34th Annual International Conference of the IEEE EMBS
San Diego, California USA, 28 August - 1 September, 2012

Indication of Abnormal Peripheral Sensory Processing of Rotational Stimulation in ADHD

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Abstract— **Attention Deficit Hyperactivity Disorder (ADHD) has been associated with motor abnormalities. Given the importance of the vestibular system in motor control, the investigation of the peripheral vestibular response is a promising area of ADHD research, which could lead to an improved understanding and management of the disorder. This study aimed to investigate the evoked peripheral vestibular response to rotational stimuli in ADHD affected adults, using Electrovestibulography (EVestG). Data was collected from 6 ADHD affected adults (2 males, 4 females) and contrasted with that of a Control group comprised of 30 individuals (10 males, 20 females). Raw data was 120 Hz high pass filtered and analyzed using the Neural Event Extraction Routine to identify local field potentials, which represent the summed activity of the components of the inner ear. The inter field potential intervals (IFPI) were calculated as the time intervals between field potentials. Analysis of the IFPI indicated that the ADHD group exhibited significantly shorter periods between field potentials generated in the right ear during left rotational acceleration than Controls (unpaired, two-tailed Student's t-test assuming unequal variance, $p<0.05$). However there was no significant difference between groups for left ear signal during right rotational acceleration. This preliminary study provides an indication as to the possibility of lateralized, abnormal inner ear responses to kinematic stimuli in the ADHD affected population. However, further studies are required to validate and elucidate this data.**

I. Introduction

The peripheral sensory systems act as our interface with the outside world, enabling the conversion of real world stimuli into biological signals. Abnormality in these systems can contribute to an altered perception of, and reaction to, the outside world. Thus improved understanding of the senses is pivotal to understand the brain and the various disorders which can affect it. One of the least investigated of the sensory apparati is the peripheral vestibular system. Housed together with the cochlear in the labyrinth of the inner ear, the vestibular system contains 3 orthogonal, semicircular canals for the detection of angular acceleration and 2 otolithic organs for the detection of linear acceleration [1]. These structures contain specialized hair cells which bend in response to relevant movements. The direction and intensity of the movement of the hair cell will regulate the firing of connected afferent nerve fibers [1]. These neurons run through the eighth cranial nerve to synapse with vestibular nuclei located within the brainstem [1]. The information provided by the peripheral vestibular system is integrated with information from other sensory streams to provide the conscious perception of the body's kinematics [2]. Thus, disorders which are associated with motor dysfunction necessitate an investigation of vestibular function, in order to provide a comprehensive understanding of their underlying features. Attention Deficit Hyperactivity Disorder (ADHD) is one such condition [3-6].

ADHD is known by the symptoms for which it is diagnosed, namely the presence of continuous and disruptive inattention and/or hyperactivity and impulsivity [7]. However, the disorder is also associated with abnormalities of motor control and balance [3-6]. There is evidence to suggest that dysfunction of the central vestibular processing pathways may underlie some of these abnormalities. In particular, the cerebellum has been found to be reduced in ADHD [8], particularly the size of lobules VIII-X [9]. The aforementioned lobules comprise the vestibulo-cerebellum [10], which has reciprocal connections with the vestibular nuclei [11, 12]. The cerebellum acts to induce inhibitory post synaptic potentials in the vestibular nuclei [13]. It has been indicated that the vestibular nuclei may regulate the responses of the vestibular end organs via an efferent system [14]. Thus it is plausible that a peripheral vestibular dysfunction may present itself in an ADHD affected population.

Given the commonality of ADHD, which has been estimated to have a worldwide prevalence of 5.29% [15] and the difficulty in the standardization of diagnostic practices [16], it is imperative that the physiological features of the disorder are evaluated to improve the understanding and management of the disorder. The aim of this research was to conduct a preliminary investigation of the responses of the labyrinth to rotational stimuli in ADHD affected adults using Electrovestibulography (EVestG) [17].

