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Distinguishing Neuro-Markers of Math Learning Disability Using EEG Coherence

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by

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ABSTRACT

Math learning disability (MLD) is a neurodevelopmental disorder that results from specific cognitive deficits involved with numeric computation and arithmetic that cannot be attributed to low general ability. Although MLD has a significant impact on life outcomes, only a few studies have evaluated unique neurological profile differences between those with and without specific math deficits. EEG coherence has been useful for evaluating neural disconnections in children with neurodevelopmental disorders but has never been used to explain cognitive deficits found in children with MLD. The current study contributed to the literature by evaluating at-rest electrocortical signatures in those with MLD (n = 15), those without MLD, (n = 30), and those with general low achieving ability (n = 15). Specifically, the study evaluated disruptions in intra- and interhemispheric EEG coherence between three groups of children with differing math profiles. Results demonstrated those with math-specific deficits had reduced delta left hemispheric coherence relative to controls (p = .006), and reduced beta coherence in the left hemispheric central-parietal lobe (p = .034) and the right hemispheric fronto-central lobe (p = .004) in comparison to controls, not seen in low achieving students. Additionally, results demonstrated greater coherence in the control group compared to both the MLD and low achieving students. Exploratory analyses revealed left hemispheric delta coherence contributed significant variance beyond IQ for math (p = .007), but not reading ability (p = .622). Results from the current study provide support for disruption in basal electrocortical activity for children with specific math deficits.

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LIST OF ABBREVIATIONS

DD.. Developmental Dyscalculia

DMN .... Default Mode Network

EEG..Electroencephalography

IQ ....Intelligence Quotient

LA ....Low Achieving

MLD..Math Learning Disability

SLD.. Specific Learning Disability

CHAPTER 1

INTRODUCTION

Learning math skills in early childhood is vital as mathematics ability is significantly associated with greater positive life outcomes including socioeconomic status (SES), educational endurance, academic motivation, economic success, and even later ability to make health decisions (Reyna, Nelson, Han, & Dieckmann, 2009; Ritchie & Bates, 2013). Importantly, early mathematics ability is a stronger predictor of later academic achievement over other academic abilities including reading and attention skills (Duncan et al., 2007). Approximately 5-7% of children develop a specific math learning disability (MLD, or developmental dyscalculia; DD), and another 10% of elementary school children will go on to develop persistent deficits in math ability (Berch & Mazzocco, 2008; Shalev, Auerbach, Manor, & Gross-Tsur, 2000; Shalev, 2004). Although not all children with math deficits will meet criteria for a specific learning disability (SLD), this indicates that nearly 17% of children at the elementary school level have deficits in mathematics ability that hinder their later academic achievement. Although the prevalence of MLD is comparable to that of dyslexia, there has been a lack of research evaluating MLD and its treatment (Gersten, Clarke, & Mazzocco, 2007). Both disorders are neurobiological in nature, yet little research has been done evaluating neurological markers to explain the academic and cognitive deficits present in MLD.

Academic Deficits in MLD

Children with difficulties in mathematics demonstrate deficits in the acquisition of arithmetic skills not due to low intellectual ability (Shalev, 2004). Core deficits include retrieving arithmetic facts, comprehending simple math equations, learning multiplication tables, and understanding math word problems (Hale, Fiorello, Bertin, & Sherman, 2003; Shalev et al., 2000; Shalev, 2004). Math skills develop in a common sequence from addition up to higher-order math topics, like geometry. Many of the skills learned in math are based on the ability to associate concrete measurements with abstract symbols (i.e., numerical symbols). Individuals can develop deficits associated with any part of this developmental sequence; however, core math deficits occur most often in the early sequence of acquiring mathematics with skills such as counting knowledge, counting speed, and working memory (Geary, 1993). As such, most MLD research evaluates elementary-aged children (Katherine & Fisher, 2016).

Cognitive Deficits in MLD

Children demonstrating deficits in mathematics show deficits in multiple areas of math and cognition (Hale et al., 2003). Children with MLD show deficits in cognitive skills such as long-term memory storage, visual motor integration, verbal comprehension, short-term working memory, and fluid reasoning (Geary, 1993, 2003; Hale et al., 2003; Price & Ansari, 2013). Although, there is disagreement as to whether all these cognitive deficits are found in children with MLD as the definition of MLD differs by research study. Including a large range of children allows for broader categorization but may cloud true cognitive deficits of children with MLD. Notably, there is agreement that core cognitive deficits in working memory and visuospatial attention (Attout & Majerus, 2015; Geary, 2003; Rotzer et al., 2009) contribute greatly to the development of MLD and low math achievement.

Children with MLD tend to score lower on tasks of working memory and numerical ordering tasks than other children, even when IQ is matched (Attout & Majerus, 2015; Menon, 2016; Schuchardt, Maehler, & Hasselhorn, 2016). However, a recent meta-analysis concluded working memory and mathematics are more strongly related in those that have comorbid cognitive and other disorders, compared to typical learners and those with sole math difficulties (Peng, Namkung, Barnes, & Sun, 2016), meaning that children with only MLD may not display such severe working memory deficits.

Research suggests that deficits in both the visuo-spatial sketchpad and central executive are intrinsically tied to arithmetic ability (Bull & Johnston, 1997; Bull, Johnston, & Roy, 1999; D'Amico & Guarnera, 2005; Geary, Hoard, vByrd-craven, & Nugent, 2007; McLean & Hitch, 1999). However, it appears that difficulties in working memory tasks for children with math deficits are numerically related (Gathercole, Pickering, Knight, & Stegmann, 2004; McLean & Hitch, 1999). Furthermore, children with low math ability tend to have deficits in verbal working memory tasks only when they involve numerical information (e.g., digit span) (D'Amico & Guarnera, 2005; McLean & Hitch, 1999).

Visuospatial deficits are also present in children with MLD. There is an association between visuospatial and mathematics deficits such that children with both impaired visuospatial and numerical skills display a lack of numerical representation on the commonly used number line (Bachot, Gevers, Fias, & Roeyers, 2005). Additionally, children with MLD have visuospatial working memory deficits (Andersson & Östergren, 2012; Ashkenazi, Rosenberg-Lee, Metcalfe, Swigart, & Menon, 2013; Ashkenazi, Rosenberg-Lee, Tenison, & Menon, 2012). For example, children with MLD have difficulty with block tasks like block recall, which requires them to remember information that is presented within a specific visuospatial layout (i.e., remembering the order of blocks being tapped on the table).

In culmination, children with MLD have wide-ranging cognitive deficits that impact their academic skills. Although there is convergent data in the field considering broad definitions of MLD, there is consistent evidence to suggest that children with lower math skills often display working memory deficits (particularly with numerical information) and visuospatial working memory deficits, which may be related to particular neurological abnormalities.

MLD and the Brain

To evaluate neurological abnormalities of learning disabilities, noninvasive neurocognitive research often uses functional magnetic resonance imaging (fMRI) and electrocochleography (EEG) paradigms. There are two main hypotheses researchers use to evaluate learning disabilities: the common deficit/domain-general hypothesis (e.g., Swanson, 1987), and the domain-specific cognitive hypothesis (e.g., Landerl, Fussenegger, Moll, & Willburger, 2009). The common deficit hypothesis argues there are general deficits children with learning disabilities have (e.g., overall lower connectivity across the brain), while the domain-specific hypothesis argues deficits in specific learning disabilities are attributed to the specific disability a child has (e.g., a child with a reading disability presents with a different neurological profile than a child with a math disability). Research has indicated that children with learning disabilities comprise a heterogenous group, but subgroups can be evaluated using behavioral data and neurological markers (Roca-Stappung, Fernández, Bosch-Bayard, Harmony, & Ricardo-Garcell, 2017).

