Medical Sciences

Relationships between Presence or Absence of ADHD and fMRI Connectivity Writing Tasks in Children with Dysgraphia

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The relationship between presence or absence of Attention Deficit Hyperactivity Disorder (ADHD) in persisting developmental dysgraphia (impaired handwriting) and brain connectivity during writing tasks was investigated. Thirteen participants (6 males, 1 female with ADHD; 4 males, 2 females without ADHD) in upper elementary or middle school grades performed four fMRI writing tasks-two cognitive (mind wandering and planning to compose) and two transcription (handwriting and spelling). Presence or absence of ADHD was correlated with brain connectivity on all four fMRI writing tasks during scanning, rather than just on the fMRI handwriting task as predicted based on prior research. However, the nature of the fMRI functional connectivity (from which of four seeds with which of eight brain regions) for the four fMRI writing tasks varied as a function of presence or absence of ADHD. The significance of these findings is discussed for both understanding the invisible biological bases of co-occurring ADHD and persisting developmental dysgraphia and teaching students with developmental dysgraphia and co-occurring ADHD.

Developmental dysgraphia | handwriting disability | Attention Deficit Hyperactivity Disorder (ADHD) | fRMI connectivity on writing tasks | transcription in writing | translation in writing

Children and youth (ages 9 to 14) diagnosed with developmental dysgraphia (persisting impaired handwriting in otherwise typically developing learner) with and without co-occurring attention deficit hyperactivity disorder (ADHD) participated in a brain imaging study. The Mayo epidemiological studies refer to specific learning disabilities in written language (SLDs-WL) including dysgraphia as the “forgotten learning disability” (1), which may co-occur with attention deficit hyperactivity disorder (ADHD) or occur without it (2). Because SLDs-WL that impair handwriting may also impair other writing skills like spelling and may also co-occur with reading, oral language, and math specific learning disabilities or ADHD, the Mayo studies estimate that about one in five school age children and youth may experience writing difficulties at some time during their schooling (3).

Relatively fewer brain imaging studies have focused on writing disabilities than on reading disabilities, especially in developing children and youth who struggle in learning specific writing skills. Relatively more brain imaging studies of writing have investigated acquired dysgraphia also known as agraphia in which individuals (usually adults) lose previously acquired handwriting and related writing skills. For a representative study of acquired dysgraphia/agraphia in adults, see (4). However, for a representative study of typical handwriting and spelling skills in young adults, see (5). A few brain imaging studies have focused on developmental dysgraphia in children and youth who struggle to acquire handwriting and related writing skills. For example, one found evidence for differences in the left fusiform gyrus associated with visible language in written letter forms and written words for familiar letters but differences in both motor regions and fusiform regions for novel letters for which letter forms in memory and letter formation by hand are being learned (6).

Another line of research has focused on the relationship between handwriting and attention deficit hyperactivity disorder (ADHD). Nearly two decades ago Barkley pointed out that written language disorders often co-occur with ADHD (7). On the one hand, some research has shown that problems associated with movement control and movement sensation in handwriting are related to learning disabilities involving written language and ADHD (8). One behavioral neuropsychological study found that sixth graders with and without ADHD differed in motor skills for writing letters alone or in the context of written word spellings in Hebrew (9). On the other hand, when children in grades 4 to 9 were identified on the basis of presence or absence of persisting dysgraphia (impaired handwriting), without consideration as to whether there was co-occurring ADHD, it turned out that presence or absence of co-occurring ADHD varied and was correlated with impaired handwriting in English (10).

Thus, the goal of the current study was to study a sample of children and youth who had been diagnosed with dysgraphia and investigate whether presence or absence of co-occurring ADHD did or did not correlate with fMRI functional connectivity on four writing tasks during scanning. The first task was actually a resting condition which has been shown to assess mind wandering (11) which is associated with the creative flow of ideas of the writer (12). The second task was writing a letter from memory (13, 14). The third task was creating word-specific spellings by adding a missing letter. This task requires creating lexical spellings with specific word meanings and pronunciations (15, 16, 17) by adding a single letter. For a comparable behavioral task, see the *Letter Choice subtest* on the *Test of Orthographic Competence, TOC* (18). The fourth task was strategic planning before composing (19).

