The Effects of Type 1 Diabetes on Executive Functioning in Children Aged 6 to 10: An Event-Related Potential Study

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Bachelor of Arts in Psychology with Honours

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This thesis is presented in partial fulfillment of the requirements for the degree of Bachelor of Arts (Honours), Murdoch University, [2014]
I declare that this thesis is my own account of my research and contains its main content work, which has not previously been submitted for a degree at any tertiary educational institution.

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Signature:
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Full name of Degree: Bachelor of Arts in Psychology with Honours

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Year: 2014
Abstract

The relationship between Type 1 Diabetes Mellitus (T1DM) and cognition has received considerable attention and remains a controversial topic due to inconsistent findings regarding the effect T1DM has on cognition, including the domain of executive functioning. The current study aimed at examining the effect of T1DM on executive functioning in children using event-related potentials (ERPs) to determine if deficits in executive functioning are associated with the disease. Two ERP components associated with executive functioning – the N2 and P3b – were observed for differences between Type 1 diabetics and controls. A total of 97 children – 48 T1DM and 49 controls – between the ages of 6 and 10 participated in the current study. Participants performed a modified visual Flanker task while electroencephalograms (EEGs) were recorded. Both groups did not differ significantly in behavioral performance on the Flanker task. Significant differences were found posteriorly in an ERP component known as the late Positive Slow Wave (PSW), which is associated with sustaining attention in a task, between the T1DM and control groups in the incongruous and switch trials of the Flanker task. No significant differences were found in the N2 and P3b components. These results highlight that there are minimal differences in sustained attention between children with Type 1 diabetes compared to their healthy counterparts, but not in other domains of executive functioning. Directions for future research were discussed including the need to conduct a follow-up study on this sample of children, possibly in adulthood, to determine if longer disease duration has effects on executive functioning.

Keywords: Type 1 Diabetes, executive functioning, ERP, N2, P3b, children
The Effects of Type 1 Diabetes on Executive Functioning in Children Aged 6 to 10: An Event-Related Potential Study

The relationship between Type 1 Diabetes Mellitus (T1DM) and the effect it has on cognition, especially in children, has received considerable attention over the past two decades (Rovet & Alvarez, 1997; Hershey, Craft, Bhargava, & White, 1997; Northam et al. 2001; Wysocki et al., 2003; Strudwick et al., 2005; Aye et al., 2011; Blasetti et al., 2011). A constant supply of glucose to the brain is essential for normal brain development (Northam et al., 2001; Desrocher & Rovet, 2004). Children with T1DM often experience fluctuating levels of insulin (i.e., from treatment via daily injections of insulin; Desrocher & Rovet, 2004) and glucose (i.e., from varying levels of food intake and physical activity; Northam et al., 2001) therefore they are more susceptible and vulnerable to complications in brain development. This in turn may have consequences on their cognitive functioning. In this study we used event-related potentials (ERPs) to investigate the effect T1DM has on a specific domain of cognition – executive functioning – in children and to determine if the presence of T1DM is associated with deficits in this domain of cognition.

Type 1 Diabetes Mellitus is part of a group of metabolic disorders of carbohydrate metabolism. Its occurrence is attributed to the destruction of pancreatic beta cells responsible for the production of the hormone insulin, which is essential for the metabolism of glucose (AIHW, 2011). Common characteristics of T1DM include hyperglycemia (i.e., high concentrations of glucose in the blood), which is usually a consequence of poor glycemic control; Desrocher & Rovet, 2004) and hypoglycemia (i.e., critically low blood glucose concentrations), attributed to high levels of insulin from treatments and fluctuating levels of physical activity (Desrocher & Rovet, 2004).
Various domains of cognitive function have been investigated for the effect of T1DM, including intelligence, learning, memory, visuospatial abilities, psychomotor efficiency, attention and executive functioning (Desrocher & Rovet, 2004; Gaudieri et al., 2009; Ly et al., 2011), however findings have been inconsistent and equivocal. Several researchers discovered differences in cognition between children with T1DM and age-matched controls (Desrocher & Rovet, 2004; Brands et al., 2005; Gaudieri et al., 2009; Naguib et al., 2009) while others found no statistically significant differences between the two groups (Perantie et al., 2008; Aye et al., 2011).

**T1DM and Executive Functioning**

A domain of cognition known as executive functioning, has also been examined by several researchers for the effect of T1DM (see Hershey et al., 1997; Rovet & Alvarez, 1997; Northam et al., 2001; Gaudieri et al., 2008; Ly et al., 2011 and Aye et al., 2011). Executive functions (EFs) refer to the cognitive processes that enable an individual to set goals, formulate goal-directed plans and fulfill these plans efficiently (Jurado & Roselli, 2007). In other words, EFs are the cognitive processes that govern goal-directed behavior (Miller & Cohen, 2001). The ability to shift our mindsets to adapt to changes in our environments and to suppress inappropriate behaviors can be attributed to executive functioning. Therefore EFs are of significant importance for humans to function in society as it governs our ability to behave appropriately and responsibly in a socially acceptable manner (Jurado & Rosselli, 2007).

EFs are also recognized as higher-order cognitive processes associated with the frontoparietal cortex (Kiefer, Marzinzik, Weisbrod, Scherg & Spitzer, 1998; Smith & Jonides, 1999; Stuss & Levine, 2002). For example, according to Picton and
colleagues, the prefrontal cortex is responsible for a type of EF known as response inhibition (i.e. knowing when to suppress or execute a response; Picton et al., 2007). The study of EFs originated from research on individuals with frontal lobe damage. Such patients showed poor monitoring and control of behavior, as well as impairments in daily living (Jurado & Rosselli, 2007) and performance deficits on complex tasks (Miyake et al., 2000).

In children, the development of EFs throughout childhood is critical due to the role EFs play in classroom learning and academic achievement (see Bull, Johnson & Roy, 1999; Bull & Scerif, 2001; Gathercole & Pickering, 2000; Gathercole, Pickering, Knight & Stegmann, 2004; Gathercole, Lamont & Alloway, 2006; St Clair-Thompson & Gathercole, 2006). Gathercole, Lamont & Allow (2006) discovered that errors in several learning activities such as following instructions and performing mental arithmetic problems were more common and recurrent in children with poor working memory function. Several classroom activities require executive functions in order to carry them out. For example, writing a sentence employs shifting and updating of working memory (St Clair-Thompson & Gathercole, 2006). Lower levels of processing are required to identify and write out letters in a word. Putting these words into a proper sentence structure requires a higher level of processing, therefore that continuous shift between different levels of processing is essential in writing a complete sentence (St Clair-Thompson & Gathercole, 2006). Updating is necessary to monitor the progress of the sentence (i.e. how much of the sentence is written and how much more is needed to complete it; St Clair-Thompson & Gathercole, 2006). Furthermore, the proper development of EFs will enable children to become self-serving adults in future, with the skills to behave appropriately in differing situations in accordance with social norms (Jurado &
Rosselli, 2007). Therefore, deficits in executive functioning in children may be detrimental to learning and academic achievement, along with the possibility of impairments in daily living in future.

The research on whether T1DM affects executive functioning has produced mixed findings. Researchers have employed various measures of executive functioning such as the Wisconsin Card Sorting Task (WCST – a commonly used measure of set shifting; Ly et al., 2011), the Controlled Oral Word Association Test (COWAT – assesses set shifting and response inhibition; Northam et al., 2001) and the Working Digit Span Backwards Task, which is a measure of working memory (Sommerfield, Dreary, McAuly & Frier, 2003). These various studies reported significantly poorer performances in diabetics than controls on these measures. To further corroborate these findings, a meta-analysis conducted by Gaudieri et al. (2008) found that based on the different measures for executive functioning adopted by the various studies included, lower scores on these measures of EFs were found in participants with T1DM compared to controls. These findings suggest that T1DM does result in deficits in executive functioning.