Specific studies have investigated brain abnormalities and differences in children with MLD compared to neurotypical controls, most commonly while performing certain mathematics tasks. Using fMRI methodology, two main brain areas are commonly evaluated in association with MLD: the IPS and fusiform gyrus, which are both areas associated with math functioning in the brain (Ashkenazi, Black, Abrams, Hoeft, & Menon, 2013; Butterworth, 2011; Menon, 2014). Children with MLD show reduced activation in areas commonly associated with math computation including the IPS, superior parietal lobule, supramarginal gyrus and bilateral dorsolateral prefrontal cortex (Ashkenazi et al., 2012). Furthermore, strength of activation in the IPS is associated with higher math performance (Bugden, Price, McLean, & Ansari, 2012), and children with MLD display reduced activation in the IPS (Mussolin et al., 2010; Rotzer et al., 2008). There is some research to suggest that children with MLD show hyperactivation of the IPS during certain tasks, but improper task modulation in the brain while performing math (Rosenberg-Lee et al., 2015). Along with IPS modulation, greater deactivation of the angular gyrus is also associated with poorer math ability (Gruber, 2001; Wu et al., 2009).

Although research evaluating MLD using EEG methodology is scarce, there are some key findings that emphasize the utility of EEG to study clinical differences in math achievement. Research suggests unique electrocortical signals that differentiate math technique usage overlap with electrocortical signals seen in executive function tasks (see Hinault and Lemaire (2016)), and may present differently in children with math deficits. An older study evaluated neurological markers of children with “nonverbal learning disabilities” (NVL) in relation to “verbal learning disabilities,” (VLD) and found children with NVL displayed reduced right hemispheric long-distance connectivity in comparison to children with VLD (Njiokiktjien, de Rijke, & Jonkman, 2001). Additionally, children with NVL showed reduced gamma coherence over frontal and temporal lobes. More recently, when comparing children of differing mathematics ability while performing math tasks González-Garrido et al. (2018) found that children with low-achieving math ability showed greater frontal coherence, but reduced beta coherence in comparison to high-achieving math students. Although a baseline difference in IQ was noted, no children had below a 90 standard score IQ, and represented low-achieving math children, rather than children with MLD. Regardless, these findings can be used as a starting point to evaluate MLD and low achieving math students’ unique neurological signatures.

Beyond activation and electrocortical studies, a unique morphometry study of children with MLD found that those with MLD had reduced volumetric white and gray matter in the left frontal lobe and right parahippocampal area (Rotzer et al., 2008). Furthermore, morphometric analyses reveal that brain abnormalities in the right hemispheric tempo-parietal networks are associated with mathematical and working memory deficits (Rykhlevskaia, Uddin, Kondos, & Menon, 2009). Overall, findings from fMRI, EEG, and morphometry reveal that children with MLD and low achieving math abilities show neurological differences that can be explored further.

Using Coherence to Study Clinical Groups

EEG studies have been performed looking at differences between those with and without learning disabilities, but few have published resting state basal data, or observed clinical differences specifically in children with math deficits. Although some key studies were identified previously, most studies evaluating math and the brain use hemodynamic measures of neural responses. However, such measures use a reductionistic approach, prioritizing separate regions of the brain implicated in cognition and mathematics ability, rather than evaluating whole brain cognition networks. One technique that may incrementally address the neurobiological basis for cognitive and mathematics deficits while preserving a more holistic assessment of brain networks is evaluating brain coherence. Coherence from EEG data is considered a type of quantitative EEG (qEEG) analysis, which has very recently been noted to provide additional insight into clinical disorders beyond behavioral profiles (Popa, Dragos, Pantelemon, Rosu, & Strilciuc, 2020). In addition, studying the brain's basal physiology can also work to highlight distinguishing features, though this paradigm is seldom used to evaluate learning disabilities, as identification practices are primarily behavioral.

Coherence is a measure of phase consistency between different electrocortical regions (Bedat & Piersol, 2000) and is often used to estimate functional interactions between brain regions at different wavelengths (Srinivasan, Winter, Ding, & Nunez, 2007). As such, by using coherence measurements, researchers can evaluate functional integration of brain regions in relation to tasks, or at rest. Resting-state paradigms are often used to evaluate neurological clinical profiles present when individuals are not performing any specific tasks (Hanakawa, 2017), and thus coherence measurements in resting-state paradigms can be used to look at unique neurological profiles in children with MLD through functional integration present in the resting brain.

A recent article evaluated resting-state brain coherence in a large group of children with and without learning disabilities (*n* = 216) and noted some clear coherence differences such as increased theta power and reduced alpha coherence in children with learning disabilities (Jäncke, Saka, Badawood, & Alhamadi, 2019). However, results did not account for a statistically significant IQ baseline difference between groups, and should be interpreted cautiously, as observed differences may reflect this baseline difference (see Thatcher, North, and Biver, (2005)) Another recent article using coherence EEG measures evaluated clinical differences between those with dyslexia (*n* =184) and children with a non-specific reading delay (*n* = 43) to observe flow of information differentiation (Bosch-Bayard et al., 2020). Overall, research studies have used EEG coherence paradigms (both resting and non-resting state) to study clinical group differences and uncover unique electrocortical signatures (Coben, Clarke, Hudspeth, & Barry, 2008; Kam, Bolbecker, O'Donnell, Hetrick, & Brenner, 2013; Park et al., 2017; Tas et al., 2015), and as such, coherence is a well-validated method that can be applied to studying MLD.

Study Overview

In culmination, children with specific math deficits are at a disadvantage in terms of later academic and economic success, and our research efforts into uncovering the neurological underpinnings of mathematics disabilities are stunted when evaluating coherence and brain connectivity. Although research has been used to evaluate the neurological basis of math while performing math tasks, we know little about the basal physiology of math deficits in the brain. The current study adds to the growing body of literature on math deficits and the brain by providing an evaluation of basal physiology differences between three groups of elementary school aged children: neurotypical controls, children with low achieving math scores (LA), and children with specific math deficits in an otherwise average cognitive profile (MLD). Analyzing inter and intrahemispheric cortical coherence between these three groups creates a holistic view of unique neurological differences that can be used to distinguish children with these specific deficits at rest and differentiate math-specific deficits against differences due to lower cognitive ability. Given the associations between brain connectivity and behavioral interpretations of academic and cognitive abilities, the results of this study provide biological explanations of math-specific deficits. Furthermore, this study provides evidence for and against the “common-deficit hypothesis” by providing unique brain profile differences in those with math deficits, not observed by those with lower cognitive ability, as well as deficits common to both groups.

CHAPTER 2

METHOD

All experimental procedures and questionnaires given were approved by the Institutional Review Board at the University of South Carolina and all children gave verbal assent, while their parents gave written consent.

Participants

This study examined math ability in children aged 7-12. Participants for this study included 30 controls, 15 children with low achieving math ability (LA), and 15 children with specific math deficits (MLD) (N = 60). Children were recruited through local advertisements and agencies in the Columbia, South Carolina area that serve children with specific learning disabilities, including MLD. Neurotypical controls were recruited using online media outlets such as Facebook parenting groups. Participants received monetary compensation for completion of the study.