The research aim of this study was, therefore, to evaluate whether, in a sample of middle childhood and early adolescents with persisting dysgraphia, about half of whom also had a diagnosis of ADHD and half did not, co-occurring ADHD was or was not related to their handwriting or other writing tasks performed during brain scanning. The hypothesis tested was that magnitude of fMRI connectivity would be correlated with ADHD diagnosis only for the fMRI handwriting task and not for the spelling task, resting condition (mind wandering), or planning task during scanning for composing outside the scanner.

Magnitude of fMRI connectivity for each fMRI writing task was assessed from four seed points: precuneus, which human connectome brain research has shown is in the rich club of neural networks and may participate in multiple networks and thus brain

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functions (20, 21); and three identified in a meta-analyses of brain imaging studies for written words—left occipital temporal, left supramarginal gyrus, and left inferior frontal gyrus (22). Each was assessed for magnitude of connectivity with the same eight brain regions as explained in the imaging methods.

Method

Participants

Children in grades 4 to 9 who were right handed and did not wear metal that could not be removed completed comprehensive diagnostic assessment using evidence-based guidelines for diagnosing dysgraphia described in (23). These procedures include normed measures as well as parent interviews and questionnaires to rule out other neurological or neurogenetic conditions and to document past and current persisting problems in handwriting despite intervention or absence of past or current handwriting problems. Criteria for dysgraphia, based on prior research, were below -2/3 SD on two or more handwriting measures and history of persisting handwriting problems despite intervention. Of the 13 who had usable brain imaging data and met the research criteria for dysgraphia, 7 (6 males) had previously been diagnosed with ADHD by a qualified practitioner in the community, and 6 (4 males) had not, as determined by written evaluation reports parents shared with the research team with documentation in students' individual educational plans. All parents had completed postsecondary education and the majority of the parents reported that their children were of European American ethnicity. Of note, although some of the other specific learning disabilities in written language (SLDs-WL) studied also had co-occurring ADHD, the relative incidence of co-occurring ADHD was very low in dyslexia and oral and written language learning disability (OWL LD), and only occurred with sufficient frequency to investigate in those with dysgraphia.

Imaging Methods

Tasks during scanning. Each participant received training in three tasks (all but planning) outside the scanner and had to show he or she could lie still while resting and not performing a task and achieve 90% accuracy on the handwriting and spelling tasks before entering the scanner. Participants were told that after performing these tasks in the scanner they would be given a topic and asked to plan a composition which they would write after leaving the scanner, but they did not practice planning. The four conditions during scanning were in this order as follows: (a) no experimenter-defined task (RESTING STATE), (b) production of the letter that follows a visually displayed letter in alphabet order (ALPHABET WRITING task), (c) production of letter in the blank in a visually displayed letter string to create a correctly spelled word (SPELLING WRITING task), and (d) planning a composition on an experimenter-provided topic at the end of the scanning session (PLANNING task). During the fMRI writing tasks, a mirror system enabled the participant in the scanner to see the instructions and task on a screen. The tasks and writing pad recordings were all programmed, timed, and coordinated with the scanner triggers using E-prime and in-house LabView software.

The resting condition lasted for 6 min 14 s. There was no experimenter-defined writing task to perform and participants were free to self-generate their own thoughts.

The resting condition was followed by 6 s of instruction for the alphabet task. The alphabet writing task lasted for 4 min and was self-paced. After the visual display of the first letter, the child wrote the next letter in the alphabet. When the child lifted the pen off the tablet, visual display 2 appeared and the process repeated for 4 min.