This report focuses on one of the prominent differences found in this pilot study between the ADHD and Control groups, the response of the right ear signal during left rotational acceleration (R-LROT). The response of the left ear signal during right rotational acceleration (L-RROT) is also considered. Both R-LROT and L-RROT are believed to exert a largely inhibitory effect on the semicircular canals of the right and left ears respectively [18], whilst eliciting a complex otolithic response [19, 20].

This research was partly supported by the Australian Research Council and Neural Diagnostics Pty Ltd. under LP0669420 and LP0454001 Grants.

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II. Methods

A. Subjects

Participants aged 18 years and over who have been diagnosed with ADHD in accordance with DSM-IV criteria [7], underwent an EVestG recording. Ethics approval was obtained from the Human Research Ethics Committee of the Alfred Hospital and from the Standing Committee on Ethics in Research Involving Humans from Monash University.

The ADHD group was composed of 6 participants (2 males, 4 females) with a mean age of 37.3 and a range of 28-56 years. The Control group comprised recordings from 30 volunteers (10 males, 20 females) with a mean age of 37.5 years and a range of 23-65 years. The comparatively large Control group was selected to allow for the visualization of the normal variation in the labyrinth signal that is seen in the population.

B. Methodology

EVestG is a non-invasive methodology which allows for the recording of the signal developed at the inner ear. This is achieved by sampling the potential proximal to the ear drum via an electrode which has been inserted into the ear canal, relative to the potential at the ipsilateral earlobe. Left and right ear signals were recorded at rest and during rotational movements. The movements were standardized by seating subjects in a multi-axis, hydraulic chair which was programmed to undergo preset tilt sequences. Noise was reduced by placing the hydraulic chair within a sound attenuating booth (>30dB). The signal was passed through a CED 1902 pre-amplifier and digitized using the CED Micro-1401 before being transferred to a PC. Raw data was 120 Hz high pass filtered and analyzed using the Neural Event Extraction Routine (NEER) [17, 21]. NEER utilizes the complex Morlet wavelet to identify local field potentials, which represent the summed activity of the components of the inner ear. These field potentials are embedded in noise and NEER is able to extract them by dividing the signal into several logarithmically spaced scales and identifying loci where phase changes across multiple scales. A matched filter, which represents known properties of a field potential, is applied to the signal at these loci in order to identify if a field potential is present. For more information about the EVestG method and NEER please refer to [17].

One of the outputs of the NEER analysis is an array containing the time of occurrence of the field potentials. This study focused on the intervals between field potentials, referred to as the inter field potential intervals (IFPI). For each individual, in each group, these intervals were calculated as the difference between field potential (n) and field potential ($n - i$) where i is the degrees of separation (DOS) between field potentials. These IFPI are depicted in Fig. 1.

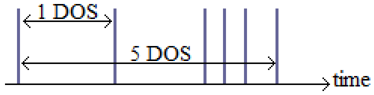

Figure 1. Representation of IFPI at various degrees of separation (DOS).

The rotational sequence begins with 20s of background recording, followed by a 3s rotation to the right. This first rotation is predominantly excitatory on the right and inhibitory on the left and is broken down into a 1.5s acceleration period onaa and a 1.5s deceleration period onbb (refer to Fig. 2 for position and velocity information about the 3s movement). The movement is followed by 17s in the rotated position and then a 3s movement back to the original seated position. Following a 17s break the subject is then rotated for 3s to the left; this movement is predominantly excitatory on the left and inhibitory on the right (and is also broken down into onaa and onbb with position and velocity information depicted in Fig. 2). Once again, the movement is followed by 17s in the rotated position, and a 3s rotation back to the original position, followed by 17s in the original position.

