Investigating the Neural Heterogeneity of Developmental Dyscalculia

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Research Highlights

- Although the behavioural and cognitive heterogeneity of developmental dyscalculia (DD) has been investigated, its neural heterogeneity is under-researched.
- Case-control design empowers researchers to probe individual idiosyncrasies, transcending the constraints imposed by summary statistics derived from group comparisons.
- Graph theory metrics provided insights into the topological organization of the brain areas that underpins mathematical tasks, extending researchers' understandings of their brain activations.
- Three dyscalculia-at-risk cases not only demonstrated different behaviorual and neural profiles, but also showed similar neural deficits, providing insights into potential early biomarkers of DD.

Abstract

Developmental dyscalculia (DD) is a heterogenous mathematics learning difficulty, affecting approximately 4 to 7% of children. Despite its prevalence, our current understanding of the neural underpinnings of DD remains limited. This study probed DD's neural heterogeneity through case study comparative analyses between dyscalculia-at-risk children (DR) with non-dyscalculia-at-risk (NDR) children. Utilizing functional near-infrared spectroscopy, brain data from resting states and a mathematical computation task (addition) were acquired and analysed, using Graph theory assessing brain global and nodal network indicators. By comparing DR cases' network indicators and activation with NDR children's data, three DR cases demonstrated lower nodal efficiency, providing insights into potential early biomarkers of DD. Moreover, the thorough investigation of single cases can offer valuable insights for devising personalized interventions for children with DD.

Key words

Neural Heterogeneity, developmental dyscalculia, graph theory, case-control design, symbolic/nonsymbolic addition

Introduction

Developmental dyscalculia (DD) is defined as a particular learning disability with continuous challenges learning academically necessary math skills that cannot be explained by intellectual disability or educational deprivation (American Psychiatric Association, 2013). It affects approximately 4 to 7% of school-aged children (Butterworth, 2019). Children with DD were found to show poor performance in symbolic (e.g., Arabic digits) and/or nonsymbolic (e.g., dots arrays) arithmetic (Butterworth, 2010; Lu et al., 2021; Price & Ansari, 2013). With a limited studies that have been conducted in this area, its underlying mechanisms remain controversial (De Smedt et al., 2013). Recent studies have recognized that DD is a heterogeneous learning disorder (Rubinsten & Henik, 2009; Träff et al., 2017) as DD might be caused by numerosity-related deficits or/and other domain-general deficits (Träff et al., 2017). With increasing awareness of the heterogeneity of DD, researchers are attempting to extend our understandings of DD to its biological origins.

The heterogeneity of DD may manifest through discernible variations in the distinct biological substrates that underpin diverse cognitive deficits. As depicted in Figure 1, it is evident that DD subtype 1's impairment in numerical quantity processing may stem from deficits in the intraparietal sulcus (IPS), while the deficit in working memory could be attributed to impairments in the frontal area. Rubinsten and Henik (2009) further proposed subtype 2 and subtype 3, both with heterogeneous cognitive profiles but shared homogeneous neural deficits, either in the IPS or the fusiform gyrus. An explanatory hypothesis for the presence of multiple cognitive deficits in DD suggests a potential shared pathophysiology,

wherein a specific brain area could participate in diverse cognitive processes. For instance, the fusiform gyrus has been implicated in tasks related to number identification, visual-spatial information processing, and the establishment of accurate mappings between Arabic digits and corresponding semantic quantities (Rotshtein et al., 2007; Rubinsten & Henik, 2009; Wilkey & Price, 2019).

Results from neuroimaging studies (Ashkenazi et al., 2012; Berteletti et al., 2014; Davis et al., 2009; Kucian et al., 2006; Rosenberg-Lee et al., 2015) indicate that the heterogeneity of DD may manifest in either weaker or stronger activations in the brain cortices when DD children participated in arithmetic problems in comparison to TD children. Berteletti et al. (2014) found decreased activations in the left middle temporal to the superior temporal gyri when DD children were solving multiplication problems compared to their TD controls while Rosenberg-Lee et al. (2015) found increased activations in occipito-temporal cortex in DD children when they were solving addition and subtraction problems.

In view of the current controversial literature regarding arithmetic, a broad field in mathematics including multiplication, addition and subtraction, two hypotheses regarding DD's brain activation in arithmetic were proposed recently by Wang & Jamaludin (2023). With reference to TD children, DD children either showed weaker activation due to failure to recruit the brain network supporting arithmetic, especially the fronto-parietal network or displayed stronger activation due to over engagement of these networks. The two hypotheses may imply that the heterogeneity of DD originates from their aberrant recruitment of brain networks related to math tasks. For example, DD children may show the impaired functioning of the prefrontal cortex, which is related to one of the core hypotheses of DD's heterogeneity—working memory deficits (Rotzer et al., 2009). With regards to the parietal cortex, as its critical roles in both numerical and spatial processing, its aberrant activation may contribute to

difficulties in processing numbers and their spatial relationship (Kucian 2016; Kucian et al., 2006; Kaufmann et al., 2009).

