15	.123		.000	1.000					
Height of Participants	.253	.125	.253	2.027	.047	.231	.259	.252	.992	1.008
Perceived Stiffness at Pre-intervention phase	.256	.125	.256	2.053	.045	.234	.262	.255	.992	1.008

<sup>a</sup>(F (2,41) = 3.828, p < 0.028) Model Adj. R<sup>2</sup> = 8.7%.

Outcome of the multiple linear regression analysis in this table revealed that, independent predictors such as height of the participants ( $p = .047$ ) and perceived stiffness at pre-intervention phase ( $p = .045$ ) were evident as predicting 8.7% of variance in changes in the levels of perceived pain at the pre-intervention observed among the OA of knee participants (refer to model *a*).

Findings from this **Table 2** implied a unique relationship as the direct contribution of perceived stiffness at pre-intervention phase on the pre-intervention level of perceived pain, clarified that among the OA participants those who perceived higher extent of stiffness in their knees, reportedly perceived higher extent of pain. This direct relationship further explained that independent of and excluding the effect of all other predictor variables, higher extent of perceived stiffness had direct influence on the increase in perceived pain. Higher tolerance index observed in collinearity statistics suggested that, very high extent of (99.2%) variance in stiffness perceived by the participants was not predicted by height of the participants.

This model further explained that every 1% increment in the stiffness perceived by the OA participants would lead to .256% increase in pain (refer to Beta Coefficient of height, having 99.2% of tolerance). Further to that, positive influence of height of the OA participants on their perceived pain was observed, which implied that those who were relatively taller individuals, they perceived higher extent of pain. This observed direct influence of height of the OA participants, independent of and excluding the effect of all other predictor variables, contributed directly on the increase in perceived pain. Thus, findings from this **Table 2** implied that among the OA participants those who perceived higher extent of pain, and were relatively taller individuals, they perceived higher extent of pain. This direct influence of both the pre-existing level of stiffness perceived and height of the OA participants on increased pain evident among the entire OA participant, however, prompted this researchers to consider group-wise evaluation of interrelationships between pain and other relevant factors, which might aggravate pain.

Table - 3 - Table of Multiple Linear Regression Analysis for explanation on Pre-Intervention level Perceived Pain  
(Conceived for the Conventional Physiotherapy group participants)

Model b: Dep. Variable: Perceived Pain at Pre-intervention phase	Unstandardized Coefficients		Standardized Coefficients		t	Sig.	Correlations			Collinearity Statistics	
	B	Std. Error	Beta	Zero-order			Partial	Part	Tolerance	VIF	
(Constant)	.086	.262		.327	.750						
Quadratic conversion of Weight	-.326	.123	-.577	-2.644	.023	-.409	-.623	-.555	.925	1.082	
Perceived Stiffness at Pre-intervention phase	.573	.204	.613	2.808	.017	.455	.646	.590	.925	1.082	

<sup>b</sup>(F (2,11) = 5.839, p < 0.019) Model Adj. R<sup>2</sup> = 42.7%.

Outcomes of this regression analysis model (refer to the model **b**) in this table revealed both linear and non-linear relationships. Model **b** explained that the independent predictors such as the perceived stiffness at pre-intervention phase (p = .017) and the quadratic conversion of weight of the participants (p = .023) were evident as predicting about 42.7% of variance in changes in the levels of perceived pain at the pre-intervention observed among the OA of knee participants, who served as the participants of control condition (refer to model **b**).

Findings from this **Table 3** implied a unique relationship as the stiffness perceived at pre-intervention phase had direct and exclusive contribution on the pain perceived by the OA participants. Perceived stiffness had strongest contribution on the pain, which one independent of and excluding the effect of all other predictor variables, had unique and exclusively direct contribution on the increase in perceived pain. Higher tolerance index observed in collinearity statistics suggested that, very high

extent of (92.5%) variance in stiffness perceived by the participants during pre-intervention phase, was not predicted by weight of the participants. This model explained that every 1% increment in stiffness perceived by the OA participants would lead to .613% increase in pain (refer to Beta Coefficient of perceived stiffness, having 92.5% of tolerance). This model also revealed negative association between the quadratic (non-linear) conversion of weight of participants and the perceived pain. Here an inhibitive bi-dimensional relationship was evident, which clarified that among the OA participants those who had relatively higher as well as lower body weight, perceived lower extent of pain as compared to their counterparts who had moderate level of body weight. Model **b** finally explained that those who perceived higher extent of stiffness, and had moderate body weight, actually suffered with higher extent of pain, but others, those who had either lower or heavier body weight, accompanied by lower stiffness, they would perceive lower extent of pain.

Table - 4 - Table of Multiple Linear Regression Analysis for explanation on Pre-Intervention level Perceived Pain  
(Conceived for the Isokinetic intervention group participants)

Model c: DV: Perceived Pain at Pre-intervention phase	Unstandardized Coefficients		Standardized Coefficients		t	Sig.	Correlations			Collinearity Statistics	
	B	Std. Error	Beta	Zero-order			Partial	Part	Tolerance	VIF	
(Constant)	.119	.184		.647	.529						
Perceived Stiffness at Pre-intervention phase	-.454	.195	-.541	-2.322	.037	-.541	-.541	-.541	1.000	1.000	

<sup>c</sup>(F (1,13) = 5.393, p < 0.037) Model Adj. R<sup>2</sup> = 23.9%.

Outcome of this linear regression model in this table revealed that the independent predictor, perceived stiffness at pre-intervention phase (p = .037) was evident as predicting 23.9% of variance in changes in the levels of perceived pain at the pre-intervention observed among the OA of knee participants, who were eventually assigned in the modified isokinetic training intervention training (refer to model **c**).

Findings from this **Table 4** implied that among the OA participants those who were evident to perceive lesser extent of stiffness in their knees, reportedly perceived higher extent of pain.

This observed indirect influence of perceived stiffness of the OA participants, had inhibitive contribution on the increase in perceived pain. Higher tolerance index observed in collinearity statistics suggested that absolute extent of (100%) variance in perceived stiffness of the participants contributed to changes in perceived pain. Model **c** further explained that every 1% reduction in the perceived stiffness of the OA participants would lead to .541% increase in pain (refer to Beta Coefficient of height, having 100% of tolerance).

Table - 5 - Table of Multiple Linear Regression Analysis for explanation on Pre-Intervention level Perceived Pain  
(Conceived for the EMG BF intervention group participants)

Model d: Dep. Variable: Perceived Pain at Pre-intervention phase	Unstandardized Coefficients		Standardized Coefficients		t	Sig.	Correlations			Collinearity Statistics	
	B	Std. Error	Beta	Zero-order			Partial	Part	Tolerance	VIF	
(Constant)	.071	.274		.259	.800						
Quadratic conversion of Weight	.373	.155	.555	2.407	.032	.228	.555	.493	.790	1.266	
Perceived Stiffness at Pre-intervention phase	.933	.302	.713	3.094	.009	.459	.651	.634	.790	1.266	

<sup>d</sup>(F (2,13) = 5.407, p < 0.020) Model Adj. R<sup>2</sup> = 37%.

Outcomes of this regression analysis model (refer to the model **d**) in this table revealed both linear and non-linear relationships. Model **d** explained that the independent predictors such as the perceived stiffness at pre-intervention phase (p = .009) and quadratic conversion of weight of the participants (p = .032)

were evident as predicting about 37% of variance in changes in the levels of perceived pain at the pre-intervention observed among the OA of knee participants, who were subjected to EMG Biofeedback intervention training (refer to model **d**).

Findings from this **Table 5** implied a unique relationship as the direct contribution of perceived stiffness at pre-intervention phase on the pre-intervention level of perceived pain, clarified that among the OA participants those who perceived higher extent of stiffness in their knees, reportedly perceived higher extent of pain. This direct relationship further explained that independent of and excluding the effect of all other predictor variables, higher extent of perceived stiffness had direct influence on the increase in perceived pain. Higher tolerance index observed in collinearity statistics suggested that, very high extent of (79%) variance in stiffness perceived by the participants was not predicted by weight of the participants. This model further explained that every 1% increment in the

stiffness perceived by the OA participants would lead to .713% increase in pain (refer to Beta Coefficient of height, having 79% of tolerance).

Further to that, non-linear positive influence of weight of the OA participants on their perceived pain was observed, which depicted a bi-dimensional relationship that clarified those who had both lower and heavier body weight, if they perceived higher extent of stiffness, would perceive higher extent of pain, while those who had moderate level of body weight, accompanied by lower stiffness, would perceive lower extent of pain. Model **c** mainly explained the unique and exclusive direct contribution of perceived stiffness, which predominantly determined the extent of perceived pain in the participants.

Table - 6 - Table of Pairwise Comparisons for Pain (WOMAC) Score Between Groups

Measurement Sessions	Groups	Mean Difference	SE	P Value	95% Confidence Interval	
					Lower Bound	Upper Bound
Pre-intervention Phase	Conventional physiotherapy	-0.25	0.38	0.51	-1.00	0.50
	Isokinetic Training	0.53	0.37	0.16	0.21	1.28
	Conventional physiotherapy	0.28	0.36	0.44	0.45	1.01
	Isokinetic Training	EMG Biofeedback	0.35	0.34	0.31	0.33
Mid-intervention Phase	Conventional physiotherapy	-0.28	0.35	0.42	-0.99	0.42
	Isokinetic Training	0.63	0.35	0.07	0.06	1.33
	Conventional physiotherapy	0.35	0.34	0.31	0.33	1.03
	Isokinetic Training	EMG Biofeedback	0.35	0.32	0.30	-0.97
Post-intervention Phase	Conventional physiotherapy	-0.33	0.32	0.30	0.50	0.30
	Isokinetic Training	1.12*	0.31	0.00	0.18	1.74
	Conventional physiotherapy	0.79*	0.31	0.01	0.05	1.40
	Isokinetic Training	EMG Biofeedback	0.14	0.34	0.68	-0.55
Post-Follow-up Phase 1	Conventional physiotherapy	0.73*	0.34	0.04	0.20	1.41
	Isokinetic Training	0.87*	0.33	0.01	0.20	1.54
	Conventional physiotherapy	0.14	0.33	0.69	-0.53	0.81
	Isokinetic Training	EMG Biofeedback	0.87*	0.33	0.01	0.21
Post-Follow-up Phase 2	Conventional physiotherapy	1.01*	0.32	0.00	0.36	1.66
	Isokinetic Training	EMG Biofeedback	0.35	0.32	0.30	-0.97

Table 6 represented pairwise comparison outcomes, which revealed that during the post intervention phase of assessment participants in the EMG Biofeedback group had significantly less pain scores in comparison with that of the participants in the Conventional Physiotherapy group and Isokinetic Training

group. In the follow up phase assessment, both during the first follow-up assessment, and during the final follow-up assessment phase, participants in the EMG Biofeedback had significant improvement in the pain scores compared to that of both the Conventional Physiotherapy and Isokinetic Training group.