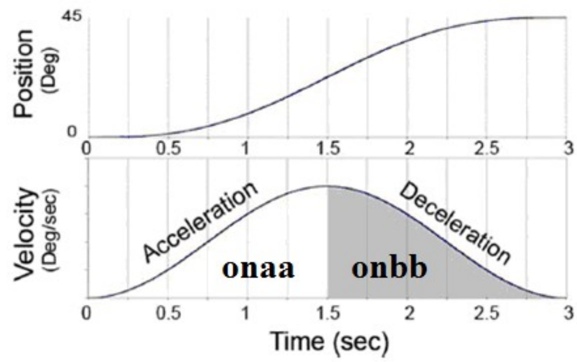

Figure 2. Kinematics during onaa and onbb sections of tilt sequence. Source: [22]

C. Data Analysis

Analysis focuses on the onaa section of the L-RROT and R-LROT tilts. Results are presented for mean group IFPI, which were calculated by taking the mean of each of the group members' mean IFPI times. Cumulative IFPI distributions were calculated for 1 – 10 DOS. Results are presented for 1 DOS to visualize the temporal properties of adjacent field potentials and 5 DOS as this result showed a clear separation between groups. One ADHD subject was excluded from analysis due to obvious artifact interference which significantly reduced the usable signal (by 30% or more). One Control subject was excluded as no data was available for the rotation sequence. Results are presented as means with error lines representing 95% confidence intervals. Excel was used to conduct an unpaired, two-tailed Student's t-test assuming unequal variance, in order to ascertain if differences between groups were significant, with $p<0.05$ considered to be significant.

III. Results

A. Mean IFPI of 1 DOS during onaa of the L-RROT and R-LROT tilts

Fig. 3, depicts the group mean IFPI (1 DOS) for tilt section onaa of R-LROT, in which the ADHD group displayed significantly shorter mean IFPI (1 DOS) than the Control group. There was no significant difference between groups during onaa of L-RROT (Fig. 4).

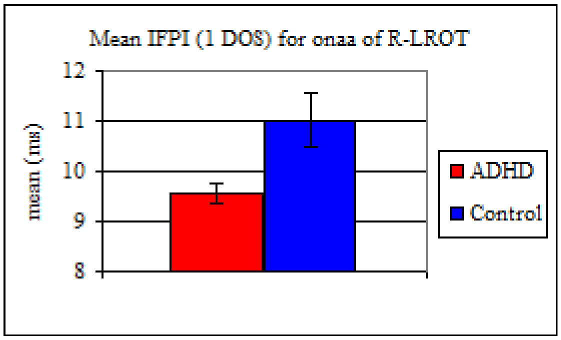

Figure 3. Mean group IFPI (1 DOS) during onaa of R-LROT. Error bars represent 95% confidence intervals. There was a significant difference between groups with p= 2.63E-05.

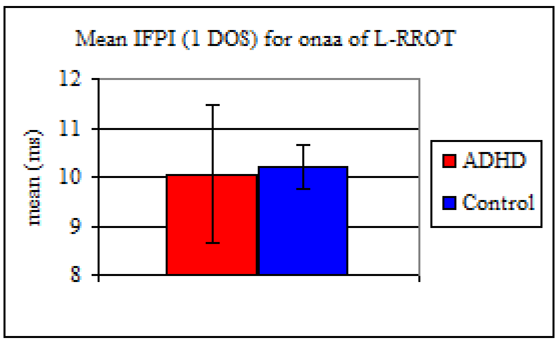

Figure 4. Mean group IFPI (1 DOS) during onaa of L-RROT. Error bars represent 95% confidence intervals. There was no significant difference between groups.

B. Cumulative frequency distributions

The cumulative distribution indicates the probability that an IFPI will occur within an interval T, where T is the value on the time-axis. The IFPI, cumulative distribution for ADHD and Control groups for the right ear signal during the onaa section of the R-LROT tilt for 1 DOS is indicated in Fig. 5.

