P300 Event-Related Potentials in Normal-Hearing Adults With Type 2 Diabetes Mellitus

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Abstract

Background: P300 event-related potentials can be used to measure auditory processing speed, working memory, and attention.

Purpose: The purpose of the study was to compare P300 event-related potentials in normal-hearing adults with those of adults with Type II diabetes mellitus.

Research Design: A two-group (with diabetes and controls) comparative study (age- and sex-matched) with a nonprobability sampling method was used.

Study Sample: Sixty-four adult participants (32 with diabetes, 32 without diabetes) between the ages of 23 and 60 years participated.

Data Collection and Analysis: Pure-tone audiometry was performed to ensure participants had pure-tone averages of ≤ 25 dB HL. Folstein Mini-Mental State Examinations were conducted, which ensured absence of cognitive impairment. Blood glucose levels were measured immediately prior to P300 testing, after which amplitude and latency results were captured. Descriptive analysis was used to calculate mean, standard deviation, median, and 25th and 75th percentiles. To study differences between adults with and without diabetes as well as the effect of glucose, linear mixed-model regression analyses were performed when left and right ears were combined, and simple linear regression analyses were performed when left and right ears were analyzed separately.

Results: For P300 latency results, a significant statistical difference ($p < .001$) was observed between participants with and without diabetes (352.46 ms, $SD = 36.36$; 314.09 ms, $SD = 32.08$), respectively. A significant statistical difference ($p < .001$) in amplitude was observed between participants with and without diabetes, respectively (12.10 μV, $SD = 3.70$; 15.08 μV, $SD = 2.82$). Glucose was a key moderator of only amplitude after adjusting for diabetes status. Glucose had no effect on amplitude and latency for adults without Type II diabetes mellitus (DM).

Conclusions: Type II DM decreases amplitude and increases latency; in addition, adults with Type II DM, attention, and working memory, as denoted by P300 amplitude, may deteriorate with increased glucose levels on the day of testing.

Interest on the impact of diabetes mellitus (DM) on cognitive function is increasing as the incidence of DM has increased in recent years due to an increase in longevity, urbanization, obesity, and changes in the lifestyle of the population (Andreadou et al., 2012; International Diabetes Federation, 2017). Recently, it was estimated that, in Africa, there are 14.7 million individuals who have DM, the majority of which are diagnosed with Type II DM (International Diabetes Federation, 2017).

Type II DM is caused by an inadequate compensatory insulin secretory response and a resistance to insulin action (Wrighten et al., 2008). Type II DM affects the sensory systems, which damages cognitive processes such as information processing speed, general intelligence, psychomotor efficiency, learning, verbal and working memory, attention, executive function, and delayed and immediate recall (Hazari et al., 2015; Hissa et al., 2002; Wrighten et al., 2008). A neurophysiological test that can be used to determine the degree to which processing speed, executive function, and memory are reduced by Type II DM is the P300 event-related potential (Wrighten et al., 2008). P300 is a far-field noninvasive late cortical neurophysiological technique that is based on an "oddball" paradigm during which a response is elicited when the participant attends to and detects a change in stimulus in a sequence of standard stimuli (frequent), from the other (infrequent) stimuli (Andreadou et al., 2012; Lombard, 2005). The P300 reflects information processing that is associated with memory and attention mechanisms and is dependent on internal cognitive processes (Somani & Shukla, 2014). The latency (240–400 ms) component indicates the speed of processing, and amplitude (8–15 μV) demonstrates attentional ability (Lombard, 2005; McPherson, 1996). The known neural generators of the P300 are said to be the hippocampus, thalamus, inferior parietal lobe, temporal lobe, dorsolateral prefrontal cortex, cingulate cortex, and amygdala (Lombard, 2005; McPherson, 1996; Somani & Shukla, 2014).

The hippocampus, in particular, is said to be affected by Type II DM, resulting in slower processing of auditory information (Sadeghi et al., 2016). This occurs due to rearrangement and changes to the electrophysiological properties of the hippocampal neurons and reductions in functional connectivity of the hippocampus as a result of insufficient insulin availability and/or dysfunctional glucose regulation (Wrighten et al., 2008; Zhou et al., 2010). Previous studies found that P300 latencies were increased and amplitudes decreased in individuals diagnosed with Type II DM (Alvarenga et al., 2005; Andreadou et al., 2012; Chen et al., 2003; Hamed et al., 2013; Hissa et al., 2002; Kurita et al., 1996; Mochizuki et al., 1998; Singh et al., 2013; Tandon et al., 1999). This increase in latencies and decrease in amplitudes indicates that Type II DM results in delayed auditory temporal processing (Alvarenga et al., 2005).

