Evaluating a novel brain-computer interface and EEG biomarkers for cognitive assessment in children with cerebral palsy

By

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Table of Contents

List of Figures

List of Tables

Chapter One: Introduction

Problem Summary

Standardized neuropsychological assessments and research instruments are typically administered with verbal queries, pictures and manipulatives that require verbal or motor responses. Requiring verbal or motor responses means that the assessments are often inaccessible to people with physical and communicative impairments, especially those who cannot talk or point [1,2]. The lack of accessible cognitive tests [1,3] causes those who are most vulnerable, due to physical and communication impairments, to be dismissed as “untestable” and excluded from medical standards-of-care. Consequently, to the inability to be evaluated, they are denied optimal participation in medical decision-making, prevented from receiving full assessments of neurological status, and unable to consistently monitor the effects of their medical/pharmacological treatment. This barrier also precludes research on cognitive symptoms both in the early acute phases of recovery from illness or injury and in the final stages of progressive diseases. Overall, the inability to accurately test the cognitive ability of a severely physically impaired individual leads to improper medical and educational decisions that cost schools and medical insurance providers over $40 billion yearly, while significantly impacting the quality of life of the patients [4,5]. Brain-computer interfaces (BCIs) and brain network science may provide an option to identify a person’s cognitive ability without the need for physical movement.

Literature review

The following sections provide a high-level overview of the concepts one must know to understand Chapters 2-4. It is not necessary to read them in order, and one can also skip directly Chapter 5. Further chapter specific background is added within each respective chapter.

The goal of this project is to create a temporary device for cognitive assessment; therefore, only non-invasive electroencephalography (EEG) methods will be covered [6,7]. First, we will cover the standard tools used for measuring a subject's cognitive capacity and then we will dive into how EEG could be incorporated to evaluate cognitive capacity in those who cannot respond to standard assessments tools due to motor and speech impairments.

Neuropsychological assessments

Clinicians use neuropsychological assessment to yield a diagnosis that will allow them to determine appropriate intervention strategies and assess a person's performance over time. The outcomes of these tests can determine what type of care or resources a person has available to them. These resouces include medical planning and medication management, rehabilitation services, special education and vocational classes, and access to assistive technologies [6-8]. Neuropsychological assessments are usually categorized into one of five categories: intelligence quotient, academic achievement, adaptive function, cognitive function and psychological/behavioral tests. Each of these categories has multiple types of tests that measure different aspects of a person's neuropsychological status [6-8].

Intelligence tests are the most well-known forms of neuropsychological assessments. They are used to determine an individual's broad mental capacity. A common test is the Wechsler Adult Intelligence Scale (WAIS) [9]. The WAIS covers verbal comprehension, perceptual reasoning, working memory and processing speed. The test spans about 65-80 minutes and provides intelligence quotient (IQ) scores. An average score is 100, with higher scores suggesting above average intelligence and lower scores suggesting lower than average intelligence [6,7,9,10]. While the WAIS and other intelligence test have significant advantages, the diversity of testing paradigms make them hard to replicate and control for test validity when altering the tests for use with a BCI.

Achievement tests like Wechsler Individual Achievement Test [11] are typically used to measure a student's acquired knowledge in educational areas such as reading, written language, oral language and mathematics. While this may seem like an intelligence test, achievement tests are more focused on assessing developed skills or knowledge instead of examining a person's ability to act purposefully and effectively adapt to new problems [6,7,11]. Like the WAIS-IV, achievement tests have a diversity of testing paradigms, thus making it hard to replicate and control for test validity when altering the test for use in a BCI.

Adaptive behavior tests like the Vineland Adaptive Behavior Scales-II [12] are typically given to determine how well a person can handle the demands of life and measure a person's independence. Questions are usually age-based and evaluate a myriad of skills, including practical ones such as money management. They also assess social skills, like the ability to behave around others, and conceptual skills, such as planning and organization [6,7,12]. Most adaptive behavior tests are focused on day-to-day interactions, which tend to rely extensively on motor and verbal abilities [6,7,12]. While many of the theses measures are valuable, the purpose of our study is to measure cognitive capacity. In addition, we plan to use a BCI because the intended subjects have challenges with assessments that rely on motor or verbal responses.

Cognitive function assessments cover the largest diversity of neuropsychological factors. Such factors include attention, language, memory, motor and executive function [6,7]. One popular test is the Peabody Picture Vocabulary Test-IV, which is a receptive vocabulary assessment [13]. The PPVT-IV is untimed, multiple choice, has a strong test-retest reliability ranging from .91 to .94 and can be used as a proxy to measure intelligence [13]. All these factors make it a desirable test to convert into a BCI-facilitated test. The fact that it is untimed removes the need to control for time, while the multiple-choice format allows us to display all possible answers at once and reduces selection time compared to tests that allow for freeform responses. Additionally, the strong test-retest reliability allows us to compare our BCI-facilitated method with the standard PPVT-IV. Furthermore, the PPVT-IV only has one exam format which reduces the complexity of building a BCI-facilitated system.

Personality/psychological tests are used to assess an individual's personality and emotional function, which may be difficult to identify during standard clinical interviews. Due to the many cognitive domains covered by these tests, they are usually given as bundles of tests called batteries [6,7]. An example of such a test is the Minnesota Multiphasic Personality Inventory [14]. We decided against using personality/psychological tests for several reasons. The first reason is that we are not targeting the personality or emotional function of an individual. Secondly, the response modality of the BCI is significantly limited compared to verbalizing a response. Attempting to translate a test that allows free form responses into a BCI may significantly alter the results of the assessment since the response modality of the BCI is significantly limited compared to verbalizing a response.

Picking the right test to adapt for cognitive assessment is important. Based on our survey of testing methods, we believe the PPVT-IV is a strong candidate for translation to a BCI-facilitated assessment system. Before delving directly into BCIs, it is important to understand the basics of electroencephalography and how it can be used for assessing cognitive capacity of an individual.

Electroencephalography as a tool for assessment

Electroencephalography is a brain imaging technique that allows for the noninvasive recording of electrical changes of an individual's brain. Brain activity is typically from ±100μV, ranges from 1-50Hz, and is measured from the scalp using non-surgical electrodes [15,16]. Two different kinds of signals are recorded from EEG 1) spontaneous activity and 2) evoked potentials [16].

Spontaneous activity is broken down into frequency bands and the increase or decrease of their spectral power is associated with different mental states [16]. Delta waves are the slowest signal at about 4Hz or less, and are typically recorded at the frontal and parietal lobes during slow wave sleep. Theta waves range from 4-7 Hz, originate from the hippocampus, and are usually associated with light sleep. Alpha waves range from 8-15Hz, are typically recorded from the occipital lobe, and are associated with being awake but mentally relaxed. Beta waves range from 13-31Hz, are typically recorded from the frontal and parietal lobes, and represent an active and awake individual. Lastly, gamma waves represent any brain related oscillation over 32Hz [17-19] and these waves are typically associated with the occurrence of cross-modal sensory processing (i.e. processing combined sensory input like sound and sight simultaneously) (Table 1) [17,18].

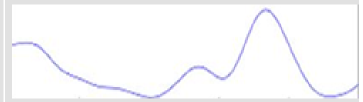
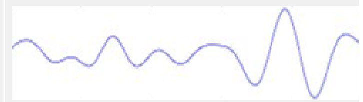
Name	Frequency Band	Details	Wave
Delta	<4Hz	• Frontal and parietal • Slowest wave • Seen during sleep	
Theta	4-7Hz	• Hippocampus • Drowsiness or light sleep • Idling or inhibiting response	
Alpha	8-15Hz	• Occipital • Relaxed, eyes closed	
Beta	13-31Hz	• Frontal and parietal • Active brain	
Gamma	>31	• Cross-modal sensory processing	

Table 1 Summary of brainwave

Evoked potentials (VP) are electrical changes that occur in response to a specific stimulus. They are normally characterized by two distinctive features: the letters P or N, and a number. The letter corresponds to the electrical change being positive (P) or negative (N) when recorded using EEG. The number corresponds to the average time in milliseconds at which the change occurs [16,20]. For example, a P100 response would signify a positive change in brain activity at 100 ms. Some evoked potentials are created using repetitive stimuli such as images or sound. For example, Itakura [21] flashed images either to the left or right visual field of three subjects and found that, when the image was initially presented on the left visual field, there was P75 and N100 present on the right occipital electrode. The electrode location of these VPs then reversed (left occipital electrode) when the image was presented on the right visual field. Itakura’s method is called a transient visually evoked potential (TVEP) [21]. If the flash is instead repeated consistently at a frequency greater than 4Hz, the result is called steady state visually evoked potentials (SSVEP). In this case, the brain activity recorded from the occipital lobe electrodes begins to synchronize with the frequency of the stimuli that is presented to the user [21-25].

Another kind of evoked potential is an event-related potential (ERP), which is evoked by an event, such as something important changing. ERPs are time locked to the event occurring [15,16]. There are numerous types of ERP waves that are stimulated by different events such as language structure or presenting important visual stimuli [26-29]. One classical example of an ERP is elicited by asking a subject to perform the oddball task. During an oddball task, a subject is asked to be mentally aware of when an important stimulus (called a target) is being presented while unimportant stimuli (called distractors) are also presented [29,30]. For example, in Campanella [30], 50 subjects viewed serially presented images of a woman or a man. In Campanella's study, the picture of the woman was the distractor and the picture of the man was the target. In total, the subject was shown either the man or woman's face 170 times, of which 30 instances were the man's face (target) while 140 displayed the woman's face (distractor). Like many others, Campanella found that time locked 300ms after presenting the image of the man's face (target), there was a positive change in the subject's brain activity i.e. a P300 [29,30].

Spontaneous activity and evoked potentials have both been used to study disease states and cognitive ability [15,19,20,29,31]. For example, Basar [19] studied the differences in alpha, beta and gamma waves between 19 schizophrenic subjects and 19 typically developing subjects. Afterwards, he compared this study to his previous study of Alzheimer's and bipolar disorder. Basar found that subjects with schizophrenia demonstrated lower gamma activity than typically developing subjects. Additionally, in all diseased states, he noted a decrease of delta activity compared to typically developing subjects [19]. Another example is Vogel [32], who analyzed EEG alpha band power in 101 typically developing adults while their eyes were closed. Vogel found that alpha band power was positively correlated to a subject's intelligence quotient (IQ).

Similar studies on disease state and intelligence have been done with ERPs. For example, Bramon [33] used an auditory P300 oddball paradigm in 37 patients with bipolar disorder and 42 typically developing (TD) subjects. Bramon found that subjects with bipolar disorder had significantly delayed P300 responses. Another example is Barratt [34], who gave intelligence assessments to 45 subjects and also had them undertake a P300 oddball experiment separately. He found that P300 amplitudes correlated positively with intelligence.

These studies suggest that spontaneous activity and evoked potentials can provide insight into the cognitive capacity of those who cannot take standard cognitive assessments due to motor and speech impairments. Another approach uses EEG to look at how the signals at different regions of the brain change with respect to time. This is accomplished by examining coherence, and phase delay analysis. To derive coherence, one measures the statistical difference between two signals within a consistent phase shift. This comparison of the two signals is usually done to estimate connectedness between two regions in the brain, and higher values imply more connectedness. Phase delay is strictly the time difference between two similar signal responses.

Gasser was one of the early thought leaders in using coherence to assess differences in intelligence [35]. He compared the coherency of 158 TD subjects with 47 subjects who had low IQ. Coherence estimates were taken from the frontal, occipital and frontal to occipital electrodes. Gasser found that children with cognitive impairments had higher coherence in the theta band in the frontal to occipital lobes [35]. Another example is Biver [36], who analyzed coherence differences in high IQ and low IQ subjects. Biver found that high IQ individuals demonstrated short interhemispheric (localized connections e.g. frontal lobe) EEG phase delays, long intrahemispheric (global connections e.g. frontal to occipital lobe) phase delays and reduced coherence across all frequency bands. He also found that delta, alpha, beta and theta bands were positively correlated with intelligence [36].

By combining these (and other) band pass, coherence and phase delay results, it is possible to find a relationship between EEG biomarkers and IQ [32,35-41].

- Delta power in the frontal cortex is negatively correlated to IQ.
- Theta power in the frontal, central, parietal and occipital lobes are negatively correlated to IQ.
- Alpha power in the frontal and occipital lobe is positively correlated to IQ.
- Beta power in the frontal and parietal lobe is negatively correlated to IQ.
- Beta power in the occipital lobe is positively correlated to IQ.
- Gamma power is negatively correlated to IQ.
- Coherence across all bands is negatively correlated to IQ.
- Short interhemispheric phase delays and long intrahemispheric phase delays are correlated to IQ.

Results for delta, theta, beta (frontal and parietal), gamma and coherence all agree with the neural efficiency theory[35]. The neural efficiency theory suggests that lower brain activation is needed to process the same information in a high IQ individual versus a low IQ individual. Thus, we would expect to see lower power band results in high IQ individuals than low IQ individuals. Alpha bands on the other hand would seem to violate the neural efficiency theory. However, increased alpha power bands are associated with a relaxed mental state and low workload. We can therefore assume that a high IQ individual would also display a lower workload (higher baseline alpha powerband) compared to a low IQ individual[39].

Low coherence, short interhemispheric phase delays and longer intrahemispheric delays suggest that brain processes are happening more locally than globally. This is in line with current functional connectivity EEG studies that suggest that higher IQ individuals use small, locally isolated and highly clustered brain regions to process information, while low IQ individuals require additional recruitment across the brain. In our studies, we expect to see a similar correlation to occur based on a subject's IQ[35,36].

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Previous studies have investigated EEG biomarkers in CP [42,43]. For example, Sobaniec found that subjects with spastic displegia cerebral palsy had longer interhemispheric phase delays and increased coherence in the theta and delta bands [44]. They also exhibited increased alpha power bands in the temporal, parietal and occipital lobes than TD subjects. Bockoski found similar results in 26 children with hemiparetic cerebral palsy [45], as did Takeshita [46] in 12 subjects with preterm diplegia. These results imply that subjects with CP should have lowered intelligence [43]. However, only 50% of subjects with CP exhibit intellectual disability [8]. This suggests that the results as they relate to functional connectivity and intelligence may not apply directly to all populations. We believe this is due to a neural compensation from a subject's underlying pathology [43]. This suggests that the brain of a person with cerebral palsy may demonstrate biomarkers of decreased intelligence due to brain network reorganization, but those markers may not adequately reflect his IQ. Thus, before these biomarkers can be used as possible cognitive assessment tools, it will be important to investigate how disease states alter the interpretation of these biomarkers.

Brain-computer Interfaces for cognitive assessments

BCIs enable humans to communicate and control software and hardware using only their brain activity [47-49]. While there are many brain imaging methods for BCIs, we will focus on EEG related methods since they are noninvasive and highly mobile, which makes them ideal temporary cognitive assessment tools.

There are four primary BCI control methods: sensory motor imagery, slow cortical potential (SCP), visual evoked potential (VEP) and event-related potential (ERP or P300) BCIs. Sensory motor imagery BCIs use changes in brain activation in the motor cortex when a user imagines moving her left hand, right hand, feet or a combination of these sources as control inputs (Figure 1) [22,50-52]. Slow cortical potentials (SCP) use increased or decreased brain activation in the frontal lobe to control their input [53-55], thus providing a binary control (Figure 2). Both SCP and motor imagery BCIs can take months to reliably control. In our study, we focus on creating a temporary device for cognitive assessments; a long training time is not adequate for our purpose [22,56,57]. For this reason, we will be focusing our review on VEP and ERP/P300 BCIs.

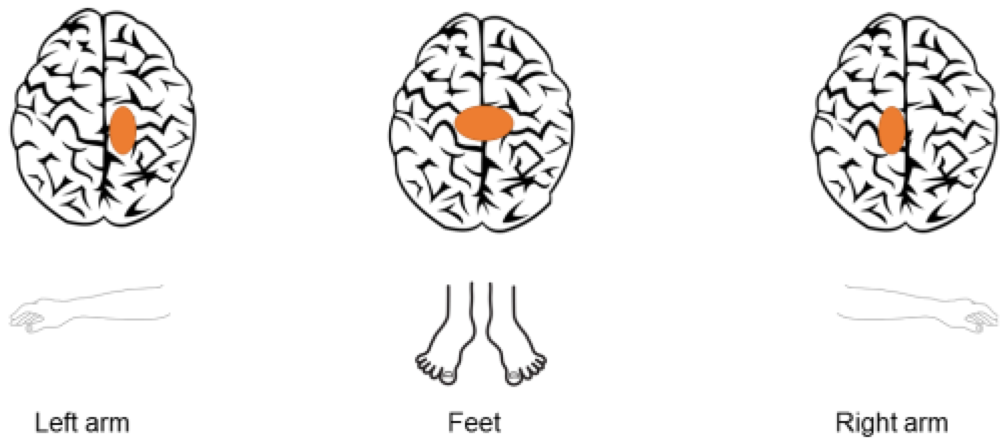

Figure 1. Illustration of brain activation for sensory motor imagery BCI

- The orange dot represents increased brain activation. The activations are with respect to what the subject using the BCI is imaging.
- Imagining left arm movement activates the right side of the motor cortex.
- Imagining right arm movement activates the left side of the motor cortex.
- Imagining the feet movement activates the motor cortex more centrally.

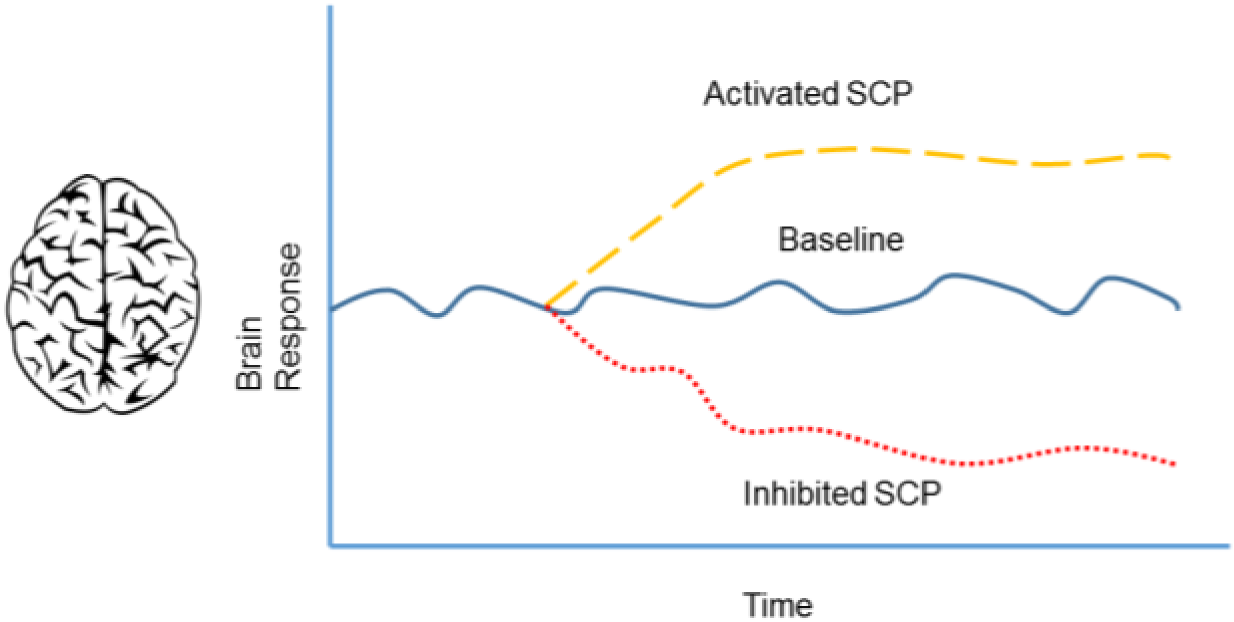

Figure 2. Illustration of brain activation from slow cortical potential (SCP) BCI

- The solid blue line represents baseline brain activity.
- The dashed yellow lined represents a user activating their slow cortical potentials for a positive BCI response.
- The dotted red lined represents a user activating their slow cortical potentials for a negative BCI response.

Visual evoked potential (VEP) BCIs use brain activity modulations in the visual cortex in response to visual stimuli presented to the user [21,22]. VEP BCIs are split into two modalities, TVEP and SSVEP. The difference is that, in regard to BCIs, the resultant response is used to classify a user's selection [21-24,58]. For example, in Itakura [21], researchers could determine if the user wanted to select the image on the right or left by detecting P75 and N100 responses. Another example is Perego, who developed a cognitive assessment BCI, which used SSVEPs [59]. Perego used four flickering Light Emitting Diodes (LED) on the sides of a monitor to provide SSVEP stimuli. The monitor displayed the cognitive assessment questions and answers to the subject and provided visual feedback on the subject's current selection. To answer a question, the subject focused their gaze on the left or right LEDs, which moved a selection cursor to the next answer. Once they had moved the selection cursor over their desired selection, the subject would focus their gaze on the top LED to submit the selection [22,23,25,59,60]. Perego's study suggests that SSVEPs could be a strong tool for cognitive assessments therefore warrant further investigation in our study (Figure 3).

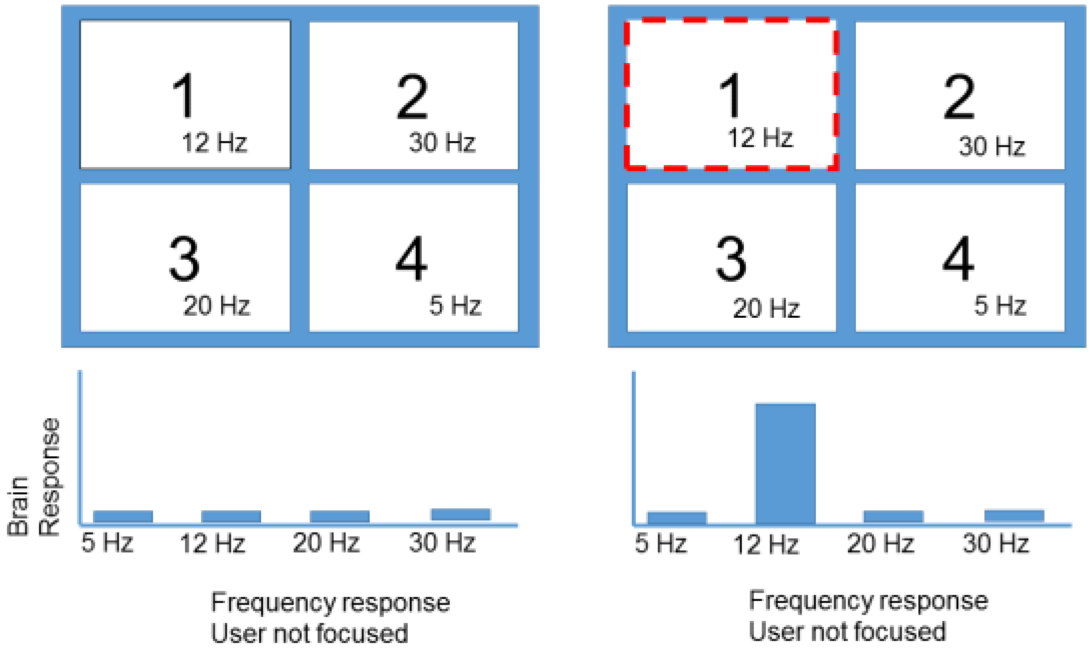

Figure 3. Illustration of brain response of visually evoked potential (VEP) BCI

- Each large number corresponds to a different selection a subject can pick. These selections are all flickering from white to black at the same time (not shown), at the frequency described below each large number.

