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Original Research Article

Mild auditory cognitive impairment in mid trimester pregnancy

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Abstract

We aimed to investigate auditory cognitive and behavioral functions during mid trimester pregnancy using Event-Related Potentials (ERPs) and neuropsychological tests, respectively. ERPs were studied by using 128-sensor net and PAS, WCST, RAVLTIM, RAVLTDR and RAVLTTS were tested for neuropsychology assessment. Total 18 subjects were recruited (n=9 in each group; control and pregnant group; 16-27 weeks). Auditory oddball paradigm was used during ERP study. Subjects counted silently only target stimuli with giving attention by ignoring standard stimuli. Value of the mean differences of the target and standard stimuli were measured across groups in six locations. The N100 and The P300 ERP components were recorded at T3, T4, T5, T6, Cz and Pz electrode sites. Higher amplitudes (4/6) and prolonged latencies (4/6) of the N100 component were found. Shorter amplitudes (1/6) and longer latencies (3/6) of the P300 component were found in the pregnant group compared to the control group. No significant difference in scores of PAS, WCST, RAVLTDR and RAVLTTS among both groups. Significantly higher RAVLTIM was observed in pregnant group. We concluded that there is mild auditory cognitive impairment during second trimester pregnancy without any deficit in executive function and auditory memory.

Keywords: Auditory cognition, Pregnancy, Standard stimuli, Target stimuli

INTRODUCTION

In cognitive science, visuospatial attention is the vital for the executive function and this visuospecial attention would be developed when audiospecial attention will work well (Smith *et al*., 2009; Wu *et al*., 2007). Audiospatial attention functionally overlaps with the brain part which is responsible for the visual attention (Smith *et al*., 2009; Wu *et al*., 2007). Then we assume that the auditory attention is important before visual attention mainly to build up the executive function. To seek any auditory dysfunction during pregnancy period is important as during pregnant condition women needs a plan to maintain their health condition properly and take care of child perfectly later on. Directed attention (DA) which needs more mental effort as these types of attention is important but not interesting in our daily life (Cimprich *et al.,* 1995). To balance various demands like maintaining families, careers, social responsibilities, relationships, and preparing for a life transition (Stark *et al*., 2000, 2001), prenatal care and preparation, pregnant women need DA, which may fatigue for them. On that case, memory and learning looks deteriorate during pregnancy (Shetty *et al*., 2002). Though pregnancy is a normal physiological condition, there are huge fluctuations of steroid hormones. Gonadal steroid hormones like estrogen, progesterone and testosterone can affect on behavior and change of neuronal activity (McEwen *et al*., 2002; Pfaff *et al*., 2005) and pregnancy can influence also cognitive functions (Bromberger *et al*., 2011; McEwen *et al*., 2012). A lots of review literature told that dramatic changes of hormone during pregnancy can

decrease cognitive functions in case of memory, attention, mood alteration, learning etc (Poser *et al*., 1986; Buckwalter *et al*., 1999). At the same time for discussion, depression and anxiety are common in women (Soares *et al*., 2008) and these symptoms of depression and anxiety can be aggravated during pregnancy (Henry *et al*., 2007; Crawley *et al*., 2008). There are studies on hormonal changes leading to mood disorder during premenstrual period (Rapkin *et al*., 2012), postpartum (O'Hara *et al*., 2009) and menopause (Freeman *et al*., 2010), though there is little investigation during pregnancy. Other research focused on mainly third trimester of pregnancy (Raj *et al*., 2014). But early assessment of cognitive dysfunction during pregnancy in first and second trimester is necessary to improve their cognitive function immediately with proper treatment and therapy. Therefore this research makes a focus to assess the auditory cognitive function during second trimester of pregnancy by the even related potential (ERP) study which is reflection of neuronal change and neuropsychology tests to seek the changes on the executive function and auditory attention and memory.