It was found that Type II DM leads to an increase in latency and a decrease in the amplitude of the P300 event-related potential (Alvarenga et al., 2005; Andreadou et al., 2012; Hazari et al., 2015; Hissa et al., 2002; Kurita et al., 1996; Singh et al., 2013). Two of the six studies included participants up to the age of 65 years (Hazari et al., 2015; Kurita et al., 1996). The remaining studies included participants of 70 years of age and older in their study population (Alvarenga et al., 2005; Andreadou et al., 2012; Hissa et al., 2002; Singh et al., 2013). In the studies conducted by Andreadou et al. (2012), Hazari et al. (2015), Kurita et al. (1996), and Singh et al. (2013), the experimental and control groups were matched by age and gender. Only Alvarenga et al. (2005) stated that they matched their experimental and control groups by gender, age, and hearing loss, whereas Hissa et al. (2002) only matched their experimental and control groups by age. P300 event-related potential is influenced by an increase in age leading to an increase in the latency and a decrease in the amplitude (Bourisly, 2016;

Dinteren et al., 2014; Tsolaki et al., 2015). As increasing age (range: 56–60 years) causes this aforementioned effect on the P300, it is not clear whether the results obtained from Alvarenga et al. (2005), Andreadou et al. (2002), Hissa et al. (2002), and Singh et al. (2013) were from Type II DM and/or the participants' age as the researchers used participants above the age of 60 years.

In addition to age, individuals with a sensorineural and peripheral hearing loss presented with P300 waves with smaller amplitudes and longer latencies, yet several studies did not control for hearing loss (Reis et al., 2015; Reis & Iorio, 2007). Alvarenga et al. (2005) and Hissa et al. (2002) did perform standard audiometric testing, but the researchers still included participants in the research studies who presented with a hearing loss. Participants did undergo standard audiometric testing, but again, researchers did not indicate whether they excluded participants that presented with a hearing loss (Hamed et al., 2013). Tandon et al. (1999) did not indicate whether they excluded participants if they had a hearing impairment or not. Kurita et al. (1996) indicated that they excluded individuals with a hearing impairment on the basis of lack of response to P300 stimuli at 70 dB. This suggests that participants with a mild-to-moderate loss were still included; however, the researchers did not do formal audiometric testing but ensured that stimuli were audible for P300 testing. Hazari et al. (2015) mentioned that they excluded participants with auditory disorders in their research study, but the researchers did not mention whether they excluded individuals with hearing impairments. Although there appears to be a consensus that P300 is associated with increased latency and decreased amplitude in adults with Type II DM, only Andreadou et al. (2012) and Singh et al. (2013) controlled for hearing loss, but researchers included participants above the age of 70 years.

Thus, it is not clear whether Type II DM, advanced age, or the hearing impairment caused the increase in P300 latencies and decrease in amplitudes reported in previous research. The current research project, therefore, aimed to compare P300 event-related potentials in normal-hearing adults with Type II DM with age-matched normal-hearing adults without Type II DM.

Method

Participants

This study was conducted at diabetes clinics at a tertiary institution and at two private clinics. Ethical clearance was obtained from the Faculty of Health Sciences Research Ethics Committee (Protocol No. 40/2018) and the Faculty of Humanities Research Ethics Committee (Reference No. 14064066; GW20180202HS).

All the participants received and signed the informed consent letter to participate in the study. Participants were required to have mean hearing thresholds with a three-frequency pure-tone average of ≤ 25 dB HL at 500, 1000, and 2000 Hz and a score above 26 for the Folstein Mini-Mental State Examination. Participants with known chronic alcohol and/or smoke abuse, medication use such as sedatives and/or antidepressants, recent infectious diseases, psychiatric disorders, traumatic brain injury, middle ear pathology and/or hearing loss, neurological involvement, and cognitive impairment, which might influence the P300 results, were excluded from the study. No research participants were excluded from the study based on the exclusion criteria.

The study comprised 64 participants where 32 participants (M = 47.4, SD = 10.2) had been diagnosed with Type II DM. Participants ranged from 23 to 60 years of age (17 women, 53.13%), and 32 nondiabetic participants matched by age (M = 47.6, SD = 9.8) and sex. A power analysis indicated a minimum sample size of 30 participants in each group, which allowed for the detection of differences between 1 and 0.5 SD with 80% power and alpha set at .05. It also ensured the detection of a difference in proportions of 20% or more. Participants with Type II DM presented with a mean disease duration of 8.23 years (SD = 7.50, range: 2.25–23 years) since diagnosis by a medical practitioner. All the participants diagnosed with Type II DM made use of metformin to control their diabetes along with dietary changes, and none was insulin dependent. Any participants with comorbid disorders, such as heart disease, stroke, kidney disease, blindness, autonomic and peripheral neuropathy, cognitive decline, and loss of limbs, were excluded from the study.

Blood glucose measurements were done on the day of testing using the Bayer's Contour TS blood glucose meter. The mean blood glucose was 8.23 mmol/L (SD = 4.20) for participants with diabetes and 5.78 mmol/L (SD = 1.25) for participants without diabetes.