- Left-side images represent when a subject is not selecting, while the right-side images represent when the user is selecting the number 1. The red box indicates what the subject is selecting.

- Lower images represent the frequency component of brain activity recorded from the occipital lobe.

- When the subject selects the number 1, a frequency response occurs in the occipital lobe at 12 Hz. The frequency that is observed in the occipital lobe always matches the frequency of the subject's selection.

Event-related potential (ERP or P300) BCIs use the same oddball strategy described above, however, they typically feature a matrix that displays all the possible options a user can select. In addition, selections or groups of selections on a computer screen are flashed one at a time [22,26,61-64]. To illustrate, in these BCIs, each selection flashes sequentially but the user focuses on the one selection they want to make and ignores all others. Under these circumstances, the P300 signal is elicited only when the selection they choose is flashed. The user’s choice is then determined by detecting which selection, when stimulated, produces a P300 signal. ERP BCIs have been used extensively for communication [22,26,61-64]. By simply changing the selection set to multiple choice cognitive assessment responses, a user would be able to respond to standard cognitive assessments (Figure 4).

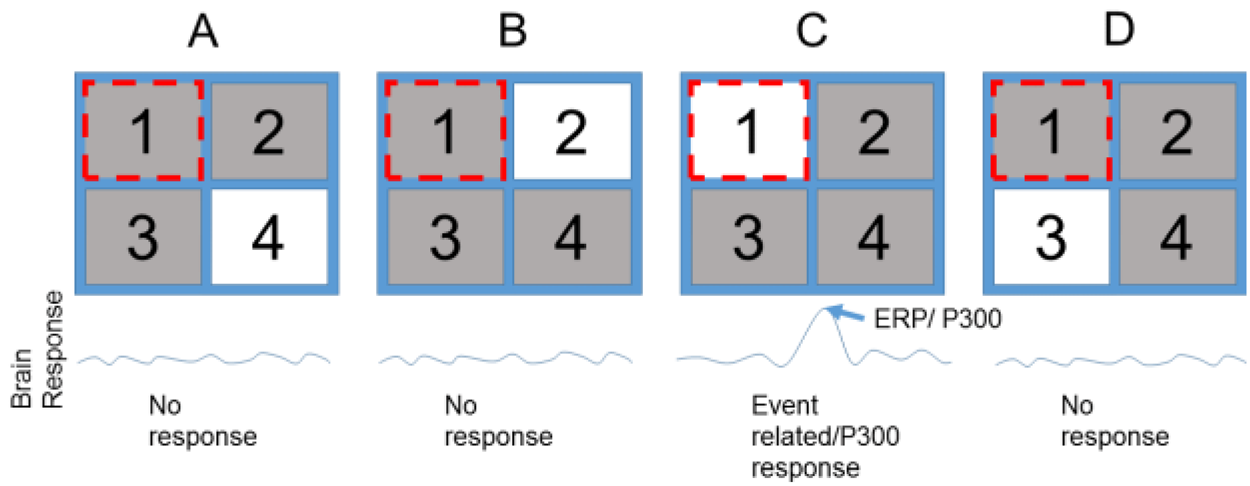

Figure 4. Illustration of brain response of an event related potential (ERP or P300) BCI

- Each large number corresponds to a different selection a subject can pick. These selections flash one at a time, as shown by having one white selection at a time.
- The red square represents what the subject is selecting by focusing their attention.
- The bottom images show cartoon images of the subject's brain activity. Images 1, 2 and 4 show baseline brain activity while image 3 shows an event-related potential.
- Brain activity is baseline except when the subject's selection (number 1) is flashed. This is shown on the third image from the left.

Both VEP and P300 systems require little to no training and can provide a high degree of control inputs [22,26,65,66], which fit our criteria for a temporary system for cognitive assessment. This suggests they are both potential candidates for future cognitive assessment BCIs.

Putting it all together

Based on the review of suitable motor-free cognitive assessment methods, the strategies that seem the most suitable are using EEG based methods such as power band analysis, modern network functional connectivity, or using BCI approaches. Powerband analysis and functional connectivity can be done passively while EEG is recorded since they do not require user input. For our BCI approach, it is possible to do SSVEP and ERP BCIs separately, but numerous studies have demonstrated a hybrid approach that could lead to increased accuracy and speed of classification [67-72]. For example, Hu [67], combined SSVEP and P300 input and asked 12 healthy subjects to type from an alphanumeric matrix that elicited both P300 and SSVEP stimuli. Hu found that by using this combined methodology, he could increase BCI accuracy by about 20% and BCI selection speed by about 50% compared to using only P300 or SSVEP. Therefore, we will be using a hybrid approach as well.

It will be important to determine to what extent the use of a BCI will affect a user's score. For this reason, it is important to first compare test results using subjects who can take both the standard assessments as well as our BCI-facilitated assessment [13].

Outline of projects

he primary goal of this research was to create a suitable solution for determining cognitive capacity in people who cannot complete standardized neuropsychological assessments due to motoric impairments. Two different approaches were taken. The first approach is covered in Chapter 2, where we used a BCI that could administer multiple-choice assessments. The BCI was tested in people with and without cerebral palsy who could take both the standard assessment and a BCI-facilitated test. This was done to determine if modifying the standard PPVT-IV to a BCI-facilitated PPVT-IV altered the psychometrics of the assessment. An essential part of the function of this BCI is the hold-release algorithm (described in Chapter 3). The hold-release algorithm was developed to integrate a simple-to-use confirmation step that prevents the BCI from moving forward in the PPVT-IV test until the subject confirms her selection.

The second approach for determining the cognitive capacity of people who cannot access standardized neuropsychological assessments due to motoric impairments was to use brain dynamics, such as power band, coherence, phase delay and functional connectivity, which are discussed in Chapter 4.

Overall, my work can be used to guide potential tools for future cognitive assesments in people with severe physical/motoric impairments.

References

[1]Sabbadini M, Bonanni R, et al 2001 Neuropsychological assessment of patients with severe neuromotor and verbal disabilities. J.Intellect.Disabil.Res. 45(Pt 2):169-179.

[2]Warschausky S, Van Tubbergen M, et al 2012 Modified Test Administration Using Assistive Technology : Preliminary Psychometric Findings. Assessment 19:472-490.

[3]Allen R 1958 Suggestions for adaptive administration of intelligence tests for those with cerebral palsy. Cerebral Palsy Review: Part II 19:6-7.

[4]NewsAmerica A Individuals with disabilities education act cost impact on local school district.

[5]Elbaum D Special needs carefor adult children: Cost of care.

[6]Benton A 1994 Neuropsylogical Assessment. Annu. Rev. Psychol 1(45):1-23.

[7]Krasuski J 2014 Lighting review of neuropsychological assessments. Amer. Phsy. Inst. 1(1):1-26.

[8]Yin Foo R, Guppy M, et al 2013 Intelligence assessments for children with cerebral palsy: a systematic review. Dev.Med.Child Neurol. 55(10):911-918.

[9]Wechsler D 2008 Wechsler Adult Intelligence Scale.

[10]Wechsler D 2011 Wechsler Abbreviated Scale of Intelligence–Second Edition (WASI-II).

[11]Wechsler D Wechsler Individual Achievement Test-Third Edition.

[12]Sparrow S, Cicchetti D, et al Vineland Adaptive Behavior Scales, Second Edition.

[13]Dunn LM, Dunn DM 2007 Peabody Picture Vocabulary Test – Fourth Edition.

[14]Arbisi PA, Polusny MA, et al 2011 The Minnesota Multiphasic Personality Inventory-2 Restructured Form in National Guard soldiers screening positive for posttraumatic stress disorder and mild traumatic brain injury. Psychol.Assess. 23(1):203-214.

[15]Nunez P, Srinivasan R 2005 Electric fields of the brain - The Neurophysics of EEG. Ox Schol 2(1):1-640.

[16]Karbowski K 1990 Sixty years of clinical electroencephalography. Eur.Neurol. 30(3):170-175.

[17]Kisley MA, Cornwell ZM 2006 Gamma and beta neural activity evoked during a sensory gating paradigm: effects of auditory, somatosensory and cross-modal stimulation. Clin.Neurophysiol. 117(11):2549-2563.

[18]Niedermeyer E 2003 The clinical relevance of EEG interpretation. Clin.Electroencephalogr. 34(3):93-98.

[19]Basar E, Basar-Eroglu C, et al 2013 Brain's alpha, beta, gamma, delta, and theta oscillations in neuropsychiatric diseases: proposal for biomarker strategies. Suppl.Clin.Neurophysiol. 62:19-54.

[20]Kothari R, Bokariya P, et al 2016 A Comprehensive Review on Methodologies Employed for Visual Evoked Potentials. Scientifica (Cairo) 2016:9852194.

[21]Yoshimura N, Itakura N 2009 A transient VEP-based real-time brain-computer interface using non-direct gazed visual stimuli. Electromyogr.Clin.Neurophysiol. 49(8):323-335.

[22]Nicolas-Alonso LF, Gomez-Gil J 2012 Brain computer interfaces, a review. Sensors (Basel) 12(2):1211-1279.

[23]Wang Y, Wang R, et al 2006 A practical VEP-based brain-computer interface. IEEE Trans.Neural Syst.Rehabil.Eng. 14(2):234-240.

[24]Zhu D, Bieger J, et al 2010 A survey of stimulation methods used in SSVEP-based BCIs. Comput.Intell.Neurosci. :702357.

[25]Guger C, Allison BZ, et al 2012 How Many People Could Use an SSVEP BCI? Front.Neurosci. 6:169.

[26]Kubler A, Furdea A, et al 2009 A brain-computer interface controlled auditory event-related potential (p300) spelling system for locked-in patients. Ann.N.Y.Acad.Sci. 1157:90-100.

[27]Furdea A, Halder S, et al 2009 An auditory oddball (P300) spelling system for brain-computer interfaces. Psychophysiology 46(3):617-625.

[28]Mirkovic B, Debener S, et al 2015 Decoding the attended speech stream with multi-channel EEG: implications for online, daily-life applications. J.Neural Eng. 12(4):046007-2560/12/4/046007. Epub 2015 Jun 2.

[29]Sur S, Sinha VK 2009 Event-related potential: An overview. Ind.Psychiatry.J. 18(1):70-73.

[30]Kajosch H, Gallhofer B, et al 2016 The bimodal P300 oddball component is decreased in patients with an adjustment disorder: An event-related potentials study. Clin.Neurophysiol. 127(10):3209-3216.

[31]Basar E, Schmiedt-Fehr C, et al 2016 What does the broken brain say to the neuroscientist? Oscillations and connectivity in schizophrenia, Alzheimer's disease, and bipolar disorder. Int.J.Psychophysiol. 103:135-148.

[32]Anokhin A, Vogel F 1996 EEG alpha rythm frequency and intelligence in normal adults. Intelligence 23(1):1-14.

[33]Schulze KK, Hall MH, et al 2008 Auditory P300 in patients with bipolar disorder and their unaffected relatives. Bipolar Disord. 10(3):377-386.

[34]Russo PM, De Pascalis V, et al 2008 Impulsivity, intelligence and P300 wave: an empirical study. Int.J.Psychophysiol. 69(2):112-118.

[35]Gasser T, Rousson V, et al 2003 EEG power and coherence in children with educational problems. J.Clin.Neurophysiol. 20(4):273-282.

[36]Thatcher RW, North D, et al 2005 EEG and intelligence: relations between EEG coherence, EEG phase delay and power. Clin.Neurophysiol. 116(9):2129-2141.

[37]Gasser T, Von Lucadou-Muller I, et al 1983 Correlating EEG and IQ: a new look at an old problem using computerized EEG parameters. Electroencephalogr.Clin.Neurophysiol. 55(5):493-504.

[38]Gasser T, Mocks J, et al 1983 Topographic factor analysis of the EEG with applications to development and to mental retardation. Electroencephalogr.Clin.Neurophysiol. 55(4):445-463.

[39]Doppelmayr M, Klimesch W, et al 2002 EEG alpha power and intelligence. Intelligence 30(3):289-302.

[40]Psatta DM, Goldstein R, et al 1991 EEG mapping in mentally retarded children by synthetic arginine vasotocin administration. Rom.J.Neurol.Psychiatry 29(1-2):9-16.

[41]Martin-Loeches M, Munoz-Ruata J, et al 2001 Electrophysiology and intelligence: the electrophysiology of intellectual functions in intellectual disability. J.Intellect.Disabil.Res. 45(Pt 1):63-75.

[42]Klingner CM, Volk GF, et al 2014 The effects of deefferentation without deafferentation on functional connectivity in patients with facial palsy. Neuroimage Clin. 6:26-31.

[43]Burton H, Dixit S, et al 2009 Functional connectivity for somatosensory and motor cortex in spastic diplegia. Somatosens.Mot.Res. 26(4):90-104.

[44]Kulak W, Sobaniec W 2003 Spectral analysis and EEG coherence in children with cerebral palsy: spastic diplegia. Przegl.Lek. 60 Suppl 1:23-27.

[45]Kulak W, Sobaniec W, et al 2005 EEG spectral analysis and coherence in children with hemiparetic cerebral palsy. Med.Sci.Monit. 11(9):CR449-55.

[46]Koeda T, Takeshita K 1998 Electroencephalographic coherence abnormalities in preterm diplegia. Pediatr.Neurol. 18(1):51-56.

[47]Galan F, Nuttin M, et al 2008 A brain-actuated wheelchair: asynchronous and non-invasive Brain-computer interfaces for continuous control of robots. Clin.Neurophysiol. 119(9):2159-2169.

[48]Chatterjee A, Aggarwal V, et al 2007 A brain-computer interface with vibrotactile biofeedback for haptic information. J.Neuroeng Rehabil. 4:40.

[49]Sung Y, Cho K, et al 2012 A development architecture for serious games using BCI (brain computer interface) sensors. Sensors (Basel) 12(11):15671-15688.

[50]An X, Kuang D, et al 2014 A Deep Learning Method for Classification of EEG Data Based on Motor Imagery. :203-210.

[51]Bai O, Lin P, et al 2008 A high performance sensorimotor beta rhythm-based brain-computer interface associated with human natural motor behavior. J.Neural Eng. 5(1):24-35.

[52]Ahn M, Lee M, et al 2014 A review of brain-computer interface games and an opinion survey from researchers, developers and users. Sensors (Basel) 14(8):14601-14633.

[53]Kubler A, Neumann N, et al 2001 Brain-computer communication: self-regulation of slow cortical potentials for verbal communication. Arch.Phys.Med.Rehabil. 82(11):1533-1539.

[54]Hinterberger T, Kubler A, et al 2003 A brain-computer interface (BCI) for the locked-in: comparison of different EEG classifications for the thought translation device. Clin.Neurophysiol. 114(3):416-425.

[55]Hinterberger T, Schmidt S, et al 2004 Brain-computer communication and slow cortical potentials. IEEE Trans.Biomed.Eng. 51(6):1011-1018.

[56]Thomas E, Dyson M, et al 2013 An analysis of performance evaluation for motor-imagery based BCI. J.Neural Eng. 10(3):031001-2560/10/3/031001. Epub 2013 May 3.

[57]Li J, Zhang L 2012 Active training paradigm for motor imagery BCI. Exp.Brain Res. 219(2):245-254.

[58]Yin E, Zhou Z, et al 2014 A dynamically optimized SSVEP brain-computer interface (BCI) speller. IEEE Trans.Biomed.Eng.

[59]Perego P, Turconi AC, et al 2011 Cognitive ability assessment by Brain-Computer Interface validation of a new assessment method for cognitive abilities. J.Neurosci.Methods 201(1):239-250.

[60]Trejo LJ, Rosipal R, et al 2006 Brain-computer interfaces for 1-D and 2-D cursor control: designs using volitional control of the EEG spectrum or steady-state visual evoked potentials. IEEE Trans.Neural Syst.Rehabil.Eng. 14(2):225-229.

[61]D'Avanzo C, Schiff S, et al 2011 A Bayesian method to estimate single-trial event-related potentials with application to the study of the P300 variability. J.Neurosci.Methods 198(1):114-124.

[62]Zickler C, Riccio A, et al 2011 A brain-computer interface as input channel for a standard assistive technology software. Clin.EEG Neurosci. 42(4):236-244.

[63]Ahi ST, Kambara H, et al 2011 A dictionary-driven P300 speller with a modified interface. IEEE Trans.Neural Syst.Rehabil.Eng. 19(1):6-14.

[64]Townsend G, Shanahan J, et al 2012 A general P300 brain-computer interface presentation paradigm based on performance guided constraints. Neurosci.Lett. 531(2):63-68.

[65]Sellers EW, Vaughan TM, et al 2010 A brain-computer interface for long-term independent home use. Amyotroph Lateral Scler. 11(5):449-455.

[66]Sellers E, Turner P, et al 2009 A Novel Dry Electrode for Brain-Computer Interface. 5611:623-631.

[67]Li Y, Pan J, et al 2013 A Hybrid BCI System Combining P300 and SSVEP and Its Application to Wheelchair Control. IEEE Trans.Biomed.Eng. 60(11):3156-3166.

[68]Yin E, Zhou Z, et al 2013 A novel hybrid BCI speller based on the incorporation of SSVEP into the P300 paradigm. J.Neural Eng. 10(2):026012-2560/10/2/026012. Epub 2013 Feb 21.

[69]Müller-Putz G, Leeb R, et al 2015 Towards non-invasive Hybrid Brain-Computer Interfaces: framework, practice, clinical application and beyond. Proceedings of the IEEE 103(6):926-943.

[70]Müller-Putz GR, Breitwieser C, et al 2011 Tools for Brain-Computer Interaction: A General Concept for a Hybrid BCI. Front.Neuroinform 5:30.

[71]Kreilinger A, Kaiser V, et al 2013 Neuroprosthesis Control via Non-invasive Hybrid Brain-Computer Interface. IEEE intelligent systems 28(5):40-43.

[72]Rohm M, Schneiders M, et al 2013 Hybrid brain-computer interfaces and hybrid neuroprostheses for restoration of upper limb functions in individuals with high-level spinal cord injury. Artif.Intell.Med. 59(2):133-142.

Chapter Two: Asynchronous brain-computer interface for cognitive assessment in people with cerebral palsy

Abstract

Typically, clinical measures of cognition require motor or speech responses. Thus, a significant percentage of people with disabilities are not able to complete standardized assessments. This situation could be resolved by employing a more accessible test administration method, such as a brain-computer interface (BCI). A BCI can circumvent motor and speech requirements by translating brain activity to identify a subject's response. By eliminating the need for motor or speech input, one could use a BCI to assess an individual who was previously thought of as untestable. We developed an asynchronous, event-related potential BCI-facilitated administration procedure for the Peabody Picture Vocabulary Test (PPVT-IV). We then tested our system in typically developing (TD) individuals (N=11), as well as people with cerebral palsy (CP) (N=19) to compare results to the standardized PPVT-IV format and administration. Standard scores on the BCI-facilitated PPVT-IV, and the standard PPVT-IV were highly correlated ($r = 0.95$, $p<0.001$) with a mean difference of 2.0 ± 6.4 points, which is within the standard error of the PPVT-IV. Thus, our BCI-facilitated PPVT-IV provided comparable results to the standard PPVT-IV, suggesting that populations for whom standardized cognitive tests are not accessible could benefit from our BCI-facilitated approach.

Keywords: P300, EEG, Cognitive Assessment, Cerebral Palsy

Introduction

Clinicians use cognitive tests that have standardized materials, procedures and normative scoring to measure cognitive abilities. Standard cognitive measures typically require motor or speech responses. Thus, a significant percentage of people with disabilities are not able to complete standardized assessments [1,2]. To more accurately measure the cognitive ability of people with severe impairments, clinicians and researchers have used assistive technology such as touch pads, switches, and eye trackers for accessible testing. However, these tools still require speech or motor input, so cognitive assessments remain inaccessible to the people with the most severe impairments [3,4].

Research on solving this issue has proved promising. A notable potential solution is to use brain activity to evaluate a person's cognitive ability, thus eliminating the need for motor or speech input to administer a test. Specifically, Connolly et al. conducted seminal work in this area [5]. Connolly collected data on brain activity via electroencephalography (EEG) to identify a subject's response to a modified version of the Peabody Picture Vocabulary Test-III (PPVT-III) [6]. Similarly, Perego et al. developed a brain-computer interface (BCI) that was used to administer the Ravens Colored Progressive Matrices Test [7]. These two studies provided a proof of concept for cognitive assessment using brain activity [7]. For these systems to move toward a clinical setting, it is important to formulate both standard design and administration methods for brain-based cognitive assessment systems. We, therefore, established design criteria based on an analysis of previous reports of brain activity based cognitive assessment tools, extensive experience in facilitated cognitive assessment, and the principles of cognitive testing psychometrics [8-10].

Only after fortifying our understanding of the concepts presented by Connolly. [5] on cognitive assessment tests can we better appreciate the importance of carefully designing interfaces for populations with impairments. The standard PPVT presents four illustrations in a quadrant array, and the subject must select one of the four that best matches a verbal prompt [1,5,11,12]. Rather than abiding by that four-illustration standard, Connolly's study modified the PPVT-III by presenting single illustrations alongside each spoken word. During the presentation, the spoken word either matched or did not match the illustration. Connolly evaluated results by manually determining post hoc whether brain activity associated with error recognition was exemplified in instances where the spoken word did not match the illustration [5]. Connolly then took those results and categorized the subjects into one of three vocabulary groups (preschool, child or adult) that estimated cognitive ability. On the other hand, the standard PPVT-III results provide individual raw scores ranging from 0-160. Using these scores, a clinician can estimate a patient's intelligence quotient. In this case, Connolly's method alters the format and psychometrics of the test and thus limits the information the clinician has to evaluate a patient's ability. Therefore, our first criterion for developing a cognitive assessment BCI is, a cognitive assessment BCI should maintain the psychometric properties of the standardized administration procedure.

Connolly's approach also necessitated manual interpretation of the brain responses. Therefore, a clinician would likely need to undergo additional training on how to interpret the brain signals, thus creating the vulnerability that results could be interpreted subjectively. These hindrances to clinical utility lead us to our second criterion: 2) Brain-based cognitive assessment systems must automatically abstract the complexity of brain activity analysis to provide results that are not difficult for the clinician to interpret, thus mitigating the risk of human-introduced inconsistency in data interpretation.