METHODS

Subjects

Total eighteen (18), education and age matched, paid volunteers were recruited with mean age±STD, 27.49±4.28 yrs (control group) and 27.19±3.00 yrs (pregnant group), without any neurological disturbances and drug history. Pregnant group took only vitamins. The subjects in the pregnant group were in 16- 27 weeks gestation (mid trimester) and the control group was non pregnant healthy females (n=9 in each group). Written informed consent was obtained from all subjects prior to testing. This study was approved by the Human Ethical Committee of Universiti Sains Malaysia (USM). ERPs were recorded in the Laboratory for MEG and ERP studies, Department of Neurosciences, Universiti Sains Malaysia (USM) by using a 128-electrode sensor net.

ERP procedure

For the presentation of stimuli, timing operations, and data collection, E-prime v 2.0 software (Psychology Software Tools, Inc, Sharpsburg, Pennsylvania, USA) was used. Each subject with head phone was comfortably seated in dimly lit, electrically shielded and sound treated room with wearing 128-sensor net. The N100 and the P300 ERP amplitudes and latencies were measured using the "auditory oddball paradigm". In this paradigm, subjects were asked to count silently target tones 60 dB sound pressure level (SPL) which were low frequency (20%) and high pitched (2000 Hz) presented binaurally, while ignoring standard tones 60 dB SPL, high frequency (80%) and low pitched (1000 Hz). Tone duration was 100 ms with a rise/fall time of 10 ms.

We used T3, T4, T5, T6, Cz and Pz areas for analysis as the N100 and the P300 ERP components reflects on these areas during auditory tasks. ERP data was filtered with low pass 30Hz and high pass 0.3Hz and sampling rate was 250 Hz.

Neuropsychology tests

PAS or COWA (controlled Oral Word Association) and WCST (Wisconsin Card Sorting Test) were done to assess executive functions and Rey Auditory Verbal and Learning Test: immediate or interference recall (RAVLT IM), delayed recall (RAVLT DR) and total score (RAVLT TS) (Rey *et al*., 1964) were tested for auditory memory assessment of both groups.

Data Analysis and Statistics

The values of the mean differences of target and standard stimuli were calculated for the amplitudes and the latencies of all the ERP components by Net-station software 5.2 (Electrical Geodesics, Inc., Eugene, OR, USA). Data was segmented as (-50-800) ms, baseline was corrected with 100 ms before the stimulation. Eye blink, eye movement and movement artifacts were detected and removed with artifact detection tools in Net Station software. As the sample size were small (9 per group), all data from both the ERP and the neuropsychology tests were analyzed with non-parametric Mann-Whitney U tests using SPSS-22 software to see significance level between groups, where P value was determined as *p<.05, **p<.01, ***p<.001.

RESULTS

With less than 3.0 % detection error, all subjects achieved well to detect the target stimuli. Figure 1 represented grand average waveform of the N100 and the P300 ERP components comparing the auditory responses within control and pregnant groups at T3, T4, T5, T6, Cz and Pz areas. Table 1 and 2 show the values of mean differences between target and standard stimuli among groups. Mann-Whitney test revealed that significant (T3, P=0.001) and non-significant (T6, Cz, Pz) shorter amplitudes of the N100 component were evoked in the pregnant group compared to the control group. Other two electrodes (T4, T5) showed non-significant higher amplitudes of the N100 component in the pregnant group (Table 1). Non-significant longer latencies of the N100 component were observed at most (T4, T5, Cz, Pz) sites in the pregnant group compared to the control group