Conversely, several researchers have reported findings that do not corroborate deficits found in executive functioning to be associated with T1DM. Hershey et al. (1997) administered the Stroop Color-Word Interference Task, a measure of response inhibition and found no significant group differences based on task errors between Type 1 diabetics and controls. Rovet and Alvarez (1997) found no significant group differences between Type 1 diabetics and controls based on performance in the WCST. With the administration of the NEPSY (a developmental NEuroPSYchological assessment), no significant differences were found between the T1DM group and controls (Aye et al., 2011).
The use of psychometric measures (e.g. WCST, COWAT, Stroop Task, NEPSY and Backwards Digit Span) has been the main method utilized to examine EFs. Though the outcomes of these behavioral measures play an integral part in understanding the importance of the role of EFs, researchers have also focused their attention on the underlying neural activity or processes associated with performance on psychometric measures of EFs (e.g. Johnstone et al., 2005; Johnstone et al., 2007; Polich, 2007; Cragg et al., 2009; Brydges et al., 2014). Examining the relationship between brain activity and behavior paves the way towards a more cohesive and holistic understanding of executive functioning.

**T1DM and Event-related Potentials**

The existence of neuroimaging technology, such as electroencephalography (EEG) and event-related potentials (ERPs), has proven to be a beneficial contribution to the research community in various domains of scientific research. EEG refers to the recording of electrical neural activity along the scalp. EEGs measure the resultant voltage changes due to ionic current flows within neurons of the brain (Niedermeyer & da Silva, 2005), therefore enabling the examination of neural activity during performance of various tasks. Despite EEGs having poor spatial resolution compared to other neuroimaging techniques [e.g. functional magnetic resonance imaging (fMRI), positron emission tomography (PET)], this is compensated by its high temporal resolution (i.e., millisecond resolution; Bokura, Yamaguchi & Kobayashi, 2001), which these other techniques do not possess. EEGs are noninvasive in nature as sensors are placed on the surface of the scalp to record neural activity. Furthermore, EEGs are relatively tolerant of subject movement compared to numerous other neuroimaging techniques (e.g. fMRI and PET scans). Various
ERPs are a derivative of EEGs that measure the electrical activity elicited in relation to cognitive, affective and sensory events. More specifically, they are voltage fluctuations in the EEG that are time-locked to sensory, motor or cognitive events (Falkenstein, Hoormann & Hohnsbein, 1999; Sanei & Chambers, 2008). ERPs are produced in response to external stimuli and appear as visual, auditory or somatosensory brain potentials. Alternatively, ERPs appear as slowly evolving neural activity observed before voluntary movements or whilst anticipating upcoming stimuli (Saneir & Chambers, 2008). Therefore, the relationship between physiological and the underlying psychological processes of physiological responses may be better understood through the examination of ERPs (Verleger, 1988). There are two ERP components associated with executive functioning – the N2 (Jodo & Kayama, 1992; Bokura, Yamaguchi & Kobayash, 2001; Johnstone et al., 2005; Jonkman, Lansbergen & Stauder, 2003; Jonkman, 2006; Johnstone et al., 2007; Cragg et al., 2009) and the P3b (Polich, Ladish & Burns, 1990; Walhovd & Fjell, 2003; Polich, 2007).

The N2 (or N200) is a negative peak observed at fronto-central areas of the scalp (Jodo & Kayama, 1992; Johnstone et al., 2007), approximately 150-400ms (often later in children) after stimulus onset (Falkenstein, Hoormann & Honsbein, 1999; Brydges et al., 2014). The N2 is traditionally associated with response inhibition (Donkers & van Boxtel, 2004; Jodo & Kayama, 1992; Johnstone et al., 2007). Response inhibition is defined as the conscious withholding of automatic, dominant and prepotent responses (Donkers & Van Boxtel, 2004). The Go/No-go task is a common task adopted by researchers to examine response inhibition (Jodo
Participants are required to respond as quickly as possible to a specific stimulus (i.e., the Go stimuli) and inhibit or withhold a response when presented with another set of stimuli (i.e., the No-go stimuli; Donkers & Van Boxtel, 2001). Jodo & Kayama (1992) shortened the response time period to “Go” stimuli in a Go/Nogo task, thereby increasing the difficulty to inhibit the Go response in No-go trials. Larger N2 amplitudes were reported, suggesting that as difficulty of the inhibitory task increases, the neural activity associated with response inhibition also increases. Similarly in children, larger N2 amplitudes in No-go trials were found in Go/No-go tasks (Johnstone et al., 2007; Cragg et al., 2009). These findings are indicative of a functional link between the N2 and response inhibition.

The relationship between the N2 and the theory of conflict monitoring has also been examined. The cognitive system responsible for conflict monitoring, serves to monitor conflicts in task performance (i.e., if task performance differs from what the task demands) and translate these conflicts to the cognitive control system (Botvinick, Braver, Barch, Carter & Cohen, 2001). According to Nieuwenhuis, Yeung, Van den Wildenberg and Ridderinkhof (2003), performing and inhibiting a single response in a Go/No-go task results in conflict, whereby the subsequent N2 effect results from this conflict. In their study, the percentage of No-go trials presented was manipulated (i.e. 20%, 50%, 80%). The N2 was reported after the No-go trials in the 20% and 50% conditions. The N2 was also observed after the less frequent Go stimuli in the 80% No-go condition, which cannot be attributed to response inhibition. According to the conflict monitoring theory, in conditions whereby a low-frequency response is required in the context of making alternative, high-frequency responses, response conflict should be largely evident (Nieuwenhuis et
al., 2003). Therefore, when a low frequency Go response was required in the 80% No-go condition, the N2 effect observed was associated with response conflict.

Van veen and Carter (2002) administered the Eriksen Flanker task (see Eriksen & Eriksen, 1974), which required participants to respond to a central target while simultaneously ignoring flanker stimuli presented on either side of the central target. The N2 observed was found to represent conflict monitoring prior to a correct response being made (Van veen & Carter, 2002; Donkers & Van Boxtel, 2004). Therefore it is clear that the N2 is not only associated with response inhibition, but with conflict monitoring as well, both of which are functions of cognitive control (Folstein & Petten, 2008).

The P3b (or P300) is a positive peak observed at central and parietal scalp sites (Picton, 1992) approximately 300-500ms (also observed later in children; Brydges et al., 2014) after presentation of stimuli (Polich, Howard & Starr, 1983; Verlger, 1988; Polich et al., 1990; Polich, 2007; Brydges et al., 2014). The P3b peak is reportedly associated with updating of working memory (Walhovd & Fjell, 2003; Polich, 2007). In adults, significantly large negative correlations between P3b latency (obtained using an auditory oddball task) and memory scores on a digit span task were reported in various studies (see Polich et al., 1983; Walhovd & Fjell, 2003) as well as positive correlations between P3b amplitudes and digit span task scores (Walhovd & Fjell, 2003). Polich et al. (1990) found similar results in a sample of children. These studies provide evidence of the relationship between the P3b and updating of working memory.

The majority of studies (e.g. Hershey et al., 1997; Northam et al., 2001; Aye et al., 2011) that investigated executive functioning in individuals with T1DM, both
including children, were based solely on behavioral measures (e.g. WCST, COWAT, Stroop Task) of EFs. Very few researchers employed the use of ERPs to examine the effects of T1DM on executive functioning.

In a study conducted by Shehata and Eltayeb (2010), which to my attention is the only ERP study involving children, the effect of T1DM on EFs in children was examined with the use of ERPs. Participants, which included 40 children with T1DM and 40 age-matched controls, were required to mentally count the number of target tones and report this number at the end of each trial, during which EEGs were recorded. Latencies and amplitudes were measured for the N200 and P300 ERP components. Statistical analyses (i.e., correlation coefficients, multiple linear regression analysis and independent samples t-tests) were conducted on ERPs recorded from electrode Cz. Significantly longer P300 and N200 latencies in the diabetic group compared to controls were reported, along with significantly lower P300-N2 amplitude in the diabetic group. These findings suggested that type 1 diabetic children experienced deficits in neural activity associated with executive functioning compared to controls.

