Agenesis of the corpus callosum (AgCC) is a congenital disorder that leads to a broad array of symptoms including cognitive, motor, and social difficulties. Parents of children with AgCC are faced with few treatment options for this often debilitating disorder. There is also a lack of research concerning how to help children and adults with AgCC achieve improved levels of functioning. This paper discusses the utility of low resolution brain electromagnetic tomography (LORETA) Z-score based neurofeedback combined with heart rate variability (HRV) training biofeedback in treating a young man with partial and congenital AgCC. The comprehensive assessment process included analysis of 19-channel quantitative-EEG (QEEG) and HRV data in combination with parent rating questionnaires, and continuous performance test measures: Integrated Visual and Auditory Continuous Performance Test (Arble, Kuentzel & Burnett, 2014) and the Test of Variables of Attention (Forbes 1998). This article illustrates amelioration of cognitive, motor, social, and sleep-based symptoms in this case, suggesting neurofeedback and biofeedback have a positive role to play in helping people with AgCC.

Introduction

This article reviews literature concerning symptoms associated with agenesis of the corpus callosum (AgCC) and the utility of low resolution brain electromagnetic tomography (LORETA) Z-score neurofeedback in combination with heart rate variability (HRV) as a treatment for this condition. AgCC is a congenital disorder that leads to a broad range of symptoms, such as delayed motor development, which may include bilateral movements including walking, bathing, brushing hair, and various activities requiring coordination. Patients with AgCC may also face difficulties in sleeping. Physically, patients with AgCC exhibit poor muscle tone, large head size, and a higher percentage of left-handedness (Moes, Schilmoeller, & Schilmoeller, 2009). Often, social deficits will be present in such cases as well. These symptoms may also be accompanied by anxiety and depressive symptoms. Due to the similarities in symptomology, these particular symptoms may sometimes be misdiagnosed as autism (Paul, Corsello, Kennedy, & Adolphs, 2014).

Researchers have investigated EEG differences in patients diagnosed with AgCC (Brázdil, Brichta, Krajča, Kuba, & Daniel, 1997). They hypothesize that, in addition to uniting the hemispheres in communication, the corpus callosum may serve to integrate and synchronize EEG activity across hemispheres. Those who have AgCC may not have synchronous EEG across hemispheres. Furthermore, Kuks, Vos, and O’Brien (1987) found that coherence levels at frequency bands below 4 Hz in individuals with congenital AgCC were significantly lower than those without. Specific cognitive dysfunction is seen in patients with AgCC, especially with respect to verbal processing. This is often the by-product of connectivity issues related to AgCC. (Hinkley et al., 2012). Quantitative EEG (QEEG) allows for the identification of amplitude, coherence, phase shift, and phase lock abnormalities (Thatcher & Lubar, 2015). LORETA Z-score neurofeedback allows clinicians to utilize neurofeedback with age-matched normative databases to create treatments that target specific neural modules and hubs that indicate dysregulation and instability across neural networks related to symptoms (Thatcher, 2013). LORETA neurofeedback is able to target specific Brodmann areas (BAs) related to functions that are impaired in AgCC including difficulty comprehending social cues, executive functioning, attention, poor skilled motor movements, balance, poor social skills, and anxiety (Thatcher, 2012).
At the ADD Centre, LORETA neurofeedback is combined with HRV training. HRV training utilizes biofeedback of heart rate and breathing rate in order to attain synchrony of the two. HRV is measured as the variation in the interbeat intervals between heartbeats (the time between consecutive R waves) measured in milliseconds in the electrocardiogram. This variability in the R-to-R interval is designated as the standard deviation of the R-to-R interval (or SDRR). After correction of artifacts, this index is designated as the standard deviation of the normalized R-to-R interval (or SDNN). The SDNN is one of the standard measures of HRV. Through training, the SDNN increases. It is maximized when the synchrony of respiration and heart rate is attained. This is usually achieved with diaphragmatic breathing at the person’s resonance frequency. The result can be improved cognitive and mental clarity (Reid-Chung, Thompson, & Thompson, 2013).

**A Single Case of Agenesis of the Corpus Callosum Seen at the ADD Centre**

Client B is a 20-year-old male who came to the ADD Centre for an assessment in 2013. He had a previous diagnosis of AgCC, which was identified as being partial and congenital. B’s mother had gestational diabetes and toxemia during pregnancy. At birth he had a low body weight and a larger head, which is common in people with AgCC, although that diagnosis was not made by his physicians. Medically, B had recurring ear infections coupled with croup. He had experienced mild hearing loss. B was nonverbal until the age of 2.

B experienced issues with bilateral coordination and his mother found his movements to be “floppy.” He had difficulties with motor function, planning, and difficulties in visual perception and orientation. At age 3, he was diagnosed as having sensori-motor integration problems and underwent treatment. This was the official diagnosis; however, autistic features were also noted by some doctors.

At age 6, he was seen by a doctor for an MRI. At this time, he presented as having a global developmental delay, hypotonia, and mild dysmorphic features. The MRI findings showed “mildly dysgenic rostrum and laminae terminalis of the corpus callosum with slight underrotation of the left hippocampus.” There was normal myelination and sulcation and ventricles were within normal limits.