Inclusion criteria for a child to be LA or MLD consisted of: a.) current/previous specific math learning disability diagnosis (including documentation), and/or b.) score below the 25th percentile on the Woodcock-Johnson Tests of Achievement – 3rd Edition (WJ-III Ach) Math Calculation subtest and/or Math Fluency subtest. Using this criteria, 30 children were identified. To be considered as MLD, a discrepancy approach was used to ensure that lower math scores deviated from a child’s general IQ. It should be noted that this classification system does not include all variables typical in a full evaluation for a math learning disability (i.e., history, instruction information, etc.). As such, inclusion criteria to the MLD group was used for the purposes of identifying children with notable math deficits within an average cognitive profile in comparison to low achieving children not meeting criteria for MLD. If a child had a math subtest score that was at least 15 standard score points (1 SD) below their IQ, they were classified as MLD. If a child did not have any math subtest scores at least 15 points below their IQ, they were identified as having low achieving math scores that could be explained by lower cognitive ability. The average discrepancy (using the child's lowest math subtest score and GIA) for the MLD group was 24.3 points (approximately 1.5 SD discrepancy from IQ), while the average discrepancy for the LA group was 8 points. The creation of these two groups increased statistical power by making groups more homogenous and allowed for the differentiation between LA and MLD children to determine unique brain profile markers in children with specific math deficits.

Inclusion criteria for control children consisted of: a.) no current or previous IEP in school or qualifications for special education services, and b.) score at or above the 25th percentile on the WJ-III Ach Math Calculation and Math Fluency subtests. The control group included children of average (SS between 90 and 115; $n = 15$) and high achieving math ability (SS above 115; $n = 15$). Children were excluded if their General Intelligence Ability (GIA) (Woodcock-Johnson Tests of Cognitive Ability – 3rd Edition; WJ-III Cog) fell below a standard score of 70. Children were also assessed with the Broad Reading Cluster to determine if there were any notable reading deficits. Only two children were identified as having a reading composite below 70; however, the exclusion of these two participants did not result in significant differences in results, so they were retained. Participants had a mean age of 9.58 ($SD = 1.38$) and 53.3% of the sample was male (46.7% female). Participants were overwhelmingly Caucasian, making up 83.3% of the ethnic makeup of the participant population, with 8.3% African American, 1.7% Hispanic, and 6.7% Asian.

Procedures

Each testing session lasted approximately three hours, including multiple breaks from testing. Participants and their guardians arrived at the lab and guardians gave written consent to testing procedures while children provided verbal assent. Parents completed parent-report questionnaires while children completed neuropsychological testing. Children were first fitted with an EEG cap and resting-state EEG data was collected, both eyes open and eyes closed in three-minute intervals. After EEG data was collected, participants completed multiple cognitive and academic tests. During testing, breaks were provided as necessary, but no breaks exceeded 20 minutes. Most children only used 3-4 breaks per testing session with each break lasting 5-10 minutes. After study completion, guardians received monetary compensation. All data used in the study was de-identified following testing to ensure confidentiality.

Materials

Woodcock-Johnson Tests of Cognitive Ability – 3rd Edition. The WJ-III (Woodcock, Mather, McGrew, & Wendling, 2001) was used in this study because data was collected before the fourth edition of the WJ was released. The WJ-III is an individually administered cognitive assessment appropriate for individuals aged two to 90+. The WJ-III Cog provides multiple subtests in each of the Cattell-Horn-Carroll (CHC) factors of intelligence. All standard battery subtests were administered to obtain a

GIA score used to rule-out general lower cognitive ability for children scoring low on math measures used in the inclusion criteria.

Woodcock-Johnson Tests of Achievement – 3rd Edition. Math achievement was represented by the WJ-III Ach (Woodcock, McGrew, & Mather, 2001). Similar to the WJ-III Cog, the WJ-III Ach is an individually administered achievement assessment that is appropriate for individuals aged two to 90+. The WJ-III Ach provides scores in different areas of math, reading, and writing. For this study, the Broad Mather Cluster score was evaluated, which combines the Calculation, Math Fluency, and Applied Problems subtests. This score is for all intents and purposes, the average of these three subtests. Additionally, individual scores on the math subtests were used for inclusion criteria into the MLD and LA groups.

EEG Recording and Analysis

Participants were fitted for a standard 19-electrode cap, with ground electrodes placed on the ears. Figure 2.1 displays the international 10-20 electrode recording placement. Baseline, resting-state EEG recordings for eyes closed and eyes open data were recorded for a minimum of three minutes. Only eyes closed data was used in the current study since this type of data is one of the most common paradigms to evaluate clinical group differences (e.g., Murias, Webb, Greenson, & Dawson, 2007). EEG activity was recorded using a BrainMaster Discovery 24E amplifier (Wigton & Krigbaum, 2015) with Neuroguide 6.6.4 Software (Thatcher, 2011). Data was sampled at 256 Hz, with a 60Hz notch filter to remove excess noise caused by the surrounding environment. All impedance values for electrodes were maintained below10KΩ throughout data recording, with reference electrodes maintained below 5KΩ.

Prior to data processing, EEG data was cleaned using the Neuroguide Software (Thatcher, 2011). First, EEG data were manually inspected to choose a minimum of ten seconds of artifact-free data. An automatic selection function was then applied to automatically select data within the sample that models the artifact-free selection. Data were visually inspected to ensure accurate selection. Additionally, automatic ocular correction was employed to remove eye-movement artifacts from data. Data was filtered using a high band pass of 1 Hz and a low band pass of 30 Hz. EEG data was referenced using a linked-ears electrode reference.

The power spectrum was calculated using Welch's transformation for delta (1–4 Hz), theta (4–8 Hz), alpha (8–13 Hz), and beta (13–30 Hz) frequency bands, which estimates power spectral density and reduces signal noise. Coherence measures were obtained using the Neuroguide software. Neuroguide uses a normed database to provide coherence values in raw Z-scores, minimizing discrepancies in coherence due to age.

Data Analysis

Continuous demographic variables were evaluated with one-way analyses of variance (ANOVA) and discrete demographic variables were evaluated with Chi-square analyses. To analyze coherence by brain area, electrodes were separated into frontal (FP1, FP2, F7, F3, Fz, F4, and F8), temporal (T3, T4, T5, and T6), central (C3, Cz, and C4), parietal (P3, Pz, and P4), and occipital (O1 and O2) lobes. Using methods similar to Coben, Clarke, Hudspeth, and Barry (2008), interhemispheric coherence was calculated by averaging all electrode coherence connections within each lobe. This included 21 frontal, 6 temporal, 3 central, and 3 parietal averaged connections. Occipital connections were not averaged because there was only one coherence connection (O1-O2). One-way

ANOVAs were performed to determine interhemispheric coherences group differences (control, LA, and MLD) at each specified wavelength.

Intrahemispheric coherence was analyzed in two different ways. First, coherence was analyzed by mean short/medium and long electrode distances by hemisphere (Coben et al., 2008) to evaluate global connectivity and integration of information across electrode distances. Left short/medium distances were: Fp1–F3, T3–T5, and C3–P3 and right distances were: Fp2–F4, T4–T6, and C4–P4. Left long electrode distance was defined as F3– O1 and right electrode distance was defined as F4–O2. Mixed ANOVAs were used to analyze differences between groups (control, LA, and MLD) and within hemisphere (L, R) at each specified wavelength.