Participants were examined using the Folstein Mini-Mental State Examination, which is a brief 30-point neuropsychometric test for cognitive functions that reflects memory, orientation, attention, ability to follow written and verbal commands, copying, and writing (Folstein et al., 1975). All participants obtained a score of 26 or higher (maximum = 30) and were included in the study and showed no cognitive impairment; the mean score was similar for both groups (diabetic: 29.69, SD = 0.93; nondiabetic: 29.94, SD = 0.25).

Audiological Assessment

Pure-tone audiometry and immittance measurements were conducted using the Interacoustics (AT 235) audiometer. Air-conduction pure-tone thresholds from 125 to 8000 Hz were conducted. All participants were required to present with a three-frequency pure-tone average of ≤ 25 dB HL at 500, 1000, and 2000 Hz, with Type A tympanograms and present ipsilateral (500–4000 Hz) reflexes at all the specified frequencies (Helleman & Dreschler, 2015). Participants presented with mean pure-tone average thresholds of 10.05 dB HL for the diabetic (SD = 5.34) and 11.72 dB HL for the nondiabetic (SD = 5.80) groups. A three- rather than four-frequency pure-tone average was selected due to mean age typically reported of adults who presented with Type II DM (Helleman & Dreschler, 2015). The increased mean age in adults with Type II DM means that several potential participants may present with initial audiometric symptoms of presbycusis and, consequently, elevated high-frequency hearing thresholds. There were 46 ears out of 128 who had 4000 or 8000 Hz behavioral pure-tone thresholds of ≥ 25 dB; thus, there were no relationship between this category and latency (p = .220) or amplitude (p = .500).

No asymmetries between the two ears for all participants were present as defined as a difference of 15 dB HL between the left and right ears at three contiguous frequencies (Djalilian, 2017). Figure 1 shows the mean behavioral pure-tone thresholds across the frequency range for both groups.

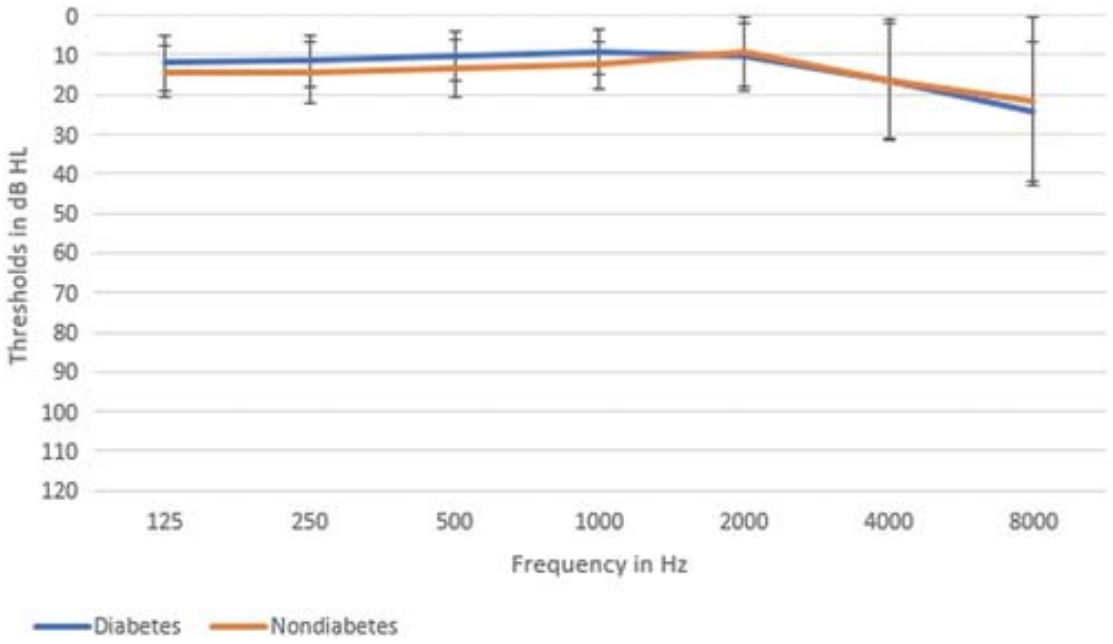

Figure 1. Mean behavioral pure-tone thresholds for participant groups with (n = 64 ears) and without Type II diabetes (n = 64 ears).