Amongst the limited ERP studies examining the effects of T1DM on executive functioning, the majority of studies have focused on these effects in adults. Pozzessere et al. (1991) compared P300 latency in adults between T1DM and healthy controls with the use of aural stimuli. Participants were required to count the number of rare tones, which had a frequency of 4000Hz, presented throughout the session and report the total number at the end of the session. An increase in P300 latency in diabetics compared to controls was discovered. Similar findings were reported by Kramer et al. (1998) and Cooray et al. (2008), in relation to the P300 latency variable. However, these researchers found conflicting results based on the
P300 amplitudes. According to the study conducted by Kramer and colleagues, participants were also presented with aural stimuli and required to keep track of and report the number of target tones they counted. P300 amplitudes of diabetic patients and healthy controls were reported to be similar. In a study conducted by Cooray et al. (2008) participants were required to make a response when they heard a low-pitch tone (900 Hz) or a high-pitch tone (1900 Hz). Responses were made using keypads placed in both hands, whereby a left hand response was for a low-pitch tone and a right hand response was for a high-pitch tone. P300 amplitudes of diabetics were reported to be significantly smaller than controls. These reported differences in P300 latency and amplitudes suggest that deficits in executive functions associated with the P300 (e.g., updating of working memory) are experienced by individuals with T1DM.

**The Current Study**

A plethora of studies, both behavioral and electrophysiological, have implicated the effect of T1DM on executive functioning. However, the lack of electrophysiological studies examining this effect in children is evident. The current study aims to build on the findings of the Shehata and Eltayeb (2010) study by administering a modified visual Flanker task (see Richardson et al., 2011) to examine the N2 and P3b ERP components in children with T1DM and age-matched controls.

The current study compares both behavioral performance and electrophysiological activity (in the N2 and P3b ERP components) of children with T1DM against age-matched controls. The first aim of the study is to determine if there are differences between children with T1DM and controls in performance on
the flanker task, by observing and comparing the accuracy levels and reaction times between the respective groups of children (i.e., T1DMs vs. controls). Secondly, the current study aims to determine if there are electrophysiological differences (i.e., differences in brain activity) between the two groups of children by examining the amplitudes of the N2 and P3b ERP components of these children. Finally, the current study aims to determine whether these differences, if any, can be attributed to the presence of T1DM.

As aforementioned, the N2 is associated with cognitive control, which includes response inhibition and conflict monitoring. Larger N2 amplitudes are observed with lower error rates in Go/Nogo tasks, therefore, to be specific, the N2 is associated with successful response inhibition (Falkenstein, Hoormann & Honsbein, 2002). In lieu with the results of psychometric measures of executive functions (i.e., the COWAT, which measures response inhibition), poorer performances of participants with T1DM are indicative of possible deficits in response inhibition (Northam et al., 2001). Furthermore, lower N2 amplitudes were observed in children with T1DM compared to controls (Shehata & Eltayeb, 2010). Therefore, we predicted that there would be a difference observed in N2 amplitudes between children with T1DM and controls, with the former having lower N2 amplitudes. This difference suggests that children with T1DM would experience more difficulty executing cognitive control, including successful response inhibition, compared to healthy controls.

It is argued that P3b amplitudes are indicative of underlying processes responsible for the updating of representations in working memory (Fabiani, Karis & Donchin, 1986). Changes in P3b amplitudes are associated with memory
performance (Shehata & Eltayeb, 2010), such that lower P3b amplitudes are indicative of poorer updating of representations in working memory. Previous studies examining P300 amplitudes in cohorts with T1DM (both adults and children) reported lower P300 amplitudes in T1DM participants compared to controls (Cooray et al., 2008; Shehata & Eltayeb, 2010). Based on these findings, it was predicted that there would be a difference between P300 amplitudes of children with T1DM and controls. This difference would signify that children with T1DM would experience deficits in updating of working memory in relation to their healthy counterparts.

Furthermore, compared to the congruous trial of the Flanker task, the incongruous and reversed trials require cognitive control. An interaction effect with trial type is predicted for the N2 amplitude. Both the incongruous and reversed trials require responses either opposite to the congruous trial, opposite to flanker stimuli or both, all of which elicit response inhibition and response conflict (i.e., cognitive control associated with the N2). This interaction effect suggests that if children with T1DM experience deficits in executive functioning compared to controls, the differences in N2 amplitude would be predominately evident in the incongruous and reversed trials due to the higher levels of cognitive control required to perform them compared to the congruous trial.

An interaction effect with trial type is also predicted for the P3b amplitude. The constant and subconscious updating of each representation associated with each of the three trial types to working memory is essential to performing the task. Due to the higher cognitive load required to perform the incongruous and reversed trials, as well as their lower frequency in the task, the need to update the representations associated with them is higher. This interaction effect suggests that if children with
T1DM experience deficits in executive functioning compared to controls, the differences in P3b amplitude would be predominately evident in the incongruous and reversed trials as a result of their higher cognitive load.

In light of the predictions made, it was hypothesized that mean N2 and P3b amplitudes of Type 1 diabetics would be lower than controls, predominately in the incongruous and reversed trials. In terms of behavioral performance on the flanker task, it was hypothesized that Type 1 diabetics would demonstrate lower accuracy levels and slower reaction times in all trials, but more so in the incongruous and reversed trials due to more cognitive control required in performing these trials.

Method

Participants

Ninety-seven children (see Table 1) participated in this study conducted by Project K.I.D.S (Kids’ Intellectual Development Study), which is a research program dedicated to examining the cognitive, social and neuropsychological development of children. This study was conducted in conjunction with Princess Margaret Hospital (PMH), Perth. PMH is the only diabetic referral center for children in Western Australia, therefore almost all children diagnosed with T1DM are referred to and receive treatment at PMH. T1DM participants (N = 48) were recruited from outpatient clinics at the Department of Endocrinology and Diabetes in PMH. Age-matched controls (N= 49) were recruited from Project K.I.D.S. via advertisements in local schools’ newsletters.
Table 1

Descriptive statistics and demographics of the controls and T1DM groups.

<table>
<thead>
<tr>
<th></th>
<th>Controls</th>
<th>T1DM</th>
</tr>
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<tbody>
<tr>
<td>Participants (N)</td>
<td>49</td>
<td>48</td>
</tr>
<tr>
<td>Age [M (SD)]</td>
<td>7.90 (.98)</td>
<td>7.90 (1.13)</td>
</tr>
<tr>
<td>Males (N)</td>
<td>27</td>
<td>27</td>
</tr>
<tr>
<td>Right-handers(N)</td>
<td>42</td>
<td>44</td>
</tr>
</tbody>
</table>

Materials

A modified visual flanker task (see Richardson et al., 2011) was administered to participants. Each trial comprised of five fish presented on a blue background (see Figure 1). Each fish had an arrow on its body depicting direction, with the middle fish as the target. Participants responded by pressing keys on a keyboard (red felt patches on the “Z” and “/” keys) associated with the direction of the target. There were three conditions: the congruous condition (probability = 0.5) whereby all the fish were green and the arrows pointed in the same direction; the incongruous condition (probability = 0.25) whereby all the fish were green and the arrows on the flankers (i.e., fish other than the target) pointed in the direction opposite to the arrow on the target; and a reversed condition (probability = 0.25) whereby all the fish were red with arrows that pointed in the same direction, however a response opposite to the direction of the target was made. There were eight practice trials and a total of 352 experimental trials administered in two blocks. Within each trial, stimuli were presented for 300ms and a keyboard response was required to continue to the next trial. Immediate feedback was presented following responses for each trial. The word
“Great!” followed a correct response, and an incorrect response was followed by “Oops!”, which was presented on screen. The entire task was administered as a game whereby participants had to feed the hungry target fish. Participants were instructed to respond as quickly and accurately as they could.