## 4. DISCUSSION

Findings of the two-way repeated measure of ANCOVA revealed that, at the post-intervention phase of assessment, compared to both the Modified Isokinetic Training and conventional physiotherapy intervention, EMG Biofeedback intervention was better effective in reducing perceived pain in OA participants. As these trend of improvement continued both in post-follow-up 1 & 2 periods of assessments, sustainably better improvement following EMG biofeedback intervention could be confirmed. Improvement in the activity of muscle spindle, golgi tendon organ, maximal voluntary isometric contraction and thereby causing enhancement in knee joint functionality, strength of the muscle, gait and functional activities in participants suffering from osteoarthritis of knee, were hypothesized as the key factors, which perhaps facilitated reduction of pain perceived amongst the OA participants.

Outcomes of this experiment prompted us to hypothesize on the path of independent predictors, which either had direct or mediated contributions on aggravated pain perceived by the OA participants. The SEM outcome, however, clarified that only height and pre-existing level of stiffness had direct impact on increased pain. Apart from that, some additive influences were also apparent, although those did not have any significant impact on perceived pain. As taller individuals had higher peak torque in extensor muscles, which evidently did not have any legitimate effect on pain. The factor of coefficient of variation of extensor muscles, on the contrary got inhibitive impacts, which depicted that

taller individuals, who had higher stiffness, had lower level of coefficient of variation, which in turn had direct influence on pain. This influence of coefficient of variation of extensor muscles, although insignificant, implied that lower extent of coefficient of variation may have additive impact on aggravated pain. Thus, the multifactorial outcomes evident in the SEM gave rise to the question that, dispositional characteristics (viz., height & weight; muscle-strength etc.) of the OA participants were possibly diverse in nature, and hence, group-wise evaluation of those pre-disposing factors, might emphasize on newer extrapolative and causal relationships of dispositional and functional factors behind perceived pain evident among the OA participants.

### 4.1 Discussion on outcomes from regression analyses

Here, we would like to discuss on the outcomes of multiple linear and non-linear regression analyses, which were carried out to detect in-depth predictive relationship between the aforementioned factors and perceived pain, evident among the OA participants. These analyses were conceived on the whole group and in separate intervention groups as well. Table 2 represented (Model **a**) outcomes of regression on total sample, which suggested those who were evident as having higher extent of pre-existing stiffness, and those who were taller individuals, evidently perceived higher extent of pain. Thus, this report substantiated the outcome of the SEM, and provided with more details on extent of unique and relative contribution of the independent predictors. Outcomes of regression analyses on three different groups separately, however, documented interesting features associated with predictive influence on the pain perceived by the OA participants.

Up on inclusion of relevant predictor independent variables, as it was done in case of the whole sample, Table - 3 was conceived considering participants of control condition. The model **b** revealed stiffness as main contributing factor for pain, and along with that interestingly weight of the participants arose as significant determinant of perceived pain. Perceived stiffness had strongest contribution on the pain. Here, height of individuals did not emerge as significance predictor, and instead weight was evident to have a non-linear (second-order or quadratic) negative relationship with pain. The model **b** explained that those who perceived higher extent of stiffness, if they had moderate level of body weight, would perceive higher extent of pain. But others, those who had either lower or heavier body weight, accompanied by lower stiffness; they would perceive lower extent of pain. Next model (model **c**, refer to Table 4) was conceived for the participants of EMG biofeedback intervention condition. The model **c** revealed stiffness as the only contributing factor explaining increase in pain. The model **d** (refer to Table 5) on the other hand explained that multiple factors, such as stiffness and quadratic version of weight were associated with pain. Here the model clarified that, those who perceived higher extent of stiffness, if they had either lower or heavier body weight, would perceive higher extent of pain. But others, those who had moderate level of body weight, accompanied by lower stiffness, they would perceive lower extent of pain.

These pre-existing status of the OA participants triggered us to pay attention to the level of stiffness in general. Although no analysis of variance was not performed, overall, the descriptive information provided us with an impression that, with the advent of the different forms of training introduced in the present study, level of stiffness in participants of all of the intervention groups got reduced. When group wise scenario were paid attention, during the mid-term phase of assessment participants of the Conventional Physiotherapy group were evident as perceived more stiffness than that of their counterparts in the other intervention groups. In the post intervention phase of assessment, trainees of the EMG Biofeedback group were observed to perceive less stiffness compared to that of the participants in the Conventional Physiotherapy group.

Here it could be assumed that performance of exercise in any form is beneficial for the participants with Knee OA especially, in reducing the perceived stiffness of the knee joint. It could be postulated that exercises improves the movement of the synovial fluid, lubricates the cartilage effectively and lengthens the muscle which could be the reason for the decreased level of stiffness among the participants with osteoarthritis of knee.

#### 4.2 Discussion on level of pain

Post-intervention findings evidenced beneficial impacts of the intervention techniques, and a close scrutiny of the comparison across the groups at the post intervention phase of assessment revealed that, the participants of the EMG Biofeedback group had less perceived pain compared to that of the trainees of the Conventional Physiotherapy group. Follow up phase of assessment confirmed that the participants of the EMG Biofeedback perceived lower level of pain compared to that of the participants in the Conventional Physiotherapy and the Isokinetic Training group. An identical trend was observed in the final follow up phase of assessment too. This observation suggests that the EMG Biofeedback group were able to sustain the effects of training after cessation of the intervention.

These beneficial outcomes of the intervention techniques employed, however, got supported by the findings of Durmus, Alayh and Canturk<sup>16</sup>, although methodological discrepancies were evident. As the present study was carried out following a

protocol of interventions 2 sessions/week for 10 weeks, but the previous one<sup>16</sup> considered a protocol of 5 sessions/week for 4 weeks. The other point of discrepancy pertained to implementation of follow up assessment in the study, as Durmus and co-researchers<sup>16</sup> did not have any follow up assessment done on the participants after the intervention whereas in our study we had two follow up assessment, 4 and 8 weeks after the intervention session.

The EMG Biofeedback protocol of the researcher<sup>16</sup> consisted of one isometric exercise for the quadriceps, whereas in this present study, in addition to that of the static quadriceps exercise, many other types of exercises were introduced. Although duration of the intervention employed in the research by<sup>17</sup> was different from that of the current study, findings of this study are also supported by the work of researchers<sup>17</sup>. Further to the aforementioned inconsistencies, most of the experiments using EMG Biofeedback were introduced to participants who underwent arthroscopic knee surgery or anterior cruciate ligament reconstruction<sup>18,19,20</sup>.

Findings of the present study could be partially attributed to the increase in the strength of the quadriceps and Hamstring muscle, improved co-contraction of the flexor and extensors of the knee and most of the exercises included in the EMG Biofeedback protocol were non weight bearing and isometric exercises which could also be a reason for the reduction in pain among the participants in the EMG Biofeedback.

Finally, we had to dig out by all possible means, the reason behind observed dichotomous contribution of weight (quadratic relationship) evident amongst the control and EMG biofeedback participants in particular. Excess weight is always considered to be a modifiable risk factor for OA<sup>21</sup>. The lowering of body weight has been suggested as a significant part of OA treatment. Weight loss has been suggested as an important part of the treatment for OA. There have been reports of pain and physical handicap being reduced in persons with OA and obesity following a moderate weight loss<sup>22,23</sup>. When comparing women with bilateral knee OA (13 obese, BMI >30kg/m<sup>2</sup>, and 15 with morbid obesity, BMI >40kg/m<sup>2</sup>), it was shown that the women with morbid obesity had a higher BMI. Vasconcelos et al<sup>24</sup>., stated the degree of obesity had no effect on the symptoms of discomfort, stiffness, or functional issues, according to the study (evaluated by WOMAC). In patients with osteoarthritis, excess weight, and adiposity, sometimes known as obesity, had a negative influence, increasing pain perception. According to Fowler-Brown, a 5 kg/m<sup>2</sup> rise in BMI was linked to a 32% increase in the risk of OA, and leptin was responsible for around half of the total effect of obesity on knee OA<sup>25</sup>. The Osteoarthritis Research Society International (OARSI) highly advised overweight people with lower limb OA to lose weight and maintain a lower weight level<sup>26</sup>. As Picavet and colleagues<sup>27</sup> postulated, probably the question of kinesiophobia, or the fear of increasing pain through movement, as well as pain catastrophizing, predict more severe pain and disability in chronic pain patients.

As the regression reports confirmed, in all of the cases either higher or lower (only for the isokinetic group) extent of perceived stiffness emerged as the most significant factor behind increased feelings of pain, while quadratic version of weight emerged as additive factor behind the feeling of pain evident among the participants of both conventional and EMG-BF training groups. Based on the outcomes associated with conventional physiotherapy group, it could be hypothesized that individuals evident with either higher or lower bodyweight, irrespective of their perceived high stiffness, felt lesser extent of pain compared to those who had moderate bodyweight and higher stiffness. Thus, the interesting pre-existing feature of the participants here clarified that neither higher nor lower bodyweight, along with higher stiffness was found associated with higher extent of pain. This pre-existing characteristic feature of OA participants contradict the existing literatures<sup>21-24</sup>. In EMG-BF group, however, both lower and higher bodyweight along with higher stiffness were associated

with high extent of perceived pain. As higher bodyweight has always been considered as detrimental<sup>21-24</sup>, association between lower bodyweight and heightened pain, perhaps hint upon existence of lots of female participants in the EMG-BF group, who had lower bodyweight, but higher extent of stiffness, consequently that led to higher feelings of pain<sup>28-30</sup>. These researchers and quite a few other contemporary research investigators opined on various aetiological explanations on the problems particularly faced by the female individuals suffering from OA, viz., weakness of quadriceps muscle<sup>30,31</sup>, less cartilage volume<sup>32</sup>, greater genetic susceptibility<sup>28</sup> and loss of cartilage due to lower levels of insulin like growth factor I (IGF-I)<sup>29</sup>. Apart from all those factors, metabolic syndromes, such as, High cholesterol levels, diabetes mellitus, coronary vessel disease and ulcerative gastritis were also evident to aggravate problems pertaining to OA of knee<sup>33</sup>.

All of these aforementioned possibilities might have interplayed behind presence of the dichotomous interactions between the weight of the OA participants and the extent of pain perceived by them. We recommend future studies on similar sample, following identical protocols conducting regression evaluations on both pre- and post intervention outcomes, to avail more in-depth information on predictive roles of health and physical crisis indices on the nature and extents of problems perceived by the individuals suffering from OA of knee.