Apart from observed activation differences from arithmetic tasks (Rapin, 2016), DD children may also show abnormal resting-state functional connectivity (RSFC) in large-scale brain networks. RSFC refers to the temporal correlation of spontaneous neural activations across brain regions without any cognitive load (Biswal et al., 1995). Jolles et al. (2016) examined the functional connectivity in children with DD. They found that DD children showed enhanced connectivity between the left and the right IPS, between the right IPS and the right superior frontal gyrus, and between the left IPS and the left frontal lobe. A negative relationship between hyperconnectivity of the IPS with the prefrontal and the parietal cortex and mathematics skill was also observed. However, it remains unclear the reasons behind hyperconnectivity within these networks. Adopting a Graph Theoretical framework, which analyses network structures and connectivity patterns, could provide valuable insights into the intricate organization of brain networks and their potential implications for mathematical competency. The excessive edges observed within these specific brain nodes could potentially account for this hyperconnectivity phenomenon (Hillary et al., 2014).

Within the existing literature, the majority of studies investigating the mechanisms of DD have predominantly employed whole-group analyses, comparing DD groups to non-DD groups. However, DD's complex heterogeneity, as depicted in Figure 1, becomes more intricate upon closer individual scrutiny. Contrasted with whole-group analyses, the case study methodology offers an intricate exploration of individual cases, providing a nuanced comprehension of the distinct attributes and experiences of dyscalculic individuals. This approach allows for the examination of specific cognitive, neural, and behavioural dimensions contributing to dyscalculia (Yin, 2018). For instance, Träff et al. (2017) conducted a case study

that observed a DD case exhibiting extensive cognitive impairments, extending beyond deficits solely related to magnitude/numerical quantities and attention/working memory. To quantitatively capture the heterogeneity of DD, an innovative design termed the case-controls design has gained traction, combining the advantages of single-case methodology and whole-group analysis. In this approach, a DD case is contrasted to a group of non-DD or typically developing (TD) children (Dinkel et al., 2013; Träff et al., 2017; Van Viersen et al., 2013). By doing so, it facilitates the establishment of a comprehensive and multi-dimensional taxonomy of DD.

To advance understandings of underlying neural mechanisms of DD, the current research adopted a single-case methodology to investigate brain activations during mathematical tasks and the architectural configurations of brain networks derived from graph theory during resting states (please see supplementary information for graph theory metrics' explanations).

Method

Participants

Sixty-four children in first grade (age: 6.17 – 8.1; $M_{age} = 7.08$; male = 37) were recruited across five primary schools. Informed written consent was obtained from the legal guardian of the children and all study protocols were approved by the Institutional Review Board of the Research Integrity and Ethics Office of local university. None of the participants had any other neurological disorders. Only complete and valid data collected from these children were included in the analysis. Ten children were excluded from the study because they met various exclusion criteria. Data from the remaining fifty-four participants were entered into the final analysis.

Measures

A comprehensive diagnosis of DD encompassing both domain-general and domain-specific assessment was conducted, including the Wechsler Individual Achievement Test, Third Edition (WIAT-III; Wechsler, 2009) and the Wechsler Intelligence Scale for Children, fourth edition, (WISC-V; Wechsler, 2003). The criteria for identifying individuals within the dyscalculia at risk (DR) category were satisfied when children achieved scores below 85 (equivalent to the 16th percentile) on either the Mathematics or Math Fluency subtest of the WIAT-III, and neither of the subtest scores surpassed 90. This criterion is informed by recommendations highlighted in Moeller et al. (2012)'s literature review and Iuculano et al. (2015)'s empirical study.

Procedure

Procedure for resting state

To elicit a condition analogous to the resting state, the research employed the freeplay paradigm introduced by Kim et al. (2020). Within this paradigm, children were afforded the opportunity to engage in unstructured play independently with basic toys (depicted in Figure 2) for a duration of eight minutes.

Procedure for the experimental task

The experimental protocol was designed to encompass one-digit symbolic and nonsymbolic addition tasks. The task paradigm drew inspiration from three prior neural studies concerning mathematics tasks of varying formats (Gu et al., 2017; Kucian et al., 2011; Venkatraman et al., 2005), with necessary modifications implemented based on the cognitive and developmental demands of the young participants in this study. The sequential progression of the experimental procedure is detailed in Figure 3. It was initiated with a thirty-second fixation phase aimed at establishing a baseline state, during which children were instructed to

maintain stillness and direct their gaze towards a cross depicted on the screen. Subsequently, a forty-two-second block dedicated to symbolic or non-symbolic addition tasks, encompassing a series of six trials, was presented to the participants. Within this block, children were required to identify the correct answers to a set of addition problems. This task block was succeeded by an eighteen-second rest period. Alternating runs of symbolic and non-symbolic addition tasks were conducted, with a total of four runs per task type (Park & Brannon, 2014). The sequence of presenting the symbolic and nonsymbolic blocks was counterbalanced across different participants. Every task block encompassed six individual trials, each lasting for a duration of seven seconds (refer to Figure 3 for an illustration of a symbolic trial and a nonsymbolic trial). Each trial initiation involved a one-second fixation image featuring a centrally located cross. Following this, a symbolic or nonsymbolic addition problem was presented on the screen for a period of five seconds. During this interval, participants were required to provide responses by pressing the "s" button if the correct answer was situated on the left side of the screen, and the "j" button if the correct answer was positioned on the right side of the screen. This response window was succeeded by a one-second inter-stimulus interval (ISI).