P300 Event-Related Potential

The Eclipse Interacoustics AEP system was used to elicit the P300 event-related potential. The AEP system was calibrated as specified in ISO 389-6-2007 before data collection commenced using ppeSPL (peak-to-peak equivalent sound pressure level) and nHL (normal hearing level; Interacoustics, 2017). Calibration was done using an oscilloscope and measured in dB ppeSPL, resulting in stimuli being reported in dB nHL. Testing was performed in a quiet room, with participants in a reclining and comfortable position with eyes open but downcast to minimize eye movements. Electrode sites were cleaned using NuPrep skin prep gel and pasted with Ten20 conductive paste to ensure impedances were kept below 5 kΩ and the difference between the two electrodes did not exceed 2 kΩ (Mohammadkhani et al., 2013). Two-channel recording was undertaken with the inverting (reference) electrode placed on the left and right mastoids, the noninverting electrode (active) placed on Fz (high forehead; Hall, 2007), and the ground electrode placed on the Fpz (low forehead; Mohammadkhani et al., 2013). Although simultaneous recording at multiple electrode sites is often recommended, the comparative research design did not include source analysis, nor did it aim to describe any developmental changes (Picton et al., 2000). The clinical two-channel electrode montage was therefore deemed sufficient for the aim of the project. Stimuli were delivered through ER-3A insert earphones. Tone burst stimuli of 1000 Hz for the frequent stimulus and 2000 Hz for the rare stimulus were used with a 20% likelihood occurrence of the infrequent target stimulus (Mohammadkhani et al., 2013). Stimuli were presented at 75 dB nHL at 0.6/s with a rarefaction polarity. A bandpass filter of 0.1–100 Hz was used for response acquisition, and the artifact rejection level was set at ± 80 μV. Analysis time of 1,000 ms and prestimulus time of 100 ms were used. A total of 240 stimuli, of which 20% were the infrequent stimulus, were presented into each ear of participants. A minimum of three traces were averaged together per ear (Zukerman et al., 2007). The largest peak was defined as the P300 wave that occurred between 240 and 400 ms following stimulus onset, of which the trough was marked at the largest negative deflection within 50 ms of the P300.

Any trials contaminated with eye blinks were excluded from averaging and additional trials completed. Participants were instructed to count the number of rare stimuli. P300 waves were marked from peak to trough (McPherson, 1996).

Statistical Analysis

For this research study, descriptive analysis was used to calculate the mean and standard deviation as well as the median and 25th and 75th percentiles of the P300 results using Stata 15, with a $p \leq .05$ recorded as statistically significant (StataCorp, 2017). In order to study the differences between adults with and without diabetes as well as the effect of glucose, linear mixed-model regression analyses were done when left and right ears were combined and simple linear regression were done when left and right ears were analyzed separately. Residual analyses were done to determine the distribution of the residuals and to detect outliers.

Results

Table 1 displays the mean and median latencies and amplitudes of participants with and without DM. In the mixed-model analyses, including random intercepts for pairs did not contribute to the model, and random intercepts were only kept for individuals (as left and right ears were combined on individuals). Since pairs were not significant in the mixed model, linear regression was used for the left and right analyses. Residual analysis identified one individual for latency and two for amplitude as outliers, and these were excluded from the analyses; their matched pairs were also excluded. Table 2 displays the comparison between DM and non-DM using either linear mixed models or just linear regression. Coefficients for interaction terms are not given only the *p* values. Figures 2 and 3 show examples of P300 waveforms for participants with normal hearing with no history of Type II DM and participants with Type II DM, respectively.

Table 1. P300 latencies and amplitudes with regard to mean, standard deviation, median, and interquartile range (IQR; 25, 75th percentiles), $N = 64$.

	Diabetes mellitus		Non–diabetes mellitus	
Variable	***M* (*SD*)**	***Mdn* (IQR)**	***M* (*SD*)**	***Mdn* (IQR)**
Amplitude	12.10 (3.70)	12.12 (9.50, 14.25)	15.08 (2.82)	14.93 (13.05, 17.05)
Latency	352.46 (36.36)	348.50 (330.50, 371.50)	314.09 (32.08)	313.50 (289.00, 332.00)

Note. N = total number of participants.

Table 2. Effect of diabetes mellitus and glucose on amplitude and latency.

Variable	Effect of diabetes mellitus alone	Effect of glucose alone	Effect of diabetes mellitus after adjusted for glucose	Effect of glucose after adjusted for diabetes mellitus status
Amplitude				
Both ears				
Coefficient	−3.26	−0.27	−3.04	−0.09
SE	0.59	0.11	0.63	0.10
p value	.001*	.013*	.001*	.342
Left ear				
Coefficient	−3.70	−0.28	−3.51	−0.08
SE	0.74	0.13	0.80	0.12
p value	.001*	.036*	.001*	.526
Right ear				
Coefficient	−3.15	−0.26	−2.91	−0.10
SE	0.77	0.13	0.84	0.13
p value	.001*	.045*	.001*	.448
Latency				
Both ears				
Coefficient	34.43	0.90	37.23	−1.32
SE	5.48	1.12	6.37	0.98
p value	.001*	.423	.001*	.176
Left ear				
Coefficient	32.81	0.50	36.93	−1.63
SE	7.85	1.35	8.45	1.28
p value	.001*	.711	.001*	.206
Right ear				
Coefficient	36.06	1.14	38.85	−1.11
SE	7.73	1.35	8.38	1.27
p value	.001*	.403	.001*	.386

*Statistical significance.