Figure 1. Examples of trials in the three stimulus conditions: Congruous, Incongruous and Reversed.

EEG Acquisition and Preprocessing

EEGs were recorded throughout the flanker task using a 38-channel NuAmp amplifier with Easy-Cap™. Electrodes were placed at 33 sites (i.e. Fp1, Fp2, F3, F4, F7, F8, Fz, FC1, FC2, FC5, FC6, FCz, FT9, FT10, C3, C4, Cz, T7, T8, CP1, CP2, CP5, CP6, P3, P4, P7, P8, Pz, PO9, PO10, O1, O2, and Iz), with AFz as the ground electrode. Two electrodes situated above and below the left eye recorded eye movements. EEG was recorded with a DC-35-Hz band-pass, with a sampling rate digitized at 250 Hz. EEGs were referenced to the right mastoid during recording and referenced to linked mastoids after recording. Input impedances were brought to 5 kΩ prior to recording. Processing of the EEGs was conducted using functions from the EEGLAB toolbox (Delorm & Makeig, 2004; Delorme et al., 2011) in MATLAB 2012b.

The EEG recordings were filtered between .01 and 30 Hz with a zero phase band-pass filter from the MATLAB Signal Processing toolbox. Epochs ranging from 100ms prior to stimulus onset to 700ms after stimulus onset were extracted and
baseline corrected around the pre-stimulus interval. Epochs were screened manually and noise or artifacts discovered were removed.

**ERP Analysis**

ERP data was only analyzed for correct trials, where the response occurred between 200ms and 1500ms after stimulus onset. Two ERP analysis strategies were used: a conventional *a priori* ANOVA approach and a modern mass univariate analysis approach (Groppe, Urbach & Kutas, 2011).

ANOVAs were performed on ERP data recorded from electrodes FCz for the N2 component and Pz for the P3b component based on previous studies that examined these electrodes for the respective ERP components (e.g., Brydges et al., 2014). The time periods analyzed were chosen from visual inspection of the Mean Global Field Power (Skrandies, 1990; Hamburger & Van Der Burgt, 1991), which provides a reference-free measure of activity across all electrodes. For the N2 component, data values were extracted between 250-400ms and between 300-400ms for the P3b.

Mass univariate analysis of ERPs was conducted using a permutation test based on the *t*-max statistic with a family-wise alpha level of 0.05 (Blair & Karniski, 1993) from EEGLAB. Specifically, a large number of *t*-tests (i.e., both independent samples and repeated measures) were performed on all time points and electrodes of interest and 5000 permutations of the data between 200 and 1500ms after stimulus onset. A *t*-test was performed every 4ms during the analyzed time period (i.e., at 200ms, 204ms, 208ms etc.). The *t*-scores from each comparison were converted to their absolute values and the greatest *t*-score in each of the 5000 permuted sets of tests (i.e., the "*t*-max" of each set of tests) were recorded and used to estimate the *t*-max distribution of the null hypothesis (i.e., no difference between groups or within
conditions). The $t$-max distribution therefore represents a range of critical $t$-scores, both negative and positive, whereby any $t$-score that falls outside of this range would be significant.

**Procedure**

Testing was conducted at Project K.I.D.S, which was located at the Neurological Development Unit (NDU) on the campus of the University of Western Australia. Project K.I.D.S. was held during the school holidays over a period of 6 days, with each child participating in two full days of testing. Participants were dropped off in the morning and spent the day at the unit. Various cognitive, social and neuropsychological assessments were conducted throughout the day. Trained members of the Project K.I.D.S. staff conducted the various assessments. EEG caps were placed on participants’ heads, with the application process taking approximately 45 minutes. They performed the flanker task on a computer, along with two other cognitive measures, while EEGs were recorded. Instructions for the flanker task were presented on screen and were read aloud by experimenters. Short breaks were given between experimental blocks and between each experimental task. Breaks were also given between all the other assessment measures to incorporate lunch and time for social activities. The data obtained from the neurocognitive tasks other than the Flanker task were not presented in this study.

**Results**

**Behavioral Data**

The descriptive statistics associated with accuracy (i.e., percentage of correct trials) in the three trial conditions of the flanker task (i.e., congruous, incongruous and reversed), are reported in Table 2. Outliers (N=3) were excluded on the basis of
more than 25 percent errors in the congruous trial type of the Flanker task. Therefore, the data of 94 out of 97 participants was analyzed.

Table 2

Accuracy levels (expressed as percentage of correct trials) of the Controls and T1DM groups in each condition of the Flanker task.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Controls</th>
<th>T1DM</th>
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<tbody>
<tr>
<td></td>
<td>M  SD</td>
<td>M  SD</td>
</tr>
<tr>
<td>Congruous</td>
<td>90.26  7.35</td>
<td>90.74  7.33</td>
</tr>
<tr>
<td>Incongruous</td>
<td>86.70  10.44</td>
<td>86.21  9.86</td>
</tr>
<tr>
<td>Reversed</td>
<td>84.72  9.48</td>
<td>82.75  12.40</td>
</tr>
</tbody>
</table>

Mean accuracy (represented as percentages of correct trials) of the controls group was numerically larger than the T1DM group. To test the hypothesis that the differences in accuracy are attributed to group membership (i.e., control vs. T1DM), in addition to the possibility that the effect may interact with trial type (i.e., congruous vs. incongruous vs. reversed), a 2 (control vs. T1DM) x 3 (congruous vs. incongruous vs. reversed) mixed design ANOVA was performed.

Prior to examining the main and interaction effects for accuracy, it was found that the assumptions of homogeneity of covariances (via Box’s M) and variances (via Levene’s test) across groups were both satisfied. The assumption of sphericity was tested and rejected based on the Mauchly’s test of sphericity and therefore, the Greenhouse-Geisser corrected F tests were used in this investigation.

There was a main effect of trial type on the accuracy data, $F(1.84, 169.40) = 42.60, p = .000, \eta^2_{\text{partial}} = .316$, with congruous trials having the highest performance and reversed trials having the lowest (Congruous $M = 90.50$; Incongruous $M = 86.46$; Reversed $M = 83.74$). There was no difference in task accuracy between controls ($M$
Moreover, the interaction between trial type and group was not significant, $F(1.84, 169.40) = 1.40, p = .249, \eta^2_{partial} = .015$. Pairwise comparisons (Bonferroni-adjusted) revealed a significant difference between the congruous and incongruous conditions ($M = 4.05, p < .001$), congruous and reversed conditions ($M = 6.77, p < .001$) and incongruous and reversed conditions ($M = 2.72, p = .002$).

The descriptive statistics associated with reaction times in the three trial conditions (i.e., congruous, incongruous and reversed) are reported in Table 3. Mean reaction time of the T1DM group was numerically larger (i.e., longer) than the control group. To test the hypothesis that the differences in reaction times are attributed to group membership (i.e., control vs. T1DM) in addition to the possibility that the effect may interact with trial condition (i.e., congruous vs. incongruous vs. reversed), a 2 (control vs. T1DM) x 3 (congruous vs. incongruous vs. reversed) mixed design ANOVA was performed.

Table 3

<table>
<thead>
<tr>
<th>Condition</th>
<th>Controls</th>
<th>T1DM</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>SD</td>
</tr>
<tr>
<td>Congruous</td>
<td>936.59</td>
<td>246.77</td>
</tr>
<tr>
<td>Incongruous</td>
<td>1075.74</td>
<td>288.27</td>
</tr>
<tr>
<td>Reversed</td>
<td>1082.67</td>
<td>287.98</td>
</tr>
</tbody>
</table>

Prior to examining the main and interaction effects for RT, it was found that the assumptions of homogeneity of covariances and variances across groups were satisfied. The assumption of sphericity was tested and rejected based on the
Mauchly’s test of sphericity, therefore, the Greenhouse-Geisser corrected $F$ tests were used in this investigation.