## 5. CONCLUSION

With the intention of reduction in pain perceived by the participants, compared to both modified isokinetic training and conventional physiotherapy, electromyography biofeedback intervention was evident as sustainably better effective technique in reducing pain perceived by the participants. Bodyweight and level of stiffness perceived by the participants had significant impacts on the extent of perceived pain. In rehabilitation of knee osteoarthritis patients, along with the existing therapies EMG biofeedback intervention may be effectively applied. Portable EMG devices are affordable hence, when compared to the benefits, cost factor appear negligible. The study emphasises on the inhibitive impact of heavier bodyweight and significance of regular stretching, strengthening and range of motion exercises, which facilitate reduction in stiffness thereby enhancing the reduction in pain as well.

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## 7. CONTRIBUTION OF AUTHORS

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Collected data and performed the experiments: NaBR SrS, SoS, FoH, MaA  
Contributed with materials/analysis tools: SrS, SoS, AmS  
Analysed the data: NaBR SoS  
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## VISUAL ATTENTION PROCESSING BY N100 ERP COMPONENT ANALYSIS AND TOPOGRAPHIC MAP DISTRIBUTION IN PREGNANT WOMEN

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### KEYWORDS:

Event-related potential, N100, pregnancy, visual oddball, visual sensory processing

### ABSTRACT

**Background:** Pregnancy related changes in bodily mechanism are identifiable using various methods. Several studies were implemented to measure the cognitive functions in pregnant women using event-related potential (ERP) technique.

**Aim:** We therefore investigated the amplitudes and latencies of the N100 ERP component in pregnant women, to assess their visual sensory processing and visual attention. Besides, topographic scalp distribution was assessed to get more detailed information on it.

**Methods:** A 128 ERP net was used to get the amplitudes and latencies of the N100 ERP component. Control and pregnant groups were divided with  $n = 18$  in each group. In the pregnant group, we used 2<sup>nd</sup> and 3<sup>rd</sup>-trimester women together. Normal healthy women were in the control group. For the ERP study, all the participants pressed the button '1' and '2' if they saw 'O' (standard) and 'X' (target) stimuli, respectively.

**Results:** Mean differences in values of standard and target stimuli were collected for amplitudes and latencies of the N100 ERP component. Topographic mapping distribution was done using Net station software based on the grand averaged N100 component waveforms. There was significantly smaller amplitude of the N100 component at C4 and significantly shorter latencies of the N100 component at P3, P4, and T6 areas found in the pregnant group compared to the control group. Topographic scalp distribution showed that the central area was activated for both groups during both stimuli. Additionally, the pregnant group showed more activated areas comparing to the control group during both stimuli.

**Conclusion:** We concluded that pregnant women have higher visual attention and a good speed of visual sensory processing, which might be a positive effect of the pregnancy/placental hormone like human chorionic gonadotropin (hCG), human placental lactogen (HPL), progesterone etc.

## 1. INTRODUCTION

The influence of the pregnancy hormone on attention and memory is variable in pregnant women. Attention can be more<sup>1,2</sup> or less<sup>3,4</sup> during pregnancy. There were limited studies to assess visual attention and sensory processing in pregnant women. Different event-related potential (ERP) components can assess the visual attention and sensory processing of the participants. ERP can record neuronal activity within a few milliseconds using different tasks<sup>5</sup> which are non-invasive and easy to handle<sup>6</sup>. Different ERP components can be expressed in different ways. N100 ERP component is one ERP component, which gives us information about visual sensory processing during visual oddball stimuli, and it is usually 90 to 200 ms<sup>7</sup>. N100 can also change with attention<sup>8</sup>. N100 reflects the negative polarity 'N' and the timing of the component is 100 ms after stimuli and its deflection can be found at most of the recording sites over the scalp<sup>9</sup>. The amplitudes and latencies of N100 are variable depending on visual parameters<sup>10</sup>.

Higher amplitudes of N100 were found when the stimulus was an attention task but when the inter-stimulus interval (ISI) was longer, then amplitudes of N100 decreased<sup>11</sup>. No change in amplitudes of the N100 component was found during simple reaction time tasks<sup>9</sup>. Researchers believe that there is a close relationship between sensory processing and the amplitude of N100. According to previous studies, sensory input increases during attention tasks and vice versa<sup>12,13</sup>. Longer latencies of the N100 component proved longer processing time<sup>14</sup> when the task is complex or difficult as that task needs more active attention<sup>15</sup>. Wu et al., (2014), performed a study on pregnant women using the go/no-go visual association task. Amplitudes and latencies of the N100 ERP component have no significant difference between groups. Topographic scalp mapping also showed the same distribution between groups<sup>16</sup>. Topographic scalp mapping showed the activation area of the ERP component based on more or less attention.

Previous studies used various types of stimuli including faces, names, basic words in ERP study in pregnant women<sup>17,18</sup>. Raz (2014) used a visual oddball task using face and shape in pregnant women<sup>19</sup>. In this present study, we used a simple oddball task where the standards were 'O' and targets were 'X' stimuli in the pregnant women to assess neural activities to unpredictable and recognizable events<sup>20</sup>.

Besides, during stimuli of the visual oddball paradigm, the N100 ERP component is evoked. N100 component is called vertex potential as it is found out at Cz area<sup>7</sup>. The deflection of the visual N100 component is widely distributed at the scalp regions and it peaks mainly over frontal regions<sup>9</sup>, indicated that the N100 ERP component is directly related to the cognitive function, mainly visual attention<sup>21</sup>. There is a lack of studies to assess visual sensory processing and visual attention using N100 ERP component analysis at the same time in pregnant women. Therefore, this study aims to investigate the amplitudes and latencies of the N100 ERP component in ERP study using visual oddball stimuli during pregnancy to assess visual sensory processing and attention for their rehabilitation purpose.

## 2. METHODOLOGY

### 2.1. The ethical statement, Participants, Study location

We received human ethical approval from the ethical committee of Universiti Sains Malaysia (USM) (USM/JEPEM/15090294) before experimenting.

There were two groups: control (healthy) and pregnant groups (n=18 in each group). All the participants were enlisted through noticeboard advertisement, internet, and personal communication with following inclusion and exclusion criteria. Women from both groups were 20-40 years old which is considered as childbearing age<sup>22</sup>, they were not under treatment or medication for any major diseases like heart disease, kidney disease, liver disease, etc. as those conditions might affect cognitive function<sup>23,24,25</sup>. We selected the women who were highly educated for both the group as higher education leads to higher cognitive function<sup>26,27</sup>. Moreover, for the control group, women were not pregnant and it was tested with a pregnancy kit before experiments. We did not take any history of the menstrual phase because in this study we aimed to investigate between pregnant and non-pregnant women. Pregnant women were selected based

### 3.2. Results on the N100 ERP component

Table 1: Amplitudes and latencies of the N100 ERP component for control and pregnant groups:

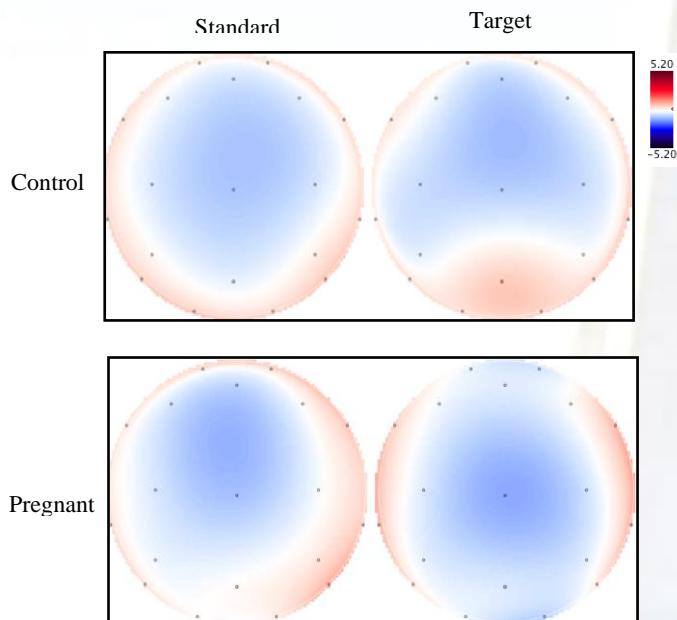
Site	Control (G1)	Pregnant (G2)	Control (G1)	Pregnant (G2)	Amplitude p-value: N100	Latency p-value: N100
Amplitudes of N100 component in $\mu$ V (mean $\pm$ SD)		Latencies of N100 component in ms (mean $\pm$ SD)				
<b>Fp1</b>	5.15 $\pm$ 1.96	5.57 $\pm$ 2.52	109.56 $\pm$ 47.67	107.25 $\pm$ 46.99	0.704	0.972
<b>F3</b>	2.69 $\pm$ 1.47	3.12 $\pm$ 1.45	106.44 $\pm$ 34.69	112.00 $\pm$ 45.16	0.388	0.730
<b>F7</b>	2.82 $\pm$ 1.94	2.85 $\pm$ 1.97	113.11 $\pm$ 40.63	109.00 $\pm$ 49.80	0.730	0.580
<b>Fp2</b>	4.95 $\pm$ 2.12	6.79 $\pm$ 3.41	98.44 $\pm$ 33.81	100.50 $\pm$ 37.80	0.105	0.972
<b>F4</b>	3.88 $\pm$ 1.34	2.95 $\pm$ 1.59	100.44 $\pm$ 36.99	88.25 $\pm$ 26.87	0.062	0.416
<b>F8</b>	2.57 $\pm$ 1.05	3.62 $\pm$ 3.67	115.33 $\pm$ 49.57	107.50 $\pm$ 43.05	0.918	0.653
<b>C3</b>	2.19 $\pm$ 1.25	1.77 $\pm$ 1.30	104.00 $\pm$ 35.03	98.00 $\pm$ 49.06	0.334	0.467
<b>C4</b>	<b>4.25 <math>\pm</math> 2.05</b>	<b>2.58 <math>\pm</math> 1.08</b>	104.00 $\pm$ 41.64	108.50 $\pm$ 32.85	<b>0.002*</b>	0.569
<b>T3</b>	1.76 $\pm$ 1.37	1.97 $\pm$ 1.54	152.89 $\pm$ 51.51	131.50 $\pm$ 51.62	0.704	0.151
<b>T4</b>	2.61 $\pm$ 2.53	3.29 $\pm$ 2.46	158.89 $\pm$ 36.09	140.00 $\pm$ 48.82	0.490	0.522
<b>P3</b>	2.44 $\pm$ 1.79	2.82 $\pm$ 2.39	<b>172.89 <math>\pm</math> 35.58</b>	<b>129.00 <math>\pm</math> 51.30</b>	0.756	<b>0.010*</b>
<b>T5</b>	2.39 $\pm$ 2.23	2.25 $\pm$ 2.37	170.22 $\pm$ 33.16	160.50 $\pm$ 36.28	0.581	0.367
<b>P4</b>	3.20 $\pm$ 2.05	3.15 $\pm$ 1.87	<b>156.67 <math>\pm</math> 27.96</b>	<b>124.25 <math>\pm</math> 46.66</b>	0.972	<b>0.021*</b>
<b>T6</b>	2.39 $\pm$ 2.51	3.01 $\pm$ 2.45	<b>170.89 <math>\pm</math> 9.58</b>	<b>144.00 <math>\pm</math> 41.85</b>	0.214	<b>0.046*</b>
<b>O1</b>	2.17 $\pm$ 1.90	3.05 $\pm$ 3.20	169.78 $\pm$ 31.23	167.00 $\pm$ 22.70	0.730	0.323
<b>O2</b>	3.07 $\pm$ 3.11	3.19 $\pm$ 1.90	166.00 $\pm$ 27.96	158.25 $\pm$ 28.95	0.558	0.185
<b>Fz</b>	4.07 $\pm$ 1.34	4.24 $\pm$ 1.74	93.78 $\pm$ 29.56	93.50 $\pm$ 40.47	0.890	0.716
<b>Cz</b>	3.68 $\pm$ 1.52	4.33 $\pm$ 3.54	110.00 $\pm$ 44.21	104.25 $\pm$ 39.85	0.972	0.917
<b>Pz</b>	4.58 $\pm$ 3.81	5.68 $\pm$ 5.55	157.33 $\pm$ 42.47	135.00 $\pm$ 41.22	0.535	0.053