The operands for symbolic stimuli were Arabic numbers, while nonsymbolic stimuli were presented as dots similar to those on the face of a dice. For all questions, the operands were ranged from 1-5 and problems involving ties (such as 2+2=4) were not included (Venkatraman, 2005). For each addition problem, two answer alternatives within the range of 3 to 9 were provided. One alternative was the correct answer, while the other was designed to exhibit a distance effect (DE) of one or two units (Pica et al., 2004; Venkatraman, 2005). The assignment of the correct answer to the left or right side of the screen was randomized and balanced across all trial instances. To maintain variety and prevent repetition, the same mathematical problem was never reintroduced within the same task block. The sequence of problems and corresponding answer options were presented in a random fashion for each block.

The execution of the experimental paradigm was programmed using E-Prime (E-Prime, Psychology Software Tools Inc. Inc., Pittsburgh, PA).

Modality and equipment

In this study, neural data was recorded at 8.14 Hz using a continuous wave functional near infra-red spectroscopy system (NIRSport2, NIRx Medical Technologies LLC, Glen Head, NY, United States). Fifteen LED sources containing 760-nm and 850-nm laser light and fourteen detectors which comprise 39 channels were formed to cover the frontal and parietal areas to demonstrate oxy-haemoglobin (HbO) changes during freeplay and addition task. The layout of optodes is illustrated in Figure 4 based on the international 10-20 standard system.

Data Analysis

Resting-state data

The FC-NIRS software (Xu et al., 2015) was used to analyse the resting-state data, with two main procedures to be included: pre-processing and brain network construction and analysis. The pre-processing procedure comprised quality control, band-pass filters, motion detection and correction, and time selection. First, channels were excluded if the signal-to-noise ratio was less than 2 (Xu et al., 2015). Low-pass filter was set to 0.1 Hz and high-pass filter was set to 0.01 Hz, replicating standards reported in Paranawithan et al (2022). Motion artifacts were detected through calculating the moving standard deviation within a two-second sliding time window and corrected by Spline interpolation method (Brigadoi et al., 2014). Standard deviation values larger than five standard deviations away from the mean of the moving standard deviation were labelled as artifacts. To construct functional connectivity and brain network with stability, the analyses excluded the first minute of resting state data acquired and focused on the last seven-minute duration (Wang et al., 2017).

Brain network construction and analysis

In fNIRS studies, nodes are defined as channels and edges are defined as the functional connectivity between channels (Cai et al., 2019; Qi et al, 2021). Functional connectivity was calculated by performing Pearson correlation analyses between the time series of every pair of nodes for each participant (Wang et al., 2020). Accordingly, a 39 x 39 (channels) symmetric correlation matric was generated for each participant in this study. Subsequently, the Pearson's R-values were converted to normally distributed z-scores through the function $z' = 0.5*[\ln(1 + r) - \ln(1-r)]$ to construct a binary undirected graph (Price et al., 2018; Wang et al, 2018; Zhao et al., 2019). If the correlation value between two nodes equals or exceeds a given threshold, it was set to 1. Otherwise, it was set to 0. The threshold was determined by sparsity, which refers to the ratio of the number of actual edges and the maximum number of edges in a network. The sparsity values ranged from 0.1 to 0.5 with an interval of 0.01 (Xu et al., 2015).

Area under curve (AUC) was calculated for each network indicator to allow threshold-independent comparisons between different groups (Cai et al., 2019). The normalized clustering coefficient (Gamma) were computed as the ratio of clustering coefficient (Cp) of a real network and mean value of Cp of a randomized network. The normalized characteristic path length (Lambda) was computed as the ratio of characteristic path length (Lp) of a real network and mean value of Lp of a randomized network. 1000 matched random networks that have the same numbers of nodes and edges as the real brain network were set to calculate the mean normalized clustering coefficient and normalized characteristic path length.

Task data

The HomER-2 software was used to analyse the fNIRS task-based data (Huppert et al., 2009). First, the signal-to-noise ratio of the data was calculated through the coefficient of variation (CV) within the thirty-nine channels and within each block. Data points were omitted

from analysis if the coefficient of variation (CV) for each channel surpassed 15%, and if the CV for each block exceeded 10% for two wavelengths (Van Hedel et al., 2021). The motion artifact was detected by channel in HomER-2. This function found the data-points exceeding a threshold in change of amplitude (1) and a threshold in change of standard deviation (5) within a given period of time (0.5) and then marked those points from the beginning of the window to 1 second later as motion artifacts (Brigadoi et al., 2014). The detected motion artifacts were corrected through Spline interpolation method wherein the degree of Spline function was set to 0.99 as suggested in previous research (Cooper et al., 2012; Scholkmann et al., 2010). Only data between 0.01 and 0.03 Hz were retained for the subsequent steps (Niu et al., 2013). The optical density data was further converted to the concentrations of HbO based on the modified Beer–Lambert law (Delpy et al., 1988; Tak & Ye, 2014). The first five seconds of data within each block were discarded due to unstable fluctuations, resulting in the averaging of thirty-six seconds of data across different blocks.