There was a main effect of trial type on the RT data, $F(1.73, 158.85) = 52.06, p = .000, \eta^{2}_{\text{partial}} = .361$, with congruous trials having the fastest RTs and reversed trials having the slowest (Congruous $M = 959.37$; Incongruous $M = 1106.67$; Reversed $M = 1099.46$). There was no difference in task RTs between controls ($M = 1031.67$) and diabetics ($M = 1078.67$), $F(1, 92) = .752, p = .388, \eta^{2}_{\text{partial}} = .008$.

Moreover, the interaction between trial type and group was not significant, $F(1.73, 158.85) = .380, p = .653, \eta^{2}_{\text{partial}} = .004$. Pairwise comparisons (Bonferroni-adjusted) revealed a significant difference between the congruous and incongruous conditions ($M = -147.303, p = .000$) and the congruous and reversed conditions ($M = -140.10, p = .000$) but not between the incongruous and reversed conditions ($M = 7.21, p = 1.00$).

**ERP Data**

The descriptive statistics associated with N2 (recorded at FCz between 250-400ms after stimulus onset) and P3b amplitudes (recorded at Pz 300-400ms after stimulus onset) in the three trial conditions (i.e., congruous, incongruous and reversed) are reported in Table 4. Apart from the three previously excluded outliers, an additional two outliers were excluded due to insufficient trial numbers. Therefore the ERP data of 92 out of 97 participants was analyzed.

As seen in Table 4, the mean N2 amplitude of the T1DM group was numerically smaller than the controls group across conditions. To test the hypothesis that the differences in N2 amplitudes are attributed to group membership (i.e., control vs. T1DM) in addition to the possibility that the effect may interact with trial
condition (i.e., congruous vs. incongruous vs. reversed), a 2 (control vs. T1DM) x 3 (congruous vs. incongruous vs. reversed) mixed design ANOVA was performed.

Table 4

*N2 and P3b amplitudes (µV) of the Controls and T1DM groups in each condition of the Flanker task.*

<table>
<thead>
<tr>
<th>Condition</th>
<th>N2 Controls M</th>
<th>SD</th>
<th>T1DM M</th>
<th>SD</th>
<th>P3b Controls M</th>
<th>SD</th>
<th>T1DM M</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congruous</td>
<td>.58</td>
<td>5.29</td>
<td>-.25</td>
<td>5.58</td>
<td>5.23</td>
<td>7.50</td>
<td>2.82</td>
<td>6.16</td>
</tr>
<tr>
<td>Incongruous</td>
<td>-.09</td>
<td>6.33</td>
<td>-.95</td>
<td>6.35</td>
<td>5.12</td>
<td>7.89</td>
<td>3.25</td>
<td>7.92</td>
</tr>
<tr>
<td>Reversed</td>
<td>-1.01</td>
<td>6.58</td>
<td>-1.49</td>
<td>5.89</td>
<td>3.71</td>
<td>9.33</td>
<td>1.62</td>
<td>8.45</td>
</tr>
</tbody>
</table>

Prior to examining the main and interaction effects for N2 amplitude, the assumption of homogeneity of covariances and variances across groups were tested and satisfied. The assumption of sphericity was tested and satisfied based on the Mauchly’s test of sphericity, $\chi^2(2) = 2.86, p = .239$.

There was a main effect for trial type on N2 amplitude, $F(2, 180) = 3.25, p = .041, \eta^2_{\text{partial}} = .035$, with congruous trials having the least negative N2 amplitude and reversed trials having the most negative N2 amplitude (Congruous $M = .16$; Incongruous $M = -.52$; Reversed $M = -1.25$). There was no difference in N2 amplitudes between controls ($M = 1031.67$) and diabetics ($M = 1078.67$), $F(1, 90) = .45, p = .506, \eta^2_{\text{partial}} = .005$. Moreover, the interaction between trial type and group was not significant, $F(2, 180) = .07, p = .929, \eta^2_{\text{partial}} = .001$. Pairwise comparisons (Bonferroni-adjusted) revealed no significant differences between the congruous and incongruous conditions ($M = .68, p = .541$), the congruous and reversed conditions...
(M = 1.42, p = .054) and the incongruous and reversed conditions (M = .73, p = .606).

Mean P3b amplitudes of the T1DM group was numerically smaller than the controls group across conditions. To test the hypothesis that the differences in P3b amplitudes are attributed to group membership (i.e., control vs. T1DM) in addition to the possibility that the effect may interact with trial condition (i.e., congruous vs. incongruous vs. reversed), a 2 (control vs. T1DM) x 3 (congruous vs. incongruous vs. reversed) mixed design ANOVA was performed.

Prior to examining the main and interaction effects for P3b amplitude, the assumption of homogeneity of covariances and variances across groups were tested and satisfied. The assumption of sphericity was tested and rejected based on the Mauchly’s test of sphericity, $\chi^2(2) = 25.11, p = .000$. Therefore, the Greenhouse-Geisser corrected F tests was used in this investigation.

There was no main effect for trial condition on P3b amplitude, $F(1.61, 144.48) = 2.83, p = .074, \eta^2_{\text{partial}} = .030$. There was no significant difference in P3b amplitudes between controls (M = 4.69) and diabetics (M = 2.56), $F(1, 90) = 2.13, p = .148, \eta^2_{\text{partial}} = .023$. Moreover, the interaction effect between trial type and group was not significant, $F(1.61, 144.48) = .08, p = .890, \eta^2_{\text{partial}} = .001$.

**Mass-univariate Analysis**

The prior use of conventional ANOVAS to examine the effects of group and trial type on the N2 and P3b amplitudes may have overlooked or missed out on effects that possibly occurred outside of the time period examined or effects that could have occurred in electrodes other than the focal electrodes (i.e., FCz and Pz). Therefore, to further examine the effects of group and trial condition on N2 and P3b amplitudes that may have been missed out by conventional ANOVAs, a mass
univariate analysis approach was conducted for all electrodes and all time points between 100 and 700ms.

To compare the ERPs between the controls and T1DM groups for the trials participants got correct in each condition (i.e., congruous, incongruous and reversed) of the Flanker task, these ERPs were submitted to an independent samples, two-tailed permutation test based on the $t$-max statistic (Blair & Karniski, 1993) using a family-wise alpha level of 0.05. Difference waveforms were calculated across 33 scalp sites at all time points between 100 and 600ms (i.e., 126 time points) with 4158 comparisons. It is important to note that higher significance is associated with larger number of brain areas (i.e., more electrodes) and longer time periods where positive or negative differences are observed.

In the congruous condition, critical $t$-scores of ± 3.91 (df = 95), which corresponded to a test-wise alpha level of .000174, were derived. The $p$-values of all the independent samples $t$-tests were equivalent to .29. There were no statistically significant differences in ERPs between the diabetic and control groups at any time point or electrode analyzed, which suggests that all $t$-scores fell within the critical $t$-score range. The raster diagram and butterfly plots depicting no statistical significant differences in the congruous condition are presented in Figure 2.
**Figure 2.** Raster diagram illustrating each time point and each electrode where a t-test was conducted between ERPs of the controls and T1DM groups in the congruous condition (a). Grey rectangles represent time points where no significant differences were found between groups in the congruous condition; Butterfly plots of amplitudes (b) and t-scores (c) depicting difference waveforms between the controls and T1DM groups in the congruous condition. Each waveform in each plot represents the data at one of 33 scalp electrodes. Vertical dashed lines represent the time window analyzed (100 to 600ms) and horizontal dashed lines represent the significant alpha level ($\alpha = .05$).

