Neuroimaging and Occupational Therapy: Bridging the Gap to Advance Rehabilitation in Developmental Coordination Disorder

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To cite this article: Meisan Brown-Lum & Jill G. Zwicker (2017): Neuroimaging and Occupational Therapy: Bridging the Gap to Advance Rehabilitation in Developmental Coordination Disorder, Journal of Motor Behavior, DOI: 10.1080/00222895.2016.1271295

To link to this article: http://dx.doi.org/10.1080/00222895.2016.1271295

Published online: 06 Feb 2017.

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Neuroimaging and Occupational Therapy: Bridging the Gap to Advance Rehabilitation in Developmental Coordination Disorder

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ABSTRACT. Developmental coordination disorder (DCD) is a neurodevelopmental disorder characterized by poor motor skills that interfere with a child’s ability to perform everyday activities. Little is known about the neural mechanisms that implicate DCD, making it difficult to understand why children with DCD struggle to learn motor skills and selecting the best intervention to optimize function. Neuroimaging studies that utilize magnetic resonance imaging techniques have the capacity to play a critical role in helping to guide clinicians to optimize functional outcomes of children with DCD. The authors’ goal is to describe how neuroimaging research can be applied to occupational therapy and rehabilitation sciences by highlighting projects that are at the forefront of the field and elucidate future directions.

Keywords: developmental coordination disorder, magnetic resonance imaging, occupational therapy, rehabilitation

A significant number of children in North America (5–6%) have a neurodevelopmental disorder called developmental coordination disorder (DCD; American Psychiatric Association, 2013), but the reported prevalence in other countries ranges from a low of 1.8–3% in the United Kingdom (Lingham, Hunt, Golding, Jongmnas, & Edmond, 2009) to a high of 19% in Greece (Tsiotra et al., 2006). At the core of DCD is difficulty in the acquisition and execution of motor skills that significantly interferes with activities of daily living, school, work, leisure, and play (American Psychiatric Association, 2013). Similar to children with other types of developmental disabilities, children with DCD tend not to outgrow their disorder (Cantell, Smyth, & Ahonen, 2003; Cousins & Smyth, 2003; Hellgren, Gillberg, Gillberg, & Enerskog, 1993). In addition to motor difficulties, children with DCD may develop a host of emotional and psychosocial issues, including low self-esteem, anxiety, and depression (Zwicker, Harris, & Klassen, 2013). Despite its prevalence, little is known about the cause of DCD and how it develops, making it difficult to understand why children with DCD struggle to learn motor skills and to determine the best intervention to optimize function. Advances in neuroimaging techniques over the last 10 years have made it possible to study the developing human brain, its mechanisms and pathways, which together have the potential to inform rehabilitation intervention for children with DCD. Research in this field has the capacity to play a critical role in helping to guide clinicians to optimize functional outcomes of children with DCD using evidence-based rehabilitation interventions. Our goal in this article was to bridge occupational therapy, rehabilitation sciences, and neuroimaging research. In the present article, we start by discussing the basic science of brain imaging techniques to help rehabilitation practitioners gain a better understanding of how to interpret imaging research and its capacity to inform clinical practice. Then, we highlight some current research that has begun to elucidate the neural correlates of motor impairment in children with DCD and how we think that neuroimaging can advance rehabilitation interventions for these children. Finally, we will discuss some limitations of magnetic resonance imaging (MRI) research and conclude with future directions in this field.