Statistical analysis

Based on case-controls design, the software application "SINGLIMS_ES.exe," developed by Crawford et al (2010), was employed to conduct a comparative analysis of the distinctions in brain network configurations and activation patterns among each child exhibiting DR and the cohort of forty-five NDR children. Outcome measures include t-values, p-values and effect size (z_{cc}), which indicate an estimate of the average difference between a case's score and the score of a randomly chosen participant of the normative population (Van et al., 2013). To address the issue of multiple comparisons, false discovery rate correction (FDR) was employed during data analyses of comparing regional nodal characteristics across thirty-nine channels. Only outcomes that remained statistically significant after FDR adjustments were reported.

Results

Demographic information of DR and NDR groups

Out of the study's recruited participants comprising fifty-four individuals, a subset of nine children satisfied the criteria indicative of being dyscalculia-risk (DR: 6 boys; mean age = 7.12), while the remaining cohort of forty-five children were categorized as belonging to the non-dyscalculia-risk group (NDR: 21 boys; mean age = 7). A Bootstrap technique, commonly employed for random sampling from an original dataset (Chong & Choo, 2011; Hesterberg, 2011, p. 11), was implemented to ensure balanced sample sizes: nine individuals were randomly drawn from the initial pool of forty-five NDR children to form pairs matched with the nine children identified as DR. To ensure reliable t-test outcomes, this random sampling procedure was repeated 1000 times, a statistically robust approach (Xu et al., 2015), resulting in the computation of averaged T-values, P-values, and descriptive statistics using Matlab R2021a software. First, the findings revealed that, following 1000 iterations of comparisons with NDR children, those classified as DR consistently achieved significantly lower scores in Mathematics, Math Fluency, Total Reading, and Basic Reading. Conversely, no noteworthy distinctions between DR and NDR children were observed in terms of Working Memory and Full-Scale IQ indicators (see supplementary information Table 2).

Results of cognitive measures

Upon conducting the single case methodology analyses, it emerged that two cases exhibited notably divergent performance outcomes (see supplementary information Table 3). Specifically, in Case 1, there was a pronounced disparity in Verbal Comprehension and Math Fluency scores when compared to his NDR peers. Nonetheless, his scores in Working Memory and Mathematics exhibited marginal differences from those of his NDR counterparts (i.e., p = 0.05 ~ 0.06). Conversely, in Case 2, discernibly lower performance levels were observed in Fluid Reasoning, Mathematics, and Math Fluency as compared to his NDR counterparts.

Results of resting state

Global network properties. Employing single-case methodology, the investigation revealed significant differences between two cases selected from the set of nine DR cases and the cohort of NDR children, particularly in terms of global network properties. One of these cases was identified as Case 2, while the other case was labelled as Case 3. Case 2 exhibited a significant increase in clustering coefficient, heightened local efficiency, and an extended characteristic path length. On the other hand, Case 3 demonstrated a considerable decrease in global efficiency and a prolonged characteristic path length when compared to the NDR children, see supplementary information Table 4. A salient commonality between these significantly disparate cases is the extended characteristic path length, signifying the minimal number of edges between two nodes.

Nodal network properties. In relation to regional nodal degree properties, it is worth noting that solely two cases, drawn from the potential pool of nine cases, exhibited significantly distinct values in comparison to the forty-five typically developing children. Interestingly, both cases showcased notably reduced nodal degree in comparison to the typically developing children, although in distinct channels. Specifically, Case 1's decreased nodal degree was observed in channel 9, whereas Case 3 displayed this phenomenon in channel 10, see supplementary information Table 5.

For regional nodal efficiency property, among the three cases aforementioned, a consistent pattern of significantly reduced nodal efficiency in comparison to the NDR children was observed, albeit through distinct neural pathways (refer to supplementary information Table 6). Case 1 exhibited diminished nodal efficiency spanning from the remote left prefrontal area (channel 4), through the right frontal region (channel 9), extending to the right parietal region (channel 39). Conversely, Case 3 showed decreased nodal efficiency across two extensive neural domains, involving adjacent channels 1, 3 and 10 in the frontal area and

adjacent channels 34, 35 and 36 in the parietal area. In contrast, Case 2 displayed a discernibly different profile, manifesting reduced nodal efficiency exclusively within channel 27, an observation distinct from the broader reduction in nodal efficiency observed across multiple brain areas in the other cases.

Results of neuroimaging tasks

Channel-by-channel comparisons were conducted between the nine DR cases and the NDR children on the averaged oxyhaemoglobin concentration in both symbolic and nonsymbolic addition tasks. Only in the symbolic addition task, Case 2 showed significantly decreased activations in both channel 5 and channel 31, findings that maintained significance even after the application of FDR correction, see supplementary information Table 7. None of the DR cases showed aberrant activation in the nonsymbolic addition task.