B’s mother says that, as a child, B had a temper and was emotionally reactive. He required a regular routine and would otherwise experience anxiety. This anxiety was still evident at the time of assessment when he was 20.

At school, the client experienced issues with socializing. He had very few friends. As well, he had severe academic delays. He was unable to complete any elementary or high school regular courses and instead undertook intense remedial education to address learning disabilities at the Arrowsmith School, a special facility that has a combination of computer, fine motor, and visual exercises to address specific learning problems. Furthermore, he had issues with motor coordination to the degree that tasks like drawing a straight line or walking in a straight line were difficult. Writing was also difficult and his written vocabulary was lower than age norms. In addition, his mathematical skills were considered to be much below age expectations. His mother also commented at the assessment that he had instances of emotional outbursts. During the intake interview his mother described many treatments that were tried in the past. His mother had hoped that neurofeedback might be able to offer improvements in some symptoms.

**Assessment**

The initial assessment for B included a clinical interview with B and B’s parent as well as two standardized continuous performance tests (Integrated Visual and Auditory Continuous Performance Test [IVA] and the Test of Variables of Attention [TOVA]). B’s mother also filled out questionnaires including: The Attention Deficit Disorder-Q (ADD-Q; Sears & Thompson, 1998), Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) rating for Attention Deficit Hyperactive Disorder (ADHD) Snap version, and Conners’ Parent Rating Questionnaire for symptoms of ADHD. The ADD Centre staff also performed a 19-Channel QEEG assessment as well as a single-channel EEG recording at CZ (the vertex). Event-related potentials (ERPs) were also recording during the initial assessment on B; however, the ERPs were indiscernible and were therefore excluded from this paper. Impedance was measured at all sites and was below 5 kohms. The 19-channel assessment was read at the ADD Centre using Neuroguide and was also sent to Evoke Neuroscience for analysis. The two reports were used to set up a LORETA neurofeedback training program for B that combined neurofeedback with HRV training. The results are summarized in the figures below with data showing pre–post comparisons.

**Treatment Program for Client B: LORETA Z-Score Neurofeedback Combined with HRV**

The client attended two sessions per week of LORETA Z-score neurofeedback combined with HRV biofeedback. To maximize effective training time in each session, HRV was practiced for about 10 min at the beginning of each session.

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while the 19-channel EEG electrocap was being applied. The goal for B’s HRV training was to master breathing at approximately six breaths per minute, to try to achieve synchrony between his breathing and heart rate, and thus to maximize the change in his HRV. The Thompson “Setting Up for Clinical Success Suite” on the BioGraph® Infiniti by Thought Technology, Ltd. (Montreal, Quebec) was used for the HRV training. Upon completion of the HRV training at six breaths per minute, the LORETA Z-score training session was started using Neuroguide LORETA neurofeedback.

Once the impedance readings at each site were measured and under 10 kohms at all sites, the session would commence. Each training segment/round would involve 5 min of feedback where the screen would play only if approximately 80% of brainwaves matched the training thresholds (so-called Z-tunes setting). Six such rounds were completed during a session with short breaks in between. Upon completion of six screens, a digit span task or reading recall task was completed.

The LORETA Z-score neurofeedback program was set to bring selected parameters to within ±2 SDs for those BAs that correlated with his major symptoms. We typically find connectivity to be the most important target in training, and thus it was not surprising that his program emphasized, for the most part, alpha (8–12 Hz) coherence. See the chart below for a full list of training parameters. Note that the program included training of BAs that are involved in the affect, executive, and salience networks. We will not speculate regarding what compensatory means exist for between-hemisphere communication for all the areas trained. Suffice it to say that agenesis of the anterior corpus callosum does not mean that there are no connections between the hemispheres: There are other commissures, albeit smaller than the corpus callosum. Whatever the precise mechanism(s), this neurofeedback training program clearly succeeded in symptom amelioration for this client.

The matching process between symptoms and BAs also emphasized coherence between frontal and parietal areas in the right hemisphere, which might account in part for his improvements is sustaining attention span (Table 1).

Over the course of 40 training sessions, protocols were modified at three intervals due to updating the assessment of the brain maps, which was done after each block of 10 sessions—that is, his program was updated after 10, 20, and 30 sessions. For progress assessment purposes, 8 min of data is collected with impedance measures under 5 kohms to ensure high quality data. Then a complete reassessment, which mirrored the initial assessment, was done after 40 sessions. At each assessment B and his mother were consulted regarding the current symptom picture.