NEUROIMAGING RESEARCH

An important application of neuroimaging research in rehabilitation sciences is to build our knowledge of the neural correlates associated with DCD and to help identify rehabilitation interventions that promote motor learning. Essential to our understanding of atypical brain development in children with DCD is the ability to quantify imaging data safely and reliably, as well as to relate these data to behavioral outcomes associated with intervention. Advanced MRI techniques, such as functional MRI (fMRI) and diffusion tensor imaging (DTI), have enabled investigation into the relationship between brain structure, microstructure, connective pathways, and behavioral outcomes in both healthy and impaired pediatric populations (Dubois et al., 2014). In addition to advances in imaging techniques, there have also been innovative approaches to analyze imaging data, such as repeating scans over time and advances in software packages to interpret the data, which together have allowed for novel inferences that will help facilitate a greater understanding of brain development in children with DCD. In recent years, several neuroimaging studies conducted in children with DCD have begun to elucidate behavioral theories with associated brain regions and pathways that differ in children with DCD (for a detailed review, see Brown-Lum & Zwicker, 2015). In the sections that follow, we briefly review MRI and highlight clinical implications of selected brain

Correspondence address: Jill G. Zwicker, BC Children’s Hospital Research Institute, K3-180, 4480 Oak Street, Vancouver, BC, Canada, V6H 3V4. E-mail: jill.zwicker@ubc.ca
imaging studies that have been conducted about DCD and other neuromuscular disorders as examples of the contribution of neuroimaging research to advance rehabilitation sciences and clinical care.

WHAT IS MRI?

MRI uses strong magnetic fields and radio waves to create detailed images of biological tissues noninvasively and without the use of radiation. When inside an MRI scanner, the magnetic field temporarily realigns the hydrogen atoms in the body. Radio waves cause these aligned atoms to produce signals, which are used to create images. Different images can be obtained to characterize brain structure and function. For example, T1 images are commonly used to examine brain anatomy; these images distinguish gray matter from white matter (Ugurbil et al., 1999). T2 images also differentiate brain tissue, but are well suited to detect demyelination, inflammation, and subtle white matter changes (Barkovich & Raybaud, 2011). A specific T2-weighted scan, T2*, is used for fMRI, which provides an indirect measure of brain activity. DTI measures water diffusion, which can provide detailed information about brain microstructure. For a summary of MRI techniques and their respective strengths and limitations, see Table 1. In this article, we discuss in greater depth two MRI techniques most commonly reported in DCD literature: fMRI and DTI.

CLINICAL IMPLICATIONS OF FMRI

An area of growing interest in DCD is the use of fMRI. fMRI is an imaging technique that indirectly measures neural activity and generates a functional map of the brain. T2*-sensitive sequences form the basis for blood oxygen level-dependent (BOLD) imaging, which is the standard technique used to generate images in fMRI studies. It is most relevant to detecting regional changes or differences in cerebral blood flow as an indirect measure of regional activity (Chavhan, Babyn, Thomas, Shroff, & Haacke, 2009). In response to a neural activity, an increase in oxygenated hemoglobin flows into the capillaries of the brain with a corresponding decrease in the amount of deoxygenated hemoglobin (Mattay & Weinberger, 1999). Research in this area over the last decade has established that the BOLD signal is an effective method that indirectly reflects neural activity (Chavhan, Babyn, Thomas, Shroff, & Haacke, 2009; Heeger & Ress 2002; Kimberly & Lewis, 2007). Current research suggests that children with DCD activate different brain regions (see Table 2 for details) compared to typically developing children to perform behavioral tasks such as finger tapping and visual-motor tracing tasks (Debrabant et al., 2013; Kashiwagi et al., 2009; Querne et al., 2008; Reynolds et al., 2015; Zwicker et al., 2011). Although brain differences may be the result of the different tasks used across studies, accumulating evidence in recent years show that children with DCD are neurobiologically different from typically developing children.