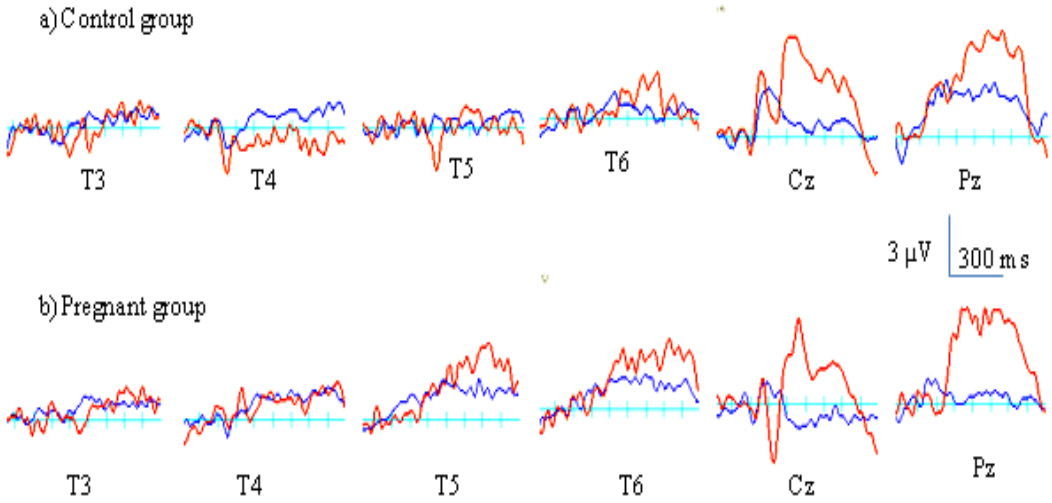

Figure 1. Grand average waveform of the N100 and the P300 ERP components during target and standard stimuli within control (a) and pregnant (b) groups at T3, T4, T5, T6, Cz and Pz locations (n=9 in each group). Standard stimuli (blue color) and target stimuli (red color).

Table 1. The mean differences of amplitudes and latencies of the N100 ERP component between control and pregnant groups.

N100ERP	Electrode sites	Control Group	Pregnant Group	P Value
Amplitude in µV (mean ± SD)	T3	1.30 ± 1.39	0.25 ±0.40	0.001
	T4	0.48 ±0.95	1.02 ±0.48	NS
	T5	1.24 ± 1.04	1.31 ±1.00	NS
	T6	1.15 ± 1.01	1.05 ±0.95	NS
	Cz	1.47 ± 1.08	0.88 ±0.59	NS
	Pz	1.25 ± 1.10	1.15 ±0.70	NS
Latency in ms (mean ± SD)	T3	128.00 ± 20.59	119.56 ± 25.10	NS
	T4	117.33 ± 25.92	125.833± 26.38	NS
	T5	115.11 ± 29.51	125.79 ± 25.62	NS
	T6	117.79 ± 22.37	112.44 ± 27.38	NS
	Cz	92.00 ± 7.48	109.33 ± 31.18	NS
	Pz	105.33 ± 25.06	125.79 ± 30.21	NS

where other two electrodes (T3, T6) showed shorter latencies of the N100 component (Table 1). The P300 amplitudes and latencies were not significant between groups across the all areas except significantly larger latency at T5 area (P= 0.02) in pregnant group compared to the control group (Table 2). Non-significant higher amplitudes of the P300 ERP component were found at T4, T5, T6, Cz and Pz areas where only one site showed non-significant smaller amplitude of the P300 in pregnant group compared to the control group (Table 2). In case of the P300 latency, equal number of electrode positions evoked longer latencies (significant at T5, P=0.02 and non-significant at T3, T6) and shorter latencies (non-significant at T4, Cz, Pz) of the P300 component in pregnant group compared to the control group (Table 2). Neuropsychology test results were shown among the two groups in Figure 2 and Table 3. PAS (P=0.45) and WCST (P=0.19) scores were not significantly difference among groups. Auditory memory test, RAVLT test results revealed that RAVLTIM (immediate memory) was significantly (P=0.03) higher in the pregnant group compared to the control group. Other two tests

Table 2. Shows the mean differences of amplitudes and latencies of the P300 ERP component between control and pregnant groups.