An alternative to the manual interpretation of brain activity is the brain-computer interface (BCI) [13-17]. A BCI translates brain activity into computer commands that allow a subject to control devices or make determinations from a display, thus removing the need for manual interpretation of brain activity [18]. For example, Iversen et al. used a non-invasive electroencephalography slow-cortical potential (SCP) BCI for cognitive assessment in three people with amyotrophic lateral sclerosis (ALS) [19]. SCP BCIs rely on a subject's capacity to control their EEG activity by creating either positive or negative EEG polarizations. In Iversen's study, all three subjects could use the BCI for cognitive assessment. These results were encouraging and demonstrated the potential for BCIs in cognitive assessment. However, SCP BCIs require multiple months of training before one can control them. For that reason, they are not regularly used in clinical settings [19]. Thus, our third criterion: 3) A brain-based cognitive assessment systems must be quick to set up for an individual patient. From our experience, and from conversing with clinicians who administer cognitive assessment tests, we determined the preferred set-up and calibration time to be an hour or less.

Perego et al. developed another cognitive assessment BCI, which used Steady State Visually Evoked Potentials (SSVEPs) [7]. SSVEP BCIs function by presenting visual stimuli that all flicker simultaneously but at different frequencies. When the BCI subject focuses his/her visual attention on one of the flickering stimuli, an oscillatory signal with a similar frequency to the stimulus manifests in the occipital electrodes of the subject's EEG. The BCI determines the subject's selection by determining which presented frequency best matches the frequency recorded in the subject's EEG.

Perego used four flickering Light Emitting Diodes (LED) to provide SSVEP stimulus, placed on the top, bottom, left, and right of a monitor. The monitor displayed the cognitive assessment questions and answers to the subject and provided visual feedback on the subject's current selection. To answer a question, the subject focused their gaze on the left or right LEDs, which moved a selection cursor to the next answer. Once they had moved the selection cursor over their desired selection, the subject would focus their gaze on the top LED to submit the selection. Using an SSVEP BCI removed many drawbacks of SCP BCIs. SSVEP BCIs present two benefits; the first is that they are quick to calibrate (within 5 minutes). Secondly, they allow subjects to make self-paced decisions by not requiring them to select a BCI command until they focus their gaze on a LED. In the BCI literature, this form of functionality is called asynchronous control [20,21].

Asynchronous control is a crucial feature for cognitive assessment BCIs. Those people in most need of cognitive assessments may have some form of cognitive impairment that prevents them from responding at the same pace as a non-impaired person. Also, the difficulty of the test questions will almost certainly vary between tests and within a test. If a person must rush to answer a question, due to limitations of the BCI, then the results of the cognitive assessment may not accurately measure a person’s capacity. Thus, our fourth criterion: 4) A brain-based cognitive assessment system must have asynchronous control.

Perego’s study also allows us to glean information on the applicability of SSVEP BCIs. Perego’s BCI was only usable in 57% of his subjects, and six out of the seven subjects unable to use the BCI were people with cerebral palsy (CP). Other studies have also shown mixed results when using SSVEP BCIs in populations with CP. Lower classification accuracy is usually attributed to the involuntary movements and muscle contractions in the neck, which are typical of CP. SSVEP BCIs rely heavily on occipital electrodes, which are the electrodes closest to the subject’s neck [7,22,23]. These electrodes are profoundly affected by muscle artifacts from the neck, which can significantly alter signal quality. This unintentional interference can ultimately lead to decreased BCI performance in people with CP. Another issue is that most SSVEP BCIs function like an eye-tracking system, requiring a person to focus and maintain their vision on the stimulus that corresponds to their selection [7,17,23]. For populations with conditions that include oculomotor impairments, maintaining such a gaze may be too difficult. While some SSVEP systems can be operated with closed eyes, or function using covert orienting of attention, these systems typically reduce the selection set to only two illustrations [24]. The reduced selection set means many cognitive assessment tests would have to be modified to a two-choice format, creating psychometric incompatibilities and violating our first design criterion.

An alternative to SSVEP BCIs is the visual event-related potential (ERP) BCI [25]. Like SSVEP BCIs, ERP BCIs use visual stimuli of flashing objects to elicit brain responses for control. In an ERP BCI, each object (or group of objects) flashes one at a time. The flashing elicits an ERP brain response only to flashes emitted by the object the subject is interested in selecting. By determining which flashing object elicited the ERP response, an ERP BCI can identify the subject's desired selection. Like SSVEP BCIs, ERP BCIs are easy to learn and can incorporate asynchronous control [26]. The primary advantage of ERP BCIs over SSVEP BCIs is that they do not rely as heavily on occipital electrodes for classification and do not require subjects to maintain visual fixation on the flashing object they want to select. For these reasons, ERP BCIs have a potential advantage over SSVEP BCIs in people with CP. Thus, our final criterion is that: 5) the BCI must be able to function in the population it is targeting.

In summary, our criteria are as follows:

1. A cognitive assessment BCI should maintain the psychometric properties of the standardized administration procedure.
2. Brain-based cognitive assessment systems must automatically abstract the complexity of brain activity analysis to provide results that are not difficult for the clinician to interpret.
3. Brain-based cognitive assessment systems must be quick to set up (one hour or less).
4. Brain-based cognitive assessment system must have asynchronous control, thus allowing the subject to control the pace of the assessment.
5. The BCI must be able to function in the population it is targeting.

Using the criteria above, we developed an asynchronous ERP/SSVEP BCI, which retains the test and result format of the Peabody Picture Vocabulary Test (PPVT-IV) [27]. We administered the BCI-facilitated PPVT-IV to people without impairments and to people with CP. We chose the PPVT-IV because it has a strong test-retest reliability ranging from .91 to .94 across two different versions, Form A and Form B [27]. The strong retest reliability allowed us to compare our BCI-facilitated PPVT-IV with the standard PPVT-IV.

Methods

The Institutional Review Board of the University of Michigan approved recruitment and data collection protocols. In total, we recruited 11 people without impairments and 19 individuals with CP. Participants were ages 8-27, and were drawn from the University of Michigan Health System and surrounding areas. Subjects or their parents signed informed consent forms and filled out demographic surveys.

Subjects attempted the standard PPVT-IV and the BCI-facilitated PPVT-IV. Subjects took the tests in a pseudo-random order. We used two matched difficulty versions of the PPVT-IV, Form A and Form B, to minimize practice effects. We used Form A for the standard PPVT-IV and Form B for the BCI-facilitated PPVT-IV. To document perceived workload of our BCI-facilitated PPVT-IV and the standard PPVT-IV, subjects filled out a NASA Task Load Index survey (NASA-TLX) after each test [28,29].

BCI Setup

The BCI was set up and calibrated for each subject using a 32-electrode (Locations: F3, F4, FC3, FCZ, FC4, T7, C3, CZ, FZ, FC5, FC1, FC2, FC6, C5, C1, C2, C4, T8, CP3, CPZ, CP4, P3, P4, PO8, C6, CP5, CP1, CP2, CP6, PZ, PO7, and OZ) EEG cap (Electro-Cap, Inc.), with a sampling rate of 600hz. Online classification only used 16 channels (F3, Fz, F4, T7, C3, Cz, C4, T8, CP3, CP4, P3, Pz, P4, PO7, Oz, and

PO8), to match the classification montage of our previous studies for future comparison [30,31]. We reserved the other channels for future analysis. [30-32]. Before taking the BCI-facilitated PPVT-IV, subjects responded to 60 PPVT-like questions where the computer provided the correct answer to the subject by highlighting the answer. Each question was presented on a monitor and showed four different illustrations. A spoken word was played through a pair of speakers that corresponded to the correct answer. The subject made his or her selection by focusing their attention on the corresponding flashing box of each illustration. We called theses boxes the selection boxes (figure 5). The subject did two 30 question runs which took about 7 minutes per run. The data collected from these runs were used to calibrate the BCI.

NASA-TLX

The NASA-TLX is a survey instrument that is commonly used to assess the workload of a task. It consists of six questions, and each question features a 21-point scale that the subject uses to convey the perceived difficulty of the task they did. The questions ask subjects to rate their perceived performance, mental demand, physical demand, temporal demand, the degree of effort and level of frustration about the task they performed [28].

Peabody Picture Vocabulary Testing

We licensed the PPVT-IV from Pearson Education, Inc for research purposes. The standard PPVT-IV contains 228 questions separated into 12 sets of increasing difficulty. Each question consists of a page with four illustrations in color. In the standard administration method, the examiner speaks a word when each question is presented. To respond, the subject must either point to or say the number of the illustration that best matches the word spoken by the examiner [27].

The test procedure involves identifying the subject's basal and ceiling set. The basal set is identified as the first set the subject completes with one or fewer incorrect responses. The starting set is based on age and is labeled the basal set if the subject meets the basal set criterion. Otherwise, the subject goes down one set at a time until they answer a set with one or fewer errors. After determining the basal set, the subject moves through the test questions until they have completed all the sets, or until they submit eight or more incorrect responses in one set. The final set is labeled the ceiling set, and the number of incorrect responses is subtracted from the highest question tested to determine the raw PPVT-IV score. Using the PPVT-IV normative conversion score tables, the raw PPVT-IV scores are converted into standardized scores that are utilized in statistical analyses.

When the subject took the standard PPVT-IV, we used the standard PPVT-IV protocol outlined above [27]. The BCI-facilitated PPVT-IV used the same logic flow as the standard PPVT-IV. However, the subject viewed illustrations on a 28-inch monitor (running at 120 Hz refresh rate), and the subject heard each question spoken a from computer speakers (Figure 5).

The BCI-facilitated PPVT-IV displayed both ERP and SSVEP stimuli in the selection box to the subject, thus enabling us to test the performance of both ERP and SSVEP BCI modalities in people with CP (Figure 5). The checkerboards (SSVEP box) in each selection box flickered continuously at unique frequencies, eliciting SSVEP responses. The SSVEP boxes flashed as follows: the upper left-hand corner flashed at

5 Hz, the upper right at 15 Hz, the lower left at 20 Hz, and the lower right at 24 Hz and the cancel SSVEP box at 30 Hz (Figure 5). The numbers in each selection box and the X in the cancel box elicited ERP responses. Only one number or the X flashed at a time, prompting an ERP response only when the subject's choice flashed (Figure 5). Subjects responded to the BCI-facilitated PPVT-IV by focusing their attention on the selection box that corresponded to the illustration they wanted to choose (Figure 5). During online testing sessions, we only used ERP responses to determine BCI state and commands. However, offline, we tested subject responses using both SSVEP by itself and hybrid SSVEP and ERP.

Classification

We used a three-stage classifier for ERP classification. During the first stage (stage 1), we applied the weights derived using stepwise linear discriminant analyses (SWLDA) during the calibration step to the subject's EEG responses. SWLDA uses feature space reduction to find suitable features in a subject's data to classify between two classes. In our case, the two classes were whether an EEG response contained an ERP or not. After establishing the features, the SWLDA classifier can then classify a subject's EEG. EEG classification produces a value called the classification value. The classification values are either a negative or positive value, depending on whether a subject does or does not exhibit an ERP response. The larger the positive or negative magnitude of the classifier value, the more likely the EEG response falls into either category. Thus, a large positive classifier value strongly suggests an ERP occurred compared to a small positive classifier value. After all selection boxes on the computer display had flashed at least once (called a flash sequence), our three-stage classifier entered its second stage called certainty.

We developed the certainty algorithm (Stage 2) to generate values corresponding to the probability that the subject is making a choice from the display. The certainty algorithm takes the SWLDA classifier values calculated for each flash sequence in stage one and performs a t-test, then normalizes the results. The outputs are the probabilities that a subject is selecting, which we termed ‘certainty values’ [33]. To better estimate the certainty values of each selection box, we averaged the classifier values from different flash sequences for each selection. Averaging provides a better result than using only one ERP instance because it reduces the signal to noise issues of EEG. In our application, we averaged up to five of the most recent flash sequences. If certainty was reached before five sequences, we moved on to the next classification stage without waiting for more sequences.

In our application, we used the certainty algorithm as a gatekeeper that prevented the BCI from making any decisions until one of the selection boxes reached a certainty value of 90% [33]. In literature, this form of BCI is called an asynchronous BCI since it prevents the BCI from making a choice until the subject is ready to respond. These steps prevent false positives and allow subjects to take their time to think about which illustration they want to choose. Once a subject has made his/her choice, he/she can then focus on the respective selection box allowing the BCI to reach the 90% certainty threshold. Once the threshold was met, we labeled the selection box the subject choose the ‘target,’ and our classification system entered stage 3; hold-release [30].

During the hold-release stage, we dimmed all illustrations except the target. At this point, the cancel box in the middle of the screen began to flash with the other selection boxes (Figure 5). We asked subjects to continue focusing their attention on the selection box they chose (i.e. the target) if no color change occurred on the illustration they were selecting. If their illustration dimmed, they were instructed to focus their attention on the cancel box.

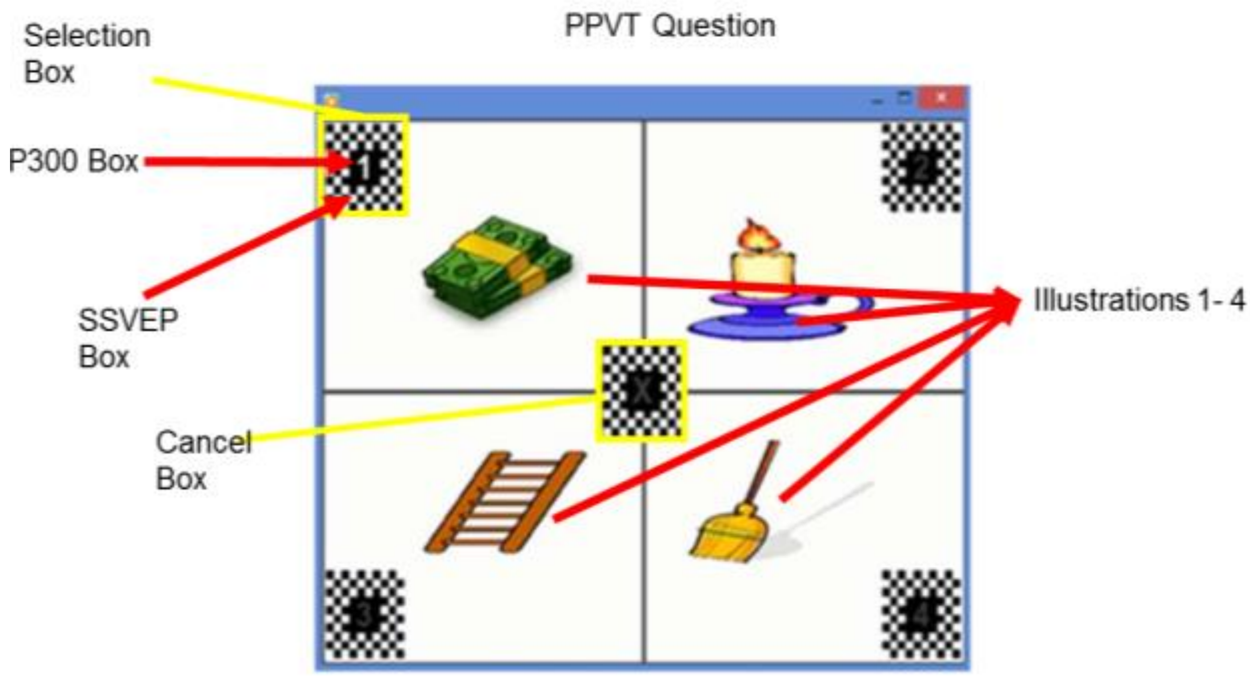

Figure 5. Labeled image of BCI-Facilitated PPVT-IV screen

- The entire screen is one PPVT question
- Each PPVT question has four illustrations
- Each checkered square with a number is considered a selection box
- The center selection box is the only selection box with an X, and we call this the cancel box
- Checkerboard patterns all flicker at different frequencies eliciting VEPs. We call these the SSVEP boxes.
- The numbers and the letter X flash only one at a time and elicit ERP/P300s. We call these the P300 boxes.

The hold-release algorithm produces a decision when any one of three conditions is met. The first condition uses as a threshold (called the positive threshold) the smallest classifier value that separated ERPs from non-ERP. In the original hold-release paper, this threshold was set to 99% accuracy difference between ERP and non-ERPs, determined from the subject's training data. In our study, the positive hold-release threshold was set to the mean plus the standard deviation of the classifier values for the attended labels in the calibration data. This represented a threshold that separated ERPs from non-ERP with 85% accuracy. We changed the method of setting the positive threshold to explore how a lower threshold would impact hold-release performance. If the classifier value of either the target or cancel box was above the positive threshold, that was considered the choice of the subject. The second condition was whether the target was a negative classifier value. In this case, the cancel selection was classified as the choice of the subject. The final condition was invoked when both the target and cancel box had positive classifier values, but those values were below the positive threshold. In this case, the subject's choice was whichever had the largest classifier value (Figure 6).

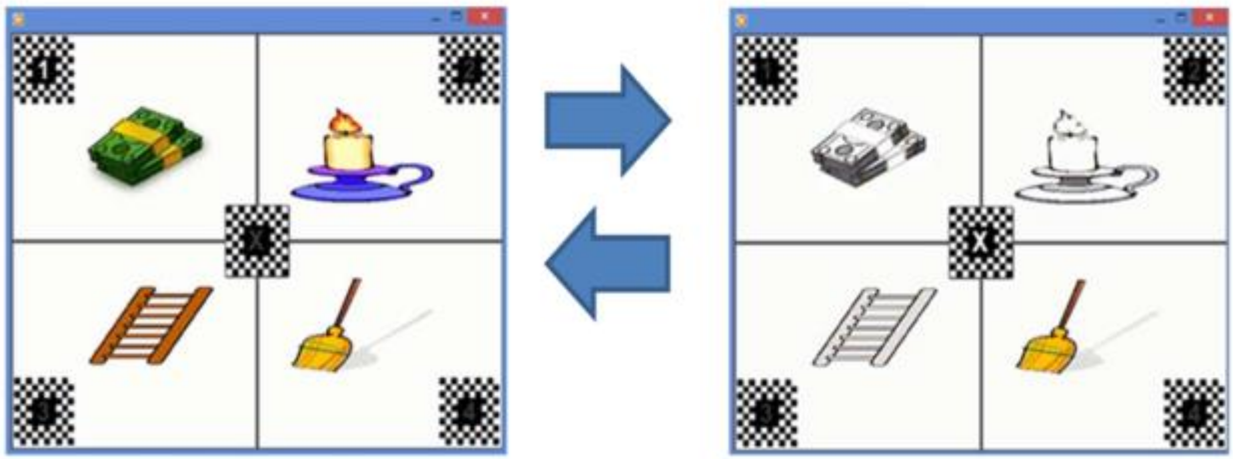

Figure 6. Example of hold-release confirmation step

- During the confirmation step, all illustrations are dimmed except the target selected by the certainty algorithm. Aside from the target, subjects can also select the cancel box (centrally located X label) to cancel their selection and try the question again.

To further increase accuracy, the hold-release algorithm can be adjusted to prevent classification until the subject selects the target selection box a predetermined number of times (called number of times to verify). In the original hold-release paper (Chapter 3), two times to verify were used. In our study, four times to verify were used to increase BCI accuracy. In contrast to the original paper, we increased the times to verify because, in real-time, classification accuracy dropped compared to the original hold-release paper. We hypothesized that the decrease in accuracy was because of the decreased number of items displayed to the user (11 versus 4).

Two other variations (3 total variations) of the original hold-release algorithm were used to test potential optimization methods. In the first variation, the third hold-release condition was ignored. Thus, the classification was not altered, even when both illustrations had positive classifier values but were still below the positive classification threshold.

In the second variation, the third hold-release condition was applied when the target had a classifier value larger than the cancel box. Otherwise, the times to verify were not altered. This modification biases the BCI into choosing the target, thus, increasing the speed of confirmation if the target was selected correctly initially.

SSVEP Classification

For SSVEP offline analysis, we used a two-second long windowed Fast Fourier Transform (FFT). Windowing began from the moment a question was presented to the subject until the moment the subject made a P300 selection. The classified selection box was determined by which of the 5 EEG frequencies collected and averaged from P07, P08 and Oz had the highest frequency power.

Hybrid Classification

For hybrid classification, we applied same classification techniques as with the SSVEP and ERP BCIs. However, the final classification was whichever BCI modality reached a result first.

Analysis

Across all subjects and both CP vs. TD groups, we calculated the mean and standard deviation for the following measures: time/set, time/question, time/attempt at a question, time in classification stages 2 and 3; the number of cancellations/question and the number of attempts/question.

The mean and standard deviation of the difference in the PPVT-IV scores for the two administration methods (standard and BCI-Facilitated) were calculated. The Pearson correlation between the scores was determined. NASA-TLX scores and the time required for test administration were evaluated using paired t-tests.

An MANOVA was used to compare SSVEP, ERP (using SWLDA) and hybrid BCI accuracy. An ANOVA was used to test hold-release accuracy based on changes to the third hold-release rule, and a t-test was used to compare the accuracy of our 3-stage classifier (SWLDA ►Certainty ► Hold-release) to only using SWLDA and certainty. Accuracy for certainty was taken each time certainty was met and whether certainty's classification of the target was equal to the subject's final selection (counting the selections that led to cancellations). Accuracy for hold-release was based on whether hold-release canceled or confirmed a subject's selection correctly.

Results

Out of all 30 subjects, eight people with CP did not complete the study. For the 21 who did complete the test, standard scores on the BCI-facilitated PPVT-IV, and the standard PPVT were highly correlated ($r = 0.95$, $p<0.001$) with a mean difference of 2.0 ± 6.4 points, which is within the measurement agreement of the PPVT-IV (Figure 7).