<table>
<thead>
<tr>
<th>Neuroimaging Modality</th>
<th>Description of the modality</th>
<th>Strength(s) of the modality</th>
<th>Limitation(s) of the modality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Structural MRI (T1 images)</td>
<td>Reveals information about the structure of the brain. In T1 weighted images, white matter is brighter than gray matter and CSF appears dark.</td>
<td>Reveals information about brain anatomy.</td>
<td>Does not provide information about brain activity; is sensitive to small movement and noise created by the scanner.</td>
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<tr>
<td>fMRI</td>
<td>Measures brain activity associated with a cognitive task and responses to the glucose/oxygen utilization as a result of increase blood flow.</td>
<td>Good spatial resolution and can provide information about neural activity that can be linked to behavior.</td>
<td>It is an indirect measure of brain activity. It does not provide information about the source of the activation (cause) or direction of the activity.</td>
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<tr>
<td>fcMRI</td>
<td>Functional connectivity reveals information about the patterns of communication among distinct brain regions.</td>
<td>Correlated regions imply that they interact as a network.</td>
<td>fcMRI does not tell us the direction or causality of the interaction.</td>
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<tr>
<td>DTI</td>
<td>Measures water diffusion in tissue to map and characterize the magnitude, the degree of anisotropy, and the orientation of diffusion anisotropy as indirect indices of tissue microstructure.</td>
<td>Is sensitive to water diffusion behavior in tissue that provides an indirect measure of neuropathology and tissue microstructure.</td>
<td>Is sensitive to image noise and artifacts created by the scanner. Does not distinguish regions of crossing fibers that can lead to challenges in the interpretation of DTI data.</td>
</tr>
</tbody>
</table>

Note: CSF = cerebrospinal fluid; DCD = developmental coordination disorder; DTI = diffusion tensor imaging; FA = fractional anisotropy; fcMRI, functional connectivity resonance imaging; fMRI = functional magnetic resonance imaging; MRI = magnetic resonance imaging.
# TABLE 2. Summary of Neuroimaging Findings that Inform the DCD Literature