Next, coherence was analyzed by group, hemisphere, and region, using previously established intrahemispheric coherence analysis methods for observing clinical group differences (Kam, Bolbecker, O'Donnell, Hetrick, & Brenner, 2013; Park et al., 2017; Tas et al., 2015; Thatcher, Krause, & Hrybyk, 1986). F3 –C3, F3–P3, F3–T3, C3–P3, C3–T3, P3–T3 electrode pairs were used on the left hemisphere and F4–C4, F4–P4, F4–T4, C4– P4, C4–T4, P4–T4 electrode pairs were used on the right hemisphere. Mixed ANOVAs were used to analyze differences between groups (control, LA, and MLD), within hemisphere (L, R), and within brain area (fronto-central, fronto-parietal, fronto-temporal, central-parietal, central-temporal, and parietal-temporal) at each specified wavelength. For all repeated measures analyses, if Mauchley's Test of Sphericity was broken, a Greenhouse-Geisser correction was applied.

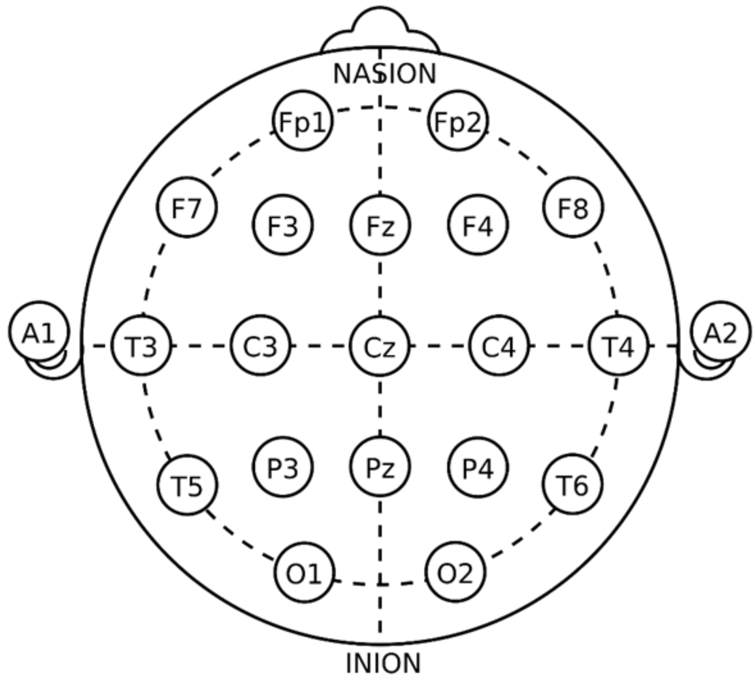

Figure 2.1. International 10-20 system.

CHAPTER 3

RESULTS

Descriptive statistics

Participant characteristics are presented in Table 3.1. All variables were homoscedastic. Of note, there was a significant difference in age between groups, however, no differences passed Bonferroni-corrected pairwise comparisons. Chi-square analyses for gender and ethnicity indicate no significant differences between the three groups. All math subtests and the broad math cluster demonstrate significant, expected differences between all groups (*p's* $< .001$), such that the control group had higher math scores than both the MLD and LA groups. As noted in Table 3.1, the control group had significantly higher general IQ than the MLD and LA groups (*p's* $< .001$). Both the control and MLD group had average IQ, while the LA group had low average IQ. This was expected given that MLD children generally have math deficits in an otherwise average cognitive profile (Geary, 2003). IQ was not used as a covariate as the MLD groups displayed average IQ. Considering IQ is positively correlated with coherence (Thatcher, North, & Biver, 2005), differences between the control and LA groups, demonstrate specific, expected, IQ-related differences in coherence.

Interhemispheric Coherence

Interhemispheric coherence results are depicted in Table 3.2. Bonferroni - corrected pairwise comparisons were performed to explore significant ANOVA differences. In occipital alpha, the MLD group showed reduced coherence compared to the LA group (p = .030). In the beta wavelength, the control group showed greater coherence compared to the LA group in the temporal (p = .027) lobe, while the control group had greater coherence compared to both the MLD (p = .034) and LA (p = .016) groups in the parietal lobe. Differences between groups did not survive Bonferroni-corrections for theta temporal coherence and there were no group differences in delta coherence. Results suggest that those with MLD show reduced alpha occipital coherence, even compared to those with low achieving math abilities. Additionally, MLD and LA groups showed reduced beta coherence in the parietal lobe, while only the LA group showed reduced coherence in the temporal lobe. As such, interhemispheric coherence markers of specific math deficits may lie within reduced alpha occipital coherence.

Intrahemispheric Coherence

Electrode Distances. Mixed ANOVAs were performed by wavelength to determine interactions within hemisphere and between groups by differing electrode distances. Bonferroni-corrected pairwise comparisons were used to explore significant differences. Results for small-medium electrode distances are depicted in Table 3.3. In the beta wavelength, the control group showed significantly greater coherence than the LA group (p = .004). Specifically, there was a group X hemisphere interaction such that in the left hemisphere, the control group had greater coherence than both the LA (p = .013) and MLD (p = .018) groups, while in the right hemisphere the control group had greater coherence than the LA group (p = .005) (Figure 3.1). This provides evidence to suggest there may be no distinct neurological markers of math deficits within short-medium electrode distance integration, beyond differences explained by lower ability.

For long electrode distances, there was only a group X hemisphere interaction in the delta wavelength. As depicted by Figure 3.2 the controls and LA groups showed modulation of coherence across hemispheres. The controls showed greater left hemispheric coherence and reduced right hemispheric coherence ($p < .001$) while the LA group showed the opposite coherence pattern (n.s.). The MLD group showed low stable coherence across both hemispheres with no coherence modulation. Overall, this provides some evidence to suggest the MLD group has lower stable delta coherence that differs from regular coherence patterns for children without specific math deficits for long-range information integration.

Group, Region, and Hemisphere Interactions. Mixed ANOVAs were performed by wavelength to determine interactions within hemisphere and region, and between groups (Table 3.5). In the beta wavelength, there was a main effect of group such that the control group showed greater coherence than both the LA ($p = .006$) and MLD ($p = .023$) groups. Additionally, there was a group X hemisphere X region three-way interaction (Figure 3.3). In the left hemisphere, the control group showed greater coherence than the LA group in the fronto-central ($p = .024$), fronto-temporal ($p = .028$), fronto-parietal ($p = .044$), central-temporal ($p = .042$), and tempo-parietal lobes ($p = .020$). Additionally, the control group showed greater coherence than the MLD group in the fronto-parietal ($p = .022$), central-parietal ($p = .034$), and tempo-parietal ($p = .030$) lobes. In the right hemisphere, the control group showed greater coherence than the LA group in the fronto-parietal ($p = .006$) and central-parietal ($p = .005$) lobes. The control group showed greater coherence than the MLD group in the fronto-central ($p = .004$) and fronto-parietal ($p = .011$) lobes.

In the delta wavelength, there was a main effect of group, such that the control group showed significantly greater coherence than the MLD group (p = .028). The group X hemisphere interaction indicates that in the left hemisphere, the control group showed significantly greater coherence than the MLD group (p = .003) (Figure 3.4). Results suggest that beta left hemispheric coherence in the central-parietal lobe and right hemispheric coherence in the fronto-central lobe may indicate specific neurological clinical differences for children with math deficits that are not solely due to low achievement in mathematics. Importantly, there were significant noted differences in delta left hemispheric coherence such that children with math deficits showed reduced coherence, not seen in the LA group.