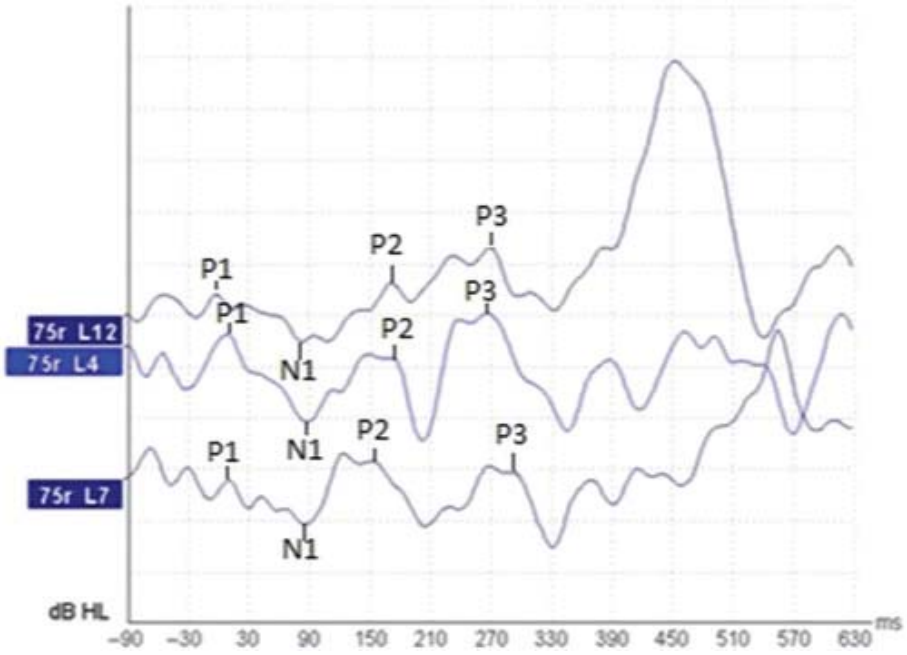

Figure 2. Examples of P300 waveforms for participants with normal hearing with no history of Type II diabetes mellitus. From the figure, it can be seen that the P300 waves occur before 330 ms when comparing it to Figure 3 when the P300 waveform occurs only from 330 ms and later when diagnosed with Type II diabetes mellitus.

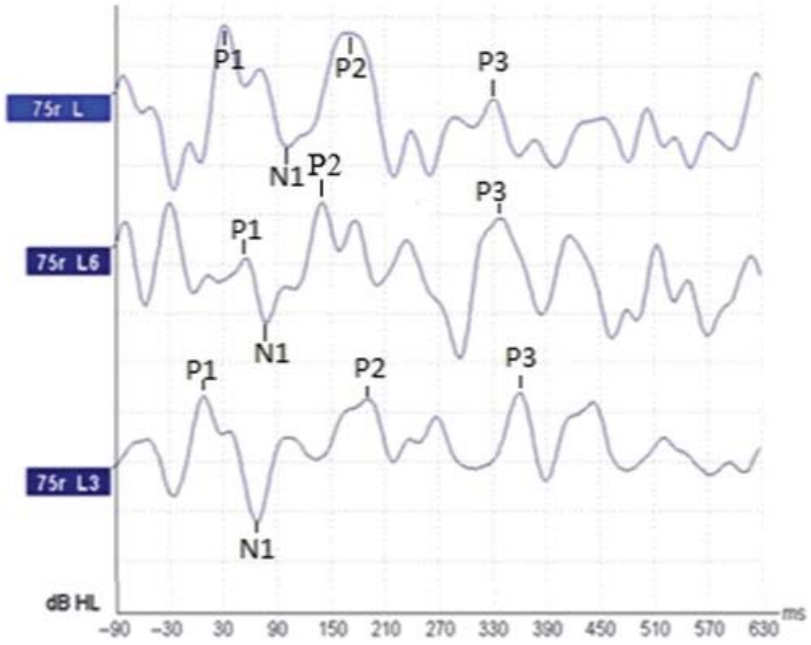

Figure 3. Examples of P300 waveforms for participants with Type II diabetes mellitus. From Figure 3, it can be seen that the P300 waves occur after 330 ms when having a history of Type II diabetes, where comparing it to Figure 2 when the P300 waveform occurs before 330 ms when having no history of Type II diabetes.

Table 1 displays that the mean amplitude was lower when compared between participants with Type II DM (12.10 μV, *SD* = 3.70) and participants without Type II DM (15.08 μV, *SD* = 2.82). Table 2 displays that there was a significant statistical effect of DM on amplitude ($p < .001$). The amplitude decreased by −3.26 μV for both ears and by −3.70 and −3.15 μV for the left and right ears, respectively, for the participants with diabetes compared to the participants without diabetes.

There was a statistically significant effect of glucose on amplitude ($p = .013$). For every 1 mmol/L increase in glucose, the amplitude of participants with diabetes decreased with −0.27 μV for both ears. When calculated separately for left and right ears, the difference was also statistically significant. For the left and right ears, respectively, there was a decrease of −0.28 ($p = .036$) and −0.26 μV ($p = .045$) in amplitude with every 1 mmol/L increase in glucose.