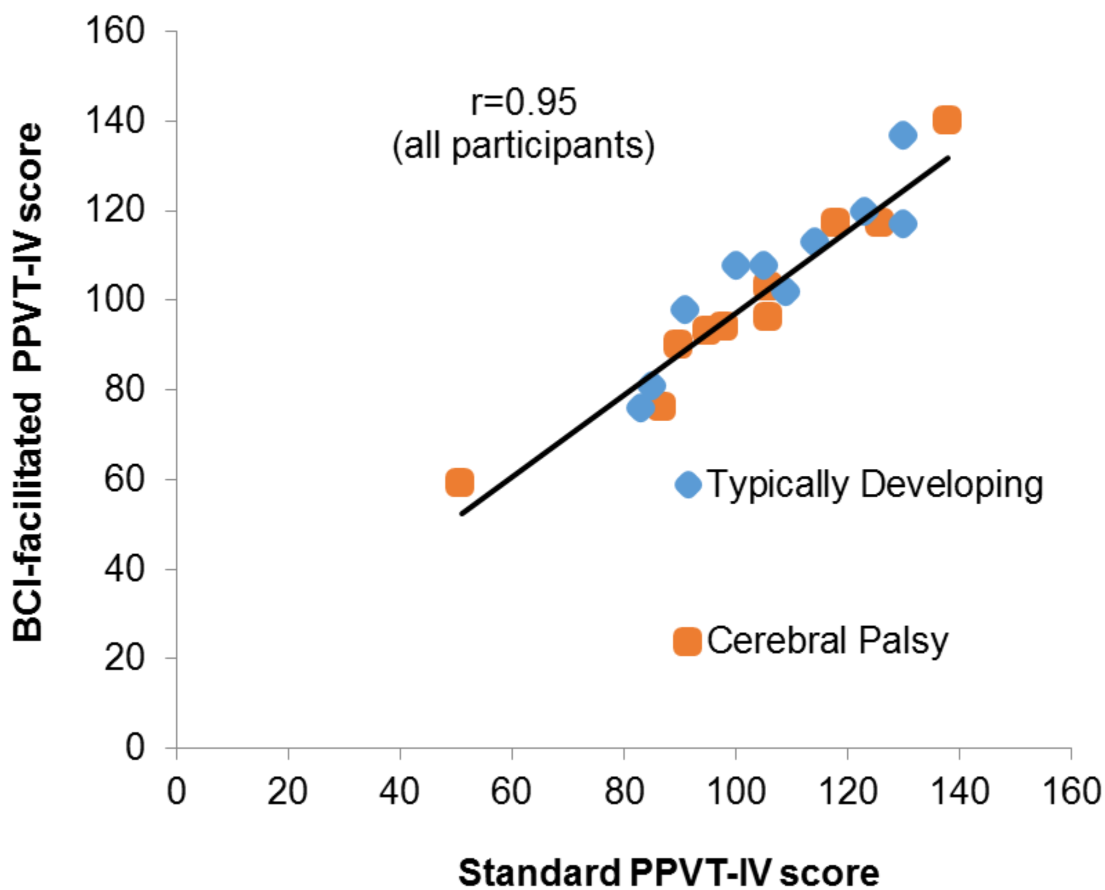

Figure 7. Correlation between Standard and BCI-facilitated PPVT-IV

- Blue diamonds represent the typically developing subjects, and yellow squares represent subjects with cerebral palsy.
- The correlation coefficient r = 0.95.

The BCI-facilitated test took about four times longer to complete than the standard PPVT-IV ($p<0.05$), with a mean of 43.05 ± 13.00 minutes compared to 12.1 ± 3.28 minutes for the standard test.

The NASA-TLX ANOVA results showed that people with CP perceived the BCI-facilitated PPVT-IV as more mentally demanding, physically demanding and requiring more effort by ($p<0.05$) than did the TD subjects. This group difference was not noted with the standard version. There was also a significant difference in perceived performance ($p<0.05$) between those with CP and TD subjects. Subjects with CP believed they did worse on the BCI-facilitated test compared to the standard test, while TP subjects believed they did similarly on both test formats. However, both groups did equally on both test formats (Table 2).

		Mental Demand	Physical Demand	Temporal Demand	Perceived Performance	Effort	Frustration
ALL	ALL Standard	10.13 ± 6.545	2.067 ± 5.521'	4.60 ± 4.501	4.867 ± 4.673	9.533 ± 6.696	5.600 ± 5.841
	ALL BCI	13.35 ± 4.2924	5.882 ± 5.5210'	4.824 ± 4.127	5.412 ± 4.731	13.12 ± 6.274	7.941 ± 6.544
BCI	TD BCI	13.00 ± 3.625	5.333 ± 4.534	4.889 ± 2.134	8.222 ± 4.438#	11.56 ± 5.657	7.222 ± 4.629
	CP BCI	13.75 ± 5.625*	6.500 ± 6.866**	4.750 ± 4.234	2.250 ± 2.581#	14.88 ± 6.312##	8.750 ± 7.723
Standard	TD Standard	11.75 ± 6.325	2.625 ± 1.976	5.625 ± 5.132	7.000 ± 5.503***	10.88 ± 6.336	4.250 ± 4.152
	CP Standard	8.285 ± 6.873*	1.428 ± 0.7868**	3.429 ± 3.780	2.429 ± 2.149***	8.00 ± 7.371##	7.143 ± 7.4258

Table 2, NASA-TLX results summary

- NASA TLX results of CP and TD means for perceived: Mental Demand, Physical Demand, Temporal Demand, Perceived Performance, Effort and Frustration.
- Symbols:’, *, **, ***, # and ## correspond to statistical significance between each respective group.
- Entries with no symbols had no statistically significant differences

Offline processing found no significant differences between our modified hold-release rules. Therefore results were averaged during our analysis. The accuracy of using our 3-stage classifier (97.78 ± 4.06) was significantly higher ($p < 0.001$) than using only SWLDA and certainty (82.34 ± 0.97) together. Accuracy for hold-release to determine the choice of a subject between the target and cancel box was 85.18 ± 4.29. SSVEP classification accuracy was 27.29 ± 3.298, and hybrid classification accuracy was 52.23 ± 5.613. Due to the low accuracies of the SSVEP and hybrid systems, we did not use these results for further analysis.

A mean of 24.57 ± 17.41 seconds was needed to answer a BCI-facilitated PPVT-IV question. It took subjects about 1.29 ± 0.67 attempts per question to answer them correctly. It took a mean of 3.85 ± 4.28 seconds for a selection to reach certainty and a mean of 6.26 ± 4.44 seconds for hold-release to determine a subject choice (about 12.13 ± 9.60 individual flashes). Questions were canceled a mean of 0.29 ± 0.67 times per questions (Table 3).

	Time/ Set	Time/ Question	Time/ Attempt	Time in Stage 2/ Attempt	Time in Stage 3/ Attempt	Sequences to reach Certainty	Flashes to Confirm or Cancel	Number of Cancelations/Set	Number of Cancelations/ Question	Attempts/ Question
All Mean	338.21± 97.05 seconds	24.57± 17.41 seconds	18.58± 6.39 seconds	3.85± 4.28 seconds	6.26 ± 3.44 seconds	6.29 ± 6.76 Sequences	12.13± 9.60 Flashes	3.46 ± 3.28	0.29± 0.67	1.29± 0.67
CP BCI Mean N =15	363.68± 108.41 seconds	26.70± 19.91 seconds	19.22± 6.76 seconds	4.03± 4.41 seconds	5.21± 3.36 seconds	6.63 ± 6.92 Sequences	13.31± 10.63 Flashes	4.24 ± 3.77	0.35± 0.76	1.35± 0.76
TD BCI Mean N = 11	313.14± 77.35 seconds	22.37± 14.07 seconds	17.86± 5.86 seconds	3.64± 4.13 seconds	5.77± 4.01 seconds	5.91 ± 6.55 Sequences	10.79± 8.07 Flashes	2.69 ± 2.51	0.23± 0.55	1.23± 0.55

Table 3. Three stage classifier results summary

- There were no significant differences between groups

The subjects who did not complete the BCI-facilitated PPVT-IV had a mean age of 10.6 ± 2.9 years old. One subject was screened ineligible due to the inability to take the standard PPVT-IV. Two subjects did not complete the BCI-facilitated test because we could not establish reliable training weights. Offline we looked at the subjects training data sets and found that for one subject's data was inconsistent and for the other subject we had forgotten to add the hold-release thresholds.

The remaining five subjects showed difficulty in maintaining their attention and interest after the one-hour setup and calibration process. For example, some children would only look at the BCI for a few seconds and then look away from the BCI or talk to their parent. We asked subjects how they were feeling, if they wanted to stop or if they wanted to take a break before resuming. All subjects who struggled with attention and interest verbally told us they were bored, tired or wanted to stop the test.

Discussion

Our findings demonstrate that our BCI-facilitated PPVT-IV provides equivalent results to the standard PPVT-IV. This suggests that our BCI-facilitated PPVT-IV could potentially be useful in testing populations for whom standardized testing is inaccessible.

The BCI-facilitated PPVT-IV takes approximately four times longer than the standard PPVT-IV. The additional time it took to take the BCI-facilitated assessment is due to the slow selection speeds of ERP BCIs [34,35]. That established, a typical cognitive assessment session lasts more than two hours, and our cognitive assessment BCI's test time is within that two-hour window of time. While in those sessions a subject normally takes more than one test, this would mean a patient using our technology would have to make additional visits compared to TD developing patient.

The NASA-TLX results showed that our BCI-facilitated PPVT-IV was perceived as having a higher physical demand than the standard PPVT-IV. The BCI-facilitated test does not require movement. Therefore, we believe this increase in physical demand was due to fatigue from sitting during the set-up and calibration period, and the increased test length compared to the standard test. Upon asking the BCI subjects why they felt the BCI-facilitated method was more physically demanding, we received comments that supported our impressions. We believe the increase in mental demand and effort was because the BCI-facilitated test required people to focus their attention on making selections, compared to verbalizing a selection as in the standard PPVT-IV. For populations without impairment or those that can take the standard test easily, such as those in our study, we expected the BCI-facilitated test to be more challenging than simply replying verbally. The results of our study support this as our BCI-facilitated assessment was perceived as more physically challenging (but not mentally challenging). However, we believe that for populations with severe movement and speech impairments for whom actual physical movement is a great burden, the BCI-facilitated test will be less challenging than the standard PPVT-IV, and perhaps the only accessible option.

There was no significant difference between the PPVT-IV scores of subjects with or without CP. However, on the NASA TLX, subjects with CP reported significantly lower perceived performance for both the standard and BCI-facilitated PPVT-IV, suggesting that the CP subjects had lower confidence than the TD subjects.

Accuracy using SSVEP was poor and only slightly above chance. Previous studies have shown varied performance gains from using a hybrid BCI approach [36-41]. Studies using SSVEP in subjects with cerebral palsy have reported low SSVEP accuracy. These studies suggest that muscle artifacts in the neck may interfere with the signal of the electrodes most used in SSVEP classification. While these studies suggest the presence of muscle artifacts as a possible reason for decreased SSVEP/hybrid BCI accuracy in subjects with CP, this does not explain the poor performance in typically developing people. For this reason, we believe the most probable cause of low accuracy in our SSVEP/hybrid BCI classification may be due to other factors, such as design errors with the SSVEP setup.

Our 3-stage classifier significantly increased the accuracy compared to other classification methods we used (SWLDA and Certainty, SSVEP or hybrid). Along with accuracy gains, our 3-stage classifier also allowed the BCI to function asynchronously. Asynchronous functionality allows subjects the time to think as much as needed to provide their best answer, while a confirmation step reduces incorrect selection.

Two other variations of the original hold-release algorithm were used offline to test potential accuracy differences. In the first variation, the third hold-release condition was ignored. In the second variation, the third hold-release condition was applied when the target had a classifier value larger than the cancel box. When these changes were applied to both conditions, there was a decreased accuracy for hold-release system compared to the original paper [26]. This is most likely due to our comparatively lenient positive hold-release threshold of 85% vs. 99% compared to the original hold-release paper.

Confirmation steps usually require a subject to respond to a secondary prompt or make another choice to confirm. To illustrate, Perego's cognitive BCI used an indirect selection method and a secondary response [7]. Subjects would first indirectly scroll through the possible choices and then provide a second command to confirm their final choice. This form of verification can become quite slow as the number of responses in a cognitive test increase. For example, in a two-choice test, 2-3 actions are required to select, but if presented with six choices (as is in Perego's study), it may take the subject 2-7 actions or more to confirm a choice. These additional steps break the flow of the assessment and may become frustrating to a subject, leading to changes in assessment results. Using hold-release allows for a more natural confirmation step compared to using a secondary prompt to confirm a subject's choice. In our implementation, the subject only needs to provide an additional response if their choice is being classified incorrectly. Otherwise, the subject continues focusing on their choice until the BCI progresses to the next question.

Other research groups have also developed asynchronous BCIs. Typically, probabilistic models of ERP's, ERP amplitude, classifier values, SSVEP, or EEG power bands are used to determine when a subject is making a choice [42]. Some groups have also combined two methods to increase the reliability of their asynchronous BCI. These hybrid systems typically combine an ERP based method (probabilistic models of ERP's, ERP amplitude or classifier values) along with a frequency-based method (EEG power bands, spectral analysis or SSVEP responses). Frequency-based methods rely heavily on occipital electrodes to determine whether a subject is selecting a response with the BCI, making SSVEP BCIs less suitable for people with CP [36,42-45]. Our method has the advantage of not requiring frequency-based analysis, reducing the likelihood of incorrect classification due to neck muscle artifacts.

In our approach, we used our certainty algorithm for asynchronous BCI functionality. Based on the classification methods described above, we will now consider how our BCI met the criteria we outline previously.

1. The first criterion, a cognitive assessment BCI should maintain the psychometric properties of the standardized administration procedure. Results from the difference analysis suggest that our BCI-facilitated PPVT-IV yields adequate measurement agreement with the standard version of the PPVT-IV, though more extensive analyses with larger samples would be important in this regard.
2. The second criterion was that brain-based cognitive assessment systems must automatically abstract the complexity of brain activity analysis to provide results that are not difficult for the clinician to interpret. Our adapted BCI provided an output that matched the format of the standard PPVT-IV. Therefore, our approach meets the second criterion.
3. Our third criterion was that brain-based cognitive assessment systems must be quick to set up (one hour or less). While our current system does fall within an hour of setup, there were still subjects who could not complete the test due to the lengthy setup time. Most of the setup time was spent applying gel to each electrode. New dry electrode technology developed by companies such as Wearable Sensing have the potential of removing this barrier and reducing setup time to less than 10 minutes [34].

4. Our fourth criterion was that a brain-based cognitive assessment system must have asynchronous control, thus allowing the subject to control the pace of the assessment. Due to our certainty and hold-release algorithms, we satisfied our fourth criterion.
5. Our fifth criterion was that the BCI must be able to function in the population it is targeting. We tested our technology with people who have cerebral palsy and selected a BCI modality that appears to function well in this relatively high-functioning population. Before we can fully say we met our fifth criterion, testing should be done to people with a higher severity of cerebral palsy.

Limitations

There were some limitations with our system and methodology. First, all subjects that went fully through our study were able to take both standard and BCI adapted PPVT-IV. While this allowed us to validate the measurement agreement of the system, future studies should focus on subjects with more significant motor and speech impairments. Furthermore, our sample size was small, thus precluding more extensive psychometric analyses of reliability and validity. Additionally, our implementation of an SSVEP BCI did not provide the accuracy needed to allow for either SSVEP or hybrid control. Lastly, we only tested our BCI on the PPVT-IV, which is an untimed multiple choice test. Different BCI adaptions would be required for time-sensitive assessments or assessments with different presentation formats and response demands.

Conclusion

Here, we presented a BCI that can administer the PPVT-IV, a test of receptive vocabulary. Our BCI provided equivalent results to the standard PPVT-IV, suggesting that our BCI-facilitated PPVT-IV could be used for cognitive assessment in populations for whom standardized tests are not accessible [41,42]. Our method was only applied to the PPVT-IV, a multiple-choice format test with a quadrant stimulus array. However, our system can be extended to other visual multiple-choice tests. Also, we demonstrated a novel, natural confirmation step that significantly increases BCI accuracy without the need for a secondary prompt.

References

[1]Yin Foo R, Guppy M, et al 2013 Intelligence assessments for children with cerebral palsy: a systematic review. Dev.Med.Child Neurol. 55(10):911-918.

[2]Bagnato S, Neisworth J 1994 A national study of the social and treatment "invalidity" of intelligence testing for early intervention. School Psychology Quarterly, Sch Psych Quart 9(2):81.

[3]Wagner BT, Jackson HM 2006 Developmental memory capacity resources of typical children retrieving picture communication symbols using direct selection and visual linear scanning with fixed communication displays. J.Speech Lang.Hear.Res. 49(1):113-126.

[4]Meyers AR, Andresen EM 2000 Enabling our instruments: accommodation, universal design, and access to participation in research. Arch.Phys.Med.Rehabil. 81(12 Suppl 2):S5-9.

[5]Byrne JM, Dywan CA, et al 1995 An innovative method to assess the receptive vocabulary of children with cerebral palsy using event-related brain potentials. J.Clin.Exp.Neuropsychol. 17(1):9-19.

[6]Byrne JM, Dywan CA, et al 1995 An innovative method to assess the receptive vocabulary of children with cerebral palsy using event-related brain potentials. J.Clin.Exp.Neuropsychol. 17(1):9-19.

[7]Perego P, Turconi AC, et al 2011 Cognitive ability assessment by Brain-Computer Interface validation of a new assessment method for cognitive abilities. J.Neurosci.Methods 201(1):239-250.

[8]Kaufman J, Van Tubbergen M, et al 2013 A comparison of visual inspection time measures in children with cerebral palsy. Rehabilitation Psychology .

[9]Warschausky S, Van Tubbergen M, et al 2012 Modified Test Administration Using Assistive Technology : Preliminary Psychometric Findings. Assessment 19:472-490.

[10]Warschausky S, Van Tubbergen M, et al 2004 Adapting cognitive evaluations for children with motoric and communicative impairments.

[11]Spaulding TJ, Hosmer S, et al 2013 Investigating the interchangeability and diagnostic utility of the PPVT-III and PPVT-IV for children with and without SLI. Int.J.Speech Lang.Pathol. 15(5):453-462.

[12]Dunn LD,Douglas 2007 Peabody Picture Vocabulary Test - Fourth Edition.

[13]Birbaumer N, Ghanayim N, et al 1999 A spelling device for the paralysed. Nature 398(6725):297-298.

[14]Birbaumer N, Cohen LG 2007 Brain-computer interfaces: communication and restoration of movement in paralysis. J.Physiol. 579(Pt 3):621-636.

[15]Buch E, Weber C, et al 2008 Think to move: a neuromagnetic brain-computer interface (BCI) system for chronic stroke. Stroke 39(3):910-917.

[16]Cincotti F, Mattia D, et al 2008 Non-invasive brain–computer interface system: Towards its application as assistive technology. Brain Research Bulletin 75(6):796-803.

[17]Daly I, Billinger M, et al 2013 On the control of brain-computer interfaces by users with cerebral palsy. Clin.Neurophysiol. 124(9):1787-1797.

[18]Allison BZ, Wolpaw EW, et al 2007 Brain-computer interface systems: progress and prospects. Expert Rev.Med.Devices 4(4):463-474.

[19]Iversen IH, Ghanayim N, et al 2008 A brain-computer interface tool to assess cognitive functions in completely paralyzed patients with amyotrophic lateral sclerosis. Clin.Neurophysiol. 119(10):2214-2223.

[20]Aloise F, Arico P, et al 2013 Asynchronous gaze-independent event-related potential-based brain-computer interface. Artif.Intell.Med. 59(2):61-69.

[21]Leeb R, Friedman D, et al 2007 Self-Paced (Asynchronous) BCI Control of a Wheelchair in Virtual Environments: A Case Study with a Tetraplegic. Comput.Intell.Neurosci. :79642.

[22]Daly I, Billinger M, et al 2013 On the control of brain-computer interfaces by users with cerebral palsy. Clin.Neurophysiol. 124(9):1787-1797.

[23]Hwang HJ, Lim JH, et al 2012 Development of an SSVEP-based BCI spelling system adopting a QWERTY-style LED keyboard. J.Neurosci.Methods 208(1):59-65.

[24]Lesenfants D, Partoune N, et al 2011 Design of a novel covert SSVEP-based BCI.

[25]Farwell LA, Donchin E 1988 Talking off the top of your head: toward a mental prosthesis utilizing event-related brain potentials. Electroencephalogr.Clin.Neurophysiol. 70(6):510-523.

[26]Alcaide-Aguirre RE, Huggins JE 2014 Novel hold-release functionality in a P300 brain-computer interface. J.Neural Eng. 11(6):066010.

[27]Dunn LM, Dunn DM 2007 Peabody Picture Vocabulary Test – Fourth Edition.

[28]Hart SG, Staveland LE 1988 Development of NASA-TLX (Task Load Index): Results of Empirical and Theoretical Research. Advances in Psychology 52:139-183.

[29]Carswell CM, Lio CH, et al 2010 Hands-free administration of subjective workload scales: acceptability in a surgical training environment. Appl.Ergon. 42(1):138-145.

[30]Alcaide RE, Huggins JE 2014 Novel hold-release functionality in a P300 Brain-Computer Interface. Journal of neural engineering 11(6):066010.

[31]Thompson DE, Huggins JE 2011 A multi-purpose brain-computer interface output device. Clinical EEG and Neuroscience (October):230-235.

[32]Thompson DE, Gruis KL, et al 2013 A plug-and-play brain-computer interface to operate commercial assistive technology. Disabil.Rehabil.Assist.Technol.

[33]Aref A, Huggins J 2012 The P300-Certainty Algorithm: Improving accuracy by withholding erroneous selections. EEG & Clinical Neuroscience Society, EEG & Clin Soc .

[34]Slater JD, Kalamangalam GP, et al 2012 Quality assessment of electroencephalography obtained from a "dry electrode" system. J.Neurosci.Methods 208(2):134-137.

[35]Donchin E, Spencer KM, et al 2000 The mental prosthesis: assessing the speed of a P300-based brain-computer interface. IEEE Trans.Rehabil.Eng. 8(2):174-179.

[36]Li Y, Pan J, et al 2013 A Hybrid BCI System Combining P300 and SSVEP and Its Application to Wheelchair Control. IEEE Trans.Biomed.Eng. 60(11):3156-3166.

[37]Matthews R, McDonald NJ, et al 2007 Novel Hybrid Bioelectrodes for Ambulatory Zero-Prep EEG Measurements Using Multi-channel Wireless EEG System. Foundations of Augmented Cognition Lecture Notes in Computer Science 4565:137-146.

[38]Millan JD, Rupp R, et al 2010 Combining Brain-Computer Interfaces and Assistive Technologies: State-of-the-Art and Challenges. Front.Neurosci. 4:10.3389/fnins.2010.00161.

[39]Pfurtscheller G, Allison BZ, et al 2010 The hybrid BCI. Front.Neurosci. 4:30.

[40]Rohm M, Schneiders M, et al 2013 Hybrid brain-computer interfaces and hybrid neuroprostheses for restoration of upper limb functions in individuals with high-level spinal cord injury. Artif.Intell.Med. 59(2):133-142.

[41]Yin X, Xu B, et al 2015 A hybrid BCI based on EEG and fNIRS signals improves the performance of decoding motor imagery of both force and speed of hand clenching. J.Neural Eng. 12(3):036004.

[42]Nicolas-Alonso LF, Gomez-Gil J 2012 Brain computer interfaces, a review. Sensors (Basel) 12(2):1211-1279.

[43]Yin E, Zhou Z, et al 2014 A dynamically optimized SSVEP brain-computer interface (BCI) speller. IEEE Trans.Biomed.Eng.

[44]Yin E, Zhou Z, et al 2013 A Speedy Hybrid BCI Spelling Approach Combining P300 and SSVEP. IEEE Trans.Biomed.Eng.