Exploratory Hierarchical Regressions

Given previous results indicating the importance of general left hemispheric delta coherence for differentiating those with and without math disabilities, an exploratory hierarchical regression was performed to determine if these neurological correlates predict math ability, beyond IQ itself. IQ was used in the first block of predictors to ensure that IQ was accounted for in predicting math ability, given its high predictive value in determining academic skill ability. Specifically, the Broad Math Cluster score was used to determine general math ability. This cluster consists of the three main math subtests from the WJ-III Ach: Math Calculation, Math Fluency, and Applied Problems. Results for the regression shows homoscedastic residuals and all VIF values were less than 10, indicating no collinearity.

Overall, both regression models were statistically significant (*p's* < .001) (Table 3.6). IQ by itself significantly predicted math ability (F (1,58) = 121.83, p < .001, R^2 =

.677). Importantly, adding coherence variables as predictors (*F* (7,52) = 24.62, $p < .001$, $R^2 = .768$) substantially explained more variance in math ability than IQ alone ($p = .007$, R^2 change 9.1%) (Figure 3.5). Delta left hemispheric fronto-central, fronto-parietal, and central-parietal coherence variables were all significant predictors of math ability. Both fronto-central and central-parietal beta weights were positive, suggesting that as coherence in these areas increase, math ability increases, while as coherence in fronto-parietal increases, math ability decreases.

To determine divergent validity in predicting math ability, delta left hemispheric coherence variables were also used to predict the Broad Reading Cluster. As previously established, coherence is positively correlated with intelligence (Thatcher, North, & Biver, 2005). Using delta left hemispheric coherence to predict reading ability provides evidence to determine if these coherence variables are correlates of math ability specifically, or general intellectual/academic ability. Results for the regression showed homoscedastic residuals and all VIF values were less than 10, indicating no collinearity. When predicting reading ability using IQ and coherence variables, both models were significant (*p's* < .001) (Table 3.6). IQ significantly predicted reading ability (*F* (1,58) = 119.41, $p < .001$, $R^2 = .673$), and adding coherence variables also resulted in a significant model (*F* (7,52) = 17.23, $p < .001$, $R^2 = .699$). Importantly, adding these coherence variables did not add significant variance for predicting reading ability beyond IQ ($p = .622$, R^2 change 2.6%). Additionally, none of the coherence variables were significant predictors of reading ability (*p's* > .4).

These results suggest that left hemispheric coherence at the delta wavelength not only may work to differentiate those with and without math disabilities but are also highly associated with math ability and not reading ability. As such, left hemispheric coherence at the delta wavelength may be particularly important for predicting math ability, and not academic abilities generally.

Table 3.1. Group Characteristics (N = 60)

Variables	Control		MLD		LA			
	M	*SD*	*M*	*SD*	*M*	*SD*	*F*	*p*
IQ ***	110.40	11.59	99.20	11.32	88.33	7.22	22.35	< .001
Age *	9.17	1.42	10.20	1.21	9.80	1.26	3.28	.045
Broad Math Cluster ***	117.37	14.34	87.13	17.53	85.80	11.07	34.08	< .001
Calculation ***	114.17	15.28	87.67	19.11	89.40	13.51	19.50	< .001
Math Fluency ***	105.90	11.52	78.00	6.16	84.20	11.21	44.14	< .001
Applied Problems ***	115.73	10.85	93.53	16.24	88.33	11.18	30.34	< .001

*$p < .05$, ** $p < .01$, *** $p < .001$

Table 3.2. Interhemispheric Coherence

	F	*p*	*Post hoc*
Alpha			
Frontal	.53	.590	
Temporal	.17	.848	
Central	2.67	.078	
Parietal	2.74	.073	
Occipital *	3.69	.031	MLD < LA
Beta			
Frontal	1.27	.289	
Temporal *	3.72	.030	Con > LA
Central *	3.69	.031	(n.s)
Parietal **	5.74	.005	Con > MLD, LA
Occipital	.23	.795	
Theta			
Frontal	.03	.971	
Temporal *	3.18	.049	(n.s)
Central	2.40	.100	
Parietal	2.60	.083	
Occipital	.99	.378	
Parietal			
Frontal	.37	.692	
Temporal	1.30	.281	
Central	1.21	.305	
Parietal	1.24	.299	
Occipital	.01	.99	

*$p < .05$, ** $p < .01$, *** $p < .001$

Table 3.3. Short-medium Electrode Distance Intrahemispheric Coherence

	F	p	η_p^2	*Post hoc*
Alpha				
Group	.38	.688	.013	
Hemisphere ***	17.40	< 001	.234	L > R
Group X Hemisphere	.18	.837	.006	
Beta				
Group **	6.39	.003	.183	Con > LA
Hemisphere *	6.09	.017	.096	L > R
Group X Hemisphere *	3.42	.040	.107	In L, Con > LA, MLD In R, Con > LA
Theta				
Group	1.88	.161	.062	
Hemisphere ***	13.26	<.001	.189	L > R
Group X Hemisphere	.95	.394	.032	
Delta				
Group *	3.44	.039	.108	
Hemisphere *	5.71	.020	.091	L > R
Group X Hemisphere	1.65	.201	.055	

*p < .05, ** p < .01, *** p <.001

Table 3.4. Long Electrode Distance Intrahemispheric Coherence

	F	*p*	η_p^2	*Post hoc*
Alpha				
Group	2.86	.065	.091	
Hemisphere	.54	.467	.009	
Group X Hemisphere	.08	.926	.003	
Beta				
Group	2.73	.074	.087	
Hemisphere **	8.68	.005	.120	L > R
Group X Hemisphere	1.88	.162	.062	
Theta				
Group	2.22	.119	.075	
Hemisphere	1.77	.188	.030	
Group X Hemisphere	2.51	.090	.081	
Delta				
Group	.90	.414	.030	
Hemisphere	.64	.428	.011	
Group X Hemisphere **	5.51	.006	.162	Con, L > R

$*p < .05$, $** p < .01$, $*** p < .001$

Table 3.5. Intrahemispheric Coherence Interactions

	F	p	η_p^2	*Post hoc*
Alpha				
Group	2.16	.124	.071	
Group X Region	1.05	.388	.036	
Group X Hemisphere	.225	.799	.008	
Group X Region X Hemisphere	1.51	.176	.050	
Beta				
Group **	6.77	.002	.192	Con > LA, MLD
Group X Region	.81	.542	.028	
Group X Hemisphere	2.19	.121	.071	
Group X Region X Hemisphere *	2.50	.031	.080	In FC FP, Con > LA, MLD In CP, Con > LA
Theta				
Group	2.54	.088	.082	
Group X Region	.38	.862	.013	
Group X Hemisphere	.93	.401	.032	
Group X Region X Hemisphere	1.68	.115	.056	
Delta				
Group *	4.29	.018	.131	Con > MLD
Group X Region	.32	.914	.011	
Group X Hemisphere *	4.68	.006	.125	In L, Con > MLD
Group X Region X Hemisphere	.89	.513	.030	