In the incongruous condition, critical t-scores of $\pm 3.96$ (df = 95), which corresponded to a test-wise alpha level of .000146, were derived. Significant differences were found specifically at electrode PO10 between 576 and 592ms and at electrode O2 between 580-588ms. All significant corrected $p$-values were between
.025 and .05. The raster diagram and butterfly plots depicting significant differences are presented in Figure 3. The grand averaged difference waveforms for the electrodes at which significant differences were found are presented in Figure 4.

Figure 3. Raster diagram illustrating each time point and each electrode where a t-test was conducted between ERPs of the controls and T1DM groups in the incongruous condition (a). Red rectangles indicate the time points/electrodes where significant differences are found, whereby ERPs are positive. Grey rectangles indicate time points/electrodes where no significant differences were found. Note that electrodes are organized along the y-axis somewhat topographically. Electrodes on the left and right sides of the brain are grouped in the figure’s top and bottom, respectively. Midline electrodes are shown in the middle. Within those three groupings, y-axis top-to-bottom corresponds to scalp anterior-to-posterior; Butterfly plots of amplitude (b) and t-scores (c) illustrating difference waveforms between the
controls and T1DM groups in the incongruous condition. Each waveform in each plot represents the data at one of 33 scalp electrodes. Vertical dashed lines represent the time window analyzed (100 to 600ms) and horizontal dashed lines represent the significant alpha level ($\alpha = .05$).

*Figure 4.* Grand averaged event-related brain potential waveforms for the controls and T1DM groups elicited in electrodes PO10 and O2 by the trials in the incongruous condition of the Flanker task.

In the reversed condition, critical t-scores of $\pm 3.96$ (df = 95), which corresponded to a test-wise alpha level of .000147, were derived. Significant differences were found specifically at electrode(s) IZ between 488 and 600ms, O2 between 516 and 512ms, O1 between 536 and 572ms, and PO10 between 568 and 588ms. All significant corrected $p$-values were between .003 and .048. The raster diagram and butterfly plots depicting significant differences are presented in Figure
5. The grand averaged difference waveforms for the electrodes where significant differences were found are presented in Figures 4 and 6.

Figure 5. Raster diagram illustrating each time point and each electrode where a $t$-test was conducted between ERPs of the controls and T1DM groups in the reversed condition (a). Red rectangles indicate the time points/electrodes where significant differences are found, whereby ERPs are positive. Grey rectangles indicate time points/electrodes where no significant differences were found. Note that electrodes are organized along the y-axis somewhat topographically. Electrodes on the left and right sides of the brain are grouped in the figure’s top and bottom, respectively. Midline electrodes are shown in the middle. Within those three groupings, y-axis top-to-bottom corresponds to scalp anterior-to-posterior; Butterfly plots of amplitude (b) and $t$-scores (c) illustrating difference waveforms between the controls and
T1DM groups in the reversed condition. Each waveform in each plot represents the data at one of 33 scalp electrodes. Vertical dashed lines represent the time window analyzed (100 to 600ms) and horizontal dashed lines represent the significant alpha level ($\alpha = .05$).

**Figure 6.** Grand averaged event-related brain potential waveforms for the controls and T1DM groups elicited in electrodes O1 and IZ by the trials in the reversed condition of the Flanker task.

**Discussion**

The current study investigated the effect of T1DM on executive functioning in children using ERPs. It aimed to determine if there are behavioral differences in executive functioning between children with T1DM and controls by comparing the accuracy levels and reaction times of the two groups on the flanker task. It also
aimed at determining if there are differences in neural activity associated with executive functioning between children with Type 1 diabetes and controls by comparing the N2 and P3b amplitudes of the two groups.

In contrast to the hypothesis that the mean accuracy level of the T1DM group would be lower than the control group and that this difference would be significant in the incongruous and reversed trials, no significant difference was found in task accuracy between the two groups based on the interaction with trial type. It was hypothesized that the mean reaction time of the T1DM would be longer than the control group in the incongruous and reversed trials, however no significant difference was found in reaction time between the two groups based on the interaction with trial type. These findings suggest that the effect of T1DM on behavioral aspects of executive functioning in children is small.

It was also hypothesized that the mean N2 amplitude would be lower in the T1DM group than the control group in the incongruous and reversed trials, however no significant difference was found in N2 amplitudes between the groups based on the interaction with trial type. Finally, in contrast to the hypothesis that the mean P3b amplitude of the T1DM group would be lower than the control group in the incongruous and reversed trials, no significant difference was found in P3b amplitude between the two groups based on the interaction with trial type. These findings suggest that the effect of T1DM on the EFs associated with the N2 (i.e. response inhibition) and the P3b (i.e. updating working memory) was subtle. These results corroborate the findings of Hershey et al. (1997), Rovet and Alvarez (1997) and Aye et al. (2011), all of which conducted behavioral studies using psychometric measures of executive functioning and found no significant differences in executive functioning between Type 1 diabetics and healthy controls. The current results also
support the finding by Kramer et al. (1998) of no difference in P300 amplitudes between the T1DM and control groups.

In contrast to our hypotheses, a significant difference in a posterior positive ERP component with a late onset was found between the T1DM and control groups in the incongruous and reversed trials. This finding was unpredicted and surprising. It is important to recognize that this unexpected finding can be attributed to the use of the mass univariate analysis approach. Due to the exhaustive analysis of effects at all electrodes across all time points, we were able to find an effect that was clearly missed out by conventional parametric analyses. Therefore, this result highlights how effective and thorough the mass univariate analysis approach is in examining effects in ERPs.

We postulated this ERP component to be a late positive slow wave (Garcia-Larrea & Cezanne-Bert, 1999). Late positive slow waves (PSWs) are presented as secondary peaks or “bumps” that overlie the slope following the P3b peak (Johnson & Donchin, 1985; Garcia-Larrea & Cezanne-Bert, 1999), resulting in a lag in the return to baseline by decreasing the gradient of the negative-going slope (Garcia-Larrea & Cezanne-Bert, 1999). It is postulated that the PSW is associated with decision making (Johnson & Conchin, 1985) or the amount of processing necessary for decision making (Ruchkin et al., 1982), the difficulty of responses required (Kok & Looren de Jong, 1980) and response selection (Falkenstein et al., 1994). The PSW has also been suggested to represent processes that occur after a response has been made, which include the subject’s preparation for the upcoming trial and evaluating the accuracy of the response (Ruchkin et al., 1990; Falkenstein et al., 1994; Garcia-Larrea & Cezanne-Bert, 1999). The late PSW is also associated with sustained attention to task performance (Gevins et al., 1996).
The differences between the groups may be attributed to the difficulty in sustaining attention associated with T1DM. It has been previously reported that T1DM has a consequential effect on sustained attention. Ryan, Vega and Drash (1985) found that participants with T1DM performed significantly poorer than controls in tasks that require sustained attention. A meta-analysis conducted by Brands et al. (2005), further corroborated these findings. As aforementioned, the PSW is associated with sustained attention in a task. Given the negative effect T1DM has on the domain of sustained attention, this could be a possible explanation for the significant differences found between children with T1DM and controls in the PSWs.

Although we postulate the PSW to be the ERP component that garnered significant differences between the two groups, alternative ERP components could be responsible for this difference. Such a component is the Late Directing Attention Positivity (LDAP), which is an enhanced contralateral positivity, which is evident at lateral posterior electrodes (Eimer, Van Velzen & Drimer, 2002). The LDAP is proposed to be responsible for direction of spatial attention from central to peripheral visual fields (Harter, Miller, Price, Lalonde & Keyes, 1989), and is therefore associated with visuospatial abilities. A typical task employed to elicit the LDAP involves the presentation of a central cue (e.g., an arrow pointing either left or right), which is indicative of the direction that peripheral stimuli would appear (i.e., left or right of cue; Harter et al., 1989; Eimer et al., 2002). The LDAP is said to present itself approximately 500ms after cue onset during the interval between onset of cue and onset of peripheral stimuli (Eimer et al., 2002).