\* Note: significant = p $\leq$ 0.05

Significantly smaller amplitude was evoked at right central; C4 ( $p=0.002$ ), but non-significant higher amplitudes were found at most of the electrode locations (14 out of 19 locations: Fp1, F3, F7, Fp2, F8, T3, T4, P3, T6, O1, O2, Fz, Cz, and Pz) in the pregnant group than in the control group. Besides, significantly shorter latencies of the N100 ERP component were found in the pregnant group at biparietal; P3 ( $p=0.010$ ), P4 ( $p=0.021$ ) and right posterior temporal; T6 ( $p=0.046$ ) areas, and non-significantly shorter latencies were originated most of the locations (at 13 areas: Fp1, F7, F4, F8, C3, T3, T4, T5, O1, O2, Fz, Cz, and Pz) in the pregnant group compared to the control group (Table 1).

### 3.3. Results on topographic scalp distribution

Topographic scalp distribution showed that the N100 component is distributed over the central areas for both control and pregnant groups while, during target stimuli, N100 distribution was more frontal in the control group and more localized at the central area in the pregnant group. More activation area was found at the central area in the pregnant group during both stimuli comparing with the control group (Figure 1).



**Figure 1:** Topographic scalp distribution of the N100 ERP component was shown between control (upper panel) and pregnant (lower panel) groups during standard and target visual stimuli. The blue color distribution is the reflection of the N100 component. Note that, deeper color indicated more activation areas.

## 4. DISCUSSION

The aim of this study is to assess the amplitudes and latencies of the N100 ERP component in pregnant women to understand their visual sensory processing and visual attention. Pregnant groups evoked significantly smaller amplitude at right central (C4) and significantly shorter latencies at bi-parietal and right posterior temporal (P3, P4, and T6) areas compared to the control group. The more activated area was found in the pregnant group at the central area during both stimuli.

Smaller amplitudes and shorter latencies of the N100 ERP component were studied in different patient groups; however, there was no study yet on the N100 component in the pregnant group. Therefore, we hope this information will be beneficial to assess visual sensory processing and visual attention in pregnant women.

As mentioned earlier, a lower amplitude of the N100 component is found when interstimulus interval (ISI) is longer<sup>11</sup>, which is consistent in this study. In our study, ISI time (1.4 sec) is longer than stimuli time (1sec). Other studies mentioned that the lower amplitude of the N100 component reflects the less sensory input/process due to lack of attention<sup>12,13</sup>. In two ways we can discuss the present results. First, amplitudes and second is the latencies with combining significant and non-significant results. Firstly, the significantly lower amplitude was found at the right central (C4) area only but non-significantly higher amplitudes were found at most of the sites in the pregnant group compared to the control group. Topographic scalp distribution results showed the reflection of the amplitude of the N100 ERP component results as we found a slightly higher activated area in the pregnant group than the control group. Higher activated area and higher amplitudes (non-significant) of the N100 indicated higher attention<sup>8,16</sup>. Therefore, our results on amplitudes of the N100 component indicated higher attention in the pregnant group comparing with the control group. Depending on the experimental paradigms, visual attention was variable in pregnant women. No change, reduced and higher visual attention was found in previous literature based on their paradigms<sup>11,12,13,16,17-20</sup>. Our present paradigm was different from their experimental design. And we found higher visual attention in the pregnant group. Significantly shorter N100 amplitude at C4 area might be due to the effect of longer ISI in the experimental paradigm<sup>11,12</sup>.

The second type of discussion is based on the significant and non-significant smaller latencies of the N100 component in the pregnant group. We found both significant and non-significantly smaller latencies at most of the sites in the pregnant group (Table 1). One study on migraine patients showed that they have longer latency of the N100 ERP component, and the authors concluded it as a reduced speed of visual information processing<sup>28</sup>. Taking these notations, we can say that pregnant women have a good visual sensory information processing system as we found significantly lesser latencies of N100 at bi-parietal and right posterior temporal (P3, P4, and T6) areas and non-significantly smaller latencies at most of the sites in the pregnant group (Table 1). It might be a positive effect of the pregnancy/placental hormones like human chorionic gonadotropin (hCG), human placental lactogen (HPL), progesterone, etc. Progesterone level is 30 to 70 times higher in pregnant women than the non-pregnant women even having menstrual period<sup>29</sup>. The study showed that progesterone, within physiological ranges, has no definite meaningful effect on cognition<sup>30</sup>. Therefore, the effect of progesterone in non-pregnant women is not comparable with pregnant women in any trimester. Hence, we assume that the higher cognitive function is the positive effect of progesterone hormone in pregnant women.

## 5. CONCLUSION

We assessed visual attention and visual sensory processing of pregnant women by analysing amplitudes and latencies of the N100 ERP component in the ERP study. Although not significant, higher amplitude and lesser latencies of the N100 component, however, postulated that pregnant women in our sample had higher visual attention and better visual sensory processing time. Evidence of slightly higher activation areas for both stimuli in the pregnant group confirmed the consistency in the results of this ERP study. Based on the outcomes of this study, we assume that the pregnancy related hormones had beneficial effect on attention processing of the pregnant women, and we recommend future replicated studies following rigorous methodology, which would arrive at decisive conclusions.

## 6. ACKNOWLEDGMENT

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## 7. LIMITATIONS

1. Small sample size. We need a larger sample size for more reliable information.
2. Collection data from different trimester groups.

## 8. AUTHORS CONTRIBUTION

**Conceived and designed the experiments:** FR

**Collected data and performed the experiments:** DA, TB

**Contributed with materials/analysis tools:** FR, TB

**Analysed the data:** DA, TB

**Wrote the manuscript:** DA, TB

**Checked and edited the format:** FR, TB

**Final approval:** DA, TB, FR

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## SYNTACTIC MALAY LANGUAGE PROCESSING IN PREGNANT WOMEN: ANALYSIS OF THE N400 COMPONENT

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### KEYWORDS:

syntactic language, N400 ERP component, pictorial stimuli, pregnancy.

### ABSTRACT

**Background:** Language is one of the fundamental ability of human being. Occasionally pregnant women experience a lack of focus, memory, and language difficulties. There is a complex and dynamic connection between idiom and language. Understanding and processing of language contain subject and object marking Wh-questions together with event-related potentials (ERP) might evident an important tool for evaluation of syntactic language processing.

**Aim:** So far there is no study yet on syntactic language processing in pregnant woman by means of Wh-questions and ERP methods. Therefore, we investigated the neural mechanism of syntactic language processing using pictorial stimuli in pregnant women using event-related potential (ERP) study.

**Methods:** Twenty Malaysian women, matched for age and education level, were recruited into: the control (n=10), and the pregnant (n=10) groups. Simple (SS session: subject-subject) and complex (OM session: object marker) questions in Malay along with pictorial stimuli were used in the ERP study. Participants were asked to press button '1' if the upper picture and button '2' if the lower picture was correct.

**Results:** Amplitudes and latencies of the N400 ERP component were analysed with 19 electrode channels. We performed two types of comparative analyses: between the groups and within the groups with the cortical mapping distribution. Both types of analyses revealed that the pregnant group had significantly higher amplitudes of the N400 component during simple Malay questions. Moreover, the right frontal distribution was seen in the pregnant group during both stimuli.

**Conclusion:** Pregnant women have higher syntactic Malay language processing with the activated right frontal area. These might be due to the effects of pregnancy hormones.

## 1. INTRODUCTION

As a basic human skill, language demands a complex pattern of cognitive function, which follows certain rules including the rules of syntax. Syntax conveys the meaning from the relationships between words in a sentence. In cognitive science research, the syntax has been related to psychological reality<sup>1,2</sup>. In view of this relationship, some researchers used pictorial stimuli to study the central neural processing areas of language, attention, and memory<sup>3,4</sup>. There are few studies about syntactic language processing in different healthy patients and control groups. Alzheimer's patients have intact syntactic language processing<sup>1,2</sup>, and Parkinson's patients exhibit impaired syntactic language processing, which provides useful information regarding deficits in the dopaminergic system<sup>5</sup>. Elderly healthy subjects showed a decline in syntactic language processing<sup>6</sup>. Zaidil et al. analysed syntactic language processing on normal healthy Malaysian women using simple and complex questions in the Malay language along with pictorial stimuli. They found that complex questions evoked lateralization in the temporo-parietal areas<sup>7</sup>. Their study was conducted at a preliminary level, as there are no previous studies

related to syntactic language processing on women. In women, attention deficits, poor memory, and reading difficulties are evident during pregnancy due to hormonal changes<sup>8,9</sup>. However, there are some studies concerning attention, memory, and executive function in pregnant women<sup>10,11</sup>. Extending the research performed by Zaidil et al., we studied syntactic language processing using pictorial stimuli in pregnant women.