For behavioural indicators, a significant deviation from the norm was observed in the responses of both Case 1 and Case 2. Specifically, Case 1 showcased impaired abilities across both symbolic and nonsymbolic tasks, where he not only exhibited significantly lower accuracy (with marginal significance in nonsymbolic addition) but also responded significantly faster than NDR children. In contrast, while Case 2's accuracy in both tasks was within the normal range, he nonetheless responded significantly faster than NDR children in both tasks (see supplementary information Table 8).

Discussion

This study juxtaposed the architectural configurations of brain networks and patterns of brain activation during arithmetic tasks exhibited by individuals with DR with those exhibited by NDR children. The comprehensive findings revealed that significant cases exhibited diverse constellations of deficits spanning from behavioural performance to the

neural indicators as summarized in Table 1 below. A detailed case-by-case examination is detailed as below.

Table 1

Summary of the Aberrant Neural Indicators and Cognitive Measures

Case ID	Global Properties	Nodal Properties	Task-based Brain Activation	Domain-general Abilities	Domain-specific Abilities
1, boy	Not Applicable	**Lower** nodal degree (ch4), **Lower** nodal efficiency (ch 4, 9, 39)	Not Applicable	Verbal comprehension, Working memory	Mathematics, math fluency, (non)symbolic accuracy and reaction time
2, boy	**Longer** characteristic path length, **higher** clustering coefficient and **higher** local efficiency	**Lower** nodal efficiency (ch27)	**Lower** activation in symbolic addition (ch5, 31)	Lower fluid reasoning,	Mathematics, math fluency, symbolic and nonsymbolic reaction time
3, girl	**Lower** global efficiency; **longer** characteristic path length;	**Lower** nodal degree (ch10); **Lower** nodal efficiency (ch1, 3, 10, 34, 35, 36).	Not Applicable	Not Applicable	Not Applicable

Case 1 - Inefficient Nodal Network Properties subtype

Case 1's brain activation on all channels in the two conditions was within the normal range. However, this Case showed significantly less efficient brain network properties than NDR children. Specifically, Case 1 exhibited diminished nodal degree in channel 4, coupled with reduced nodal efficiency in channels 4, 9, and 39. Despite these local discrepancies, his global network properties did not exhibit significant differences when compared to those of NDR children. Notably, channel 4 corresponds to the left inferior prefrontal gyrus (Brodmann 1909). The observed impairments in nodal degree and efficiency within this region might

signify an inherent dysfunction in Case 1's utilization of this area. The literature underscores the involvement of the left inferior prefrontal gyrus in a range of cognitive functions, including semantic processing (Devlin et al., 2003; Poldrack et al., 1999), language processing (Gabrieli et al., 1998; Zhang et al., 2004), and working memory (Baldo & Dronkers, 2006; Öztekin et al., 2009). Moreover, this brain region has demonstrated activation across diverse arithmetic tasks (Delazer et al., 2003; Kong et al., 2005; Menon, 2016). The observed reductions in nodal degree and efficiency in this region may reflect attenuated connections and diminished efficiency of information transfer with other brain regions. This scenario potentially contributes to compromised verbal comprehension, working memory capabilities, and mathematical performance, aligning with the presentation of Case 1. Notably, the evidence of a significantly weak positive correlation between nodal efficiency in this region and math fluency ($r = 0.31$, $p = 0.046$) and accuracy in nonsymbolic addition ($r = 0.329$, $p = 0.033$) further bolsters the notion that decreased nodal efficiency might exert a negative influence on mathematical performance.

An additional insightful result exhibited by Case 1 showed lower nodal efficiency on channel 4, 9, and 39. They are located in the left inferior prefrontal gyrus, right inferior prefrontal gyrus and fusiform gyrus respectively, comprising the front-parietal network which has been reported to support mathematical task processing (Emerson & Cantlon, 2012). Specifically, the inferior prefrontal gyrus is activated in working memory processing while the fusiform gyrus is activated in number form decoding and building visuo-spatial representation of numerical quantity (Fias et al., 2013; Menon et al., 2020). In the study conducted by Zhao et al. (2019) involving adults, a shift in connectivity patterns emerged following arithmetic training, transitioning from left parietal-right frontal to right parietal-left frontal regions. Remarkably, despite the precise nature of this connectivity shift, a strong and consistent correlation was detected among three brain regions: the left inferior prefrontal gyrus, the right

inferior prefrontal gyrus, and the fusiform gyrus, all within the frontal-parietal network. Based on such observations, it may suggest that the lower nodal efficiency among these identified areas may hinder information transfer efficiency and overall coordination within the frontal-parietal network during the execution of mathematical tasks.

Case 2 - Inefficient Brain Network Properties and Under-Activation subtype

Case 2's brain activations on channels 5 and 31 were significantly lower than NDR children. Channel 5 is located in the left inferior frontal gyrus (IFG) and channel 31 is located in the left intraparietal sulcus (IPS). The involvement of the left IFG in arithmetic has been discussed in Case 1 and the activation of the left IPS in arithmetic has been reported in studies of Bugden et al. (2012) and Houser et al. (2015).