<table>
<thead>
<tr>
<th>Author</th>
<th>Brain regions/pathways implicated and theories associated with reported results</th>
<th>Strengths and limitations</th>
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</thead>
<tbody>
<tr>
<td><strong>Structural MRI</strong></td>
<td></td>
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<tr>
<td>Caeyenberghs et al., 2016</td>
<td>The DCD group displayed global network values similar to typically developing group. The group with ASD was found to have altered global network parameters that were different than typically developing and DCD groups. Findings support the hypothesis that DCD and ASD have a low degree of overlap in abnormalities in connectivity and the co-occurrence of DCD+ASD have a distinct neural signature.</td>
<td>First to investigate the structural networks between ASD and DCD using graph theory. A limitation to the study is that the authors were not able to get individual brain network data, which limited them from examining the relationship between motor and/or cognitive performance with the graph metrics.</td>
</tr>
<tr>
<td>Langevin et al., 2015</td>
<td>Cortical thinness in frontal, parietal, and temporal lobes was correlated with lower motor and attention assessment outcomes in children with DCD and ADHD. Supports the hypothesis that DCD and ADHD share common neurobiological markers.</td>
<td>This is study is the first to examine cortical thickness in motor and attention disorders. However, it was not clear whether the larger and older age range of the control group would have affected the findings. Also, the associated functional task to regions of cortical thinness lacked specificity. Future studies with larger sample sizes would help confirm these findings.</td>
</tr>
<tr>
<td>Lloyd et al., 2010</td>
<td>Negative correlation between a trail tracing motor skill test and gray matter volume of the left cerebellar posterior lobe; and positive correlation between a measure of error in movement and gray matter volume of the medial frontal cortex. Supports the hypothesis that the cerebellum and parietal lobe are implicated in DCD.</td>
<td>This is the first study to report on gray matter volume in children with DCD. The study lacked a control group.</td>
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<tr>
<td><strong>fMRI</strong></td>
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<td>Debrabant et al., 2013</td>
<td>Decreased activation in right dorsolateral prefrontal cortex, left posterior cerebellum, and right temporoparietal junction during a finger tapping paradigm (visuomotor reaction time task (unpredictive &gt; predictive). Corroborates findings from Querne et al. (2008) in support of the internal modeling deficit hypothesis.</td>
<td>First to report on the neural correlates of predictive motor timing in children with DCD. It would have been useful to include a measure of attention and/or executive function as a covariate as these skills are likely to influence performance. Included both left- and right-handed children, which may have reduced ability to detect hemispheric brain differences.</td>
</tr>
<tr>
<td>Kashiwagi et al., 2009</td>
<td>Left posterior parietal cortex and left postcentral gyrus were implicated in a visual-motor task that involves tracking an object using a joystick. Supports the internal modeling deficit hypothesis.</td>
<td>This is one of the first to study neural correlates of children with DCD. A limitation to the study is that the group with DCD was mixed with ADHD and dyslexia and that there was an outlier that may have driven the results.</td>
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<table>
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</tr>
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<tr>
<td>Licari et al., 2015</td>
<td>Decreased activation in the left superior frontal gyrus, left inferior frontal gyrus, and increased activation in the right postcentral gyrus in children with DCD. Supports suspected deficits in cortical regions associated with working memory and executive functioning in children with DCD and adds preliminary support for deficits in the mirror neuron system.</td>
<td>This is the first study to investigate cortical activation patterns that contribute to increased motor overflow in children with DCD. However, the authors did not report activation deficits to explain motor overflow seen in children with DCD. Supports suspected deficits in cortical regions associated with working memory and executive functioning in children with DCD and adds preliminary support for deficits in the mirror neuron system.</td>
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<tr>
<td>Querne et al., 2008</td>
<td>Activation of left anterior cingulate cortex by using a go-no-go motor inhibition task. Supports the attentional network deficit in children with DCD as part of the internal modeling hypothesis.</td>
<td>This is one of the first to use fMRI to look at inhibition in children with DCD. The sample size in this study was small (n = 9 DCD; n = 10 controls). The relationship between motor skills and attention was not addressed. The conclusion that children with DCD may be characterized by an abnormal brain hemispheric specialization during development could not be confirmed in this cross-sectional study. Supports the attentional network deficit in children with DCD as part of the internal modeling hypothesis.</td>
</tr>
<tr>
<td>Reynolds et al., 2015</td>
<td>Decreased cortical activation in the precentral gyrus, posterior inferior parietal lobule, posterior cingulate, precuneus complex during observation of a finger sequencing task; region of interest analysis showed lower activation in the pars opercularis during imitation of finger sequence task. Provides some support for the hypothesis that dysfunction in the mirror neuron system may be implicated in children with DCD.</td>
<td>This is the first study to use fMRI to investigate MNS function in children with DCD. Limited by small sample size (n = 14 DCD; n = 12 controls) and uncorrected whole brain analyses. Only some MNS activations were different in DCD (and some brain areas not associated with MNS were activated in children with DCD), findings will need to be replicated in larger samples to confirm MNS hypothesis. Provides some support for the hypothesis that dysfunction in the mirror neuron system may be implicated in children with DCD.</td>
</tr>
<tr>
<td>Zwicker et al., 2010</td>
<td>Trail tracing task was associated with increased BOLD signal in the frontal, parietal and temporal regions when first performing the task. Supports the hypothesis that DCD is associated with impairment in motor learning and motor control; may indirectly provide support for internal modeling hypothesis.</td>
<td>This is the first study to provide neuroimaging evidence that supports clinical observations that children with DCD exert greater effort and cognitive fatigue with performing motor based activity. Findings should be interpreted with caution given the small sample size (n = 7 DCD; n = 7 control children). Supports the hypothesis that DCD is associated with impairment in motor learning and motor control; may indirectly provide support for internal modeling hypothesis.</td>
</tr>
<tr>
<td>Zwicker et al., 2011</td>
<td>Trail tracing task was associated with underactivated BOLD signals in the frontal, parietal, and cerebellar regions in motor learning paradigm. Supports the hypothesis that DCD is associated with impairment in motor learning and motor control; may indirectly provide support for internal modeling hypothesis.</td>
<td>This is the first neuroimaging study to use serial scans to investigate motor learning in children with DCD. The small sample size (n = 7 DCD; n = 7 control children) limits the generalizability of the study findings. The length of time between sessions may have been too short to fully capture learning. Supports the hypothesis that DCD is associated with impairment in motor learning and motor control; may indirectly provide support for internal modeling hypothesis.</td>
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<tr>
<td><strong>fcMRI</strong></td>
<td>McLeod et al., 2014</td>
<td>Decreased functional connectivity between the primary cortex, and the striatum and the angular gyrus was observed in children with DCD and ADHD. Supports the hypothesis that a common neurophysiological substrate exists that underlie both motor and attention problems.</td>
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<tr>
<td><strong>DTI</strong></td>
<td>Debrabant et al., 2016</td>
<td>Positive correlation between a visual-motor tracing task and FA in the retrolenticular limb of the internal capsule within the DCD group; decreased nodal efficiency at the cerebellar lobule VI and the right parietal superior gyrus was significantly implicated children with DCD compared to typically developing children. Sensorimotor functioning is impaired in children with DCD; hypothesized that mild cerebral palsy and DCD may share similar deficits in the sensory pathway.</td>
</tr>
<tr>
<td>Langevin et al., 2014</td>
<td>Lower FA in frontal regions of the corpus callosum, parietal regions and left superior longitudinal fasciculus; FA was positively correlated with scores on assessments of both motor and attention. The corpus callosum underlies difficulties in motor and attention functioning, supports shared neurobiological basis for DCD and ADHD.</td>
<td>First study to examine possible shared mechanisms underlying DCD and ADHD. There are limitations inherent with deterministic tractography as it assumes a single orientation of a fiber per voxel. Restricted seeding in M1 limits other possible differences in brain microstructure.</td>
</tr>
<tr>
<td>Zwicker et al., 2012a</td>
<td>Lower mean diffusivity and axial diffusivity were reported in the motor and sensory pathways in children with DCD; lower axial diffusivity was associated with poorer motor function. Motor and sensory pathway—particularly the corticospinal tract and posterior thalamic radiation are implicated in children with DCD.</td>
<td>This was the first neuroimaging study to use DTI to look at white matter pathways in children with DCD. Diffusivity values showed a trend towards significance, which was likely due to small sample size (n = 7 DCD; n = 9 typically developing children).</td>
</tr>
</tbody>
</table>