[45]Wang Y, Wang R, et al 2006 A practical VEP-based brain-computer interface. IEEE Trans.Neural Syst.Rehabil.Eng. 14(2):234-240.

Chapter Three: Novel Hold-release Functionality in a P300 Brain-computer Interface

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Abstract

Assistive technology control interface theory describes interface activation and interface deactivation as distinct properties of any control interface. Separating coBCIntrol of activation and deactivation allows precise timing of the duration of the activation. We propose a novel P300 BCI functionality with separate control of the initial activation and the deactivation (hold-release) of a selection. Using two different layouts and off-line analysis, we tested the accuracy with which subjects could 1) hold their selection and 2) quickly change between selections. Mean accuracy across all subjects for the hold-release algorithm was 85% with one hold-release classification and 100% with two hold-release classifications. Using a layout designed to lower perceptual errors, accuracy increased to a mean of 90% and the time subjects could hold a selection was 40% longer than with the standard layout. Hold-release functionality provides improved response time (6-16 times faster) over the initial P300 BCI selection by allowing the BCI to make hold-release decisions from very few flashes instead of after multiple sequences of flashes. For the BCI user, hold-release functionality allows for faster, more continuous control with a P300 BCI, creating new options for BCI applications.

Keywords: P300, EEG, speller, activation/deactivation, assistive technology

Introduction

A brain-computer interface (BCI) is an assistive technology interface intended to provide operation of technology directly from the interpretation of brain signals to benefit those with the most severe physical impairments. The science of assistive technology describes the human/control interface as “the boundary between the human and assistive technology.” For a BCI, the human/technology interface characterizes the utility the BCI provides [1]. Here we consider the characteristics of BCIs as human/technology control interfaces and present a novel P300 BCI functionality. For the three most commonly used electroencephalography (EEG)-based BCIs: P300 [2], steady-state visual evoked potential (SSVEP) [3], and motor imagery [4], we performed a literature search to define the most common BCI control interface characteristics and identify novel BCI control methods.

Human/Technology Interface Characteristics

The human/technology interface can be characterized by 1) the control interface, 2) the selection set, 3) the selection method and 4) the user interface [1]. The control interface is described as the hardware between the human and technology through which information is exchanged. For non-invasive EEG BCIs, the control interface would be the electrodes, amplifier, and computer that convert the user’s brain signals to BCI commands. The selection set of a human/technology interface is the group of available choices a user can make. Examples of selection sets include the letters/numbers on an alphanumeric matrix or the directional arrows on a control display [1]. The selection method describes how a command from a user will be interpreted by the BCI, either directly or indirectly. Direct selection allows a user to directly select any item from the selection set, while indirect selection requires an intermediary step before a user can select [1].

The final component is the user interface, which describes the characteristics of the interface between the user and the BCI. Three types of characteristics describe the user interface: 1) spatial, 2) sensory and 3) activation/deactivation. The spatial characteristics describe the dimension, number, and shape of the targets. The sensory characteristics describe the feedback provided to the user, whether auditory, visual or somatosensory [1]. The activation/deactivation describes the quality of the human/technology interaction. The effort describes the quality of interaction (how difficult it is to use the BCI), displacement (how much movement is required to respond), flexibility (the number of ways in which the BCI can be used), durability (how reliable the BCI hardware is), maintainability (how easily the BCI can be repaired) and the method of activation or release (the ability to make/activate or stop/deactivate a selection and how that selection is made) [1]. It is important to distinguish between activation and deactivation because they can both be given distinct functionality. Using activation as a control input can be thought of as a trigger or momentary switch. In this case, only the activation causes an effect, and the duration with which the activation is held does not alter the outcome. Using both activation and deactivation allows for more complicated control functionality, and the control input can act as a button. For example, on a television remote control, you can activate and hold one of the volume keys to keep increasing the volume. In this case, holding a selection causes continued change, while releasing it keeps the current state.

Literature search

We performed a literature search on EEG-based P300, SSVEP, and motor imagery BCIs to 1) describe typical BCI implementations using the human/technology interface characteristics and 2) identify P300, SSVEP, and motor imagery BCIs with novel selection or activation/release methods.

We search PubMed [5] from 1991-2014 using the terms: brain-computer interface control, brain-computer interface asynchronous, brain-computer control interface, brain-computer interface hybrid, brain-computer interface novel control, analog control brain-computer interface, analog control brain-computer interface, and proportional brain-computer interface. This generated over 600 unique publications. Review articles were identified by articles that did not focus on one study but instead described basic information on P300, SSVEP and motor imagery BCIs. Older review articles were dropped if a more recent article covered similar material. We used 13 review articles to categorize the typical implementation of P300, SSVEP and motor imagery BCIs per the characteristics of the selection set, selection method, and user interface. Insufficient information was present in the literature to categorize the lifespan of BCI hardware, durability, or maintainability. All P300, SSVEP, and motor imagery articles using typical implementations were excluded to identify 47 candidate novel interfaces articles.

Literature results

Over 99% of P300 studies used selection sets of characters or images. Selection sets typically had 36 items (6x6 matrices) [6] but ranged from 4 to 84 items (4 independent options [7] to a 7x12 [8] matrix). P300 BCIs primarily used a direct selection method with activation as the only control method. Although P300 signals could be used for indirect selection, most examples of this approach still used the P300 signal to directly select from nested menus [2]. Only Citi et al. [9] used the P300 in a truly novel BCI paradigm to control a computer mouse in two dimensions by combining the P300 amplitudes of the filtered output. This implementation allowed for indirect selection and could also allow for deactivation. With only one published alternative control method for using the P300, this suggests that P300 BCIs have little flexibility. P300 BCIs tended to require less effort than SSVEP or motor imagery BCIs. P300 accuracy increases substantially if a person can maintain a steady gaze [10], but gaze control is not strictly necessary [11-13]. Thus, P300 have low to medium displacement, as little to no eye movement is required for some layouts (Table 4).

SSVEP BCIs are more flexible than P300 BCIs and have been used in direct and indirect selection methods and for activation/deactivation [3,14]. SSVEP selection sets typically consist of flashing characters or objects [3]. The number of objects is typically four [15] but ranges from 2 to 48 [16,17]. Displacement varies depending on the type of SSVEP BCI. Like P300 BCIs, the accuracy of SSVEP BCIs increases if the user can maintain gaze [18]. Newer SSVEP systems such as eyes-closed SSVEP BCIs eliminate the displacement issue, but such BCIs have a small selection set [19](Table 4). This suggests that displacement of SSVEP BCIs varies depending on the application.

Motor imagery BCIs have greater flexibility than SSVEP BCIs and have been used for direct and indirect selection and activation/deactivation. Direct selection motor imagery BCIs tend to have smaller selection sets, typically 2-4 selections [20-22] because the number of selections is limited to the number of distinguishable imagined actions [23,24]. Selection set size for indirect selection motor imagery BCIs is limited by the number of selections presented to the user and the precision of control. Motor imagery BCIs require more effort to learn and use than P300 or SSVEP BCIs [25-27]. Required displacement of motor imagery BCIs varied greatly with simple protocols such as binary selection requiring no displacement while more complex protocols such as controlling robotic devices required the user to monitor the activity of the robot (Table 4).

BCI	Selection Set	Selection Method	Activation/ Deactivation	Flexibility	Effort	Displacement
P300	36	Direct	Activation	Low	Low	Low-Medium
SSVEP	4 selections	Direct and Indirect	Both	Medium	Medium	Low-Medium
Motor Imagery	2-4 selections	Direct and Indirect	Both	High	High	Low-High

Table 4. Assistive functionality BCI overview

- Selection set of a human/technology interface is the group of available choices a user can make.
- The selection method describes how a command from a user will be interpreted by the BCI, either directly or indirectly.
- Activation/deactivation describes the control option of the human/technology interaction.
- Flexibility describes the number of ways in which the BCI can be used
- Effort describes how difficult it is to use the BCI
- Displacement describes how much movement is required to respond

Our literature search shows that P300 BCIs utilize the same activation/release methods, producing less flexibility in P300 BCIs compared to SSVEP and motor imagery BCIs. This may result from the low signal-to-noise ratio of the P300, which often requires multiple P300 responses to accurately determine a user's selection, reducing the response speed of the P300 BCI. Thus, P300 BCIs are typically used for direct selection from large sets of predetermined choices, such as a keyboard. In this application, the advantage of a large selection set is considered more important than rapidly changing between selections.

However, speed is a critical factor for many applications that do not naturally have quantified discrete outputs. For example, in applications such as BCI control of the position of a reclining seat, it is desirable to sustain a command (such as 'recline') until the desired condition is met (seat angle) or a safety concern arises. While motor imagery BCIs are often thought of as BCIs of choice for analog outputs, the time needed to learn sufficient motor imagery control for functional use can be prohibitive [25-30]. While SSVEP has been used for rapid response applications, there is no equivalent of this for P300 BCIs.

Several P300 based systems have used different classification and feature extraction techniques to increase accuracy for classification of single P300 flashes. This includes using principal component analysis, independent component analysis, and neural networks. However, accuracies tend to be under 60% [31-35]. This can be largely attributed to the tendency for single trial studies using P300 to have a large matrix of choices (36 vs. two selections). However, in some situations, it may be beneficial to have a limited number of choices for a quick response. Results from studies that use fewer selections suggest that fewer averages are needed to achieve a high classification accuracy. For example, Kubler [36] used an auditory P300 BCI for binary selection on twenty subjects and achieved 66% accuracy with one sequence, 78% accuracy with two sequences, and 93% with 25 sequences. Further insight on how presentation methods can affect accuracy can be derived by evaluating data from rapid serial visual presentation (RSVP) BCIs that use the P300 signal but only display one option to the user at a time [37-39]. For example, in Blankertz [38], users were able to achieve 83% classification accuracy after their selections flashed on the screen about four times. Similar results were found in other RSVP studies [37-39]. While accuracy is still significantly less than ideal, findings from these studies and an abundance of others suggest that a smaller number of selections (if presentation rarity is maintained i.e. how often the subject's selection is presented) and a presentation method that increases discernibility will yield an increase in P300 classification accuracy [38,40-42]. Thus, requiring less P300 events to occur for a correct classification can be reached.

Hold-release Functionality

We propose a novel P300 BCI functionality in which the initial activation and the deactivation (hold-release) of targets in a P300 BCI can be separately controlled. This would allow P300 BCIs to be used in applications that require indirect selection or applications that require quick changes between states. Further, it would allow confirmation-cancelation of a selected target by either holding the selection or switching attention to a release target.

In a potential real-world application, the targets on the BCI display would have different activation/deactivation characteristics. Some items would be hold-release enabled to allow fine adjustment, for example, reclining a wheelchair (Figure 8: B1), changing the temperature (Figure 8: A3 and B3), or increasing the volume of a television (Figure 8: A2 and B2). Safety-critical items, such as unlocking/locking a door (Figure 8: D1 and E1), could require a hold-release confirmation-cancelation step, where a short hold period was required before activation. The remaining items would perform traditional discrete P300 actions, such as turning on lights or changing a television channel. (Figure 8: C1, A2, and A3). Once the user selected a target with a hold-release response (for adjustment or confirmation) then the screen would change to a hold-release mode (Figure 8, right panel), in which only the previously selected target and a release target would be active, and the rest of the targets on the BCI matrix would not be selectable. If the BCI had correctly identified the desired target, the user would hold the selected target and the BCI would perform the action either until the user wanted the action to stop (reclining wheelchair or changing television volume) or for a specified duration to confirm the selection (thereby preventing inadvertent activation of a safety-critical action). Thus, hold-release functionality would expand the utility of P300 BCIs in ways that mirror the multiple control modes available on existing assistive technology and other BCI modalities [1,15,43-45].

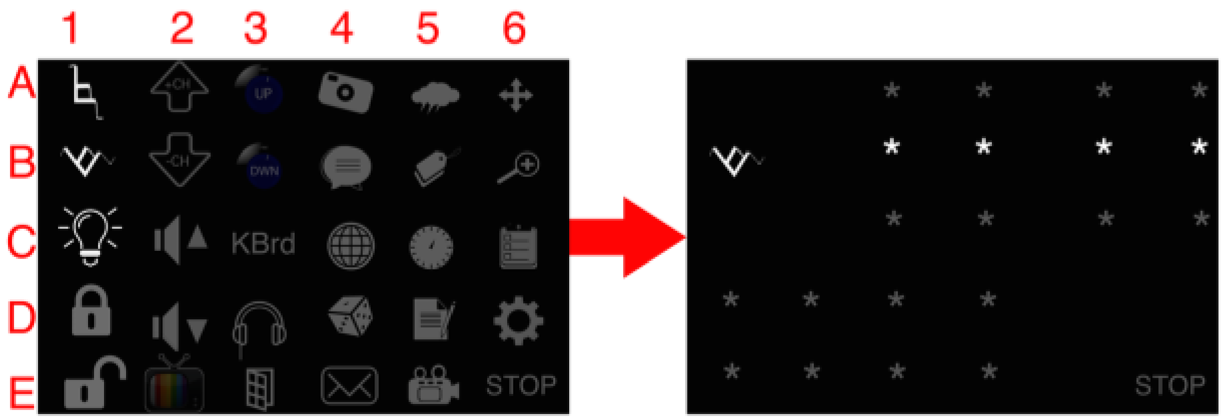

Figure 8. Concept image of future hold-release enabled BCI

- Example BCI matrix with targets for different actions. Some actions are enabled for hold-release functionality and others are not.
- Right: After the subject selects an action that is hold-release enabled, in this case, recline wheelchair, the screen changes to a hold-release mode.
- In this case, the subject can then recline their chair until they want to stop.

During the holding process, the only information required by the BCI is when the user changes their selection (e.g. stops increasing/decreasing volume or recline a wheelchair). The binary nature of the release decision allows the BCI to make the decision from very few flashes instead of after multiple sequences of flashes. For the BCI user, this means a faster response time and a more continuous control than using the traditional P300 BCI method.

To test the feasibility of P300 hold-release functionality, we asked subjects to perform hold-release tasks with two P300 BCI display layouts. Our first layout was a standard P300 BCI speller matrix. The second was designed to reduce perceptual issues known to decrease P300 BCI classification accuracy and represented a change in the layout that would indicate the entry into the hold-release mode. The feasibility of hold-release functionality was determined through off-line analysis.

Methods

Layouts

To get data to develop and test hold-release functionality, we created a 5x6 matrix for a P300 speller with two selectable objects; one object was an 'X' in the upper left-hand corner of the matrix, and the other was 'O' in the lower right-hand corner (Figure 9). For this feasibility study, the locations of these "selectable targets" were chosen to maximize the distance between targets, minimizing the potential for inadvertent reactions to the incorrect target. The two selectable targets represent how hold-release would be used in a real-world application. The user would select on a standard BCI matrix with all the targets active. Then the screen would change to hold-release mode, in which only the previously selected target and the “release target” would be active. The user would then hold the target (‘X’ in our case or raise/lower volume in case of figure 8) until the user wants to change the state (‘O’ in our example or stop in Figure 9). The rest of the objects on the BCI matrix would not be selectable, and responses from their flashes would not be used to determine the state the user was selecting.

Two variations of the layout for the operating matrix were tested (Figure 9), both representing realistic usage options where a subject must alternate their selection between two targets (e.g., for volume control or wheelchair reclining). In layout 1, the non-selectable objects of the matrix contained numbers to provide the visual clutter typical of P300 BCIs. Layout 2 was designed to remove two common perceptual issues in P300 spellers; adjacency response errors and double flashing errors. Adjacency response errors can happen when a flash occurs adjacent to the item the BCI user is selecting. This can cause the user to erroneously produce a P300 for an object that is not being selected. Double flash errors happen when the item the user is selecting is flashed twice in a row. This can cause the BCI user to miss the second flash or have a delayed reaction to the second flash [46-50]. To remove adjacency response errors, we surrounded each selectable object with white space. All other locations were filled with ‘*’ characters for reduced visual clutter while keeping rarity of stimuli equal to a traditional BCI display. To remove double flashes, we ensured that the row and column containing a selectable item were never flashed sequentially. Layout 1 represents an eventual application in which activating a hold-enabled-selection results in the appearance of the release target, but no other changes. Layout 2 represents an eventual application in which activating the hold-enabled-selection results in activation of the release target and other changes to the display to eliminate perceptual errors and indicate the entrance into the hold-release mode.

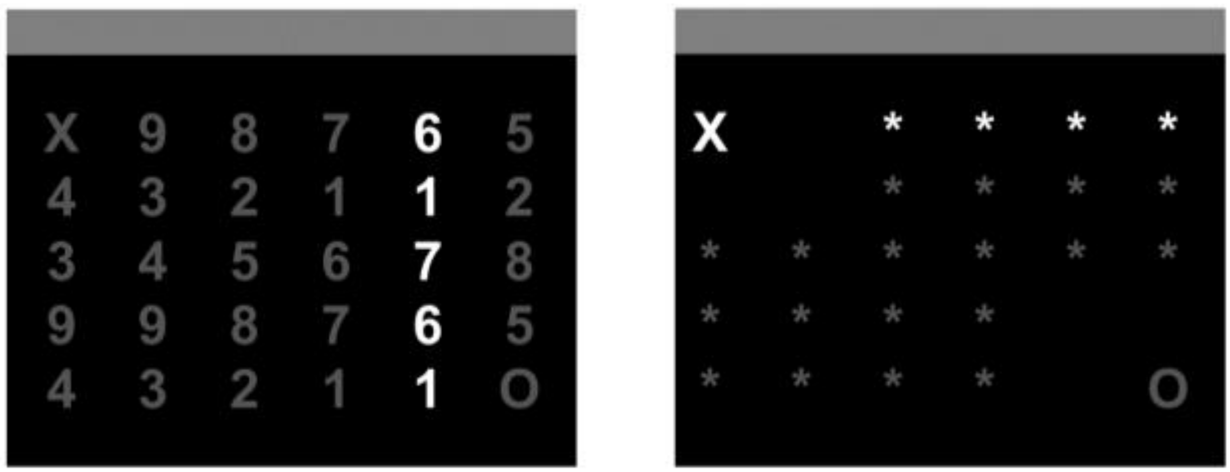

Figure 9. Different layouts tested using hold-release technology

- Left image is layout 1 which represents a typical event-related potential BCI typing matrix with numbers providing visual clutter.
- The right image is layout 2 which has asterisks instead of numbers and whitespace to reduce perceptual errors.
- Illuminated areas represent a flash group.

Protocol

We tested seven able-bodied subjects ages 27 ± 13 years (2 females and five males) using a 16-channel EEG electrode cap from Electro-Cap International (electrode locations in figure 10). Subjects sat in front of a computer screen that contained one of our BCI layouts. We instructed our subjects to select and hold an object until a tone sounded to indicate a switch of the target object. Subjects “held” the object by counting how many times it flashed. The target in the upper left corner was designated as the starting target. Subjects performed ten hold-release runs, five using layout 1 and 5 using layout 2. The order in which they used the layouts was pseudo-random. The tone played five times per run, creating five transitions between objects. The timing for the tone was pseudo-random and happened after 10-60 flashes (1560-9360 ms). All tones were separated by at least ten flashes, no tones played when a group that contained a selectable object was flashing, and no tones played during the first or last 5 seconds of each run. Each run lasted about a minute, containing 330 flashes and a total of 120 hold-release decisions. During the collection, subjects were not given feedback regarding whether the object they were holding was selected.

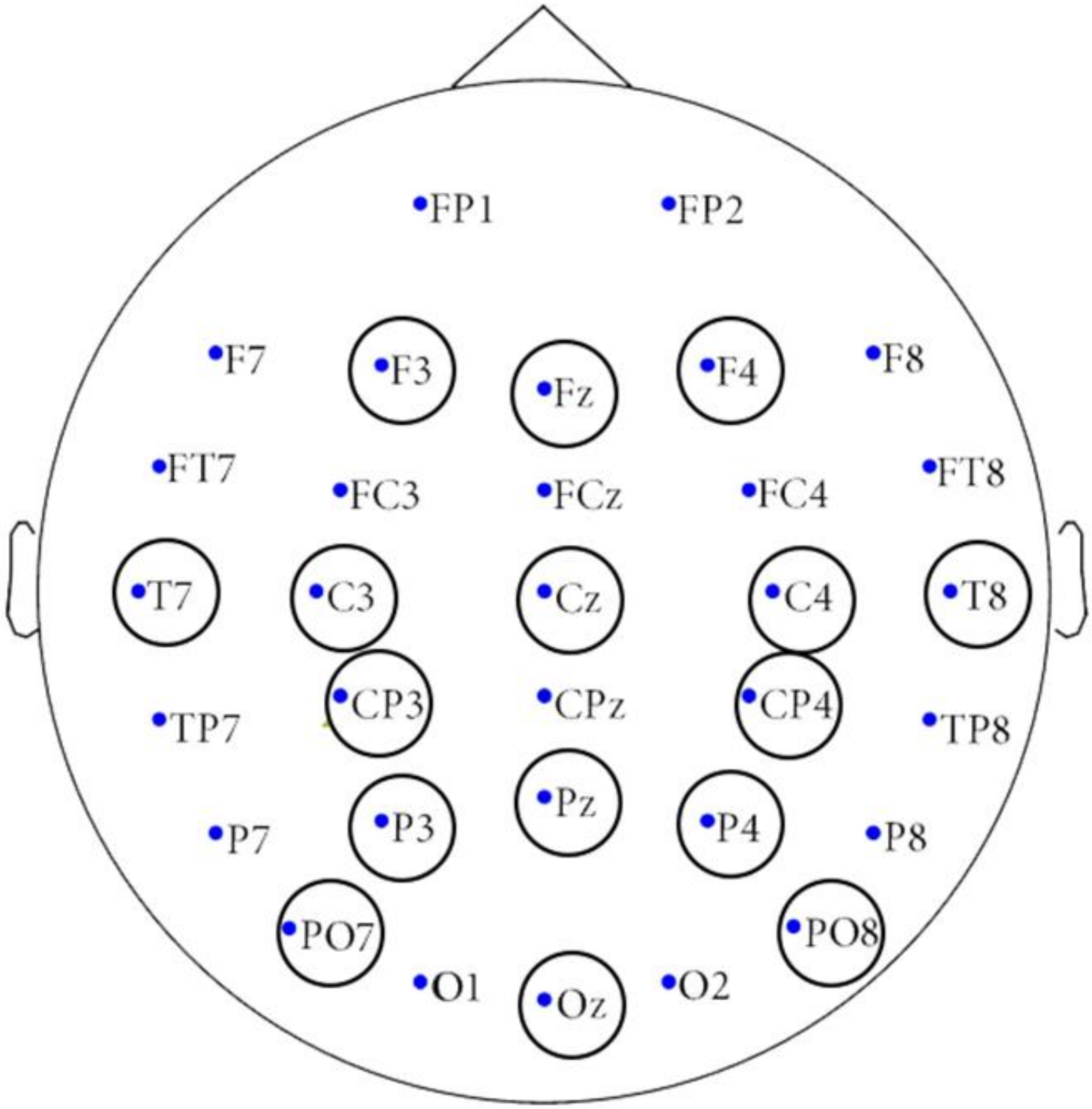

Figure 10. Electrode cap montage

- Circles denote electrode locations used for the study.