Researchers have identified the left IPS as a pivotal region involved in tasks related to symbolic ordinal processing (Matejko et al., 2019), symbolic number processing (Vogel et al., 2017), and arithmetic processing (Artemenko et al., 2020). It is established that impairment to this region can contribute to dyscalculia (Ashkenazi et al., 2008). A matter of ongoing debate in the current literature pertains to the level of activation within these specific brain regions. While certain studies emphasize overactivation (Davis et al., 2009; Dinkel et al., 2013; McCaskey et al., 2018; Üstün et al., 2021), others underscore underactivation (Ashkenazi et al., 2012; Berteletti et al., 2014; Kucian et al., 2006). The notably reduced activation observed in Case 2's aforementioned brain areas aligns with the concept of underactivation. This finding suggests that Case 2 struggled to effectively engage these critical regions for successful arithmetic processing (Berteletti et al., 2014). A potential explanation for this perspective is that his challenges lay in utilizing these essential areas for efficient mental calculations, which could account for his notably quicker completion of the symbolic addition task. This expedited

completion might stem from his difficulty in engaging the necessary brain regions that are typically involved in the more time-intensive process of mental calculation.

In addition, Case 2 exhibited both a higher clustering coefficient and local efficiency, where a higher clustering coefficient indicates that more neighbouring nodes are connected to each other, thus correlating with a higher local efficiency. A correlation analysis between the clustering coefficient and the local efficiency on NDR participants indicated a significantly high positive relationship, $r = 0.851$, $p < 0.001$. It is also reasonable that Case 2 has both a higher clustering coefficient and higher local efficiency, which indicate that his brain network orient towards a cliquish (i.e., a pattern in which certain groups of brain regions tend to be more interconnected with each other than with regions outside of those groups) organization of the brain (Klados, et al., 2013).

Lastly, Case 2 displayed lower nodal efficiency on channel 27, which is located in the right IPS. The observed decrease in nodal efficiency within the right IPS potentially underscores the reduced activations witnessed in mathematics tasks. Scholars have proposed that the frontal-parietal network responsible for mathematics skills finds its foundation in the IPS (Iuculano & Menon, 2018; Jolles et al., 2016; Menon & Chang, 2021). Should its efficiency in processing information with other distant brain regions be compromised, it could lead to an inability to effectively orchestrate interactions between the inferior frontal gyrus and fusiform gyrus during mathematical tasks.

Case 3-Inefficient Brain Network Properties subtype

In the case of Case 3, the obtained data illuminated impairments within her brain network properties. Specifically, she showed longer characteristic path length and lower global efficiency in global network properties. It is worth noting that the global efficiency and characteristic path length are inversely related, substantiated by a correlation analysis

encompassing all NDR participants (r = -0.908, p < 0.001). Thus, the observation of longer characteristic path length coupled with lower global efficiency in Case 3 aligns with the theoretical underpinnings of the reverse relationship between these two global network metrics.

Moreover, the observed reduction in global efficiency in her case aligns with the prior investigations encompassing cohorts with ADHD (Wang et al., 2020), athletes (Pi et al., 2019), and research exploring differing complexity levels of mathematical tasks (Klados et al., 2013). Taken together, these studies consistently suggest that individuals with diminished global efficiency tend to display less optimal brain functioning.

Conclusion

The primary objective of this research was to delve into the neural underpinnings of DR's heterogeneity. Despite the distinct neural profiles observed in the three cases, a shared characteristic emerged: diminished nodal efficiency in comparison to NDR children. This shared trend is visually depicted in Figure 5, illustrating the deviant brain network properties and activation patterns of these cases. Collectively, these findings highlight the central importance of enhanced nodal efficiency within key regions such as the IFG and IPS, which play crucial roles in supporting mathematical competency.

The present investigation accentuates the critical relevance of the brain's structural arrangement in facilitating mathematical abilities, surpassing the confines of mere brain activation during mathematical tasks. Despite the heterogeneity typically associated with DD, the three identified cases consistently exhibited lower nodal efficiency in their brain networks, potentially affecting their mathematical performance. Acknowledging the preliminary nature of the "brain norm" established using the NDR children's data, it is anticipated that future neuroimaging research with larger sample sizes will establish a more comprehensive

"developmental brain norm." This norm could potentially aid in the early detection of aberrant brain indicators in children with DD, with an aim towards facilitating timely interventions.

Figure 1. Framework for the origins of DD and their underlying neurocognitive deficits