The difference between the participant groups with and without diabetes was significant on amplitude after adjusting for glucose for both ears ($p < .001$) and for the left ($p < .001$) and right ($p < .001$) ears calculated separately. However, glucose had no significant effect on amplitude after adjusting for diabetes status for both ears ($p = .342$) and the left and right ears ($p = .526$, $p = .448$), respectively.

Table 1 displays that the mean latency was higher when compared between participants with Type II DM (352.46 ms, *SD* = 36.36) and participants without Type II DM (314.09 ms, *SD* = 32.08). Table 2 displays that there was a significant statistical effect of DM on latency ($p < .001$). Latency increased with 34.43 ms for both ears for the participants with diabetes compared to the participants without diabetes and with 32.81 ($p < .001$) and 36.06 ms ($p < .001$) for the left and right ears, respectively.

There was no statistically significant effect of glucose on latency. For every 1-mmol/L increase in glucose, latency increased by 0.90 ms for both ears ($p = .423$), and when calculated separately, the latency increased by 0.50 ms ($p = .711$) in the left ear and 1.14 ms ($p = .403$) in the right ear.

The difference between the participant groups with and without diabetes regarding latency was also significant after adjusting for glucose for both ears ($p < .001$) and for the left ($p < .001$) and right ($p < .001$) ears calculated separately. However, glucose had no significant effect on latency after adjusting for diabetes status for both ears ($p = .176$) and for the left and right ears ($p = .206$, $p = .386$, respectively).

For combined ($p = .350$, $p = .590$) as well as for left ($p = .387$, $p = .938$) and right ($p = .891$, $p = .591$) ears separately, the interaction terms between DM and glucose were assessed and were found not to be statistically significant for either amplitude or latency, respectively. Viewing the results in Table 2, the p values unadjusted for multiple testing are shown. If we use the Bonferroni correction for multiple testing, then the significant associations stay significant except where the p values were .036 (becomes .108) and .045 (becomes .135) for the left and right ear effect of glucose alone.

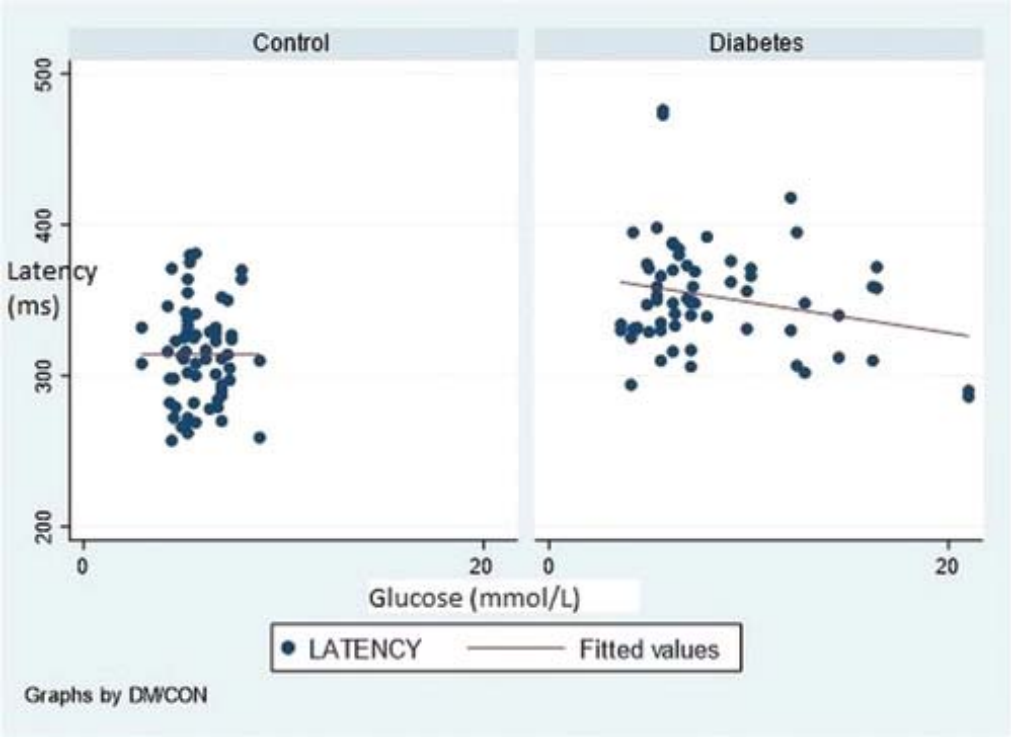

Figure 4. Effect of glucose levels (mmol/L) on P300 latency (ms) for the control and group with Type II diabetes mellitus.

As can be seen from Figures 4 and 5, with latency and amplitude, it does appear as if the relationship between glucose and latency and amplitude is different between controls and diabetes, but the interaction terms were not significant for latency ($p = .47$) and amplitude ($p = .41$), respectively. It is possible that the linear line could have been influenced by the extreme values above 20 mmol/L, and power may have been too low for the interaction term to be significant because of relatively low numbers.