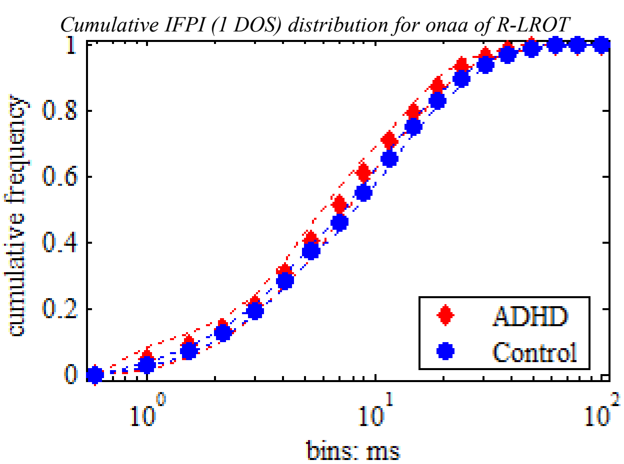

Figure 5. Cumulative frequency distribution of IFPI from the onaa section of the R-LROT tilt. Dashed lines represent 95% confidence intervals.

The cumulative distribution at 5 DOS (Fig. 6) shows a greater separation between the ADHD group and Controls than the cumulative distribution at 1 DOS. The purpose of presenting results for 5 DOS is to indicate that a greater clustering of field potentials occurs in the ADHD group. For both 1 and 5 DOS the ADHD cumulative distribution curve is shifted to the left, relative to the Control group, with this effect being more prominent at 5 DOS.

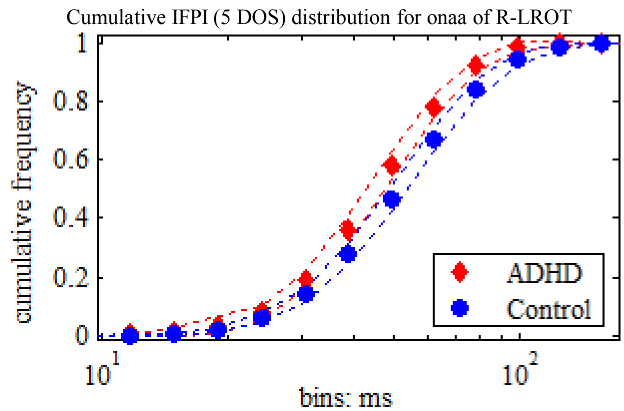

Figure 6. Cumulative frequency distribution of IFPI at 5 DOS from the onaa section of R-LROT. Dashed lines represent 95% confidence intervals.

IV. Discussion

Impairment in inhibitory control has been characterized as a feature of ADHD [23, 24]. Thus, the increased activity, as indicated by decreased IFPI, during R-LROT may be an indication of the presence of inhibitory impairment of the peripheral vestibular system in ADHD. However, this finding was not replicated in L-RROT. This result may be the outcome of a small sample size or it may indicate a lateralized deficit in peripheral vestibular function in individuals with ADHD. ADHD has previously been associated with a lateralized dysfunction of the right frontal cortex [23]. It has been suggested that lateralized deficits may contribute to a rightwards movement overshoot in ADHD affected children [25]. Further research is required to understand whether the findings presented in this study relate to previously described right side abnormalities [23, 25].

Given the small sample size of the ADHD group, a larger study will be required to validate and elucidate these results. Any future studies will also have to investigate the influence of co-morbidities because they affected all of the subjects in the ADHD group and affect upwards of 80% of all adults who have ADHD [26]. If such an investigation was to allow for the characterization of the effects of co-morbidities on ADHD this would enable for therapies to become more personalized by indicating how treatments affect an individual's health profile.

The subtype of ADHD will also require consideration in any subsequent studies as the combined type of ADHD has been associated with more balance problems than the predominantly inattentive type [3].

Future studies should also consider the effects of medications as half of the subjects in the presented ADHD group were prescribed dextroamphetamine, which has been shown to affect the vestibular nuclei [27]. If dextroamphetamine causes a measurable change in peripheral vestibular activity, then recording and analyzing the activity of the labyrinth in response to kinematic stimuli, may allow for the objective evaluation of the effects of this medication. This may enable greater uniformity of diagnostic and therapeutic practices nationally and internationally.

V. Conclusion

This preliminary study suggested the presence of impaired sensory processing of rotational, acceleratory stimuli in ADHD affected adults. Future studies, with larger sample sizes, are required to elucidate and validate these findings.

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