Next there were 6 s of instruction for spelling followed by the spelling task that lasted for 4 min and was self-paced. After visual display 1, the child wrote a letter in the blank to complete the word spelling. When the child lifted the pen off the tablet, visual display 2 appeared and the process repeated for 4 min. The response requirement was the same for the alphabet and spelling tasks—to form one letter using the MRI-compatible stylus.

Next, instructions for planning appeared for the first time and stayed on the screen for the whole 4 min, while the child just generated ideas and planned a composition on the topic provided, but did no writing until leaving the scanner. Aural instructions for the last task were as follows: "*After you leave the scanner you will write about 'Astronauts Writing While Exploring Outer Space'. Please start thinking in the inner space of your mind now about the ideas you will write about.* Identical instructions readable by the children lying prone in the scanner were also displayed visually.

Imaging Procedures

Functional magnetic resonance imaging (fMRI) connectivity scans on a Philips 3 T Achieva scanner (release 3.2.2 with the 32-channel head coil) were used to obtain measures of functional connectivity. The following fMRI series were scanned: fMRI scan with echo-planar gradient echo pulse sequence (single shot): TR/TE 2000/25 ms; Field of view 240 × 240 × 99 mm; slice orientation transverse, acquisition voxel size 3.0 × 3.08 × 3.0 mm; acquisition matrix 80 × 80 × 33; slice thickness 3.0, 13:08 min/s. Functional images were corrected for motion using FSL MCFLIRT (24), and then high-pass filtered at sigma = 20.83. Motion scores (as given in the MCFLIRT report) were computed for each participant and average motion score (mean absolute displacement) was 1.50 ± 1.23 mm for dysgraphia group. Spikes were identified and removed using the default parameters in AFNI's 3dDespike. Slice-timing correction was applied with FSL's slicetimer; and spatial smoothing was performed using a 3D Gaussian kernel with FWHM = 4.0 mm. Time series motion parameters and the mean signal for eroded (1 mm in 3D) masks of the lateral ventricles and white matter (derived from running FreeSurfer3s recon- all on the T1-weighted image) were analyzed.

Co-registration of functional images to the T1 image was performed using boundary based registration based on a white matter segmentation of the T1 image through epi_reg in FSL. The MPRAGE structural scan was segmented using FreeSurfer software; white matter regressors were used to remove unwanted physiological components. Group maps for fMRI functional connectivity were generated for each of the 4 tasks/conditions with eight brain regions from each of 4 different seed points (in the left precuneus cortex PCC, in the left temporooicipital cortex TOC, in the left supramarginal gyrus SMG, and in the left inferior frontal gyrus, IFG Broca's area (based on the Rich Club network and a meta-analysis for written word production, see introduction). These eight regions included four associated with written language processing (Broca's, fusiform, supramarginal, and fusiform 2), one associated with executive functions (cingulate), one associated with attention (thalamus), one associated with working memory (hippocampus), and one associated with emotions such as fear and anxiety (amygdala).

fMRI time-series were averaged within regions of interest (ROIs) formed from a 15 mm sphere centered at each seed. The averaged time-series at each ROI was correlated with every voxel throughout the brain to produce functional connectivity correlation maps, converted to z-statistics using the Fisher transformation.

Individual functional connectivity values from all four seed points were extracted from the coregistered connectivity maps from the following brain region of interests (ROI) (numbers do not refer to references): 1) broca_IFG (70 67 39, x, y, z, voxel coordinates from 2 mm MNI space); 2) fusiform (29 38 24); 3) supramarginal_gyrus (69 42 46); 4) fusiform2 (59 22 29); 5) cingulate (47 61 57); 6) thalamus (51 57 41); 7) hippocampus (56 56 26); and 8) amygdala (57 62 26). Only functional connectivity values found to be statistically significant (using FSL's randomise for group analysis, *which corrects for multiple voxels comparisons*, were used in correlation analyses for presence or absence of ADHD diagnosis. An additional high threshold of 6.0 was used in the group tscore maps produced by randomise in order to further prevent false positives.