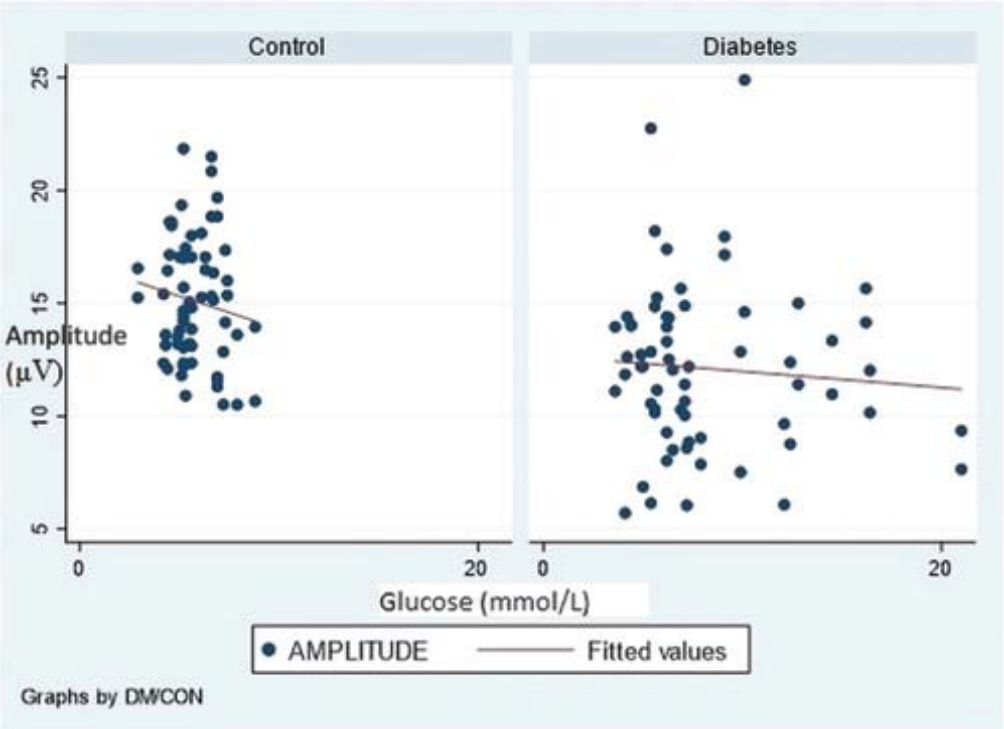

Figure 5. Effect of glucose levels (mmol/L) on P300 amplitude (μV) for the control and group with Type II diabetes mellitus.

Discussion

The current research study aimed to describe P300 event-related potentials in normal-hearing adults with Type II DM. This study reported that there was a significant decrease in P300 amplitude (12.10 μV, *SD* = 3.70) and increase in latency (352.46 ms, *SD* = 36.36) in adults with Type II DM, compared to their age- and sex-matched peers without Type II DM ($p <$ .001), which is in agreement with those reported in previous studies. Different studies conducted previously on adults with Type II DM have reported latencies and amplitudes ranging from 314.8 to 405.6 ms and 8.09 to 13.96 μV, respectively (Alvarenga et al., 2005; Andreadou et al., 2012; Chen et al., 2003; Hamed et al., 2013; Hissa et al., 2002; Kurita et al., 1996; Mochizuki et al., 1998; Singh et al., 2013; Tandon et al., 1999). However, the mean amplitude of the P300 in the current study was higher in comparison to the amplitude reported by Alvarenga et al. (2005; 1.98 μV) and Singh et al. (2013; 3.15 μV), and the mean latency was lower in comparison to that reported by Andreadou et al. (2012; 405.6 ms). This disparity in amplitude and latency with that of previous studies, despite similar participants, may be attributed to differences in the age of the participants. The P300 is influenced by advanced age (> 60 years), leading to an increased latency and a decrease in amplitude (Dinteren et al., 2014). The mean age of the participants in the studies by Alvarenga et al. (2005), Andreadou et al. (2012), Hamed et al. (2013), and Singh et al. (2013) was greater than 70 years of age, which may have further increased the latency and decreased the amplitudes reported in comparison to those of the current study, where the mean age of participants was 47.4 years.

The effect of DM was found to have a significant effect on the P300 for the total participant group. For the participant group with Type II DM, amplitude was significantly lower and

latency was significantly longer than for the participants without Type II DM. Glucose level on the day of testing did not influence latency of the P300. In contrast, glucose level was found to be a key moderator of amplitude. However, glucose had a significant effect on amplitude as a consequence of diabetes status. DM was found to have an effect on both amplitude and latency independently of the participant's glucose level as measured on the day of assessment. In addition, after adjusting for DM, glucose had no significant effect on P300 amplitude or latency. Previous research has not reported on the interaction of DM and glucose on the P300 in adults with or without Type II DM.