*p < .05, ** p < .01, *** p <.001

Table 3.6. Delta Hierarchical Regressions Predicting Math and Reading

	β	*t*	*p*	R^2 Change
Broad Math Cluster				
Model 1				
IQ ***	.823	11.04	< .001	
Model 2				.007
IQ ***	.789	11.31	< .001	
F3-C3 *	.246	2.07	.043	
F3-T3	.037	.29	.773	
F3-P3 *	-.325	-2.22	.031	
C3-T3	.194	1.03	.309	
C3-P3 *	.257	2.15	.036	
P3-T3	-.101	-.66	.512	
Broad Reading Cluster				
Model 1				
IQ ***	.820	10.93	< .001	
Model 2				.622
IQ ***	.802	10.08	< .001	
F3-C3	.117	87	.390	
F3-T3	.048	.33	.743	
F3-P3	-.063	-.38	.707	
C3-T3	.051	.24	.814	
C3-P3	.022	.16	.871	
P3-T3	-.001	-.00	.997	

*p < .05, ** p < .01, *** p <.001

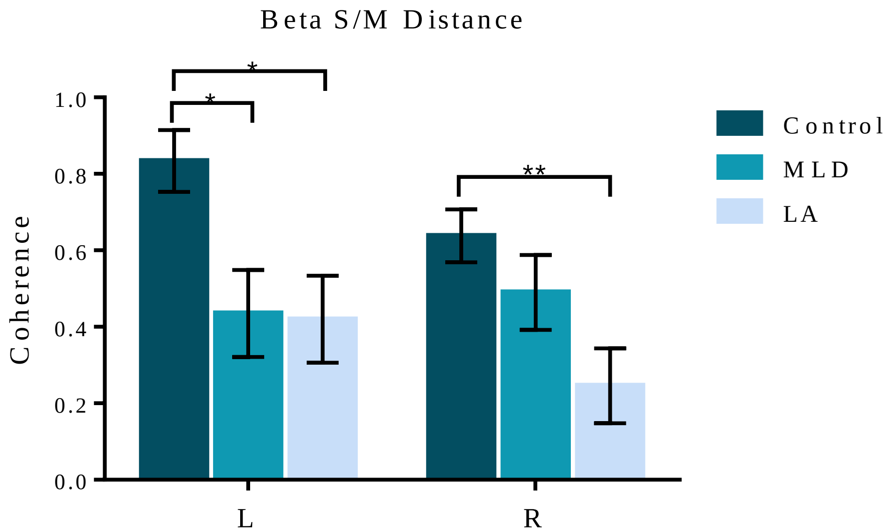

Figure 3.1. Beta S/M electrode distance coherence Group X Hemisphere.

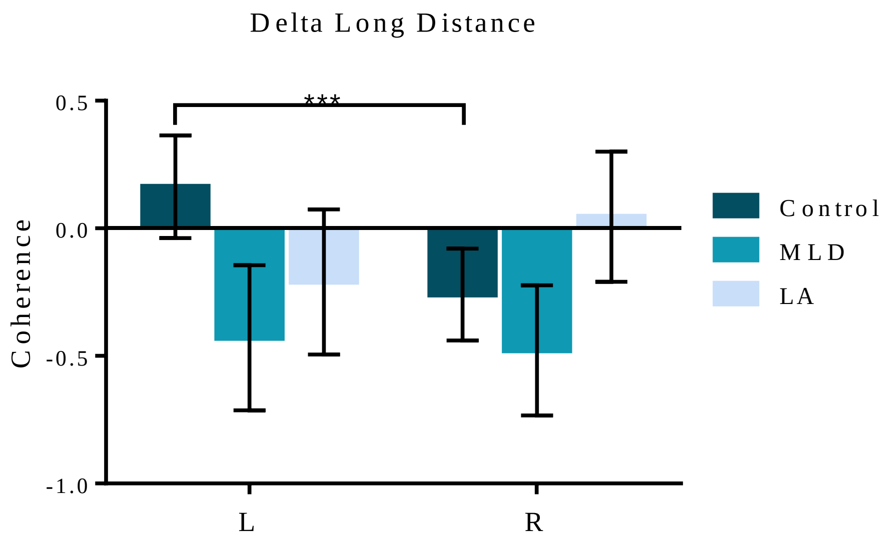

Figure 3.2. Delta long electrode distance coherence Group X Hemisphere.

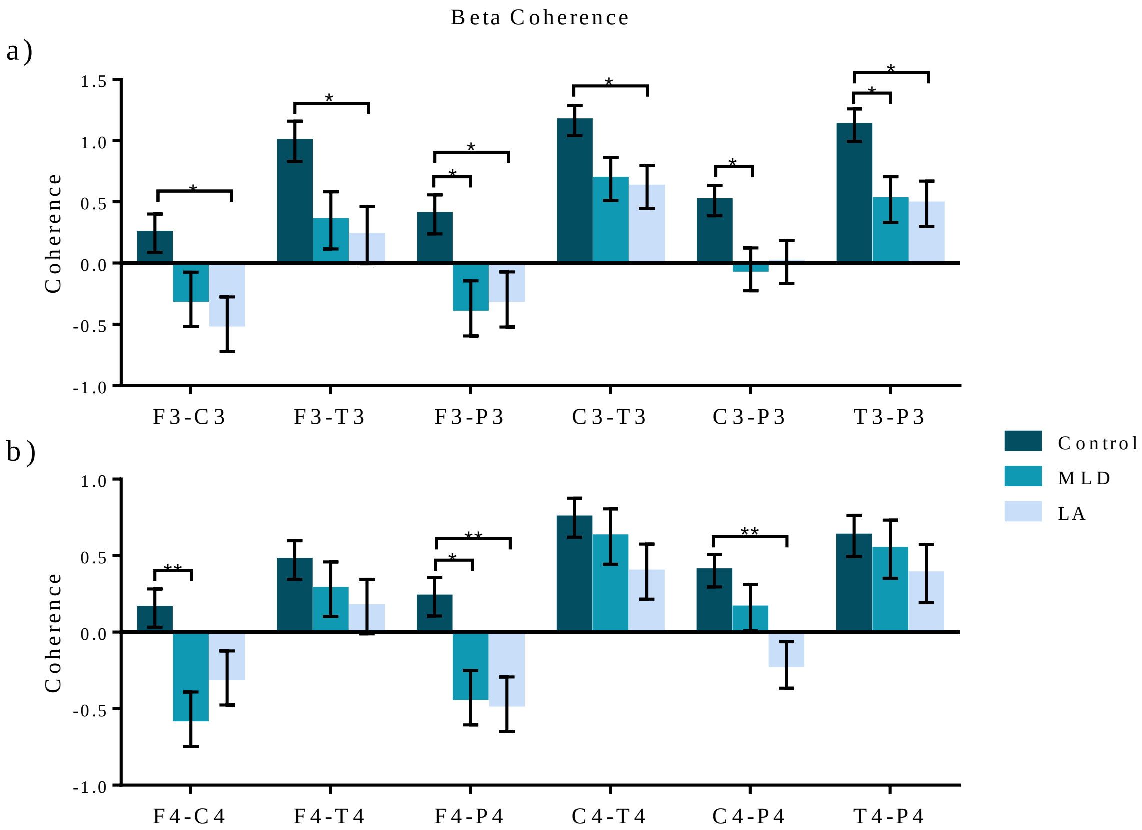

Figure 3.3. Beta Group X Region X Hemisphere. a.) Left hemisphere and b.) Right hemisphere. X-axis depicts electrode pairs across regions.