**Note**: ADHD = attention-deficit/hyperactivity disorder; ASD = autism spectrum disorder; BOLD = blood oxygen level dependent; DCD = developmental coordination disorder; DTI = diffusion tensor imaging = DTI; FA = fractional anisotropy; fcMRI = functional connectivity resonance imaging; fMRI = functional magnetic resonance imaging; MNS = mirror neuron system; MRI = magnetic resonance imaging.
As DCD was originally thought (and may still be by some) to just be the lower end of normal variance of motor abilities (Polatajko, 1999), these neuroimaging findings provide evidence to counter this (mis)perception and significantly advance our understanding of DCD as a neuromotor disorder.

For example, in a study that compared typically developing children and children with DCD, Zwicker et al. (2010) showed that children with DCD used different brain regions to complete a fine-motor trail tracing task. Children with DCD activated regions primarily associated with visual-motor and visual-spatial processing, whereas typically developing children activated brain regions associated with motor control, motor learning, and error recognition. In addition, children with DCD activated almost twice as many brain regions compared to typically developing children to complete the task. These findings have several important clinical implications for occupational therapists. First, these findings show that children with DCD use their brains differently from typically developing children when doing a fine-motor trail tracing task. In addition, these findings show that children with DCD directed more effort to complete the motor tasks (Saling & Phillips, 2007). This study provides the first neuroimaging evidence to support the clinical observation that children with DCD seem to exert great effort and experience fatigue with motor-based activities (Missiuna, Rivard, & Bartlett, 2003; Prunty, Barnett, Wilmut, & Plumb, 2014). Before obtaining a diagnosis of DCD, these children are often perceived by their teachers as lazy or unmotivated because they are generally bright children but are underperforming in the classroom (Missiuna, Gaines, & Soucie, 2006). Explaining these findings to teachers may help them to appreciate occupational therapy recommendations to reduce motor demands in the classroom (e.g., reducing the number of math questions or spelling words, having a scribe, completing tests verbally, using a computer for written output). The finding that children with DCD recruit more brain regions to complete motor tasks may also help parents, coaches, and therapists be more aware of the mental demand of motor tasks and the potential need for modifications, such as taking rest breaks or reducing expectations if engaging in motor tasks at the end of the day (e.g., written homework, swimming lessons).