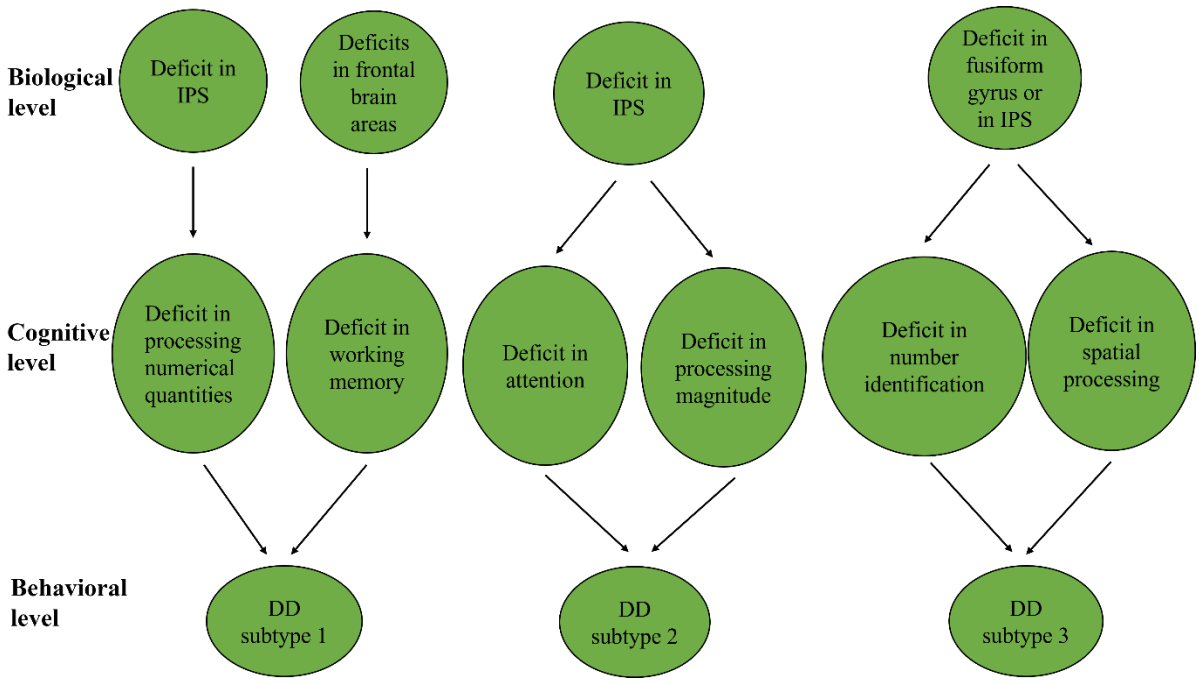


Figure 2

Toys for Freeplay

Figure 3

Semantic Flow of Experimental Procedure and A Non/Symbolic Addition Trial

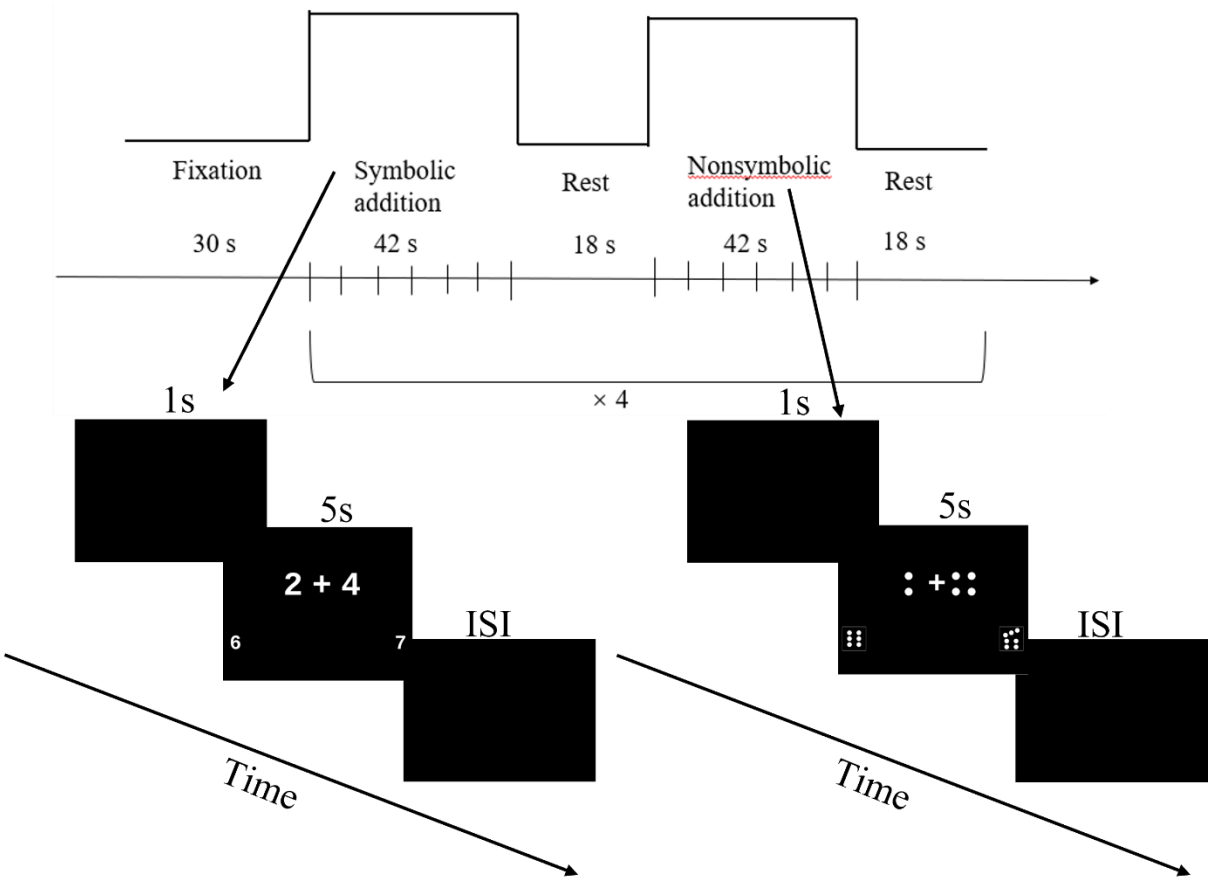
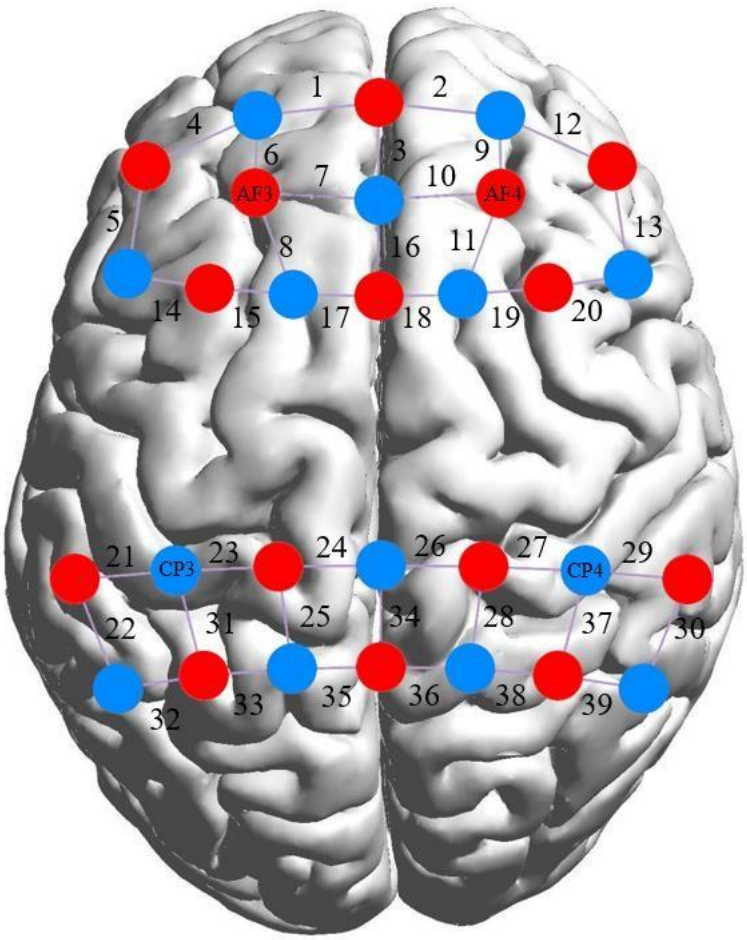