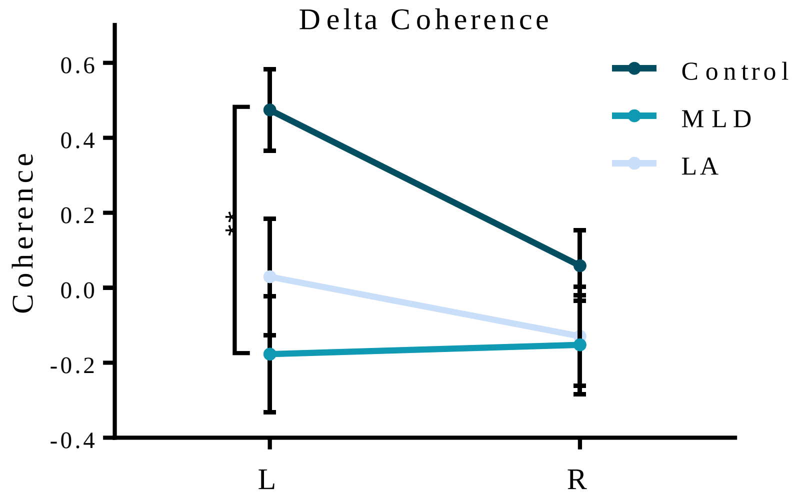

Figure 3.4. Delta coherence Group X Hemisphere.

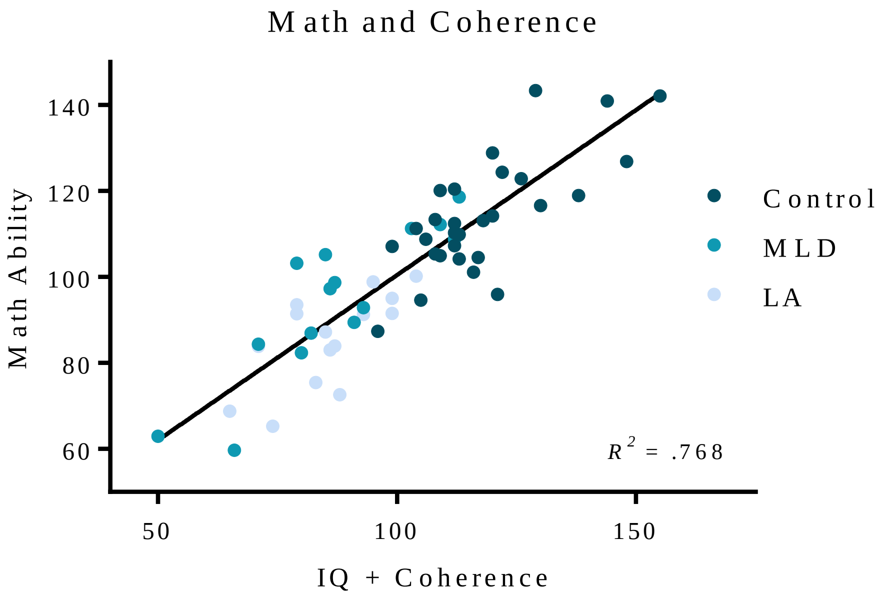

Figure 3.5. Regression Predicting Math using IQ and delta left hemispheric coherence. Electrode pairs predictors (F3-C3, F3-T3, F3-P3, C3-T3, C3-P3, and P3-T3).

CHAPTER 4

DISCUSSION

Math learning disability is a neurodevelopmental disorder that results in individuals having deficits in arithmetic, not due to low general ability. Although arithmetic abilities are highly predictive of later personal and economic success (Duncan et al., 2007; Ritchie & Bates, 2013), there is a lack of research into MLD compared to other neurodevelopmental disorders, such as dyslexia (Gersten et al., 2007). Although there has been much research into the neurological markers of mathematics in the brain, there are only a handful of studies that evaluate unique neurological profile differences between those with and without specific math deficits. The current study sought to fill this gap by providing evidence of unique electrocortical signatures present in those with MLD that differ from those without deficits, and those with general low achieving ability. Specifically, the study evaluated intra- and interhemispheric EEG coherence between three groups to identify potential brain integration disruptions in children with MLD.

Results from the current study demonstrate expected coherence differences between those without deficits and those with low achieving math ability, but also highlight important neurological distinctions in those with MLD. Although multiple areas of the brain were implicated as differences between clinical groups, the most salient results indicated that individuals with MLD may show reduced beta coherence in left hemispheric central parietal areas and right hemispheric frontal central areas. Additionally, the MLD group showed reduced left hemispheric delta coherence compared to controls, a difference that the LA group did not display. Although the neurotypical control group showed a modulation of delta hemispheric coherence with higher coherence in the left hemisphere compared to the right hemisphere (also demonstrated in the LA group, though not significantly), the MLD group demonstrated low, stable coherence across both hemispheres.

In the beta band, the MLD group showed reduced coherence compared to the controls across the left central parietal area and right fronto-central area. Moreover, controls showed greater coherence across fronto-parietal connections in both hemispheres compared to the MLD and LA groups. These results align with previous studies suggesting the importance of frontal and parietal networks in math ability. Specifically, math-gifted children show greater connectivity (as measured by fMRI) across fronto-parietal networks, and the parietal lobe across multiple task paradigms (Prescott, Gavrilescu, Cunnington, O'Boyle, & Egan, 2010; Zhang, Gan, & Wang, 2017). Morphometrically, research suggests that MLD may be a "disconnection syndrome," showing reduced fiber projections between parietal, temporal, and frontal regions (Kucian et al., 2014), which may explain reduced coherence among certain projections from these regions as measured electrocortically.

With regards to interhemispheric coherence, controls had higher coherence than the LA group within the beta band across the parietal, temporal, and central lobes. Recent research suggests that children with high math achievement express increased beta usage during math tasks in comparison to children with lower math achievement (González-Garrido et al., 2018). Additionally, a review of beta-band activity suggests that beta activity should be prominent in resting-state paradigms (Engel & Fries, 2010), and although high beta activity was observed in the control group, both the MLD and LA groups showed reduced resting-state beta coherence. As such, reduced beta at resting-state may signify abnormal basal physiology. Uniquely, the MLD group showed reduced coherence in relation to the LA group in the occipital lobe in the alpha band. This may suggest that when compared to those with lower achieving ability, those with specific math deficits show reduced integration across high frequency visual areas of the brain. Overall, these results align with clinical theories that those with MLD may have weaknesses in visuospatial cognitive abilities, as indicated by difficulties in linear and spatial numerical representations (Bachot et al., 2005; Hegarty & Kozhevnikov, 1999). Additionally, visuospatial integration significantly explains both math and written expression achievement abilities in children (Carlson, Rowe, & Curby, 2013), suggesting the importance of visual skills in math performance, even considering IQ.

In a novel finding, left hemispheric delta coherence differentiated MLD individuals from controls such that the MLD group had low stable coherence across hemispheres compared to the control group, who showed a modulation in coherence with high left hemispheric coherence compared to right hemispheric coherence. An older study using cognitive assessment data hypothesized that left hemispheric activity (and executive functions) may be predictive of mathematics ability, particularly in children with MLD (Hale et al., 2003). Although older theories suggested that MLD may result from right hemispheric deficits due to non-verbal dysfunction (Rourke, 1991), neuroimaging studies suggest multiple areas of cognition across hemispheres are necessary for math computation and differentiating MLD (e.g., Ashkenazi et al. (2013)). Additionally, as recent fMRI research suggests left hemispheric activity is more highly associated with more basic math abilities (Arsalidou & Taylor, 2011), reduced left hemispheric coherence at rest may be associated with reduced ability to perform these basic math tasks. More research is needed to confirm this association.