Results

Contrary to the tested hypothesis that presence or absence of ADHD diagnosis would be correlated only with the fMRI handwriting task, it was correlated with each of the four fMRI connectivity writing tasks. However, the correlations varied as to which of the 8 brain regions was significantly connected with which of the 4 seeds for each of the four fMRI writing tasks. Note that all the following correlations were positive, which indicates that, for the children with dysgraphia, presence of ADHD tended to be associated with greater magnitude of connectivity from a particular seed point with another brain region more so than absence of ADHD. Greater magnitude of fMRI connectivity may be an indicator of less efficiency, as proposed to explain why typically developing writers had greater white matter integrity than children with dysgraphia who had greater fMRI functional connectivity than the typically developing writers (25). The rationale was that lower white matter integrity was compensated for with greater functional connectivity, but the resulting functional writing system was less efficient.

Cognitive writing tasks. ***For resting*** (mind wandering), these correlations were significant: left occipital temporal with left inferior frontal (Broca's area), r=.353, p=.032, and with fusiform 2, r=.626, p=.001; left supramarginal with fusiform 2, r=.582, p=.001, and with thalamus, r=.451, p=.005; left precuneus with fusiform 2, r=.355, p=.043; and Broca's area with thalamus, r=.457, p=.004. Significant correlations also occurred ***for planning*** (strategic thinking before composing): left occipital temporal with Broca's, r=.345, p=.036; left supramarginal with Broca's area, r=.365, p=.026; and Broca's area with amygdala, r=.448, p=.005.

Transcription writing tasks. Correlations were significant for both the handwriting and spelling tasks. ***For alphabet writing***, left occipital temporal with thalamus, r=.415, p=.011 and with amygdala, r=.352, p=.03; left supramarginal with Broca's, r=.510, p=.001, with thalamus, r=.346, p=.036, and with amygdala, r=.422, p=.009; left precuneus with fusiform 2, r=.369, p=.025, and with amygdala, r=.361, p=.029; and Broca's with fusiform 2, r=.434, p=.007. ***For spelling***, left occipital temporal with Broca's, r=.399, p=.04, and with amygdala, r=.342, p=.038; left supramarginal, with Broca's area, r=.608, p.001; left precuneus with Broca's, r=.448, p=.005; and Broca's with fusiform, r=.537, p=.041, with thalamus, r=.448, p=.005, and with amygdala, r=.349, p=.034.

Summary. Even if, to control for multiple comparisons, p was set to $\leq$ .001, at least one connection was significantly related to presence or absence of ADHD in the handwriting, spelling, and mind wandering (flow) task; or if p < .005 close to the .001 criterion for planning to compose. That is, ADHD was related to both the transcription and cognitive tasks.

Discussion

Presence of ADHD in those with dysgraphia was associated with greater magnitude of fMRI functional connectivity for all four writing tasks during fMRI but from varying seeds: altogether fifteen seed-region connections for transcription (handwriting and spelling) skills, and nine seed-region connections for cognition (mind wandering during resting and strategic planning before composing) skills. These findings are consistent with co-occurrence of ADHD and poor handwriting observed by clinicians and reported in prior research (7, 8, 9, 10). Yet the current results also show that ADHD is related to other writing skills as well—not just handwriting.

The current findings for students with diagnosed dysgraphia but varying in presence or absence of co-occurring ADHD add to prior findings of research on ADHD and writing problems. When dysgraphia based on impaired handwriting is diagnosed first, and co-occurring ADHD is variable, ADHD affects multiple transcription and/or translation skills in writing, as shown in the current brain imaging study. When ADHD is diagnosed first and co-occurring handwriting and other co-occurring written language problems are variable, only the motor processes of handwriting were affected in another study (9). To address these complex interrelationships, future research could compare a sample for whom the primary diagnosis is dysgraphia and ADHD freely varies as to whether it is or is not a co-occurring diagnosis and a sample for whom ADHD is the primary diagnosis and handwriting or other written language disorders freely vary as to whether they are co-occurring diagnoses. These comparisons might be made for (a) developmental dysgraphia, which is a struggle in learning to write, and acquired dysgraphia, which is loss of previously acquired writing ability through various kinds of neurological insults; (b) inattentive, hyperactive, and combined subtypes of ADHD; and (c) children, adolescents, young adults, and older adults. Hopefully this brief research article based on a relatively small sample will stimulate such research in the future.