P300ERP	Electrode sites	Control Group	Pregnant Group	P Value
Amplitude in µV (mean ± SD)	T3	2.39 ± 3.84	1.54 ±0.87	NS
	T4	1.06 ±1.60	1.92 ±1.09	NS
	T5	2.78 ± 1.22	3.13 ±2.15	NS
	T6	3.07 ± 1.98	3.30 ±1.10	NS
	Cz	4.93 ± 3.11	5.64 ±2.18	NS
	Pz	5.65 ± 3.70	6.15 ±2.25	NS
Latency in ms (mean ± SD)	T3	569.33 ±262.27	674.67 ±93.53	NS
	T4	535.11 ±155.91	526.67 ±189.88	NS
	T5	505.79 ±124.84	645.78 ±86.23	0.02
	T6	560.00 ±109.20	564.44 ±163.37	NS
	Cz	430.67 ±160.81	404.89 ±123.72	NS
	Pz	526.22 ±151.86	485.33 ±140.07	NS

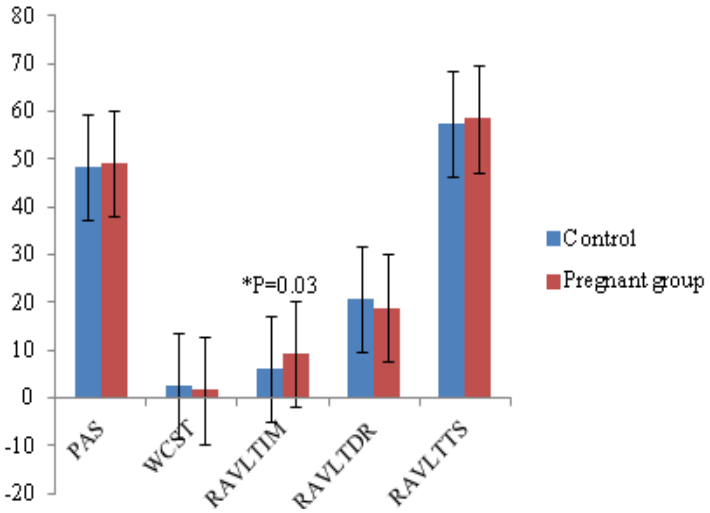

Figure 2. Bar graph shows different neuropsychology test scores among control and pregnant groups. 'I' symbol indicates error bar with standard error.

Table 3. Value of different neuropsychology test scores was shown among control and pregnant groups.

Groups	PAS	WCST	RAVLTIM	RAVLTDR	RAVLTTS
Control group	48.25 ± 8.41	2.5 ± 1.85	6.13 ± 3.36	20.88 ± 6.00	57.25 ± 15.64
Pregnant group	49.13 ± 16.63	1.63 ± 2.00	9.25 ± 2.92 *	18.88 ± 16.09	58.5 ± 17.72

(RAVLTDR: delay memory, P=0.37 and RAVLTTS: total score, P=0.44) were not significantly different among the two groups (Figure 2, Table 3).

DISCUSSION

We studied the amplitudes and the latencies of the N100

and the P300 ERP components which are the reflection of the auditory perception and the attention, respectively, evoked by the auditory oddball paradigm and at the same time neuropsychology tests (PAS, WCST, RAVLTTS, RAVLTIM and RAVLTDR) were done among the healthy control and the pregnant groups (2^{nd} trimester) to assess the executive function and the auditory memory function. The shorter amplitudes (4/6) and the prolonged latencies (4/6) of the N100 ERP component were found in the pregnant group compared to the control group. The shorter amplitude (1/6) and the longer latencies (3/6) of the P300 component were found in the pregnant group compared to the control group. PAS, WCST, RAVLTDR and RAVLTTS scores were not significant among both groups. RAVLTIM score was significantly higher in pregnant group compared to the control group.