Language and syntactic language processing might be affected by dialect. There is a complex and dynamic relationship between dialect and language. Documents support that higher dialect users have poor language processing, but it is not proved that dialect itself influences the progress of language skills over time. Also, higher dialect users have slower reading progress. The longitudinal studies used children in urban areas as participants and they used English language<sup>12,13</sup>. In Malaysia, there are various regions using their own dialect. Till now, 10 dialects were used throughout Malaysia and among them, the dialect of Kelantan is unique comparing with the other dialects<sup>14</sup>. Dialect effect of the

Malay language on Malay syntactic language processing is still not yet done.

Stimuli usually involve auditory, visual, or somatosensory tasks, which can typically be done in event-related potential (ERP) studies. In ERP studies, we can record neuronal activity during stimuli or tasks to investigate the cognitive functions in different paradigms<sup>15,16</sup>. ERP components can express the nature of cognitive functions by positive (P) or negative (N) deflections in the ERP waveforms, followed by a value that indicates the latency in milliseconds<sup>17</sup>. Depending on the stimuli pattern, different ERP components are evoked, for example, during syntactic language processing, N400 ERP components are evoked. The N400 ERP component has a negative peak and a latency range of 200-600ms. It is evoked when there is semantic incongruity within sentences and unexpected word stimuli during sentence reading<sup>18</sup>. Studies have shown that amplitude reductions in the N400 ERP component are biomarkers of cognitive function impairment<sup>19</sup> and it might happen during repeated word stimuli<sup>18</sup>. Higher amplitudes and greater latencies in the N400 ERP component have been seen in congruent wordings<sup>20</sup>. N400 component was assessed as a crucial tool for the disorder of consciousness (DOC) patients<sup>21,22</sup>. Information processing abilities were assessed in different patient groups like traumatic brain injury<sup>23</sup>, stroke<sup>24</sup>, Alzheimer's disease<sup>25</sup>, mild cognitive impairment (MCI)<sup>19</sup> using the N400 ERP component. So far there is no study yet on pregnant women to explore their syntactic language processing in any other languages. Hence, we evaluated syntactic language processing in Malay language using the N400 ERP component among Malaysian women.

The aim of this study was to determine the amplitudes and latencies in the N400 ERP component during syntactic Malay language processing with the cortical distribution, using pictorial stimuli in pregnant women.

## 2. MATERIALS AND METHODS

### 2.1. Study design

This is a quantitative cross-sectional, non-interventional study. We used a convenient sampling method during the selection of participants.

### 2.2. Ethics and sample size

This study was approved by the Human Ethical Committee of Universiti Sains Malaysia (USM) (USM/JEPeM/15090294) before the start of the experiment.

All participants were Malaysian women and recruited by notice board notifications and using personal and Internet connections. The sample size was calculated with Power and Sample Size (PS) software using a difference mean (36) and standard deviation (27.49) from the previous study of Zaidilet al<sup>7</sup>. Probability power ( $\beta$ ) was 0.8 and ( $\alpha$ ) power was 0.05. Therefore, a total of twenty participants were calculated. They were divided into two groups: the control (non-pregnant) (n=10), and pregnant (2<sup>nd</sup> and 3<sup>rd</sup> trimester together) (n=10) groups. Women from both groups were aged between 20 and 40 years<sup>26</sup>, and their educations were equalised<sup>27</sup> as age and education can affect the cognitive function/attention<sup>26,27</sup>. All the women from both groups were from the Kelantan state of Malaysia.

This study was conducted in the ERP/Magnetoencephalography (MEG) room at Hospital Universiti Sains Malaysia (HUSM), and before the experiment, all participants provided written informed consent.

### 2.3. Experimental procedure and paradigm

Siapakah yang sedangmenolakseorangbudaklelaki?  
(Who is pushing a boy?) (simple)  
Or

Datuk manakah yang seorangbudaklelakisedangtolak?  
(Which grandfather is being pushed by a boy?) (complex)

Simplex and complex questions in the Malay language: 5 sec

**Figure 1.** The experimental paradigm of visual pictorial stimuli with examples of simple and complex questions was shown in figure 1.

All participants sat in a dimly lit, sound-treated room, with a 128 ERP net on their scalp, and they were 1-meter away from a 22-inch LCD computer. They had normal or corrected vision. All stimuli were presented with E-Prime software (v2.0, Psychology software tools, Inc., Sharpsburg, Pennsylvania, USA), and data were recorded with Net Station software 5.2 (Electrical Geodesics, Inc., Eugene, OR, USA). The experimental paradigm was adopted from our previous study<sup>7</sup>. Twenty simple questions (subject-subject, SS) and twenty complex questions (object marker, OM) in the Malay language along with related pictorial stimuli were presented. All stimuli were presented for 5 sec, with 5-sec inter-stimulus intervals (ISI). Participants were asked to press button '1' if the upper picture was correct and button '2' if the lower picture was correct, related to previous simple or complex questions. The following is an example of a simple question: "Siapakah yang sedangmenolakseorangbudaklelaki?" (Who is pushing a boy?); the following is an example of a complex question: "Datuk manakah yang seorangbudaklelakisedangtolak?" (Which grandfather is being pushed by a boy?) (Figure 1).

### 2.4. Data analysis

Raw data were collected from Net Station software. Electrode impedances were less than 50k $\Omega$ . All data were filtered with 0.03-30 Hz, with a 250-Hz sampling rate. Segmentation was done from -100 to 1000ms. Eye blinks, eye movements, and movement artefacts were removed using artefact removal tools in Net Station software. The baseline was corrected to 100ms before the stimuli presentation. All values of amplitudes and latencies of the N400 ERP component were collected in 19 electrode channels, in a 10-20 system using a statistical extraction tool from the same software application. Since the sample size is small and not normally distributed, therefore nonparametric Mann-Whitney U test was used to analyse significant differences between SS and OM sessions between the pregnant and non-pregnant groups as well as SS and OM sessions within each group using SPSS 24 software  $p \leq 0.05$  was considered to indicate statistical significance.

Cortical topographic distribution was done using view tools in Net Station software after doing a grand average of N400 ERP components for both groups.

## 3. RESULTS

### 3.1. Demographic information

The mean ages (SD) of the control and pregnant groups were 31.06 (4.32) years and 28.47 (1.14) years, respectively ( $p=0.073$ ). On the other hand, the mean (SD) numbers of years of education were 14.4 (0.7) years and 15.5 (2.46) years, respectively ( $p=0.105$ ). Non-significant differences between groups indicated the age and education matched between groups.

### 3.2. Results on N400 ERP component

First, we compared the two sessions in the control and pregnant groups separately. The control group showed significantly higher ( $p=0.017$ ) N400 amplitudes at the T4 area ( $0.35\pm0.39\mu\text{V}$ ) during OM sessions than during SS sessions ( $0.21\pm0.42\mu\text{V}$ ). There were no significant differences in N400 latencies between SS and OM sessions in the control group (Table 1).

In the pregnant group, significantly higher ( $p=0.022$ ) N400 amplitudes were found at FP2 ( $0.86\pm0.27\mu\text{V}$ ,  $p=0.022$ ) and T4 ( $0.44\pm0.42\mu\text{V}$ ,  $p=0.047$ ) areas during SS sessions than during OM sessions ( $0.65\pm0.37\mu\text{V}$ ,  $0.09\pm0.52\mu\text{V}$ , respectively). SS sessions

evoked significantly prolonged latencies at O2 ( $536.8\pm91.75\text{ ms}$ ,  $p=0.028$ ) and Pz ( $512.0\pm115.90\text{ ms}$ ,  $p=0.028$ ) areas compared to OM sessions ( $437.2\pm120.99\text{ms}$ ,  $398.0\pm114.67\text{ms}$ , respectively) (Table 1).

Second, we compared SS sessions and OM sessions separately between the control and pregnant groups (Table 2). In SS sessions, the pregnant group showed significantly higher amplitudes ( $0.86\pm0.27\mu\text{V}$ ) at FP2 ( $p=0.043$ ) and shorter latencies ( $378.0\pm82.13\text{ ms}$ ) at FP1 ( $p=0.043$ ) of the N400 ERP component compared to the control group ( $0.36\pm0.64\mu\text{V}$ ,  $464.8\pm85.95\text{ ms}$ , respectively). In OM sessions, there were no significant differences in amplitudes and latencies of the N400 ERP component between groups (Table 2).

**Table 1:** Amplitudes and latencies of the N400 ERP component within groups: comparing SS and OM sessions in the control and pregnant groups at various regions of the brain.