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Classification

The hold-release process used two classifiers. An initial selection classifier (such as is typically used for a P300 BCI) assigned classification values to the flashing objects. The selection classifier used a least squares regression from training data collected by having the BCI user focus on each letter in the phrase "THE QUICK BROWN FOX" for 30 flashes per letter on a 6x6 BCI speller matrix.

The hold-release classifier used the values produced by the selection classifier to determine which object was being held. The determination of the hold state assumed that, no matter how many objects were present in the BCI display, the user was attending to one of the two selectable objects. The held object was identified by comparison of the most recent classifier values of the two objects to each other and a threshold value. The held object decision could occur as frequently as each time that a new classifier value was available for either object. Because the selectable objects were placed in distinct flash groups, a hold-release decision could be made in less than an entire sequence of flashes. The key variables in the response time of the hold-release functionality were, therefore, the amount of EEG used for classification (762 ms) and the number of flashes of the hold and released objects that were used in the decision process. Results were calculated for one flash and two flashes of hold-release objects. Since the group that flashed happened at random, it took an average of 421 ± 250 ms for a new flash of one of the hold-release objects to occur. Thus, decisions based on one flash occurred on average every 1221 ± 250 ms, and those based on two flashes occurred on average every 1642 ± 363 ms.

The hold-release classifier produced a state change when any one of three conditions was met. The first condition used as a threshold the smallest selection classifier value that separated the selected objects with 99% accuracy (calculated from the training data). The strict 99% accuracy was selected to maximally prevent unwanted state change for initial feasibility analysis. If either object returned a selection classifier value that was equal to or greater than this threshold, that object was set as the held object. The second condition was whether the selection classifier value of one of the objects was negative. Whenever an object returned a negative selection classifier value, the held object was set to the other object. The second conditions directly implemented a release of a formerly held item. These conditions were applied on an individual flash basis. The final condition was invoked when both objects had positive selection classifier values, but those values were below the threshold. This condition required data from flashes of both objects. Therefore no change occurred until the second object flashed. In this case, whichever object had the largest classifier value was considered the held object.

When analyzing data utilizing two flashes of the hold-release objects, we required the classification decision from both flashes to agree on which selectable object was being held before the hold decision changed. If both flashes did not agree, then the previous hold decision was kept.

<u>Analysis</u>

In real world applications, the hold-release functionality would be associated only with certain objects in the BCI display and the mode would activate on the selection of one of those objects. Thus, the held object would be known. For the start of each run, we, therefore, assumed that the held object was known to be the object in the upper left that the subject was instructed to observe first. This object considered the held object until information from one of the two selectable objects was available, triggering a new hold decision. Flashes of rows and columns that did not contain either selectable object did not result in a new hold decision.

Ideal algorithm performance was a release decision at the first flash of either selectable target after the occurrence of the signal tone. This allowed each flash of the selectable targets to be assigned a correct decision value. Algorithm results for both layouts were compared to this standard. With only two selectable objects, chance accuracy would be 50% during each hold-release decision. For each run, we then calculated the mean accuracy of all decisions and the number of flashes between the transition points. Then, we used a two-way ANOVA to compare accuracy across subjects and layouts.

The duration of continuous correct hold-release classification was also analyzed. Ideal performance required correctly tracking the transitions between the held objects. No tolerance was allowed for delayed classifications of a state change.

Results

Minimum accuracy for the hold-release algorithm was 80% or higher for all subjects when calculated with information from one flash of a hold-release object. Mean accuracy from one flash of a hold-release object using layout 1 was 85 ± 3.5% and mean accuracy using layout 2 was 90 ± 3.6%. Figure 11 shows an example of result data from the two layouts. Using information from two flashes (from any combination of the two selectable objects) before deciding increased accuracy to 100% for both layouts. A two-way ANOVA across subjects and layouts showed a significant difference in accuracy depending on the layout used (=0.0003).

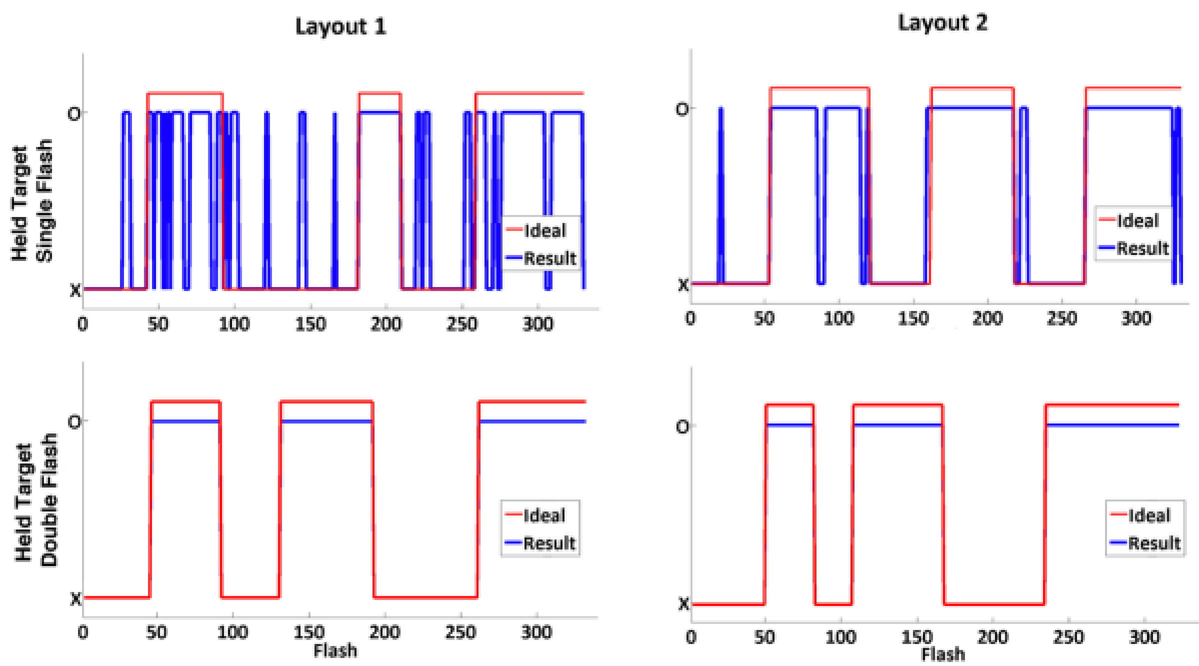

Figure 11. Sample data of hold-release protocol

- Left images are sample outcomes of our hold-release protocol using layout 1.
- Right images are sample outcomes of our hold-release protocol using layout 2.
- Top images represent when only one flash was used for classification.
- Bottom images represent when two flashes were used for classification.
- The red line shows the ideal hold result for each flash. The blue line shows which target the algorithm classified as held.

This accuracy results in sequences of continuous correct performance, which represent correct tracking of the hold condition, including transitions between hold targets. There was a significant difference ($p < 0.0001$) between the continuous correct hold-release classifications between layouts. Layout 1 tended to have a greater number of shorter continuous correct classifications while layout 2 had longer continuous correct classifications. Using two flash classifications, all subjects held the correct target for the full duration of the run (Figure 12).

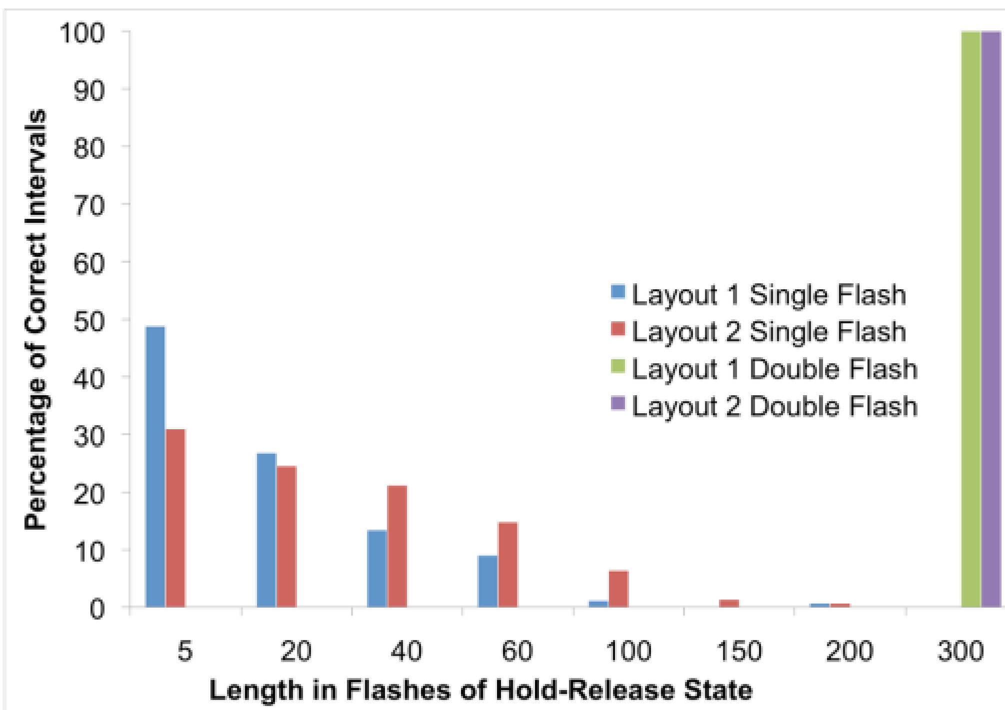

Figure 12. Length of consecutive hold-release intervals

- The length of consecutive correct performance intervals (in flashes) for all subjects by layout and single vs. double flash classification.
- Note that each run was 330 flashes.

Discussion

Our results demonstrate that hold-release functionality is possible using P300 BCIs. Using hold-release allows us to extend the use of P300 BCIs to applications that require fast and analog-like responses. Using layout 2, all subjects performed the hold-release task with an accuracy of 86% or higher from the classification of one flash of either hold-release object. Using two flashes of any combination of the two hold-release objects gave 100% accuracy.

P300 BCI spellers typically require 4-15 sequences for adequate classification accuracy (about 2 seconds per sequence)[2]. While a BCI with hold-release functionality would still require this time frame for activation of the hold-release mode, a response time advantage would be seen in the precision with which the duration of the hold was controlled. Thus, multiple sequences of flashes would be used to activate a hold-release selection, but deactivation would require only a single flash. This makes our release functionality much faster (Figure 13) than traditional P300 BCI system activation functionality, where each sequence adds to the classification time. This faster response time comes from a decrease of information needed to make a classification among fewer targets.

While motor imagery BCIs may provide faster responses than our hold-release P300 potential BCI [51,52], some BCI users have difficulty learning precise EEG-based motor imagery control [25,27-30]. SSVEP and P300 BCIs are both relatively easy to learn and have comparable responsiveness. SSVEP BCIs typically require 0.5-4 (average 1) seconds [3,15,18,53-56] for accurate classification, while hold-release functionality requires 1.23 seconds (Figure 13). The largest time requirement for our hold-release functionality is the collection of 762ms of EEG activity after each flash of a hold-release object. This window size was a default value to ensure that the P300 potential was captured. Optimization of this window size may increase the interface responsiveness without loss of accuracy and responsiveness may approach the lower bound of SSVEP systems. However, the current hold-release system is comparable to current SSVEP systems regarding response time.

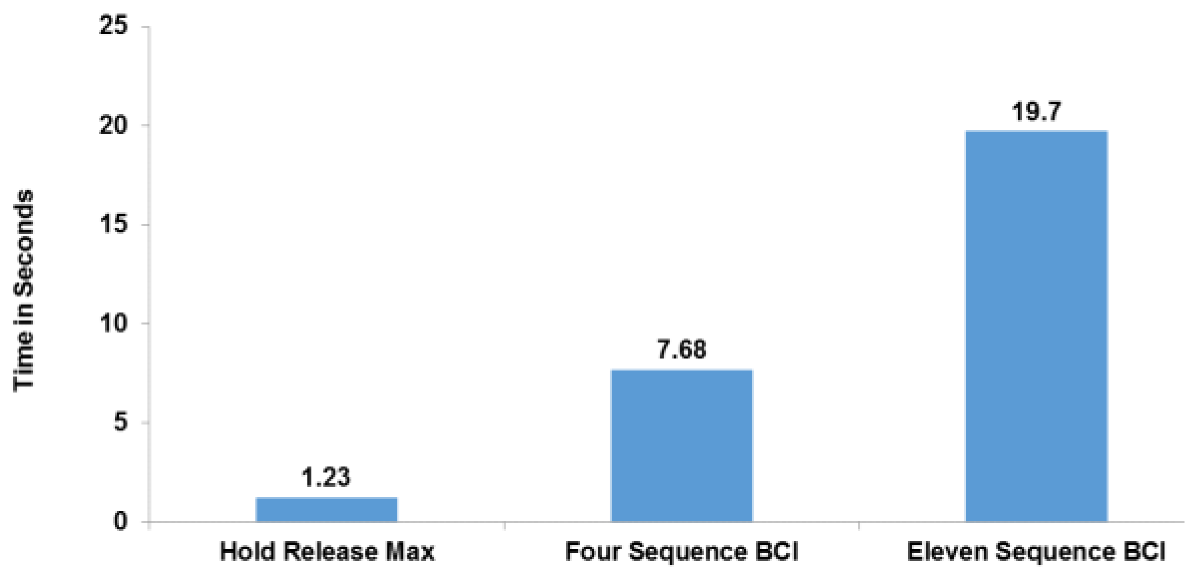

Figure 13. Comparison of standard ERP BCIs vs hold-release BCI

Since our algorithm operates using data from only one or two flashes, it can be expected to be extremely sensitive to perceptual errors in those flashes. As expected, layout 2, which was designed to reduce perceptual errors, produced a significant increase of 5% points in average accuracy from a single flash (from 85% to 90%). Furthermore, layout 2 has on average 40% longer continuous correct classifications and a larger maximum interval of continuous correct classifications compared to layout 1 (210 vs. 182 flashes).

These results support previous literature showing that BCI display characteristics have a direct effect on performance [15,46,57]. The increase in accuracy achieved from our simple changes to layout suggests that that other changes such as using color, flash brightness or frequency may further increase the robust of single flash classification using our hold-release functionality. Our layout changes are also reasonable within the applications in which hold-release functionality will be used. Many applications exist where it is important to rapidly change between two selections. For example, in the assistive technology realm, hold-release functionality has been used for volume control, item scanning and wheelchair control [1]. Our method can also be integrated with traditional P300 item selection in a two-step process to expand functionality. For example, a BCI user could use the traditional BCI speller to select the desired command from all possible commands, and then the screen could change to a hold-release screen to allow the user to have a precise termination of the command's effect. Also, the hold-release could be used to provide a seamless confirmation step, allowing a user to cancel an erroneous selection in less time than would be required to select a backspace. This means that our hold-release functionality can naturally expand the functionality of traditional P300 BCIs, changing their functionality depending on the application.

Limitations

This was a proof-of-concept study to demonstrate that hold-release functionality is possible using a P300 BCI. This study used offline data processing; we expect on-line tests to vary depending on the difficulty of the task. Future testing should also include longer duration runs to quantify better the timing of hold sequences, which in this data are limited by the one-minute duration of runs.

Some steps were taken to avoid perceptual errors, such as the maximal spatial separation of the selectable targets. The success of rapid serial visual presentation (RSVP) BCI keyboards show that such separation of targets may not be necessary [58].

Conclusion

We presented a novel BCI functionality in which activation and deactivation of a selection can be separately controlled. This functionality improves response time by allowing the BCI to make hold-release decisions from very few flashes instead of after multiple sequences of flashes. For the BCI user, this faster response time and a more analog-like control open new applications and interaction methods. Further study is needed to verify on-line function and optimize the hold-mode flash patterns and visual layout for maximum responsiveness.

References

[1]Cook Albert HS 2001 Assistive Technologies: Principles and Practice.

[2]Cecotti H 2011 Spelling with non-invasive Brain-Computer Interfaces--current and future trends. J.Physiol.Paris 105(1-3):106-114.

[3]Vialatte FB, Maurice M, et al 2010 Steady-state visually evoked potentials: focus on essential paradigms and future perspectives. Prog.Neurobiol. 90(4):418-438.

[4]Neuper C, Müller-Putz GR, et al 2006 Motor imagery and EEG-based control of spelling devices and neuroprostheses. Prog.Brain Res. 159:393-409.

[5]PubMed.

[6]Kleih SC, Kaufmann T, et al 2011 Out of the frying pan into the fire--the P300-based BCI faces real-world challenges. Prog.Brain Res. 194:27-46.

[7]Sellers EW, Donchin E 2006 A P300-based brain–computer interface: Initial tests by ALS patients. Clinical Neurophysiology 117(3):538-548.

[8]Jin J, Sellers EW, et al 2012 Targeting an efficient target-to-target interval for P300 speller brain-computer interfaces. Med.Biol.Eng.Comput. 50(3):289-296.

[9]Citi L, Poli R, et al 2008 P300-based BCI mouse with genetically-optimized analogue control. IEEE Trans.Neural Syst.Rehabil.Eng. 16(1):51-61.

[10]Brunner P, Joshi S, et al 2010 Does the P300 Speller Depend on Eye-Gaze? 7(5):10-10.

[11]Marchetti M, Piccione F, et al 2013 Covert visuospatial attention orienting in a brain-computer interface for amyotrophic lateral sclerosis patients. Neurorehabil.Neural Repair 27(5):430-438.

[12]Marchetti M, Onorati F, et al 2013 Improving the efficacy of ERP-based BCIs using different modalities of covert visuospatial attention and a genetic algorithm-based classifier. PLoS One 8(1):e53946.

[13]Riccio A, Mattia D, et al 2012 Eye-gaze independent EEG-based brain-computer interfaces for communication. J.Neural Eng. 9(4):045001-2560/9/4/045001. Epub 2012 Jul 25.

[14]Li Y, Pan J, et al 2013 A Hybrid BCI System Combining P300 and SSVEP and Its Application to Wheelchair Control. IEEE Trans.Biomed.Eng. 60(11):3156-3166.

[15]Zhu D, Bieger J, et al 2010 A survey of stimulation methods used in SSVEP-based BCIs. Comput.Intell.Neurosci. :702357.

[16]Hwang HJ, Lim JH, et al 2012 Development of an SSVEP-based BCI spelling system adopting a QWERTY-style LED keyboard. J.Neurosci.Methods 208(1):59-65.

[17]Xiaorong G, Dingfeng X, et al 2003 A BCI-based environmental controller for the motion-disabled. IEEE Transactions on Neural Systems and Rehabilitation Engineering 11(2):137-140.

[18]Walter S, Quigley C, et al 2012 Effects of overt and covert attention on the steady-state visual evoked potential. Neurosci.Lett. 519(1):37-41.

[19]Han CH, Hwang HJ, et al 2013 Development of an "eyes-closed" brain-computer interface system for communication of patients with oculomotor impairment. Conf.Proc.IEEE Eng.Med.Biol.Soc. 2013:2236-2239.

[20]Curran EA, Stokes MJ 2003 Learning to control brain activity: a review of the production and control of EEG components for driving brain-computer interface (BCI) systems. Brain Cogn. 51(3):326-336.

[21]Pfurtscheller G, Neuper C 2006 Future prospects of ERD/ERS in the context of brain-computer interface (BCI) developments. Prog.Brain Res. 159:433-437.

[22]Li Y, Long J, et al 2010 An EEG-based BCI System for 2-D Cursor Control by Combining Mu/Beta Rhythm and P300 Potential. IEEE Trans Biomed Eng .

[23]Hashimoto Y, Ushiba J 2013 EEG-based classification of imaginary left and right foot movements using beta rebound. Clin.Neurophysiol. 124(11):2153-2160.

[24]Xia B, An D, et al 2013 A mental switch-based asynchronous brain-computer interface for 2D cursor control. Conf.Proc.IEEE Eng.Med.Biol.Soc. 2013:3101-3104.

[25]Wolpaw JR, McFarland DJ, et al 1991 An EEG-based brain-computer interface for cursor control. Electroencephalogr.Clin.Neurophysiol. 78(3):252-259.

[26]Wolpaw JR, McFarland DJ 2004 Control of a two-dimensional movement signal by a noninvasive brain-computer interface in humans. Proc.Natl.Acad.Sci.U.S.A. 101(51):17849-17854.

[27]Wolpaw JR, McFarland DJ 1994 Multichannel EEG-based brain-computer communication. Electroencephalogr.Clin.Neurophysiol. 90(6):444-449.

[28]Kubler A, Neumann N 2005 Brain-computer interfaces--the key for the conscious brain locked into a paralyzed body. Prog.Brain Res. 150:513-525.

[29]Wolpaw JR, McFarland DJ, et al 1986 Preliminary studies for a direct brain-to-computer parallel interface. In: IBM Technical Symposium. Behav Res Meth :11-20.

[30]McFarland DJ, Lefkowicz AT, et al 1997 Design and operation of an EEG-based brain-computer interface (BCI) with digital signal processing technology. Behav Res Meth 29(3):337-345.

[31]Sharma N 2013 Single-trial P300 classification using PCA with LDA and neural networks. Col State U 1(1):1-52.

[32]D'Avanzo C, Schiff S, et al 2011 A Bayesian method to estimate single-trial event-related potentials with application to the study of the P300 variability. J.Neurosci.Methods 198(1):114-124.

[33]Jarchi D, Sanei S, et al 2011 A new spatiotemporal filtering method for single-trial estimation of correlated ERP subcomponents. IEEE Trans.Biomed.Eng. 58(1):132-143.

[34]Jansen B, Allam A, et al 2004 An Exploratory Study of Factors Affecting Single Trial P300 Detection.

[35]Lee WL, Tan T, et al 2013 An improved P300 extraction using ICA-R for P300-BCI speller. Conf.Proc.IEEE Eng.Med.Biol.Soc. 2013:7064-7067.

[36]Halder S, Rea M, et al 2010 An auditory oddball brain-computer interface for binary choices. Clin.Neurophysiol. 121(4):516-523.

[37]Fried-Oken M, Mooney A, et al 2015 A clinical screening protocol for the RSVP Keyboard brain-computer interface. Disabil.Rehabil.Assist.Technol. 10(1):11-18.

[38]Acqualagna L, Blankertz B 2013 Gaze-independent BCI-spelling using rapid serial visual presentation (RSVP). Clin.Neurophysiol. 124(5):901-908.

[39]Marathe AR, Lawhern VJ, et al 2016 Improved Neural Signal Classification in a Rapid Serial Visual Presentation Task Using Active Learning. IEEE Trans.Neural Syst.Rehabil.Eng. 24(3):333-343.