### Posttraining Changes

After completing 40 sessions of treatment, both qualitative and quantitative updates were done. With respect to qualitative measures, B’s mother noted that she had observed improvements in his motor skills. He was able to walk in a straighter line. He demonstrated a greater level of goal-directed movements. He was enrolled in a regular high school for the first time, albeit taking a modified program, and he tried out for a sports team and made the

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**Table 1. LORETA neurofeedback training parameters**

<table>
<thead>
<tr>
<th>Frequency</th>
<th>BAs</th>
<th>Neuroanatomical areas</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alpha coherence</td>
<td>8–12 Hz</td>
<td>9, 10, 8, 40, 11 Prefrontal cortex, parietal lobe, supramarginal gyrus</td>
</tr>
<tr>
<td>Beta coherence</td>
<td>13–20 Hz</td>
<td>7, 13, 40 Sensory association, insula, parietal, supramarginal gyrus</td>
</tr>
<tr>
<td>Hi-beta coherence</td>
<td>25–30 Hz</td>
<td>9, 10, 40 Prefrontal cortex, parietal lobe, supramarginal gyrus</td>
</tr>
<tr>
<td>Phase</td>
<td>25–30 Hz</td>
<td>7, 40 Sensory association, parietal lobe</td>
</tr>
<tr>
<td>Amplitudes</td>
<td>Frequencies outside 2 SDs were trained in these areas</td>
<td>13, 8, 40, 9, 10, 11 Insula, prefrontal, parietal lobe, supramarginal gyrus</td>
</tr>
</tbody>
</table>

*Note. BAs = Brodmann areas. See *Functional neuroanatomy* text by Thompson and Thompson (2015) for detailed descriptions of each area noted in the table above.*

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[1] Each BA is a region of the cerebral cortex, defined by the structure and organization of its cells.
roster as a substitute player without any accommodations being made for him in the selection process. At the initial assessment, a major symptom of concern was his inability to sleep through the night. His mother noted that, after training, his sleep was significantly better. For example, he was able to sleep through the whole night without waking up. In addition, he started to take naps for the first time in his life. Academically, B had made great strides over the course of his neurofeedback treatment. He was able to complete Grade 6 level mathematics. In his Grade 11 vocational mathematics class, he earned a 91%. Furthermore, B was able to complete his high school certificate and will be graduating this year. He plans on pursuing higher education. Socially, B made great strides as well. He was able to attend camp away from home for the first time. In addition, B was able to achieve an award of excellence for participation in his high school’s politics club.

The objective pre–post data also document improvements. Changes across IVA, TOVA, and HRV measures are displayed in the graphs below (Figures 1 through 6).

**Conclusion**

Throughout his life, B tried many treatments and many of these treatments were deemed successful, but his mother noted that no other treatment ever led to significant improvement across such a wide range of symptoms, in such a short period of time, the way that LORETA neurofeedback has. B improved in motor coordination, visual spatial abilities, academics, attention, impulse control, and social interactions. B plans to continue LORETA neurofeedback training to further improve symptoms. The results of utilizing LORETA neurofeedback in combination with HRV in this case of AgCC has resulted in unprecedented improvements. This case study suggests that further research is warranted. Due to the low prevalence of the condition, it may be difficult to undertake a large scale study to investigate efficacy of LORETA neurofeedback and HRV in AgCC; however, these positive results suggest that combined training of brain activation patterns and autonomic nervous system patterns might lead to improved functioning in people with other inborn neuroanatomical differences, too. For future study of AgCC a complete online neuropsychological assessment should be completed pre- and posttraining for a more comprehensive assessment of progress. CNS Vital

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**Figure 1.** Scores on the IVA test are standard scores with a mean of 100 and a standard deviation of 15. Higher scores indicate better performance. Initially, B’s response control quotient (RQ) was at 73, indicating that there was a significant degree of impulsive responding (hitting for the number 2 and not just the number 1). After training, the score rose to 86, which is just within 1 SD of the mean. His attention quotient (AQ) was at 49, indicating issues with maintaining attention. After training this increased to 56 indicating fewer instances of missing targets.

**Figure 2.** On the TOVA, scores are standard scores with a mean of 100 and a standard deviation of 15. B’s results on the TOVA improved across all dimensions. First, he increased his ability to respond consistently with his response time variability (RV) increasing from 73 to 86. This indicates a reduction in drifting attention. His score for response time (RT) also increased, from 120 to 130, indicating a fast response time (90th percentile rank) got even faster (98th percentile rank). His score for commission errors improved from 60 to 79, while his omission errors went from 40 to 94, putting him within the average range for attention on the TOVA. Scores indicated a significant improvement in both impulse control and ability to pay attention.

**Figure 3.** HRV statistics. The measure of the total power of his HRV increased significantly from 1632 to 3906, indicating healthier heart function. Finally, his low frequency power increased from 662 to 1384.

**Figure 4.** B initially started treatment with an SDNN of 61. After training this increased to 94. Scores above 75 are in the healthy range for young adults and this change indicates that his HRV had increased significantly.
Signs of online neuropsychological assessments are now being done routinely at the ADD Centre pre- and posttraining (provided by CNS Vital Signs, LLC, Morrisville, NC, at http://www.cnsvs.com). CNS Vital Signs was not available at the ADD Centre for B’s age group at the time of assessment. Based on the results of this case, it appears that it would certainly be worthwhile to try to study a series of cases with AgCC to further examine the effects of LORETA neurofeedback on symptoms.

References