DM is therefore a significant confounding variable for both P300 amplitude and latency. Clinicians must be aware of the potential effects of DM on P300, and for those patients diagnosed with Type II DM, glucose level on the day will further moderate P300 amplitude. Within the adult group with Type II DM, the current study suggested that the amplitude of the P300 can be expected to decrease by 0.27 μV with every 1 mmol/L increase in glucose level. Glucose was not found to affect P300 amplitude and latency in adults without Type II DM.

The reported effect of Type II DM on amplitude and latency of P300 supports the assertion that cognitive functions such as working memory and attention, which are linked to amplitude of the P300 response, and auditory processing, as noted by the prolonged P300 latency, will be deleteriously affected due to the physiological changes as a result of acute hyperglycemia (Singh et al., 2013; Sommerfield et al., 2004).

No significant differences were found when comparing left and right ears for either the P300 latency or amplitude. This contradicts the late latency findings reported by both Bayazit et al. (2009) and Jerger and Martin (2004), which found that auditory stimuli was processed faster in the left hemisphere, which resulted in the so called “right-ear advantage,” something that is often referred to with regard to behavioral measures of temporal auditory processing (Bayazit et al., 2009; Jerger & Martin, 2004). Both studies made use of speech stimuli, however, in contrast to the tone bursts used in this study. Speech stimuli is known to be processed by Wernicke's area in the left hemisphere (Passer et al., 2009), and speech stimuli in the right hemisphere are subject to processing delay as stimuli must cross over to the left hemisphere via the corpus callosum (Jerger & Martin, 2004). The use of tonal midfrequency stimuli in this study, which is also relatively easier to distinguish compared to speech stimuli, may therefore explain the lack of asymmetry in left and right P300 waves. Further research comparing both objective and subjective measures of temporal processing, working memory, and attention in the left and right ears may corroborate the reason for the disparity of findings.

Limitations

The current study made use of a two-channel electrode montage used frequently in clinical settings. The P300 was measured from the Fz electrode rather than from Cz or Pz midline electrodes, which are known to yield larger amplitude responses (Najafi et al., 2017; Reis et al., 2016; Zukerman et al., 2007). However, the effect of choice of electrode montage was moderated by the study design, namely, between-groups comparisons using age and gender-matched controls; the age of the participants; and the lack of source analysis or developmental changes (Picton et al., 2000). Nevertheless, replication of the study with P300 waveforms measured from Cz or Pz (Najafi et al., 2017; Reis et al., 2016; Zukerman et al., 2007) is recommended.

Participants in the current study were required to present with a normal three-frequency pure-tone average while threshold of hearing at 4000 Hz was not required to fall within normal limits. The mean threshold of hearing of the diabetic and nondiabetic groups, respectively, was 10.05 dB (*SD* = 5.34) and 11.72 dB (*SD* = 5.80), which was higher than the mean reported for 500, 1000, and 2000 Hz. However, due to the choice of P300 rare and frequent stimulus frequency (2000 and 1000 Hz), the mean threshold of hearing at 4000 Hz is unlikely to have had an effect on P300 waveforms.

Blood glucose levels were measured immediately prior to P300 testing. However, it must be noted that the participants were not tested at the same time of day, nor was time of testing after eating controlled. Variation in glucose levels may therefore be attributed to these factors rather than be representative of their typical blood glucose on a given day. In addition, blood glucose was only measured prior to and not following data collection. Variability in glycemic levels during the assessment was therefore not monitored and may have further affected P300 waveforms. The duration of Type II DM was also not controlled because the duration of disease in some participants was longer than others. Participants with a longer duration of Type II DM might have presented with prolonged P300 latencies in relation to participants with a shorter duration of disease (Hazari et al., 2015). Future researchers may want to investigate how P300 latencies and amplitudes are affected in relation to disease duration, with the addition of continual monitoring of glucose levels during assessment. The latter may provide further elucidation on the effect of glycemic fluctuations on cognitive functions such as auditory temporal processing speed and attentional abilities. As Type II DM affects cognitive processes such as delayed and immediate recall and attention, future researchers might also want to measure behavioral accuracy and reaction time.

Conclusions

Individuals diagnosed with Type II DM with normal hearing had statistically reduced P300 amplitudes ($p < .001$) and increased latencies ($p < .001$) compared to the age- and sex-matched control group with no history of Type II DM. Blood glucose level immediately prior to testing was found to be a significant moderator of amplitude but not latency of P300, but this was determined by diabetes status. Clinicians, therefore, need to be aware that the diagnosis of Type II DM is a significant confounder of accurate interpretation of P300 amplitude and latency. Moreover, for those adults with Type II DM, attention and working memory, as denoted by P300 amplitude, may deteriorate with an increase in glucose levels and is susceptible to fluctuation with changes in glucose levels. The diagnosis of Type II DM in adults will have a negative impact on daily listening skills and attentional abilities.

Acknowledgments

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