[40]Riccio A, Simione L, et al 2013 Attention and P300-based BCI performance in people with amyotrophic lateral sclerosis. Front.Hum.Neurosci. 7:732.

[41]Nicolas-Alonso LF, Gomez-Gil J 2012 Brain computer interfaces, a review. Sensors (Basel) 12(2):1211-1279.

[42]Salvaris M, Sepulveda F 2009 Visual modifications on the P300 speller BCI paradigm. J.Neural Eng. 6(4):046011.

[43]Galan F, Nuttin M, et al 2008 A brain-actuated wheelchair: asynchronous and non-invasive Brain-computer interfaces for continuous control of robots. Clin.Neurophysiol. 119(9):2159-2169.

[44]Millan JD, Rupp R, et al 2010 Combining Brain-Computer Interfaces and Assistive Technologies: State-of-the-Art and Challenges. Front.Neurosci. 4:10.3389/fnins.2010.00161.

[45]Müller-Putz GR, Breitwieser C, et al 2011 Tools for Brain-Computer Interaction: A General Concept for a Hybrid BCI. Front.Neuroinform 5:30.

[46]Townsend G, LaPallo BK, et al 2010 A novel P300-based brain-computer interface stimulus presentation paradigm: moving beyond rows and columns. Clin.Neurophysiol. 121(7):1109-1120.

[47]Martens SMM, Hill NJ, et al 2009 Overlap and refractory effects in a brain-computer interface speller based on the visual p300 event-related potential. 6(3).

[48]Chun MM 1997 Types and tokens in visual processing: a double dissociation between the attentional blink and repetition blindness. J.Exp.Psychol.Hum.Percept.Perform. 23(3):738-755.

[49]Raymond JE, Shapiro KL, et al 1992 Temporary suppression of visual processing in an RSVP task: an attentional blink? J.Exp.Psychol.Hum.Percept.Perform. 18(3):849-860.

[50]Kanwisher N, Potter MC 1989 Repetition blindness: the effects of stimulus modality and spatial displacement. Mem.Cognit. 17(2):117-124.

[51]Townsend G, Graimann B, et al 2004 Continuous EEG classification during motor imagery--simulation of an asynchronous BCI. IEEE Trans.Neural Syst.Rehabil.Eng. 12(2):258-265.

[52]Guger C, Daban S, et al 2009 How many people are able to control a P300-based brain-computer interface (BCI)? Neurosci.Lett. 462(1):94-98.

[53]Yin E, Zhou Z, et al 2014 A dynamically optimized SSVEP brain-computer interface (BCI) speller. IEEE Trans.Biomed.Eng.

[54]Guger C, Allison BZ, et al 2012 How Many People Could Use an SSVEP BCI? Front.Neurosci. 6:169.

[55]Spuler M, Rosenstiel W, et al 2012 Online adaptation of a c-VEP Brain-computer Interface(BCI) based on error-related potentials and unsupervised learning. PLoS One 7(12):e51077.

[56]Bin G, Gao X, et al 2011 A high-speed BCI based on code modulation VEP. J.Neural Eng. 8(2):025015-2560/8/2/025015. Epub 2011 Mar 24.

[57]Allison BZ, Pineda JA 2006 Effects of SOA and flash pattern manipulations on ERPs, performance, and preference: implications for a BCI system. Int.J.Psychophysiol. 59(2):127-140.

[58]Orhan U, Erdogmus D, et al 2012 Improved accuracy using recursive bayesian estimation based language model fusion in ERP-based BCI typing systems. Conf.Proc.IEEE Eng.Med.Biol.Soc. 2012:2497-2500.

Chapter Four: Intelligence and functional connectivity in people with Cerebral Palsy

Abstract

Human cognitive assessment methodologies currently require a motor or speech input, which may prevent clinicians from obtaining accurate measurements of the cognitive capacity of subjects absent motor and speech. One potential method of mitigating this issue is to use electroencephalography (EEG) biomarkers to estimate cognitive capacity. In this study, we examine the relationship between oscillatory frequency power spectra, coherence, and phase lag between frontal and parietal cortices as they relate to intelligence in people with cerebral palsy (CP) who took a Peabody Picture Vocabulary Test (PPVT)-IV. Here, we observe frontal lobe biomarkers in EEG theta and delta oscillatory bands of children with CP that are traditionally associated with lower intelligence, compared to typically developing children. However, importantly, children with CP performed equally well in the PPVT-IV, which has been used as a proxy for intelligence. Therefore, EEG theta and delta power band spectra may not be a suitable biomarker for determining intelligence in subjects with CP. We suggest this may relate to neural compensation mechanisms in CP subjects, and propose alpha band power and theta phase lag as possible candidates for EEG biomarkers of cognitive capacity in CP subjects.

Keywords: Functional Connectivity, PPVT, Intelligence, Cerebral Palsy

Introduction

Standardized cognitive assessment tests provide a valid, meaningful measure of cognitive functioning for use in treatment planning, acute evaluation after injury, medication monitoring, academic curriculum, and accommodation planning. However, these standardized cognitive tests and the evidence-based practice that they support are inaccessible to individuals who cannot provide reliable verbal or motor responses, such as individuals with severe cerebral palsy (CP) [1-4]. The lack of accessible cognitive testing can result in under-estimation of cognitive abilities due to the common but mistaken assumption that one's quality of movement and speech correlates to the quality of the mind [1,4]. Despite modifications to existing systems [1], most cognitive tests still require some degree of motor or speech input. Some studies have used brain-computer interfaces (BCI) which allow a subject to control a device using their brain activity to answer assessment questions [5-7]. Unfortunately, most BCI methods alter the tests in ways that create psychometric concerns [1,8,9]. An alternative approach in estimating cognitive ability is to use non-invasive neuroimaging techniques while correlating intelligence to various biomarkers. This is typically done with electroencephalography (EEG), magnetoencephalography (MEG) or functional magnetic resonance imaging (fMRI). One of the earliest approaches was to look at power spectral analysis of EEG [10,11].

There are two methods for investigating intelligence with power spectral analysis. The first method was used by Doppelmayr [10], who recorded EEG signals in 74 participants, who sat with their eyes closed for 3 minutes. Afterwards, participants took two different intelligence assessments, the Intelligenze-Struktur-Test (IST-70) and the Lern-und Gedachtnistets (LGT3). Both the IST-70 and the LGT-3 are multi-dimensional intelligence tests, however the IST-70 is more focused on semantic memory demands, while the LGT-3 focuses on the ability to learn new material. Doppelmayr found that lower alpha band power (8-10Hz) was positively correlated with IQ in the LGT-3 test, while the upper alpha band power (10-13Hz) correlated with IQ in the IST-70. Similar results regarding alpha band power and intelligence have also been reported by numerous other studies [10,12-14].

The second method which leads to an opposite relationship between alpha band power and intelligence, has been used by Neubauer as well as other researchers [11,15-17]. Neubauer [17] tested 47 tournament chess players of varying intelligence on mental speed, memory and reasoning tests, while recording their brain activity with EEG. Subjects with higher intelligence demonstrated decreased upper alpha band (10-13Hz) power than subjects with lower intelligence. This study suggests that more intelligent players exhibited decreased upper alpha band (10-13Hz) power because they required less mental resources to process the tasks presented to them.

In regards to alpha responses, the different relationships shown by each method is due to the testing methodology. In Doppelmayr's [10] study, EEG was recorded while subjects had their eyes closed. Therefore, alpha waves that were recorded were resting state alpha waves, also called tonic alpha waves. The subjects in the Neubauer [17] study, on the other hand, were actively performing a task while the EEG was being recorded, creating so-called phasic alpha waves [10]. Studies have demonstrated that intelligence is positively correlated to tonic alpha waves [10,12-14] and negatively correlated to phasic alpha waves [10]. Thus, it is important to consider whether experimental methods will elicit tonic or phasic alpha band responses and interpret results accordingly. Studies in subjects with intellectual deficiencies have also generated significant insight regarding brain dynamics and intelligence. For example, Psatta's study of 15 subjects and Gasser's study of 25 subjects (among others) demonstrated that delta and theta waves are increased in people who were diagnosed with intellectual deficiencies [18-21]. In most cases, tonic and phasic power band results with respect to intelligence agree except for alpha and gamma. Gamma has been shown to be negatively correlated to intelligence in the frontal and occipital lobes but positively correlated to intelligence in the parietal lobe [19].

Signal coherence and phase delay are two other biomarkers that have been correlated to intelligence in previous studies [19]. Coherence is the term for the statistical difference between two signals with respect to signal phase shift. Therefore, this comparison may estimate the connectedness between two regions in the brain, such that higher values imply more connectedness. In contrast, phase delay strictly measures the difference in time between two simultaneously recorded signal responses [19].

Seminal work from Gasser [19] first explored EEG coherence as an assessment of intelligence. The authors compared the coherency of 158 TD subjects with 47 subjects who had a low IQ. Coherence estimates were taken from the frontal and occipital electrodes, as well as the electrodes linking the frontal to occipital region. Gasser found that children with cognitive impairments had higher coherence in the theta band in the frontal to occipital lobes. Separately, a comparison of coherence between high IQ and low IQ participants revealed a positive correlation of IQ with short interhemispheric (localized connections e.g. frontal lobe) EEG phase delays, long intrahemispheric (global connections e.g. frontal to occipital lobe) phase delays and reduced coherence across all frequency bands. Furthermore, delta, alpha, beta (frontal and parietal; occipital is positively correlated) and theta bands were negatively correlated with IQ intelligence.

Altogether, we find the several distinct relationships between EEG biomarkers and intelligence [10,13,14,18-22] (Figure 14):

- Delta power in the frontal cortex is negatively correlated to IQ.
- Theta power in the frontal, central, parietal and occipital lobes are negatively correlated to IQ.
- Tonic alpha power in the frontal and occipital lobe is positively correlated to IQ.
- Phasic alpha power in the frontal and occipital lobe is positively correlated to IQ.
- Beta power in the frontal and parietal lobe is negatively correlated to IQ.
- Beta power in the occipital lobe is positively correlated to IQ.
- Tonic gamma power is negatively correlated to IQ.
- Phasic gamma is negatively correlated to IQ in the frontal and occipital lobes
- Phasic gamma is positively correlated to IQ in the parietal lobes.
- Coherence across all bands is negatively correlated to IQ.
- Short interhemispheric phase delays and long intrahemispheric phase delays are correlated to IQ

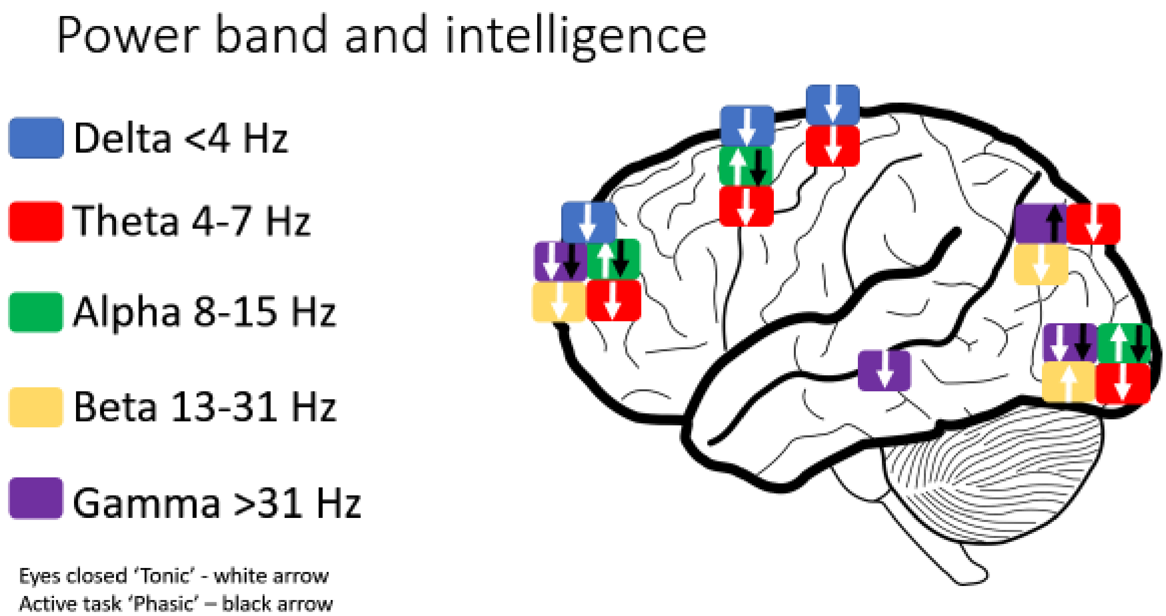

Figure 14. Summary of power band and intelligence

These results are all in accordance with the neural efficiency theory that suggests that lower brain activation is needed to process the same information in high IQ individuals compared to lower IQ individuals [19]. Low coherence, short interhemispheric phase delays and longer intrahemispheric delays suggest that brain processes are happening more locally than globally [14,19]. This is consistent with current functional connectivity EEG studies that suggest that higher IQ individuals use small, locally isolated and highly clustered brain regions to process information, while low IQ individuals require additional recruitment across the brain. Similar results have also been found in CP subject populations [23,24]. For example, Sobaniec [25] found that subjects with spastic displegia cerebral palsy exhibit longer interhemispheric phase delays and increased coherence in the theta and delta bands. Subjects also exhibited an increased alpha power band in the temporal, parietal and occipital lobes. [26] yielded similar results from 26 children with hemiparetic cerebral palsy, as did Takeshita [27] when studying 12 subjects with preterm diplegia.

Per previous literature all CP subjects should have lowered intelligence [24]. However, only fifty percent of subjects with CP exhibit intellectual disability [1]. This suggests that results related to functional connectivity and intelligence may not apply equally to all populations. We believe that this is due to a neural compensation, which may relate to subjects' pathologies [24]. If so, the brain of a CP subject may demonstrate biomarkers of decreased intelligence due to brain network reorganization, but these markers may not adequately reflect a person's IQ. Currently it is unknown whether EEG biomarkers are directly correlated with intelligence in subjects with CP.

Therefore, understanding the relationship between EEG biomarkers and intelligence in CP could allow researchers and clinicians to assess cognitive capacity in CP.

Here, we investigated the relationship between EEG power band, coherence and phase delay in CP subjects who used a brain-computer interface adapted to the Peabody Picture Vocabulary Test (PPVT)-IV.

Methods

We recruited participants ages 8 and older who could complete both a standard Peabody Picture Vocabulary Test (PPVT-IV) and a BCI-facilitated PPVT-IV. In total, 11 participants without impairments and 19 subjects with CP were recruited (ages 16.03 ± 5.71;17 male and 12 female). Out of the 30 participants overall, 8 CP subjects were excluded from the study. The PPVT-IV is a commonly used cognitive assessment for determining receptive vocabulary and can be used as a proxy for intelligence. We chose the PPVT-IV because it has a strong test-retest reliability, ranging from .91 to .94 across two different versions (Form A and Form B) [28].

The participants who did not complete the BCI-facilitated PPVT-IV had a mean age of 10.6 ± 2.9 years old. One subject was screened ineligible due to the inability to take the standard PPVT-IV. Two subjects did not complete the BCI-facilitated test because we could not establish reliable training weights. Offline, we looked at the subjects' training data sets and found that one subject's data was inconsistent, and due to an error, a different subject's data was missing the hold-release thresholds.

The remaining five subjects had trouble maintaining their attention and interest after the one-hour setup and calibration process. For example, some children would only look at the BCI for a few seconds and then look away or talk to their parent. We asked subjects how they were feeling, and if they wanted to stop or rest before resuming. All subjects who struggled with attention and interest verbally indicated they were bored, tired or wanted to stop the test.

Subjects were recruited from the University of Michigan Health System and surrounding areas. The University of Michigan Institutional Review Board approved recruitment and data collection protocols. Participants and their parents signed informed consent forms and filled out demographic surveys.

The study consisted of subjects taking the standard PPVT-IV and a BCI-facilitated PPVT-IV. Both tests were performed, to compare exam score variability between the standard and BCI-facilitated PPVT-IV. Subjects were seated in front of a computer monitor and set up with a 32-electrode electroencephalography cap, channels F3, F4, FC3, FCZ, FC4, T7, C3, CZ, FZ, FC5, FC1, FC2, FC6, C5, C1, C2, C4, T8, CP3, CPZ, CP4, P3, P4, PO8, C6, CP5, CP1, CP2, CP6, PZ, PO7, and OZ.

The BCI was set up as a hybrid BCI that combined Steady State Visually Evoked Potentials (SSVEP) and Event Related Potentials (ERP) [9,29]. During our study, we only used the ERP to classify user intent due to poor SSVEP performance. ERP classification was handled using the three-stage classifier outlined in Chapter 3 [9,29,30]. This allowed subjects to take as much time as needed to respond to each PPVT-IV question and allowed subjects to confirm their selections without needing secondary prompts.

The standard PPVT-IV was administered using the standard protocol [9,28,29]. The BCI-facilitated PPVT-IV differed by using a pair of laptop speakers to play each question's respective word and by displaying each question on a computer monitor [9,29]. To respond, the subject focused his/her attention on the number that corresponded with the image he/she wanted to select. The BCI would then move through the test after a response was registered. To help keep the subjects focused, we instructed them to say, in their head, the number they wanted to select each time it flashed.

Analysis

After the subject completed both tests, we compared the scores of the standard PPVT-IV by taking the mean and standard deviation of the difference in the PPVT-IV scores for the two administration methods (standard and BCI-facilitated). Furthermore, a Pearson correlation was taken between the scores of the standard and BCI-facilitated test.

We then examined subjects' data (total across-subjects length of 12 minutes) gathered during the calibration process described in Chapter 3. Like Langer [31], we used 40 seconds of EEG data, sampled five times. These five sample locations were randomly taken from each subject's EEG data and manually inspected for eye and muscle artifacts. If artifacts were found in the sample, then a new random sample was taken and manually inspected. This was repeated until five clean, 40-second EEG samples were collected for each subject's respective data with no overlapping data. For each subject, we concatenated their data to create 200-second chunks of data. Like Langer, no changes were done for the edge conditions since they represent an insignificant amount of the over-all data. These chunks of data were analyzed for differences in power in the delta (1-4Hz), theta (4-7Hz), lower alpha (8-10Hz), upper alpha (10-13Hz), beta 1(13-18Hz) and beta 2(18-25Hz) bands.

Coherence and phase delays were also analyzed, using the same 200-second chunks of data, broken up into the same 8 frequency bands. Afterwards, the results for the CP and TD groups were averaged separately. We separately analyzed the coherence and phase lag (interhemispheric) of the frontal lobe electrodes (F3, F4, Fz, FC3, FCz, FC4, FC5, FC1, FC2 and FC6,) and the posterior electrodes (P3, P4, PO8 PZ, PO7 and OZ). We then analyzed the coherence and phase lag (intrahemispheric) between the frontal and posterior electrodes. An ANOVA was performed on the power band, coherence, and phase lag measures, with respect to both the standard PPVT-IV scores and BCI-facilitated PPVT-IV.

Results

We found no significant differences when analyzing global (frontal to posterior) or posterior power band between subjects with CP and TD. However, when considering power from only the frontal lobe electrodes, there was a significant difference between CP and TD in the theta power bands (mean and standard deviation: TD 490 $\pm$ 410 vs. CP 1100 $\pm$ 730, $p<0.01$) and delta power bands (mean and standard deviation: TD 1900 $\pm$ 1000 vs. CP 3500 $\pm$ 230 $p<0.0001$).

There were no significant differences between TD and CP subject’s coherence and interhemispheric phase delay when analyzing the frontal and posterior electrodes. However, there was a significant difference in the global (frontal to posterior) electrodes, with CP subjects having higher coherency but not larger intrahemispheric phase delays.

Discussion

The purpose of this study was to investigate the feasibility of using EEG biomarkers as a method to assess intelligence in people with motor impairments, such as CP, for whom it is difficult or impossible to perform standardized intelligence tests. Numerous studies have investigated functional connectivity and power band analyses with respect to intelligence in typically-developing subjects, and in subjects diagnosed with intellectual impairments. Other studies have focused on understanding the power band differences in subjects with CP compared to TD subjects. However, none have explored how these EEG biomarkers relate to intelligence in subjects with motor impairments such as CP. In CP in particular this is critical, because biomarkers of intelligence suggest that subjects with CP have lower intelligence even though close to half of the subjects with CP are reported to have no intelligence impairments [1]. In our study, we compared EEG biomarkers of intelligence with PPVT-IV scores recorded using the standard PPVT and a BCI-facilitated PPVT-IV.

Power band analysis provided the most prominent biomarker in our study. Compared to TD subjects, frontal lobe power in subjects with CP was greater by nearly five times, thus suggesting that CP subjects should have lower PPVT-IV scores than TD subjects. The second metric, frontal lobe delta wave power, was also significantly higher in people with CP compared to TD. This result also suggests that CP subjects should on average exhibit lower measures of IQ as compared to TD subjects, as implied by findings from previous studies such as Gasser's [18-20]. The significant increase in theta and delta in the frontal lobe in people with CP compared to TD suggests that subjects with CP require more cognitive resources to take the PPVT-IV. This result has major implications for the current prevailing theories of power band analysis and intelligence, since it suggests that current metrics may not apply to subjects with CP. Therefore, these EEG biomarkers are not recommended for assessing the intelligence capacity of someone with severe CP who cannot take a standard cognitive exam as those methods of measurement may not be appropriate.

This theory is supported by fMRI studies that have been conducted in subjects with CP. For example, in Burton's [24] study on 11 subjects with CP and 11 typically developing subjects, he found that subjects with CP had expanded networks with larger clustering. Taken together, our results indicate that the reorganization of the brain that occurs in subjects with CP significantly alters the brain dynamics, thus altering how EEG biomarkers of intelligence should be interpreted.

Interestingly, we did not find any difference between CP subjects and healthy participants when analyzing the global power band. Previous studies rarely find significant difference in all power bands. That could explain why there was no significant difference between beta and gamma power band analysis. However, global alpha band difference between high IQ vs low IQ individuals is usually a consistent metric that usually shows significant results across studies. Since there wasn't a significant difference between age and PPVT-IV score, we would expect the CP and TD subjects to fail to display significant differences in alpha band pass power difference. Indeed, it was shown in our results that some biomarkers (in our case alpha band pass) may still be a suitable biomarker for assessing cognitive capacity in people with CP. Future studies should investigate how low/high IQ CP subjects compare to low/high IQ TD subjects.

We found no significant differences between coherence and interhemispheric phase delay when analyzing the frontal and posterior electrodes. However, we saw a significant difference in the global (frontal to posterior) electrodes, with CP subjects having higher coherency but not larger phase delays. The higher coherence suggests that a CP subject recruits more brain areas to process the same task as a TD subject, suggesting that they would possess lower intelligence [14]. Thus, on the PPVT-IV, we would predict the CP subjects would have lower scores then TD subjects, however, this is not the case.