The recruitment of neural resources is important to assess attention deficit among the pregnant women. On this aspect the ERP has a great role to assess the attention via assessment of the amplitude and the latency of different ERP components. There are not so many studies on pregnancy using the ERP to reveal the cognitive deficit. Visual attention/cognitive function were investigated once with visual oddball task with different faces and shapes among pregnant women (Raj *et al*., 2014). In their study they used pregnant women with third trimester. In this oddball task they find out pregnant group working poorer than control with smaller amplitude of the P300 ERP component. In our study we performed auditory oddball task with the standard and the target stimuli to assess the auditory perception and attention among the second trimester pregnant women and we analyzed the amplitudes and latencies of the N100 and the P300 ERP component as an indicator of the auditory perception and auditory attention, respectively (Spench *et al*., 2010). Increased amplitudes and larger latencies of the perceptual components like the P50 and the N100 components is the meaning of the mild impairment (Golob *et al*., 2007). On that basis we say that our pregnant group had mild perceptual impairment as this group evoked the increased amplitudes and prolonged latencies of the N100 ERP component in few sites also not all sites (Table 1). The shorter amplitudes and prolonged latency of the P300 ERP component indicated lack of attention (Ford *et al*., 1996; Unsal *et al*., 1995). Our results regarding the P300 component proved that the pregnant group had mild cognitive impairment as only one site (out of six) had the shorter amplitudes and three sites (out of six) reflected longer latencies of the P300 component (Table 2)

There are lots of studies to assess memory and attention during pregnancy mainly in third trimester with different neuropsychology tests. Memory testing during pregnancy was done previously (Henry *et al*., 2007; Crawley *et al*., 2008; Macbeth *et al*., 2010), and mainly the memory impairment find out during last trimester (Rendell *et al*., 2008). Some researchers investigated attention during pregnancy where the results were controversial with attention deficit (de Groot *et al*., 2003) and no changes of attention (Crawley et al., 2003). Some general memory and attention tasks were done in previous studies to assess attention. But in our study we specially used RAVLT (RAVLTIM, RAVLTDR and RAVLTTS) test where subjects need only auditory attention with memory and for executive function assessment we used PAS and WCST. We find out that there were no significant changes between the groups in PAS, WCST, RAVLTDR and RAVLTTS tests (Fig 2, Table 3). In case of RAVLTDR and RAVLTTS, our results are consistent with Christensen et al (2010) who reported California Verbal Learning Test (which is almost similar test of RAVLT) among pregnant group and found no significant auditory memory impairment among them, but this study did not mention about group of trimester (Christensen *et al*., 2010). In our study, we found significantly higher score during RAVLTIM in pregnant group compared to the control group which meant that pregnant group had improved immediate auditory memory and for the other two (RAVLTDR and RAVLTS) tests results indicated that our pregnant group had no auditory memory impairment compared to the control group (Table 3). Onyper et al., 2010 used PAS and WCST to assess executive function among pregnant women. This study found significant changes in PAS (COWAT) but no significant changes in WCST (Onyper *et al*., 2010). Therefore Onyper research (2010) concluded that the executive function in pregnant group is mild. Our pregnant group did not show any executive dysfunction (not even mild) as no significant changes in score of PAS and WCST tests (Table 3).

The decline or no change of cognitive function in pregnant group depends on many factors. Addiction (Thomas et al., 2010), education (Begum et al., 2014), economical condition, environmental condition may reflect to cognitive function. All pregnant women in our study were well educated without any addiction and they were all working in hospital area with responsible position (nurse, research assistant etc.). Then we assume that these present pregnant group showed mild auditory cognitive function impairment due to change of hormonal imbalance. We need further study to clarify the effect of various factors on cognition during pregnancy.

CONCLUSION

The results of the current study of auditory oddball tasks using the ERP study support that there are mild auditory cognitive function impairment among pregnant women in second trimester. And neuropsychology tests results support that the pregnant group has no impairment of executive function and auditory memory. To our knowledge, this is the first ERP study to examine auditory attention with auditory oddball task among pregnant

women with neuropsychology tests. The present study emphasizes the value of the ERP methodology and neuropsychology tests in together as a sensitive measure for the assessment of cognitive function in the research field of pregnancy.

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