Sites	Control group (mean $\pm$ SD)		Pregnant group (mean $\pm$ SD)		p-value (control)	p-value (pregnant)
	SS	OM	SS	OM		
<b>Amplitudes (in <math>\mu\text{V}</math>) (mean<math>\pm</math>SD) of the N400 ERP Component</b>						
<b>Fp1</b>	0.71 $\pm$ 0.32	0.56 $\pm$ 0.45	0.86 $\pm$ 0.42	0.70 $\pm$ 0.33	.333	.508
<b>F3</b>	0.23 $\pm$ 0.64	0.28 $\pm$ 0.47	0.50 $\pm$ 0.57	0.54 $\pm$ 0.27	.799	.878
<b>F7</b>	0.43 $\pm$ 0.55	0.21 $\pm$ 0.73	0.63 $\pm$ 0.50	0.55 $\pm$ 0.60	.169	.878
<b>Fp2</b>	0.36 $\pm$ 0.64	0.44 $\pm$ 0.44	<b>0.86<math>\pm</math>0.27</b>	<b>0.65<math>\pm</math>0.37</b>	.878	<b>.022*</b>
<b>F4</b>	0.24 $\pm$ 0.50	0.23 $\pm$ 0.51	0.23 $\pm$ 0.60	0.38 $\pm$ 0.36	.646	.333
<b>F8</b>	0.37 $\pm$ 0.46	0.15 $\pm$ 0.66	0.22 $\pm$ 0.67	0.41 $\pm$ 0.34	.646	.878
<b>C3</b>	0.30 $\pm$ 0.49	0.48 $\pm$ 0.43	0.49 $\pm$ 0.27	0.42 $\pm$ 0.32	.386	.799
<b>C4</b>	0.31 $\pm$ 0.37	0.45 $\pm$ 0.38	0.41 $\pm$ 0.48	0.39 $\pm$ 0.23	.169	.721
<b>T3</b>	0.33 $\pm$ 0.42	0.41 $\pm$ 0.24	0.50 $\pm$ 0.51	0.33 $\pm$ 0.70	.646	.386
<b>T4</b>	<b>0.21<math>\pm</math>0.42</b>	<b>0.35<math>\pm</math>0.39</b>	<b>0.44<math>\pm</math>0.42</b>	<b>0.09<math>\pm</math>0.52</b>	<b>.017*</b>	<b>.047</b>
<b>P3</b>	0.46 $\pm$ 0.39	0.57 $\pm$ 0.43	0.53 $\pm$ 0.30	0.42 $\pm$ 0.37	.575	.333
<b>T5</b>	0.09 $\pm$ 0.63	0.47 $\pm$ 0.38	0.48 $\pm$ 0.45	0.47 $\pm$ 0.45	.333	.721
<b>P4</b>	0.33 $\pm$ 0.57	0.54 $\pm$ 0.41	0.30 $\pm$ 0.61	0.49 $\pm$ 0.33	.285	.386
<b>T6</b>	0.37 $\pm$ 0.43	0.45 $\pm$ 0.44	0.47 $\pm$ 0.65	0.52 $\pm$ 0.41	.575	.799
<b>O1</b>	0.53 $\pm$ 0.57	0.51 $\pm$ 0.62	0.50 $\pm$ 0.45	0.48 $\pm$ 0.76	.799	.959
<b>O2</b>	0.40 $\pm$ 1.07	0.48 $\pm$ 0.59	0.61 $\pm$ 0.45	0.35 $\pm$ 0.50	.721	.093
<b>Fz</b>	0.38 $\pm$ 0.47	0.46 $\pm$ 0.40	0.43 $\pm$ 0.52	0.30 $\pm$ 0.39	.799	.575
<b>Cz</b>	0.41 $\pm$ 0.62	0.32 $\pm$ 0.43	0.46 $\pm$ 0.42	0.41 $\pm$ 0.40	.799	.646
<b>Pz</b>	0.46 $\pm$ 0.83	0.49 $\pm$ 0.53	0.62 $\pm$ 0.37	0.58 $\pm$ 0.70	.799	.799
<b>Latencies (in ms) (mean<math>\pm</math>SD) of the N400 ERP Component</b>						
<b>Fp1</b>	464.8 $\pm$ 85.95	446.0 $\pm$ 96.45	378.0 $\pm$ 82.13	407.2 $\pm$ 87.81	.878	.284
<b>F3</b>	400.4 $\pm$ 66.22	440.8 $\pm$ 90.31	401.6 $\pm$ 83.29	406.8 $\pm$ 90.12	.262	.799
<b>F7</b>	401.6 $\pm$ 64.94	417.6 $\pm$ 71.66	411.2 $\pm$ 97.28	428.4 $\pm$ 107.24	.508	.878
<b>Fp2</b>	426.4 $\pm$ 99.92	412.8 $\pm$ 93.42	363.6 $\pm$ 85.63	424.0 $\pm$ 94.96	.878	.202
<b>F4</b>	434.8 $\pm$ 97.36	400.4 $\pm$ 76.35	375.6 $\pm$ 94.72	438.8 $\pm$ 108.55	.508	.386
<b>F8</b>	402.0 $\pm$ 95.48	388.4 $\pm$ 90.16	479.2 $\pm$ 93.67	434.8 $\pm$ 113.33	.721	.445
<b>C3</b>	453.6 $\pm$ 61.69	428.4 $\pm$ 87.26	386.4 $\pm$ 65.49	376.4 $\pm$ 59.40	.284	.722
<b>C4</b>	482.0 $\pm$ 97.82	427.6 $\pm$ 90.46	466.8 $\pm$ 99.96	455.2 $\pm$ 107.34	.475	.575
<b>T3</b>	458.4 $\pm$ 79.98	468.0 $\pm$ 88.42	396.8 $\pm$ 78.38	402.0 $\pm$ 98.20	.760	.878
<b>T4</b>	436.4 $\pm$ 108.75	491.6 $\pm$ 123.57	498.0 $\pm$ 112.84	524.0 $\pm$ 75.40	.285	.721
<b>P3</b>	495.2 $\pm$ 104.37	467.2 $\pm$ 107.31	440.4 $\pm$ 115.28	442.8 $\pm$ 117.26	.594	.838
<b>T5</b>	495.2 $\pm$ 115.74	469.2 $\pm$ 92.65	467.6 $\pm$ 105.60	446.4 $\pm$ 104.21	.508	.541
<b>P4</b>	561.6 $\pm$ 85.61	501.6 $\pm$ 102.96	483.2 $\pm$ 128.72	431.2 $\pm$ 120.06	.173	.203
<b>T6</b>	518.8 $\pm$ 104.05	469.6 $\pm$ 111.29	512.4 $\pm$ 116.88	442.4 $\pm$ 135.92	.263	.221
<b>O1</b>	486.0 $\pm$ 132.32	455.6 $\pm$ 103.13	517.6 $\pm$ 105.28	464.4 $\pm$ 125.76	.333	.236
<b>O2</b>	524.8 $\pm$ 107.18	474.0 $\pm$ 116.96	<b>536.8<math>\pm</math>91.75</b>	<b>437.2<math>\pm</math>120.99</b>	.508	<b>.028*</b>
<b>Fz</b>	421.2 $\pm$ 93.81	450.4 $\pm$ 96.19	392.0 $\pm$ 88.30	411.6 $\pm$ 101.48	.109	.507
<b>Cz</b>	458.4 $\pm$ 109.27	451.6 $\pm$ 88.61	413.2 $\pm$ 88.16	382.0 $\pm$ 91.49	.799	.314
<b>Pz</b>	508.4 $\pm$ 116.61	490.8 $\pm$ 107.83	<b>512.0<math>\pm</math>115.90</b>	<b>398.0<math>\pm</math>114.67</b>	.721	<b>.028*</b>

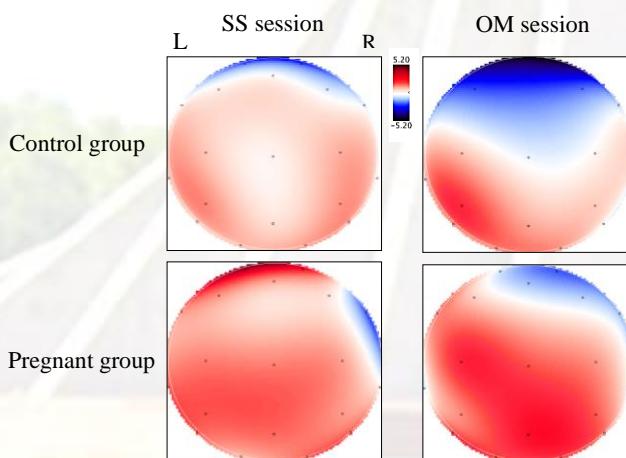
\*Note: significant =  $p\leq0.05$

**Table 2:** Amplitudes and latencies of the N400 ERP component between groups. Comparing control and pregnant groups in the SS and OM sessions at various regions of the brain.

Sites	SS		OM		p-value (SS)	p-value (OM)
	Control group	Pregnant group	Control group	Pregnant group		
	Amplitudes (in $\mu$ V) (mean $\pm$ SD) of the N400 ERP Component					
<b>Fp1</b>	0.71 $\pm$ 0.32	0.86 $\pm$ 0.42	0.56 $\pm$ 0.45	0.70 $\pm$ 0.33	.481	.631
<b>F3</b>	0.23 $\pm$ 0.64	0.50 $\pm$ 0.57	0.28 $\pm$ 0.47	0.54 $\pm$ 0.27	.436	.218
<b>F7</b>	0.43 $\pm$ 0.55	0.63 $\pm$ 0.50	0.21 $\pm$ 0.73	0.55 $\pm$ 0.60	.393	.165
<b>Fp2</b>	<b>0.36<math>\pm</math> 0.64</b>	<b>0.86<math>\pm</math> 0.27</b>	0.44 $\pm$ 0.44	0.65 $\pm$ 0.37	<b>.043*</b>	.436
<b>F4</b>	0.24 $\pm$ 0.50	0.23 $\pm$ 0.60	0.23 $\pm$ 0.51	0.38 $\pm$ 0.36	.912	.393
<b>F8</b>	0.37 $\pm$ 0.46	0.22 $\pm$ 0.67	0.15 $\pm$ 0.66	0.41 $\pm$ 0.34	.684	.436
<b>C3</b>	0.30 $\pm$ 0.49	0.49 $\pm$ 0.27	0.48 $\pm$ 0.43	0.42 $\pm$ 0.32	.579	.481
<b>C4</b>	0.31 $\pm$ 0.37	0.41 $\pm$ 0.48	0.45 $\pm$ 0.38	0.39 $\pm$ 0.23	.393	.579
<b>T3</b>	0.33 $\pm$ 0.42	0.50 $\pm$ 0.51	0.41 $\pm$ 0.24	0.33 $\pm$ 0.70	.190	.247
<b>T4</b>	0.21 $\pm$ 0.42	0.44 $\pm$ 0.42	0.35 $\pm$ 0.39	0.09 $\pm$ 0.52	.247	.280
<b>P3</b>	0.46 $\pm$ 0.39	0.53 $\pm$ 0.30	0.57 $\pm$ 0.43	0.42 $\pm$ 0.37	.971	.190
<b>T5</b>	0.09 $\pm$ 0.63	0.48 $\pm$ 0.45	0.47 $\pm$ 0.38	0.47 $\pm$ 0.45	.123	.971
<b>P4</b>	0.33 $\pm$ 0.57	0.30 $\pm$ 0.61	0.54 $\pm$ 0.41	0.49 $\pm$ 0.33	.853	.912
<b>T6</b>	0.37 $\pm$ 0.43	0.47 $\pm$ 0.65	0.45 $\pm$ 0.44	0.52 $\pm$ 0.41	.393	.631
<b>O1</b>	0.53 $\pm$ 0.57	0.50 $\pm$ 0.45	0.51 $\pm$ 0.62	0.48 $\pm$ 0.76	1.000	.796
<b>O2</b>	0.40 $\pm$ 1.07	0.61 $\pm$ 0.45	0.48 $\pm$ 0.59	0.35 $\pm$ 0.50	.853	.579
<b>Fz</b>	0.38 $\pm$ 0.47	0.43 $\pm$ 0.52	0.46 $\pm$ 0.40	0.30 $\pm$ 0.39	.631	.247
<b>Cz</b>	0.41 $\pm$ 0.62	0.46 $\pm$ 0.42	0.32 $\pm$ 0.43	0.41 $\pm$ 0.40	.853	.436
<b>Pz</b>	0.46 $\pm$ 0.83	0.62 $\pm$ 0.37	0.49 $\pm$ 0.53	0.58 $\pm$ 0.70	.684	.684
Latencies (in ms) (mean $\pm$ SD) of the N400 ERP Component						
<b>Fp1</b>	<b>464.8<math>\pm</math> 85.95</b>	<b>378.0<math>\pm</math> 82.13</b>	446.0 $\pm$ 96.45	407.2 $\pm$ 87.81	<b>.043*</b>	.353
<b>F3</b>	400.4 $\pm$ 66.22	401.6 $\pm$ 83.29	440.8 $\pm$ 90.31	406.8 $\pm$ 90.12	.739	.436
<b>F7</b>	401.6 $\pm$ 64.94	411.2 $\pm$ 97.28	417.6 $\pm$ 71.66	428.4 $\pm$ 107.24	.853	.912
<b>Fp2</b>	426.4 $\pm$ 99.92	363.6 $\pm$ 85.63	412.8 $\pm$ 93.42	424.0 $\pm$ 94.96	.123	.853
<b>F4</b>	434.8 $\pm$ 97.36	375.6 $\pm$ 94.72	400.4 $\pm$ 76.35	438.8 $\pm$ 108.55	.075	.739
<b>F8</b>	402.0 $\pm$ 95.48	479.2 $\pm$ 93.67	388.4 $\pm$ 90.16	434.8 $\pm$ 113.33	.105	.529
<b>C3</b>	453.6 $\pm$ 61.69	386.4 $\pm$ 65.49	428.4 $\pm$ 87.26	376.4 $\pm$ 59.40	.043	.218
<b>C4</b>	482.0 $\pm$ 97.82	466.8 $\pm$ 99.96	427.6 $\pm$ 90.46	455.2 $\pm$ 107.34	.739	.393
<b>T3</b>	458.4 $\pm$ 79.98	396.8 $\pm$ 78.38	468.0 $\pm$ 88.42	402.0 $\pm$ 98.20	.063	.143
<b>T4</b>	436.4 $\pm$ 108.75	498.0 $\pm$ 112.84	491.6 $\pm$ 123.57	524.0 $\pm$ 75.40	.280	.912
<b>P3</b>	495.2 $\pm$ 104.37	440.4 $\pm$ 115.28	467.2 $\pm$ 107.31	442.8 $\pm$ 117.26	.315	.684
<b>T5</b>	495.2 $\pm$ 115.74	467.6 $\pm$ 105.60	469.2 $\pm$ 92.65	446.4 $\pm$ 104.21	.631	.739
<b>P4</b>	561.6 $\pm$ 85.61	483.2 $\pm$ 128.72	501.6 $\pm$ 102.96	431.2 $\pm$ 120.06	.105	.143
<b>T6</b>	518.8 $\pm$ 104.05	512.4 $\pm$ 116.88	469.6 $\pm$ 111.29	442.4 $\pm$ 135.92	.853	.481
<b>O1</b>	486.0 $\pm$ 132.32	517.6 $\pm$ 105.28	455.6 $\pm$ 103.13	464.4 $\pm$ 125.76	.579	.853
<b>O2</b>	524.8 $\pm$ 107.18	536.8 $\pm$ 91.75	474.0 $\pm$ 116.96	437.2 $\pm$ 120.99	.684	.631
<b>Fz</b>	421.2 $\pm$ 93.81	392.0 $\pm$ 88.30	450.4 $\pm$ 96.19	411.6 $\pm$ 101.48	.436	.353
<b>Cz</b>	458.4 $\pm$ 109.27	413.2 $\pm$ 88.16	451.6 $\pm$ 88.61	382.0 $\pm$ 91.49	.481	.089
<b>Pz</b>	508.4 $\pm$ 116.61	512.0 $\pm$ 115.90	490.8 $\pm$ 107.83	398.0 $\pm$ 114.67	.971	.105