In another fMRI study that examined motor learning in children with DCD, Zwicker et al. (2011) reported that children with DCD did not show any improvement in accuracy of a fine-motor trail tracing task with equivalent practice to typically developing children. These findings confirm that children with DCD do not benefit from practice alone, and taken together with other literature, reinforce that in addition to practice, they benefit from additional information (e.g., explicit feedback, cognitive strategies) to support the acquisition of motor skills (Polatajko, Mandich, Miller, & Macnab, 2001a; Shoemaker & Smits-Engelsman, 2015). Relative to typically developing children, children with DCD underactivated brain regions associated with motor learning, namely the dorsolateral prefrontal cortex, inferior parietal lobule, and cerebellum (Zwicker et al., 2011). This study is the first to suggest that motor learning difficulties in children with DCD may be associated with underactivation of these brain regions, which are anatomically connected in a cerebello-cortico-cerebellar network. These findings are consistent with Marien et al. (2010), who conducted a case study of an adolescent with DCD using single-photon emission computed tomography (SPECT). SPECT requires the use of radioactive tracer material to be injected into the bloodstream of the patient thereby providing information about the amount of blood flow of the imaged region in three-dimensional representation. Based on these findings, the authors reported decreased perfusion in prefrontal and cerebellar brain regions, hypothesizing that a disruption of the cerebello-cerebral network is implicated in DCD (Marien et al., 2010). It seems reasonable to suggest that if we can activate this network in rehabilitation interventions for children with DCD, then perhaps we can change the child’s ability to learn motor skills. Further research is needed to confirm this hypothesis.

**CLINICAL IMPLICATIONS OF DTI**

Another MRI acquisition technique called DTI has been gaining traction in this field. DTI is an indirect measure of molecular diffusion and is an imaging technique that has been applied to infer information about gray and white matter microstructure (Mukherjee et al., 2002). During development, diffusion parameters in brain microstructure change. For example, molecular diffusion becomes increasingly restricted to the longitudinal axes of fiber tracts with increasing fiber density and myelination (Salat et al., 2005), making it a useful tool to investigate changes in brain microstructure over time. This forms the basis for neurodevelopmental studies as well as investigations about neuroplasticity in response to rehabilitation intervention (Blumenfeld-Katzir et al., 2011; Jones, Knoche, & Turner, 2013). To date, commonly reported DTI measures in DCD research are measures of diffusion, such as mean diffusivity and fractional anisotropy (FA; Debrabant, Gheysen, Caeyenberghs, Van Waelvelde, & Vingerhoets, 2013; Debrabant et al., 2016; Langevin, MacMaster, Crawford, Lebel, & Dewey, 2014; Zwicker, Missiuna, Harris, & Boyd, 2012a). Mean diffusivity is an indirect measure of the overall magnitude of water diffusion in axons, whereas FA represents the relative direction of water diffusion. An FA value of 0 is interpreted to mean that diffusion is isotropic or freely moving, whereas an FA value of 1 is representative of restricted diffusion that may indirectly reflect the degree of myelination in axons (Cascio, Gerig, & Piven, 2007; Ciccarelli, Catani, Johansen-Berg, & Clark, 2008; Dubois et al., 2014). Subcomponents of FA include measures of axial and radial diffusivity that describe the movement of water molecules parallel and perpendicular to fiber
bundles respectively. Increasing axial diffusivity may reflect an increase in axon number or size (Song et al., 2002). During the development of white matter fiber pathways, mean diffusivity and radial diffusivity decrease, whereas FA and axial diffusivity steadily increase (Partridge et al., 2004); thus, these diffusion parameters are thought to provide an indirect measure of white matter microstructure. Changes in water diffusion may be related to changes in fiber diameter, fiber density, membrane permeability, or myelination, which, in turn, may be associated with disease, development, learning, or rehabilitation (Jones et al., 2013). While DTI is exquisitely sensitive to any change in tissue microstructure, it does not address the heterogeneity of fiber orientation at any given voxel and cannot provide information about what biological or physiological changes underlie these changes (Jones et al., 2013). Despite the limitations of DTI, we hope to illustrate that data DTI studies have the potential to help inform rehabilitation sciences and clinicians. For example, using serial DTI scans, indices of diffusion can be applied to track changes in brain microstructure over time as a result of rehabilitative intervention strategies. In cross-sectional DTI studies, diffusion parameters can be applied to help identify potential pathways or regions in the brain that are implicated in neurodevelopmental disorders when compared to typically developing brains and when correlated with behavioral data, such as motor outcomes. A greater understanding of the implicated brain regions and how the brain responds to rehabilitation intervention may help to inform clinical practice.