In the flanker task of the present study, the arrow on the body of the central target could have possibly resulted in subconscious or implicit direction of attention to the flankers on either side of the central target, depending on the direction of the
arrow. In this case, it is possible that the LDAP was elicited. The current positivity was found to be significant between 500 and 600ms following stimulus onset, which is similar to the approximate onset time of the LDAP. As aforementioned, the LDAP is associated with visuospatial abilities. Researchers have found that children with T1DM display deficits in tasks that measure visuospatial abilities (Desrocher & Rovet, 2004; Gaudieri et al., 2009; Ly et al., 2011). These visuospatial deficits, which seem to be associated to the presence of T1DM, could provide an explanation for possible differences between groups in the LDAP.

An alternative ERP component that could also be responsible for the differences between groups is the error positivity (Pe). Pe is a positive deflection that follows an error in a response (Falkenstein, Hohnsbein, Hoormann & Blanke, 1991; Leuthold & Sommer, 1999; Endrass, Reuter & Kathmann, 2007), with a topographic presentation at centro-parietal regions of the brain (Endrass et al., 2007). Pe typically occurs between 400 and 700ms following the onset of stimuli (Falkenstein et al., 1991; Endrass et al., 2007). A study conducted by Nieuwenhuis, Ridderinkhof, Blom, Band and Kok (2001) reported that the Pe is associated with being consciously aware of an incorrect response, which is followed up by compensatory remedial action. The relationship between the Pe and error detection was further corroborated by Endrass et al. (2007) and Hajcak, McDonald and Simons (2003). The Pe is also associated with post-error processes reflecting recognition of an error, alteration in responses following an error, as well as evaluation of the error (Falkenstein, Hoormann, Christ, & Hohnsbein, 2000).

In the current flanker task, participants are provided with immediate feedback following an incorrect response on a trial (i.e., “Oops” appears on screen). Looking at the mean accuracy levels (i.e., percentage of correct responses) of the control and
T1DM group, the T1DM group displayed poorer accuracy levels than the control group despite this difference not being significant. This suggests that the T1DM group had a larger percentage of incorrect responses than the control group. Errors made by both groups could have possibly elicited the Pe. A larger proportion of errors being made in one group (i.e., T1DM) could be responsible for the significant difference in the error positivity ERP component.

There are various reasons behind our postulation that the ERP component associated with significant group differences is the PSW. First and foremost, the PSW is postulated to be a part of the P300 family. The P300 is suggested to be a waveform comprised of three subcomponents – the P3a, the P3b and the late positive slow wave, each of which have frontocentral, centroparietal and posterior topographies respectively (Squires, Squires, & Hillyard, 1975; Osterhout, 1999). Furthermore, the presentation of the grand averaged waveforms for electrodes at which significant differences were found (see Figures 5 and 7) match the waveforms of a typical late PSW.

The LDAP was discounted, as it typically follows an early directing attention negativity (EDAN), which is a clear negative peak at 200ms following stimulus onset (Eimer et al., 2002). As can be seen in Figure x, there are several negative peaks prior to the positive peak, each of which do not resemble the EDAN. The topography of the current ERP component was posterior, which does not match the centroparietal topography of the Pe but that of the late PSW instead. Therefore, we came to the conclusion that the significant differences found between the T1DM and control groups were in the PSW.

In comparison to the Shehata and Eltayeb (2010) ERP study, which found differences in P3-N2 amplitudes, N2 latency and P3 latency between children with
T1DM and healthy controls, the current study did not observe the latency of the N2 and P3b ERP components. Furthermore, the ERP studies involving adult Type 1 diabetics also examined the latency of the P300 (see Pozzessere et al., 1991; Kramer et al., 1998; Cooper et al., 2008) and found between group differences. Therefore it is worthwhile for a future study to replicate the current study on the same sample of children and examine the latency of the N2 and P3b components for differences between the groups.

The lack of differences between the T1DM and control groups could be attributed to the duration of T1DM in our current sample of children. The mean duration of disease is $3.82 \pm 2.55$ years. It is probable that deficits in cognition, including executive functioning, would be apparent after a longer duration of disease. This suggests that diabetes is possibly cumulative across development (Desrocher & Rovet, 2004). Northam et al. (2001) found differences in executive functioning in their sample of children, whereby disease duration was at least six years. Hershey et al. (1997) and Ly et al. (2011) conducted follow up studies and examined their original sample of diabetic children in adulthood. Both studies found significant group differences between diabetics and controls in executive functioning. These various findings shed light on the possibility that longer duration of disease plays a role in deficits in executive functioning in T1 diabetics. Therefore it would be worthwhile to conduct follow-up studies on the current sample in future to examine whether deficits in executive functioning manifest after longer disease duration.

Early age of onset of T1DM, severe hypoglycemia and hyperglycemia have received the attention of an abundance of research studies (see Hershey et al., 1997; Rovet & Alvarez, 1997; Desrocher & Rovet, 2004; Brands et al., 2005; Hershey et
al., 2005; Perantie et al., 2007; Perantie et al., 2008; Aye et al., 2011; Ly et al., 2011; Blasetti et al., 2011; Cato et al., 2014) and findings have indicated or suggested that each of these complications contribute to deficits in executive functioning based on psychometric measures amongst people with T1DM.

Several studies have employed the use of alternative neuroimaging methods to examine the effect of T1DM on brain structure in both children and adults. Aye et al. (2011) conducted Magnetic Resonance Imaging (MRI) scans on 40 children comprising of diabetics and healthy controls aged three to 10 years of age. Although no significant differences in brain volume were found between the diabetics and controls, differences in white matter and hippocampal development related to the age of onset of T1DM were found in the diabetic group compared to controls (Aye et al., 2011). Similarly, Ferguson et al. (2005) conducted MRI scans on a sample of young adults who developed T1DM early in life and found ventricular atrophy and lesions in hippocampal white matter in their sample.

The current sample comprised of children, whereby the youngest participant was 6 years of age and the oldest was 10 years of age. Onset of diabetes is considered early if diagnosis occurs before the age of 7 (Ferguson et al., 2005), although some researchers define it at a younger age (i.e., 5 years of age; Desrocher & Rovet, 2004). Given the demographics of the current sample, coupled with the fact that mean duration of diabetes was 3.7 ± 2.5 years, it is clear that onset of diabetes was definitely at an early age in this sample. Given the abnormalities in structure and development of highly important brain regions expressed in adults who developed diabetes early in childhood, it is definitely essential and worthwhile for future research to examine the effects of EOD, along with the other complications (i.e. severe hypoglycemia and hyperglycemia) associated with T1DM, on executive
functioning in a follow-up study of the current sample later in adulthood. A combination of neuroimaging techniques – ERPs and MRI, for example – could be employed to examine and determine effects, if any, on executive functioning and identify changes in brain structure associated with longer disease duration.

Another direction for future research would be to consider the influence of modality on various ERP components associated with executive functioning. The N2 has been found to be modality specific, with auditory oddball stimuli eliciting lower N2 amplitudes than visual stimuli (Falkenstein et al., 1999; Falkenstein et al., 2002). As the current study consists of solely visual stimuli, future studies could employ either auditory tasks or tasks with a mix of both auditory and visual stimuli to examine if there are significant differences in N2 and P3b amplitudes and latencies.

In conclusion, the current study found minimal effects of T1DM on electrophysiological activity associated with response inhibition and updating of working memory. However, significant effects in other domains of executive functioning such as sustained attention, represented by the positive slow wave was found, with credit to the use of mass univariate analysis. These results are encouraging and heartening for Type 1 diabetic children and their families as there are minimal negative effects at this stage of the disease. However, it seems plausible that several deficits would appear later in life for these children. The current findings contribute to the existing body of research pertaining to T1DM and its effects on domains of cognition. They also reiterate the importance for researchers in future to develop a better understanding of the relationship between T1DM and cognition across development, especially in adulthood when disease duration has been long. A deeper comprehension and examination of the nature of the various complications (i.e. severe hyperglycemia, EOD, hyperglycemia) that accompany T1DM and their
respective degrees of contribution to cognitive deficits later in life is essential so as to enable these individuals to recognize and possibly compensate for these disease related disadvantages.
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APPENDIX A
Project KIDS Information Sheet

PROJECT K.I.D.S.
Neurocognitive Development Unit
School of Psychology
The University of Western Australia
CRAWLEY 6009
Phone: 6488 7342 Fax: 6488 1006

PROJECT KIDS ACTIVITY DAY PROGRAM - INFORMATION SHEET

January, 2012

Dear Parent,

Looking for something fun for your child to do?