An exploratory analysis was used to determine whether left hemispheric delta coherence was specifically predictive of math ability, rather than general ability. Given previous results suggesting that left hemispheric delta coherence was useful in differentiating those with and without MLD (such that those with MLD show reductions in coherence across these regions), these coherence measures were regressed with IQ to predict math and determine if they added significant explained variance beyond IQ. Generally, although we use dichotomous categories for diagnosis, symptoms of clinical syndromes (including academic skills) are continuous (Krueger et al., 2018). As such, left hemispheric delta coherence that differentiated groups, could be used to predict continuous mathematics ability. Adding in coherence variables did add significant explained variance for mathematics ability but did not add significant explained variance beyond IQ for reading ability. Altogether, these results suggest that reduced left hemispheric delta coherence may be associated with lower math ability. Future studies should continue to evaluate correlates of math ability through qEEG paradigms.

Limitations

Generally, there are some limitations in this study that should be considered. Most significantly, the sample size for both the MLD and LA groups was small; however, separating participants with math ability below the 25th percentile into MLD and LA groups created more homogeneity. Additionally, having a low-achieving group helps to distinguish markers of MLD that differ from lower general ability. Importantly, IQ is highly correlated with coherence, so there are many expected differences between the control and LA group that resemble differences in ability (Thatcher et al., 2005). Creating homogenous groups not only increases statistical power but allows for greater interpretation of results. Previous similar studies including González-Garrido et al. (2018) and Jäncke et al. (2019) both evaluated individuals with low-achieving academic abilities and although excluded for low IQ, did not account for baseline differences in IQ. Distinguishing unique brain differences while accounting for expected differences due to lower ability is an important distinction made in this study, as compared to other EEG studies. Future studies should ensure adequate sample size, but also ensure that IQ is not influencing EEG coherence results when evaluating clinical group differences.

Another limitation of this study is that the control group used here was heterogenous and included half average achieving and half high-achieving children. As mentioned previously, ability is related to coherence, so the control group may have displayed heightened coherence in comparison to the other two groups, due to the inclusion of high-achieving children. Some research does suggest heightened connectivity in fronto-parietal brain regions for math gifted children during specific tasks (Prescott et al., 2010); however, there is little research to suggest that high-achieving children have significantly increased resting-state connectivity compared to average achieving children. Regardless, future studies should consider separating these two groups when evaluating learning disabilities.

Lastly, the study used a categorization method of MLD that did not consider all aspects common to a clinical or school-based diagnosis. The current study used an experimental IQ-achievement discrepancy approach for two reasons: 1) to determine if lower math ability was due to lower cognitive ability or possible specific math deficits, and 2) to confirm MLD status for children with a school/clinic diagnosis of MLD. The MLD group had either a math fluency or math calculation subtest discrepancy from their overall IQ by at least 15 standard score points (1*SD*), but the average discrepancy for the MLD group was over 24 standard score points (approximately 1.5 *SD*). Although IQ can be affected by lower working memory deficits that are associated with MLD, research suggests deficits in these areas may be more prevalent in children with comorbid cognitive disorders and low math achievement (see (Peng, Namkung, Barnes, & Sun, 2016). Similar discrepancy approaches have been used in dyslexia studies (e.g., Abbott, Reed, Abbott, and Berninger (1997) and Hook (2001)) using verbal composite scores. The broad math composite score was not used for the discrepancy evaluation here as children can have MLD in math fluency or basic calculation skills, and the math composite score averages across all math subtests. It should be noted that this type of discrepancy approach does not adequately account for a child's overall strengths and weaknesses or instructional history. This approach did however feasibly allow for an evaluation of two distinct groups (MLD, LA), but future studies could improve the categorization of MLD using additional testing and gathering information from a child's school.

Future Studies

When evaluating mathematics ability in individuals, research studies have often evaluated differences between those with and without math deficits while performing certain working memory or math tasks. Few studies have evaluated resting-state paradigms, even though resting-state can be used to assess basal physiology of individuals, and the default-mode network (Greicius, Supekar, Menon, & Dougherty, 2009). Specifically, research suggests that activity in the delta wavelength are highly associated with the default-mode network (DMN) (Neuner et al., 2014). The DMN appears to show higher activity at rest, but less activity during tasks (Broyd et al., 2009). Results from this study suggest that children with MLD cognitive profiles showed reduced coherence in the delta wavelength. These results may provide evidence to suggest that those with MLD had reduced activation of the DMN network, particularly in comparison to those with no math-specific deficits. Hypotheses concerning beta-band oscillation also indicate reduced beta-activity at rest (found for the MLD and LA groups) may be associated reduced activation of the DMN and reduced top-down control during tasks (see Engel and Fries (2010)). However, previous DMN studies evaluated power while this study evaluated coherence. Future studies should investigate the associations between coherence and DMN across wavelengths, particularly in clinical groups, such as MLD or LDs. Additionally, future MLD intervention studies may consider targeting behaviors associated with the DMN including creativity and problem-solving (Kühn et al., 2014).

Conclusions

Not only did this study evaluate basal physiology through EEG connectivity, but it also uniquely looked at neurological profiles of children with MLD. Only a handful of studies have evaluated electrocortical signatures present in MLD (or low-achieving math ability), although similar research has been conducted for other neurodevelopmental disorders including dyslexia (Bosch-Bayard et al., 2020) and autism spectrum disorder (Coben et al., 2008). Additionally, the neurological research into LDs does not always consider evaluation of separate LD types (e.g., Jäncke et al. (2019)) due to arguments that neurologically, LDs present with a common-deficit, rather than specific deficits (e.g., Swanson (1987)).

The current study provided evidence that LDs have electrocortical signatures that can present as both domain-general and domain-specific. Generally, results from this study suggested that often, the control group showed increased coherence compared to the MLD and LA groups. In contrast, some areas in the beta band, and general left hemispheric delta coherence were associated with specific deficits in children with MLD, not seen in LA children. These results are similar to those in Jäncke et al. (2019), which noted unique electrocortical signatures in subtypes of learning disabilities with additional evidence of domain-general deficits.

Studying unique neurological profiles of types of LDs, including MLD, provides a way of linking neurological differences to academic profiles. Cognitive and academic tests used to evaluate LDs measure behavioral abilities as a proxy for neurological functioning. However, brain signatures of LDs evaluate brain functioning directly. Importantly, EEG coherence allows for a low-cost, non-invasive way of analyzing integrated cortical functioning. A greater understanding of neural disconnections present in LDs improves our current treatment and identification of LDs. The current study sought to evaluate resting-state brain coherence to determine basal physiology distinct in children with MLD compared to those without any academic deficits, and those with consistent, low-achieving abilities. Results suggest domain-specific deficits in the MLD group in left hemispheric delta coherence, which uniquely predict math ability, while differentiating MLD children from neurotypical controls. Results also demonstrated possible deficits in the default mode network in children with MLD, providing evidence for targeted interventions associated with the DMN including creativity and problem-solving, which should be further explored. MLD is a seldom studied neurodevelopmental disorder, and research that bridges the gap between behavioral characteristics and neural presentations provide theoretical utility for evaluating neurological functioning in these types of disabilities.

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