Figure 4

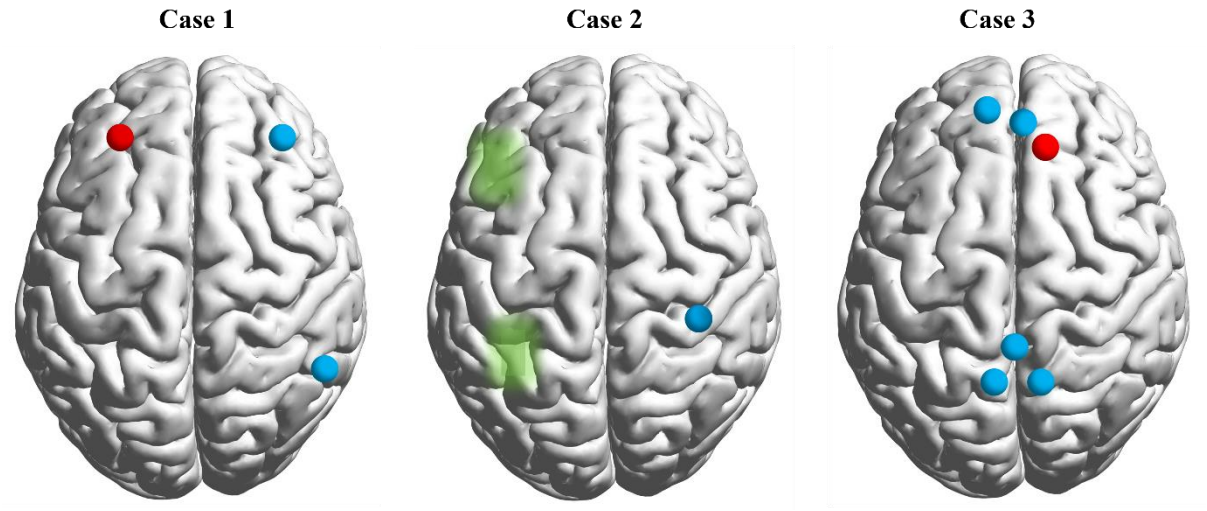
Placement of fNIRS Probes for Freeplay and Addition Task



dd

Figure 5

Regional Network Properties and Activation of Three Cases



Note: red: decreased nodal degree and efficiency; blue: decreased nodal efficiency; green: decreased brain activation.

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