\*Note: significant =  $p \leq 0.05$

### 3.3. Results on topographic distribution



**Figure 2:** Topographic cortical distribution in control and pregnant groups during SS and OM sessions. The blue color indicated a negative reflection of the N400 ERP component.

Cortical topographic distribution revealed that the control group evoked N400 reflection at the fronto-polar area (Fp1, Fp2) during simple question (SS session) and widely distributed at frontal areas (Fz, F3, F4, Fp1, Fp2) during complex question (OM session) stimuli. On the other hand, the pregnant group induced the right frontal area (F8) and right frontal areas (Fz, F4, Fp2, F8) during simple and complex questions stimuli, respectively (Figure 2). Therefore, commonly the right frontal area (F8) was found as the cortical topographic distribution for the pregnant group during both simple and complex Malay word stimuli (Figure 2).

## 4. DISCUSSION

We analysed amplitudes and latencies of the N400 ERP component to assess syntactic Malay language processing in pregnant Malaysian women and used visual pictorial stimuli. All participants selected the correct pictorial stimuli based on the simple (SS session) and complex questions (OM session) performed earlier.

We conducted two types of analyses: 1) within-group: comparing SS and OM sessions within the control and pregnant groups, and 2) between groups: comparing the SS and OM sessions between the

control and pregnant groups. In the first analysis, we found that the control group evoked significantly higher N400 amplitudes during OM sessions at the T4 area, and the pregnant group had significantly higher N400 evoked amplitudes at the FP2 and T4 areas during SS session. The pregnant group also had prolonged latencies at the O2 and Pz areas during SS session. However, the second analysis revealed that the pregnant group evoked significantly higher amplitudes of N400 components at the FP2 area and had a shorter latency of N400 components at the FP1 area only during SS sessions. Topographic cortical distribution revealed that the frontal area was induced in the control group and the right frontal area was induced in the pregnant group during both stimuli.

Lack of cognitive function was observed in some studies based on smaller amplitudes and longer latencies of N400 ERP components<sup>15</sup>. Higher amplitudes of the N400 component were found during incongruent word stimuli, as participants needed more attention to understanding incongruent words<sup>18</sup>. Poor syntactic language processing was found in older people, which was reflected by smaller amplitudes and prolonged latencies of the N400 component<sup>6</sup>.

During the comparisons of the two sessions in the control and pregnant groups, we found that the control group evoked significantly higher amplitudes of N400 components during complex questions (OM session) at the T4 location and the pregnant group evoked these during simple questions (SS session) at Fp2, T4 areas. Considering the points discussed in the previous studies<sup>6,18,20</sup>, our results indicated that the control group required higher syntactic language processing during complex questions to understand their meaning clearly, but the pregnant group required higher syntactic language processing to understand simple questions. They might have struggled to understand the simple questions, requiring them to focus more. Moreover, the pregnant group evoked significantly higher amplitudes and shorter latencies of N400 components at Fp2 and Fp1, respectively, during simple questions stimuli (SS session, Table 2), and this finding indicated that our pregnant women required higher syntactic language processing during simple questions in the Malay language, a finding that is consistent with those of other studies<sup>6,18,20</sup>. An explanation of our result, a previous study reported that the N400 ERP component is usually evoked depending on stimuli type which enters into temporal synchrony. This temporal synchrony creates a multimodal conceptual representation to make a context dependant memory of the given stimuli. The multimodal conceptual representations meaning that context dependant memory is different depending on people, time, and context<sup>28</sup>. Besides, N400 reflects the conscious experience of meaning to the stimuli<sup>29</sup>. Therefore, we predict that our pregnant group has the conscious experience or visual attention to the syntactic Malay language processing due to the creation of multimodal conceptual representation during simple question (SS session) at the fronto-temporal areas (Fp1, Fp2, T4) but not during complex question (OM session). The explanation of why simple questions creates this conceptual representation but not for complex question among pregnant women is still a big question that might be explored during our future study.

No previous study was found on topographic map distribution in pregnant women using syntactic Malay language processing. In our study, we found that control women used their frontal area to give attention to both types of stimuli and in the case of pregnant women, the attentional area was diverted to the right frontal area during both stimuli (Figure 2). The right frontal area is usually activated during complex linguistic processing<sup>30</sup>. By adopting this point, we can assume that both simple and complex questions were more or less complex patterns for our pregnant women because

the right frontal area was induced during simple questions and it was more prominent and widely distributed during complex questions in the same area (Figure 2). Numerous modalities were used to investigate the activated source localization of the N400 ERP component. fMRI and EEG-based evidence proved that the left temporal lobe is the largest source of the N400 component with the smaller distribution of the right temporal area<sup>31</sup>. Left perisylvian cortex<sup>32</sup> and bilateral inferior frontal gyri<sup>33</sup> were also found as activated areas for the N400 ERP component in EEG-based works. MEG using source localization give more confirmation about this where left superior and middle temporal gyri with inferior parietal and frontal areas were evident for source activation area for N400 component<sup>34</sup>. However, the source of N400 was within the distributed language network<sup>35</sup>. We assume that the variable findings of source localization of N400 component are due to a) on modality use as they have limitation based on temporal and special resolution, b) on sample populations as gender, clinical samples might affect differently, c) on different experimental paradigm with different languages. In our study, all the sample participants were women, we used an ERP study to reveal N400 activation with syntactic language paradigm which might lead our result differently comparing with those previous studies. Our female population chose the complex linguistic area to focus the syntactic processing in the Malay language instead of the normal language network.

We do hereby acknowledge that, there are some limitations in this study. Firstly, a small sample size might affect the present result. We need a large sample size to get more reliable information in future studies. Secondly, all participants were from the Kelantan State of Malaysia. The local language of Kelantan might affect the result also. Therefore, further study is required in other states of Malaysia among pregnant women which might be comparable with these present results.

## 5. CONCLUSION

We aimed to determine the neuronal cortical processing of syntactic language processing using pictorial stimuli in pregnant women by analysing the N400 ERP component. We found that while responding to simpler questions, pregnant women had higher syntactic processing ability in the Malay language. Besides these, while maintaining attentional focus and processing of answers to both simple and complex types of questions stimuli, pregnant women in our study had more activation in the right frontal area, which is the area of complex linguistic processing. We hypothesize that the hormonal alterations during pregnancy facilitated in observed advancement in cognitive functioning. We recommend future detailed and replicated studies to confirm this phenomena with adequate empirical evidence.

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## 7. AUTHORS' CONTRIBUTIONS

**Conception and design:** JHY, FR, TB

**Analysis and interpretation of the data:** TB, FR, NNZ

**Drafting of the article:** NNZ, TB, FR

**Critical revision of the article for important intellectual content:** TB, FR

**Final approval of the article:** NNZ, FR, TB, JHY, RAR

**Administrative, technical, or logistic support:** TB, FR, RAR

**Collection and assembly of data:** NNZ, TB, FR

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## PROSTHETIC REHABILITATION OF AN OCULAR DEFECT – A CASE REPORT

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#### KEYWORDS:

*Prosthodontic rehabilitation, Ocular prosthesis, Eye prosthesis, Case report*

### ABSTRACT

**Background:** Maxillofacial deformity especially ocular deformity can be emotionally traumatizing and affect social behaviour of an individual. In such cases, custom made aesthetic prosthesis serves as a viable option for the patient.

**Aim:** The aim of ocular prosthesis is to enable rehabilitation of the patient with normal appearance and bring back the patient in the society.