Your child is invited to attend two activity days at the Neurocognitive Development Unit at the University of Western Australia.

The PROJECT K.I.D.S. research team will be running daily activity sessions for 7 to 11 year old children during the <<month>> school holidays/weekends in <<month>>. We have been running these activity days for the past 18 years and have found that kids have a great time! Children attend for two consecutive days and participate in a range of computer tasks, word games and puzzles as well as other fun activities. We also use brain-wave technology to examine activity of the brain while each child performs a simple task. This is a non-invasive measure that records brain activity via sensors placed on the scalp. To record this activity, an elasticised cap (a bit like a bathing cap) will be put on your child’s head and a small amount of salt-water paste placed underneath each of the sensors. This often results in some pretty unusual hairstyles! Your child’s hair will be washed and dried after they’ve finished the task. You can see these games and tasks in action in a short information DVD enclosed. We encourage you to review the DVD and discuss the procedures with your child prior to completing the attached consent form. Children usually find the activities enjoyable and stimulating but if your child is at all unhappy with any aspect of the day’s testing he/she may withdraw from all or part of any activity at any time. We also ask parents some questions about their child’s learning, strengths, challenges and interests.
Children’s responses to the computer tasks, puzzles, and games will go into our research database to help us learn about children’s thinking and development. Parents’ responses to questions about their child will also go into our research database to help us get a clearer picture of each child’s developmental progress. Of course, all information will be treated in the strictest confidence. It will only be accessible for use in approved research projects and only released if we were required to do so by law. No identifying information (such as your child’s name) will be stored with the information we collect. Children will only be identified by a code number. The data are then stored securely in a password protected file on a computer stored in a locked office at the University of Western Australia and can only be accessed by myself and the members of my research team.

We will be taking some video images of the children and staff throughout the day to assist in our research and for publicity to help us secure grant funding. You can choose for your child not to be videotaped or photographed if you prefer. All children will receive certificates of achievement, and a special Project KIDS gift at the end of their second day!

Children will remain within the Neurocognitive Development Unit and playground complex for the entire day, and will be supervised in groups of no more than 4 children per team leader. Sessions will be held between 8.45am and 4.30pm, Monday to Friday/Saturday or Sunday (delete as appropriate). A healthy lunch and snacks will be provided. We endeavour to keep friends, siblings or children from the same school together as much as possible, particularly if you indicate the name of the school friend in the space provided on your registration form.

After your child has completed Project KIDS you may be offered an opportunity to participate in a trial of one of three approaches to improving your child’s working memory and problem solving skills. We also like to get in touch again over the years to follow-up and see how your child is doing with their learning and life skills. If you would like your child to participate in the current study but would prefer not to be re-contacted please indicate this on the attached consent form. This will not affect your child’s ability to attend the Activity Day Program in <<month>>.

These sessions are held at NO COST to parents.

If you are interested in your child participating in this study, please complete the enclosed registration and consent forms and return them in the reply paid envelope provided. As we only have places for a limited number of children each day, you will need to reply as soon as possible to ensure your child’s involvement. When we receive your child’s registration form, we will contact you to organise the day your child can attend. We will also send you more detailed information about your child’s Activity Sessions including a map showing you where to find us.

If you are not interested in your child participating in the Project K.I.D.S. research program, it would be greatly appreciated if you could please return the DVD in the reply paid envelope provided to help us with recycling and minimising waste.
Unfortunately, we are not able to offer places to those children who have attended PROJECT K.I.D.S. before. If you would like further information, please call Bec on 6488 7342 or email at pkids@psy.uwa.edu.au.

We look forward to meeting your child.

Professor Mike Anderson.
Research Director, Project KIDS
### RESEARCH PROGRAM REGISTRATION FORM

2012

Please complete these forms & return them in the reply paid envelope as soon as possible.

<table>
<thead>
<tr>
<th>Child's First Name</th>
<th>Child's Surname</th>
<th>Child's Sex M / F (please circle)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Child's Date of Birth</td>
<td>Child's Year at School 3 4 5 6 7 (please circle one)</td>
<td>Child's School</td>
</tr>
<tr>
<td>Parent(s)’/Guardian(s)’ Name(s)</td>
<td>Address</td>
<td></td>
</tr>
<tr>
<td>Phone Number</td>
<td>Postcode</td>
<td>Is English your child's first language? YES / NO</td>
</tr>
<tr>
<td>Home</td>
<td>Work/Mobile</td>
<td></td>
</tr>
</tbody>
</table>

**Note:** Email addresses will only be used to update parents with information relevant to their child’s attendance at Project K.I.D.S.

**Preferred Week** *(please circle one)*  
(insert date)  
(insert date)  
NB. Child attends for **two consecutive days**

Is there another child whom you would like to attend the same session? If so, please list his/her name & age & whether they are at your child’s school or another school.

Any special dietary requirements (please list)

Any special health considerations (please list)
Any additional information you think is relevant

* If you have preferred days please note them for us, but we cannot guarantee that you will be able to attend on those days if they are already booked out.

PLEASE TURN OVER AND SIGN CONSENT FORM
APPENDIX C: Project KIDS Consent Form

_______________ (insert parents/guardian's name) and
_______________ (insert child's name) have read the PROJECT K.I.D.S. Information Sheet and we have watched the PROJECT KIDS DVD. Any questions we have asked have been answered to our satisfaction. We agree to my child and family participating in the PROJECT K.I.D.S. Research Program conducted by Prof. Mike Anderson of the University of Western Australia, School of Psychology.

We understand that we can withdraw from the study at any time without concern or prejudice by informing the researchers. We know that our child can also withdraw from any of the activities at any time, without reason and without prejudice, by informing PROJECT K.I.D.S. staff.

I agree that data gathered for the study may be published provided my child's name or other identifying information is not used. We can choose to withdraw our permission for our child's image or our family's data to be used for this research project until the point of publication.

We understand that the Project KIDS staff use video recording and photographs for the purpose of assessment of each child as well as for training and publicity. We know that we can choose not to have our child photographed or videotaped by marking the box below.

   We do NOT agree to the recording of video and photographs during the day.
   We do NOT agree to our child's image to be included in publicity material.

From time to time, the Project KIDS team secure grants that enable us to pilot new training programs to help improve children's working memory or problem solving skills. We also like to follow-up former project KIDS participants to see how they are going. Please indicate below if you do not wish to be contacted for the purpose of follow-up.
We do NOT agree to being contacted for future training programs.
We do NOT agree to being contacted for follow-up studies.

When children are referred to Project KIDS from other services such as PMH or Neurosciences we routinely send a report to the referrer. If this is relevant to you, please let us know if you do not wish us to do so.

We do NOT want our child's results to be shared with the service that referred him/her.

Our signatures below indicate that we have understood the information provided.

Parent/guardian's signature: Date:
Child's signature: Date:

Preferred contact phone number or email address: ____________________________

The Human Research Ethics Committee at the University of Western Australia requires that all participants are informed that if they have any complaint regarding the manner in which a project is conducted it may be given to the research or, alternatively, to the Secretary, Human Research Ethics Committee, Registrar’s Office, University of Western Australia, 35 Stirling Hwy, Crawley, WA 6009 (telephone number 6488-3703). All study participants will be provided with a copy of the Information Sheet and Consent Form for their personal records.