The significant association between ADHD and internal brain processes while performing fMRI writing tasks observed in the current study does, however, extend prior work showing dysgraphia is an invisible disability (26). Dysgraphia with co-occurring ADHD may be an even more impairing invisible disability than dysgraphia alone. Likewise, researchers in the field of cognitive writing research are showing that for typically developing writers on-line processing prior to written production, which is not directly visible, plays an important role in written composing (27, 28, 29, 30). Asking students with dysgraphia to perform contrasting kinds of writing tasks during brain scanning is another way to assess such on-line processing prior to written production of compositions.

Future research should also compare students with ADHD who do and do not have dysgraphia or with dysgraphia who do and do not have ADHD on the resting condition in particular. Both individuals with ADHD and dysgraphia and individuals with ADHD without dysgraphia may struggle with the self-regulation of their own internal thought processes without the scaffolding provided by human teachers. At the same time those with ADHD may be very creative thinkers. Although resting has generally been regarded as a state of mind wandering in the default mode (11), more recently resting has been re-conceptualized as activating the large interconnected default network, which interacts with executive control systems, to support internally guided, self-generated thought (31, 32). Although the topic for planning the composition was not provided in the current study until near the end of the scanning session, the participants may have engaged this default network during the resting condition and again during the planning condition. Analyses of the compositions written outside the scanner after planning during scanning in another sample identified a multitude of genres reflecting the creativity and knowledge transforming not just knowledge telling of the developing writers (authors, submitted). The point is that resting may not just capture mindless wandering but rather mindful self-guided creative thinking independent of the external world. Also see Shah and colleagues (33) for the role of brain in supporting creative thought and writing.

The goal of assessment is often to develop individualized treatment plans, which are referred to as Individual Education Plans (IEPs) in US schools for those who qualify for special education services K to 12. Much has been learned about effective, evidence-based instructional approaches for teaching struggling writers (34) that can inform such treatment plans. However, the current research suggests that presence of co-occurring ADHD in students with dysgraphia should also inform those treatment plans. For those with dysgraphia with co-occurring ADHD, individual education plans should include evidence-based practices for teaching them to pay attention during transcription and translation.

Approaches that were used effectively to teach students to pay attention while writing during programmatic research with students in elementary and middle school include the following (26). To teach students to pay attention to sequential strokes while forming letters during handwriting, ask them to study numbered arrow cues for order of stroke formation before writing letters. To help them pay attention to sequential letters in words while spelling ask them to write sequential graphemes (1 to 2 letters that stand for phoneme sounds) in contrasting, alternating colors. To help them pay attention during idea generation ask them to think aloud before composing. To help them pay attention during translation teach them to make visual diagrams with genre-specific plans before composing to guide their translation during composing.

To summarize, all students including those with specific learning disabilities in written language may benefit from instructional strategies for paying attention while forming letters, spelling words, generating ideas, and planning to compose—that is during both transcription and translation (35). However, for those with dysgraphia and co-occurring ADHD it is essential that such instruction should also include explicit strategies for paying attention while transcribing (26) and translating (35) as shown is relevant in the current study.

In conclusion, this study shows the promise of integrating brain research on writing and clinical assessment of ADHD to assess internal processing for writing tasks often assessed only at the behavioral level. The internal processes provide clues to why those with diagnosed dysgraphia and co-occurring ADHD may struggle so in transcription and translation tasks. “Invisible disabilities” like dysgraphia, especially if ADHD co-occurs, inside the mental universe, unlike visible ones in the external universe involving directly observable impairment in sensory and motor systems, can interfere with writing acquisition in otherwise typically developing learners.

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