**Method:** Impression was taken by Vinyl Polysiloxane Impression material using custom tray. The impression was cast and transparent acrylic conformer was made from the mould. Adjustment was done on conformer and scleral shell was prepared. Coloration was completed on scleral shell and final prosthesis was fabricated.

**Results:** This article elaborates the rehabilitation process of a case of acquired eye defect with custom made ocular prosthesis for a patient who had his right eye surgically enucleated.

**Conclusions:** The present technique is simple but further research can be done to decrease the cost and fabrication time of the prosthesis.

## 1. INTRODUCTION

Eyes are the first features of the face to be noted. An eye defect can be caused by any of the several condition, including trauma, congenital malformation, or surgical removal of the eye due to tumor. The disfigurement due to loss of an eye can cause significant physical and emotional problems<sup>1</sup>. Therefore, a prosthetic rehabilitation to restore the form, function and aesthetic is mandatory to elevate psychological status of such patients.

Surgical procedures adapted for the removal of an eye are classified into three categories: evisceration, enucleation and exenteration. Patients requiring treatment with custom ocular prosthesis are those who have lost ocular structure through orbital evisceration or enucleation. Evisceration is the removal of the contents of the globe but leaving the sclera and on occasion the cornea in place<sup>2</sup>.

A custom-made ocular prosthesis should begin to fabricate as soon as the socket has healed. These prostheses could be either

glass of methylmethacrylate resin. But glass is not the choice of material as it breaks very easily, and the surface may deteriorate from contact with orbital fluid<sup>3</sup>. In contrast, Methylmethacrylate resin is tissue compatible, more aesthetic, durable, available, and cost effective<sup>4</sup>. This case report demonstrates the fabrication of a custom ocular prosthesis for rehabilitation of post enucleation patient.

## 2. CASE DESCRIPTION

1. A 26-year-old male patient was brought to our clinic with chief complaint of facial disfigurement because of missing right eye for 9 months (Figure 1). He had acquired this condition as a result of accident followed by enucleation was noted. On examination we have found sufficient socket volume, adequate fornix depth, superior sulcus deepening, presence of upper eyelid ptosis and slight drooping of the lower eyelid. Patient was explained about the procedure and expected outcome.

2. Before taking impression, petroleum jelly was applied to the eyebrows

and eyelashes for the easy removal of the impression material.

3. Patient seated in an upright position. Stock impression tray specially made for ocular impression was placed inside the socket before making impression to check the size and orientation.

4. Impression was taken by medium body Vinyl Polysiloxane Impression (VPS) material from 3M ESPE, USA. After the material had set, impression was removed from the socket to check voids and defects.

5. The impression thus recorded was invested using small ocular flask in Type III dental stone (Dentsply, Canada) (Figure 2). The mould created was filled with heat cure clear acrylic resin (Factor 2, USA) and cured for 40 minutes in hot water at 100 degree Celsius. This clear cured product is called conformer. Trimming and polishing of the conformer was done and tried in the socket. Some adjustment was done in the conformer to adjust the opening of the eye.

6. Center marking, and size of the Iris was marked on the conformer by taking guide from the unaffected eye (Figure 3).

7. As there was some correction on the conformer a new mould was made using Type III dental stone. Heat cure scleral acrylic resin was packed in the mould and cured.

8. Iris button was placed, and coloration was done by taking the guideline from contralateral eye. The pattern and type of vessels of the opposite eye was reproduced as close as possible. A thin layer of clear acrylic resin was placed on the prosthesis and cured (Figure 4).

9. Final prosthesis was inserted in ocular defect and patient was asked to relax for atleast 10 minutes to allow all the surrounding muscles to relax, to permit critical evaluation (Figure 5).

10. Patient was instructed on how to remove and place the prosthesis.

### 3. DISCUSSION

The use of the stock ocular prosthesis doesn't provide the exact contour and color matching to the contralateral eye. Custom made acrylic ocular prosthesis is easy to fit and adjust, unbreakable, inert to ocular fluids, long lasting and provide good aesthetic outcome<sup>2,5</sup>. Depending on clinician's choice there are many techniques that have been used in fitting and fabricating eye prosthesis. Stock or prefabricated ocular prosthesis is often used when there is limited availability of custom-made prosthesis<sup>6</sup>. The use of stock or prefabricated ocular prosthesis of appropriate size and color cannot be neglected. But a prosthesis that was properly planned and well fabricated can maintain its orientation when patient performs various movement. With the advancement of materials, the socket can be finely recorded on which custom-made prosthesis can be made with exact shape and color<sup>7</sup>. Mass produced commercially available stock eye prosthesis have been marketed since years with less clinical success. Tomar, et al.<sup>8</sup> mentioned custom-made ocular prosthesis proved to be a boon to the patients needing ocular prosthesis<sup>8</sup>. According to Beumer et al.<sup>9</sup> intimate contact between the eye prosthesis and the tissue bed is needed to distribute even pressure, so that a stock eye prosthesis should be avoided. Moreover, the voids in the stock prosthesis collect mucus and debris, which can cause irritation in the mucus and act as a potential source of infection, which could be minimized in the



Figure 1



Figure 2



Figure 3



Figure 4



Figure 5

custom-made prosthesis<sup>9,10</sup>. The method here described is a custom-made ocular prosthesis that has provided good results from patient's aesthetics, acceptance, and satisfaction points of view.

In the future, nanotechnology, biotechnology, robotics, and bio-molecular biology involving multidisciplinary team with the current fabrication technique might be revolutionary for the patients. Moreover, computer aided design and implementation of three-dimensional printing has great potential in the manufacturing of an ocular prosthesis which decrease the fabrication time, frequency of visit to the clinic and overall cost of the prosthesis.

## 4. CONCLUSION

The goal of prosthetic rehabilitation is to return the patient to a normal cosmetic appearance as soon as possible. This method provides an accurate position and alignment of the iris that mimics a natural look. A properly finished and polished custom-made prosthesis enhance physical and psychological healing for such patient. Although patient can't see with such prosthesis, but it can definitely help patient live life with self-confidence and respect, without being starred by people.

## 5. CONTRIBUTION OF AUTHORS

Conceived and designed the study: MMuiN, AmR, NbJ, ZaG, AH

Conducted the procedure: MMuiN, AmR, NbJ

Contributed with materials/ tools: MMuiN, AmR, NbJ

Wrote the manuscript: MMuiN

Checked and edited the format of the paper: MMuiN,

Final approval: MMuiN,

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### Process of Acceptance for SECTION III articles (Articles on Neuro and Rehabilitation Science)

Article ID	Reviewer	Affiliation	Assigned as	Decision
<b>MS-BD50-Res- Exp. Neuro- Rehab Sc-1</b>	Dr. Kousiki Chakrabarti	HOD &Assistant Professor Zoology, Calcutta University, India	First reviewer on <b>March 24<sup>th</sup> 2021</b>	Accepted with moderate level of revision
	Dr. Dilsad Ahmed	Research Coordinator University of Macau, Macau, Guangdong, China	Second reviewer on <b>March 26<sup>th</sup> 2021</b>	Accepted after major Change
	Prof. Dr. Asok Ghosh	Professor, Sports Science RKMV University, Kolkata, India	Final reviewer on <b>April 26<sup>th</sup> 2021</b>	Accepted for publication on <b>29<sup>th</sup> of September 2021</b>
Article ID	Reviewer	Affiliation	Assigned as	Decision
<b>MS-BD50-Res- Exp. Neuro- Rehab Sc-2</b>	Dr. Debashish Chowdhury	Sport Physician and Asst. Gen. Manager, Bangladesh Cricket Board, Dhaka, Bangladesh	First reviewer on <b>March 11<sup>th</sup> 2021</b>	Accepted after major Change
	Dr. Satyapriya De Sarkar	Gastroenterologist G D Hospital & Diabetes Institute Kolkata, India	Second reviewer on <b>March 24<sup>th</sup> 2021</b>	Accepted with moderate level of revision
	Prof. Dr. Asok Ghosh	Professor, Sports Science RKMV University, Kolkata, India	Final reviewer on <b>May 23<sup>rd</sup> 2021</b>	Accepted for publication on <b>27<sup>th</sup> of September 2021</b>
Article ID	Reviewer	Affiliation	Assigned as	Decision
<b>MS-BD50-Res- Exp. Neuro- Rehab Sc-3</b>	Asso. Prof. Dr. Santanu Dutta	Associate Professor, Dept. of CTVS, Inst. of PG Medical Education and Research Kolkata, India	First reviewer on <b>March 26<sup>th</sup> 2021</b>	Accepted after major Change
	Dr. Kousiki Chakrabarti	HOD &Assistant Professor Zoology, Calcutta University, India	Second reviewer on <b>March 29<sup>th</sup> 2021</b>	Accepted after major Change
	Prof. Dr. Asok Ghosh	Professor, Sports Science RKMV University, Kolkata, India	Final reviewer on <b>June 13<sup>th</sup> 2021</b>	Accepted for publication on <b>28<sup>th</sup> of September 2021</b>
Article ID	Reviewer	Affiliation	Assigned as	Decision
<b>MS-BD50-Res- Exp. Neuro- Rehab Sc-4</b>	Dr. Debashish Chowdhury	Sport Physician and Asst. Gen. Manager, Bangladesh Cricket Board, Dhaka, Bangladesh	First reviewer on <b>March 25<sup>th</sup> 2021</b>	Accepted with minor change
	Asso. Prof. Dr. Santanu Dutta	Associate Professor, Dept. of CTVS, Inst. of PG Medical Education and Research Kolkata, India	Second reviewer on <b>March 25<sup>th</sup> 2021</b>	Accepted after major Change
	Prof. Dr. Asok Ghosh	Professor, Sports Science RKMV University, Kolkata, India	Final reviewer on <b>June 15<sup>th</sup> 2021</b>	Accepted for publication on <b>29<sup>th</sup> of September 2021</b>
Article ID	Reviewer	Affiliation	Assigned as	Decision
<b>MS-BD50-Res- Exp. Neuro- Rehab Sc-5</b>	Dr. Satyapriya De Sarkar	Gastroenterologist G D Hospital & Diabetes Institute Kolkata, India	First reviewer on <b>March 11<sup>th</sup> 2021</b>	Accepted with moderate level of revision
	Dr. Dilsad Ahmed	Research Coordinator University of Macau, Macau, Guangdong, China	Second reviewer on <b>March 24<sup>th</sup> 2021</b>	Accepted with minor change
	Prof. Dr. Asok Ghosh	Professor, Sports Science RKMV University, Kolkata, India	Final reviewer on <b>May 20<sup>th</sup> 2021</b>	Accepted for publication on <b>29<sup>th</sup> of September 2021</b>

### Finalised by the Guest Editors

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