Coherence is a statistical measure of phase consistency between two signals. Previously, coherence has been described as an indicator of shared information processing. Thus, decreased coherence may indicate increased spatial differentiation as well as increased complexity, leading to increased speed and efficiency of information processing [10,13,14,18-22]. Phase delay is the lead or lag between two time series signals, and is also amplitude independent. This measure has not been heavily explored in the literature but it is speculated that phase delay is associated to signal transduction or processing speed [14]. Therefore, greater phase delay between frontal and posterior brain regions may correspond to slower processing and thus lower intelligence. Here, we observed that CP subjects with similar intelligence to TD subjects exhibited higher EEG coherence, but similar phase delay, between frontal and posterior regions. Based on this, we suggest that coherence may reveal cortical organization, which may or may not directly correlate with intelligence. CP subjects have brain reorganization due to their pathology, and this is reflected as a higher coherence, but overall, they can function cognitively equal to TD as shown by the lack of phase delay and equal PPVT-IV score. This suggests that phase delay may be a strong correlate to intelligence but not coherence.

The results of this study suggest that different strategies must be employed to accurately use EEG biomarkers as tools for assessing intelligence. Using EEG biomarkers found to correlate with intelligence in TD may not be the best approach in subjects with CP as they may falsely indicate lowered intelligence inconsistent with their actual cognitive capacity. There are however two biomarkers that may still be good candidates for assessing cognitive capacity: frontal to posterior alpha power band, and phase delay. Further research is required to understand how intelligence changes with respect to IQ, and to examine whether these biomarkers are also suitable for assessing cognitive capacity in other disease states.

Limitations

The primary limitations of this study are related to sample size and the task the subject had to perform. Our small subject number was a possible reason why some biomarker measures did not reach statistical significance. For example, Thatcher used a total of 442 subjects [14]. To our knowledge, Thatcher is only group that has studied neural correlates of phase delay and intelligence. Therefore, it is not well established what the subject size norms should be.

A limitation is that our study used EEG data of subjects while they performed a BCI-facilitated test. While previous connectivity studies have been done while people perform tests, most connectivity results are obtained by recording a subject’s EEG after the test with their eyes closed. Additionally, in a BCI, the subject uses their brain activity for control and that control input could affect our connectivity results.

Conclusion

Standardized cognitive tests are inaccessible to individuals without a reliable verbal or motor response. The lack of accessible cognitive testing can result in under-estimation of cognitive abilities. An alternative approach to estimating cognitive capacity is to use non-invasive neuroimaging techniques while correlating intelligence to power band analysis or functional connectivity. In this study, we investigated how accurately power band analysis and functional connectivity measure intelligence in people with CP. Our results suggest that previous findings relating functional connectivity and power band analysis to intelligence do not directly apply to subjects with CP. Subjects with CP demonstrated features that correlate with lower intelligence than TD subjects. However, they scored similarly to TD subjects on a PPVT-IV, which we used as a proxy for intelligence. We believe this is due to the neural compensation resulting from the subject's pathology.

References

[1]Yin Foo R, Guppy M, et al 2013 Intelligence assessments for children with cerebral palsy: a systematic review. Dev.Med.Child Neurol. 55(10):911-918.

[2]Bagnato S, Neisworth J 1994 A national study of the social and treatment "invalidity" of intelligence testing for early intervention. School Psychology Quarterly, Sch Psych Quart 9(2):81.

[3]Hill-Briggs F, Dial JG, et al 2007 Neuropsychological assessment of persons with physical disability, visual impairment or blindness, and hearing impairment or deafness. Arch.Clin.Neuropsychol. 22(3):389-404.

[4]Losch H, Dammann O 2004 Impact of motor skills on cognitive test results in very-low-birthweight children. J.Child Neurol. 19(5):318-322.

[5]Byrne JM, Dywan CA, et al 1995 An innovative method to assess the receptive vocabulary of children with cerebral palsy using event-related brain potentials. J.Clin.Exp.Neuropsychol. 17(1):9-19.

[6]Iversen IH, Ghanayim N, et al 2008 A brain-computer interface tool to assess cognitive functions in completely paralyzed patients with amyotrophic lateral sclerosis. Clin.Neurophysiol. 119(10):2214-2223.

[7]Byrne JM, Connolly JF, et al 1999 Brain activity and language assessment using event-related potentials: development of a clinical protocol. Dev.Med.Child Neurol. 41(11):740-747.

[8]Connolly JF, D'Arcy RC, et al 2000 The application of cognitive event-related brain potentials (ERPs) in language-impaired individuals: review and case studies. Int.J.Psychophysiol. 38(1):55-70.

[9]Huggins JE, Alcaide RE 2013 Brain-Computer Interfaces to Assess the Cognitive Capabilities of Locked-In Children.

[10]Doppelmayr M, Klimesch W, et al 2002 EEG alpha power and intelligence. Intelligence 30(3):289-302.

[11]Neubauer AC, Fink A 2009 Intelligence and neural efficiency: Measures of brain activation versus measures of functional connectivity in the brain. Intelligence 37(2):223-229.

[12]Klimesch W 1999 EEG alpha and theta oscillations reflect cognitive and memory performance: a review and analysis. Brain Res.Brain Res.Rev. 29(2-3):169-195.

[13]Anokhin A, Vogel F 1996 EEG alpha rythm frequency and intelligence in normal adults. Intelligence 23(1):1-14.

[14]Thatcher RW, North D, et al 2005 EEG and intelligence: relations between EEG coherence, EEG phase delay and power. Clin.Neurophysiol. 116(9):2129-2141.

[15]Klimesch W, Doppelmayr M, et al 1998 Induced alpha band power changes in the human EEG and attention. Neurosci.Lett. 244(2):73-76.

[16]Klimesch W, Doppelmayr M, et al 2006 Upper alpha ERD and absolute power: their meaning for memory performance. Prog.Brain Res. 159:151-165.

[17]Neubauer AC, Grabner RH, et al 2004 Intelligence and individual differences in becoming neurally efficient. Acta Psychol.(Amst) 116(1):55-74.

[18]Gasser T, Von Lucadou-Muller I, et al 1983 Correlating EEG and IQ: a new look at an old problem using computerized EEG parameters. Electroencephalogr.Clin.Neurophysiol. 55(5):493-504.

[19]Gasser T, Rousson V, et al 2003 EEG power and coherence in children with educational problems. J.Clin.Neurophysiol. 20(4):273-282.

[20]Gasser T, Mocks J, et al 1983 Topographic factor analysis of the EEG with applications to development and to mental retardation. Electroencephalogr.Clin.Neurophysiol. 55(4):445-463.

[21]Martin-Loeches M, Munoz-Ruata J, et al 2001 Electrophysiology and intelligence: the electrophysiology of intellectual functions in intellectual disability. J.Intellect.Disabil.Res. 45(Pt 1):63-75.

[22]Psatta DM, Goldstein R, et al 1991 EEG mapping in mentally retarded children by synthetic arginine vasotocin administration. Rom.J.Neurol.Psychiatry 29(1-2):9-16.

[23]Klingner CM, Volk GF, et al 2014 The effects of deefferentation without deafferentation on functional connectivity in patients with facial palsy. Neuroimage Clin. 6:26-31.

[24]Burton H, Dixit S, et al 2009 Functional connectivity for somatosensory and motor cortex in spastic diplegia. Somatosens.Mot.Res. 26(4):90-104.

[25]Kulak W, Sobaniec W 2003 Spectral analysis and EEG coherence in children with cerebral palsy: spastic diplegia. Przegl.Lek. 60 Suppl 1:23-27.

[26]Kulak W, Sobaniec W, et al 2005 EEG spectral analysis and coherence in children with hemiparetic cerebral palsy. Med.Sci.Monit. 11(9):CR449-55.

[27]Koeda T, Takeshita K 1998 Electroencephalographic coherence abnormalities in preterm diplegia. Pediatr.Neurol. 18(1):51-56.

[28]Dunn LM, Dunn DM 2007 Peabody Picture Vocabulary Test – Fourth Edition.

[29]Alcaide R, Warchausky S, et al Asynchronous brain-computer interface for cognitive assessment in people with cerebral palsy. In review J of Neuro Eng.

[30]Alcaide R, Huggins J 2013 Evaluating hold-release functionality in a P300 BCI. BCI Meeting; 1(1).

[31]Langer N, Pedroni A, et al 2012 Functional brain network efficiency predicts intelligence. Hum.Brain Mapp. 33(6):1393-1406.

Chapter Five: Closing Discussion

Standardized cognitive assessments are typically administered with verbal queries, pictures and manipulatives that require verbal or motor responses. This prevents them from being used by people with physical and/or communicative impairments [1,2]. By using assessments that require verbal or motor responses, those with physical and/or communication impairments are dismissed as untestable [1,2], thus leaving them vulnerable to not receiving the aid they need. To circumvent these issues, researchers have used assistive technologies such as touch pads, switches, and eye trackers. However, these tools still require some form of speech or motor input [3,4]. The goal of this dissertation was to investigate alternative approaches that do not require any motor or speech input to assess the cognitive capacity of an individual. The first approach involved using a BCI [5-8] that was adapted to facilitate the administration of a PPVT-IV [5,6]. The second approach used EEG biomarkers such as power band, coherence and phase delay analyses [9-14].

Our results demonstrate that our BCI-facilitated PPVT-IV performs equally to the standard PPVT-IV in subjects with mild cerebral palsy (CP), suggesting that it is potentially useful in populations for whom standardized testing may be inaccessible. We have also outlined five criteria for the development of future BCI-facilitated cognitive assessments. The criteria are as follows:

1) A cognitive assessment BCI should maintain the psychometric properties of a test.
2) Brain-based cognitive assessment systems must automatically abstract the complexity of brain activity analyses to provide results that are not difficult for the clinician to interpret.
3) Brain-based cognitive assessment systems must be quick to set up (less than one hour).
4) Brain-based cognitive assessment systems must have asynchronous control.
5) The BCI must be able to function in the population it is targeting.

When evaluating our BCI-faciliated cognitive assessment system, we were able to meet all but one of the criteria we had outlined. Specifically, our fifth criterion was only partially met because we only tested mildy impaired CP subjects [5,6]. In light of that caveat, future studies will need to test our BCI-facilicated PPVT-IV in populations who have severe impairments, before our system can be considered clinically valuable.

In order to meet these criteria, we had to develop a method for confirming a subject's selection. Confirmation steps usually require a subject to respond to a secondary prompt or make additional choices to confirm a response [7,8]. These additional steps break concentration while taking a cognitive assessment and may become frustrating to a subject. Therefore, we developed the hold-release methodology that allows for a more natural confirmation step (chapter 3) [15].

The concept of the hold-release system was inspired by assistive technology functionality in which the initial activation and the deactivation (hold-release) are separately controlled. Specifically, we applied these methodologies to a P300 BCI system. Hold-release enabled us to improve response times in binary selection (6-16 times faster) tasks compared to traditional P300 BCIs. This was made possible by allowing the BCI to make classifications after a single P300 event rather than after multiple sequences of P300 events. This change resulted in a faster and more continuous P300 BCI control, thus opening possibilities for new P300 based applications [15].

The NASA-TLX results showed that our BCI-facilitated PPVT-IV was perceived as having a higher physical demand than the standard PPVT-IV. The BCI-facilitated test does not require movement. Therefore, we believe this increase in physical demand was due to fatigue from sitting during the set-up and calibration period. Interestingly we also had 5 subjects who did not complete the BCI-facilitated PPVT-IV because they could not maintain the concentration to complete the BCI configuration step. Their fatigue compared to our other CP subjects may suggest that the subjects who were unable to finish had possible attentional impairments. This suggests that our BCI may be successful in subjects with sever motoric/verbal impairments as long as their attentional capacity is not compromised. This also suggests that revisions will be needed to our current system to function in children who may have cognitive impairments. Three major areas for improvement include: 1) BCI calibration time, 2) BCI headset setup and 3) BCI presentation method. BCI calibration method could be successfully removed if new riemannian geometry classification methods are used [16]. This method leverages previously collected data and creates a minimum distance to mean classification framework that can be used to allow a subject to use a BCI without training.

In our study, it took about thirty minutes to setup a subject with a headset and this also lead to attentional issues in subjects. New dry electrode technology developed by companies such as Wearable Sensing have the potential of removing this barrier and reducing setup time to less than 10 minutes [17]. Thus, reducing the amount of time a subject must wait to start the using the BCI.

Lastly, we could alter the presentation method to display more interesting selectable items. Instead of numbers in the selection boxes, we could use images or flash the selection using different colors [18-21]. These changes have been explored in previous research. For example, Cochocki [22] did a comprehensive study on 6 males using a P300 BCI that flashed faces with varying emotional states to a user. While there was not a significant performance increase based on the emotional state that was shown to the user, using faces was significantly faster than using the standard P300 BCI flashing. Faces seem to trigger larger areas of the brain and provide stronger P300 response, thereby increasing the ability to accurately classify a P300 response. Other BCI changes could be done strictly to increase subject attention or to create discernibility to increase P300 results. For example, Sellers found that accuracy increased in 7 subjects when they used a P300 BCI that displayed different colors and stimulation methods compared to the traditional row-column white and black presentation method [23].

CP subjects reported significantly lower perceived performance for both the standard and BCI-facilitated PPVT-IV. Since both CP and TD subjects scored similarly this suggests that CP subjects had lower confidence than the TD subjects. This is particularly troubling because self-confidence affects how a person handles failure and goal making, which attributes to long-term success. While the focus of this research was not to explore user confidence, our results may nevertheless provide an interesting insight regarding how pathology affects self-perception [24].

In addition to using a BCI, we are also assessed cognitive capacity through the use of EEG biomarkers such as power band, coherence and phase delay analyses [9-14]. Summarizing previous studies (Chapter 1 and 4), led to the following conclusions [10-12,25-29]:

- Delta power in the frontal cortex is negatively correlated to IQ
- Theta power in the frontal, central, parietal and occipital lobes are negatively correlated to IQ
- Tonic alpha power in the frontal and occipital lobe is positively correlated to IQ
- Phasic alpha power in the frontal and occipital lobe is positively correlated to IQ
- Beta power in the frontal and parietal lobe is negatively correlated to IQ
- Beta power in the occipital lobe is positively correlated to IQ
- Tonic gamma power is negatively correlated to IQ
- Phasic gamma is negatively correlated to IQ in the frontal and occipital lobes
- Phasic gamma is positively correlated to IQ in the parietal lobes
- Coherence across all bands is negatively correlated to IQ
- Short interhemispheric phase delays and long intrahemispheric phase delays are correlated to IQ

In our studies, we expect to see similar correlations to occur based on a subject's IQ. However, in previous studies and in our own subjects, people with CP exhibit biomarkers associated with lower intelligence, suggesting that they would have lower intelligence [30-33]. However, in our study, both CP and typically developing (TD) subjects scored similarly on a PPVT-IV, which is a proxy for intelligence [5,6]. This suggests that the current perception of the relationships between EEG biomarkers and intelligence may not fully apply to subjects with CP. Burton suggest that this is due to the reorganization that occurs after a brain lesion [33]. Based on their we postulate that the brain of person with CP may demonstrate biomarkers of decreased intelligence due to brain network reorganization, but that those markers may not adequately reflect a person's IQ. Based on our results we do postulate that two biomarkers may be potential candidates in CP for assessing intelligence, alpha and phase delay. In our case CP subjects had similar intelligence to TD subjects, higher coherence but, similar phase delay. Coherence is an amplitude independent statistical measure of phase consistency between two signals. Based on previous studies coherence is an indication of shared information processing [10-12,25-29]. Thus, decreased coherence means increased spatial differentiation as well as increased complexity leading to increased speed and efficiency of information processing. Phase delay is the lead or lag delay between two time series and is also amplitude independent. It is speculated that phase delay is associated to processing speed, where greater phase delay corresponds to slower processing and thus lower intelligence [12]. Taken together our results suggest that coherence may not be strictly an intelligence measure in CP, instead it may represent reorganization. Phase delay on the other hand may be correlated to intelligence since there was no significant change between TD and CP which was reflected in PPVT-IV results. Further investigation on how intelligence in CP affects phase delay and other EEG markers is needed before they can be used for cognitive assessment.

Taking this dissertation and the reviewed literature we currently recommend using a BCI to assess cognitive measures in an individual with severe motoric impairments. By using a BCI, a user can respond to standardized cognitive assessments that already have well-established norms. However, it is important to ensure that when designing these systems, the changes made to adapt the cognitive assessment for the BCI do not alter the format or psychometrics of the test.

In summary, my dissertation

1) Provides a possible solution for assessing cognitive capability (BCI-facilitated PPVT-IV) in people who may not be able to take a traditional standardized cognitive assessment.

2) Provides guidelines for the development of future cognitive assessment brain-based systems.

3) Introduces the published hold-release functionality that allows for new BCI applications.

4) Demonstrates one of the many possible uses of the hold-release algorithm and exemplifies how this new technique can create a more natural confirmation step.

5) Summarizes the findings relating intelligence to EEG biomarkers for typically developing subjects.

6) Provides the first evaluation that studies how EEG biomarkers relate to intelligence in people with cerebral palsy.

7) Highlights the potential pitfalls of using EEG biomarkers for measuring cognitive capacity in people with cerebral palsy.

References

[1]Sabbadini M, Bonanni R, et al 2001 Neuropsychological assessment of patients with severe neuromotor and verbal disabilities. J.Intellect.Disabil.Res. 45(Pt 2):169-179.

[2]Warschausky S, Van Tubbergen M, et al 2012 Modified Test Administration Using Assistive Technology : Preliminary Psychometric Findings. Assessment 19:472-490.

[3]Wagner BT, Jackson HM 2006 Developmental memory capacity resources of typical children retrieving picture communication symbols using direct selection and visual linear scanning with fixed communication displays. J.Speech Lang.Hear.Res. 49(1):113-126.

[4]Meyers AR, Andresen EM 2000 Enabling our instruments: accommodation, universal design, and access to participation in research. Arch.Phys.Med.Rehabil. 81(12 Suppl 2):S5-9.

[5]Huggins JE, Alcaide RE 2013 Brain-Computer Interfaces to Assess the Cognitive Capabilities of Locked-In Children.

[6]Alcaide R, Warchausky S, et al Asynchronous brain-computer interface for cognitive assessment in people with cerebral palsy. In review J of Neuro Eng.

[7]Perego P, Turconi AC, et al 2011 Cognitive ability assessment by Brain-Computer Interface validation of a new assessment method for cognitive abilities. J.Neurosci.Methods 201(1):239-250.

[8]Iversen IH, Ghanayim N, et al 2008 A brain-computer interface tool to assess cognitive functions in completely paralyzed patients with amyotrophic lateral sclerosis. Clin.Neurophysiol. 119(10):2214-2223.

[9]Klimesch W 1999 EEG alpha and theta oscillations reflect cognitive and memory performance: a review and analysis. Brain Res.Brain Res.Rev. 29(2-3):169-195.

[10]Doppelmayr M, Klimesch W, et al 2002 EEG alpha power and intelligence. Intelligence 30(3):289-302.

[11]Anokhin A, Vogel F 1996 EEG alpha rythm frequency and intelligence in normal adults. Intelligence 23(1):1-14.

[12]Thatcher RW, North D, et al 2005 EEG and intelligence: relations between EEG coherence, EEG phase delay and power. Clin.Neurophysiol. 116(9):2129-2141.

[13]Rubinov M, Sporns O 2010 Complex network measures of brain connectivity: uses and interpretations. Neuroimage 52(3):1059-1069.

[14]Neubauer AC, Fink A 2009 Intelligence and neural efficiency: Measures of brain activation versus measures of functional connectivity in the brain. Intelligence 37(2):223-229.

[15]Alcaide RE, Huggins JE 2014 Novel hold-release functionality in a P300 Brain-Computer Interface. Journal of neural engineering 11(6):066010.

[16]Barachant A, Bonnet S, et al 2013 Classification of covariance matrices using a Riemannian-based kernel for BCI applications. Neurocomputing 112:172-178.

[17]Slater JD, Kalamangalam GP, et al 2012 Quality assessment of electroencephalography obtained from a "dry electrode" system. J.Neurosci.Methods 208(2):134-137.

[18]Riccio A, Simione L, et al 2013 Attention and P300-based BCI performance in people with amyotrophic lateral sclerosis. Front.Hum.Neurosci. 7:732.

[19]Acqualagna L, Blankertz B 2013 Gaze-independent BCI-spelling using rapid serial visual presentation (RSVP). Clin.Neurophysiol. 124(5):901-908.

[20]Nicolas-Alonso LF, Gomez-Gil J 2012 Brain computer interfaces, a review. Sensors (Basel) 12(2):1211-1279.

[21]Salvaris M, Sepulveda F 2009 Visual modifications on the P300 speller BCI paradigm. J.Neural Eng. 6(4):046011.

[22]Jin J, Allison BZ, et al 2012 The changing face of P300 BCIs: a comparison of stimulus changes in a P300 BCI involving faces, emotion, and movement. PLoS One 7(11):e49688.

[23]Ryan D, Sellers E 2011 Improving brain-computer interface performance: Giving the P300 speller some color. East Ten St U 1(1):1-56.

[24]Bjork R, Druckman D 1994 Learning, remembering believing: enhancing human performance. :173-206.

[25]Gasser T, Von Lucadou-Muller I, et al 1983 Correlating EEG and IQ: a new look at an old problem using computerized EEG parameters. Electroencephalogr.Clin.Neurophysiol. 55(5):493-504.

[26]Gasser T, Mocks J, et al 1983 Topographic factor analysis of the EEG with applications to development and to mental retardation. Electroencephalogr.Clin.Neurophysiol. 55(4):445-463.

[27]Gasser T, Rousson V, et al 2003 EEG power and coherence in children with educational problems. J.Clin.Neurophysiol. 20(4):273-282.

[28]Psatta DM, Goldstein R, et al 1991 EEG mapping in mentally retarded children by synthetic arginine vasotocin administration. Rom.J.Neurol.Psychiatry 29(1-2):9-16.

[29]Martin-Loeches M, Munoz-Ruata J, et al 2001 Electrophysiology and intelligence: the electrophysiology of intellectual functions in intellectual disability. J.Intellect.Disabil.Res. 45(Pt 1):63-75.

[30]Stam CJ 2014 Modern network science of neurological disorders. Nat.Rev.Neurosci. 15(10):683-695.

[31]Klingner CM, Volk GF, et al 2014 The effects of deefferentation without deafferentation on functional connectivity in patients with facial palsy. Neuroimage Clin. 6:26-31.

[32]Langer N, Pedroni A, et al 2012 Functional brain network efficiency predicts intelligence. Hum.Brain Mapp. 33(6):1393-1406.

[33]Burton H, Dixit S, et al 2009 Functional connectivity for somatosensory and motor cortex in spastic diplegia. Somatosens.Mot.Res. 26(4):90-104.