DTI studies on children with DCD have reported differences in white matter compared to typically developing children. In a pilot study, Zwicker et al. (2012a) reported lower axial diffusivity (lower water diffusion along the axons) of the corticospinal tract (motor pathway) and the posterior thalamic radiations (sensory pathway) in children with DCD compared to typically developing children. Furthermore, lower axial diffusivity was moderately to highly correlated with poorer motor outcomes as measured by the Movement Assessment Battery for Children Second Edition (Henderson et al., 2007). In another DTI study, Langevin et al. (2014) reported lower FA in the corpus callosum under the parietal lobe and in the left superior longitudinal fasciculus in children with DCD, which correlated with lower motor scores on the McCarron Assessment of Neuromuscular Development (McCarron, 1997). They also reported lower FA in the corpus callosum in children with attention-deficit/hyperactivity disorder (ADHD). These authors suggest a shared neurobiological basis for DCD and attention disorders in children that may help to support the high co-occurrence of the two disorders. More recently, Debrabant et al. (2016) reported lower FA in the main sensory motor tracts (left retrolenticular limb of the internal capsule) in children with DCD compared to controls, which was predictive of poorer visual-motor performance on the Beery-Buktenica Developmental Test of Visual Motor Integration (Beery & Beery, 2004). Taken together, findings from these DTI studies suggest that children with DCD show altered development of brain pathways associated with sensorimotor function. These findings are consistent with the diagnostic criteria and observation that DCD occurs in the developmental period (American Psychiatric Association, 2013), but what causes these developmental differences is largely unknown and is the subject of further study.

NEUROIMAGING STUDIES BRIDGE BEHAVIORAL/COGNITIVE HYPOTHESES ABOUT DCD

Although DCD is a recognized developmental disorder, the cause and the underlying etiology remains unknown. Recent neuroimaging studies provide support to some of the current hypotheses to explain the motor difficulties experienced by children with DCD. One predominant theory is the internal modeling hypothesis, which suggests that children with DCD have difficulty with forming or updating an internal model of movement (Adams, Lust, Wilson, & Steenbergen, 2014; Wilson, Ruddock, Smits-Engelsman, Polatajko, & Blank, 2013; Zwicker et al., 2012b). Successful motor control is thought to result from an internal model that predicts sensory consequences of a motor command. The cerebellum is thought to receive an efference copy of the motor command and then compare the predicted movement with the actual movement; if there is a mismatch, the cerebellum sends an error signal as feedback to create a more accurate movement on subsequent occasions (Kawato, 1999). The involvement of the cerebellum has been suspected in DCD (Zwicker et al., 2009), which has since been confirmed in MRI studies that show underactivation of the cerebellum in children with DCD relative to control children (Debrabant et al., 2013; Zwicker et al., 2011). Cerebellar network — connections to frontal and parietal areas—also seem to be implicated in DCD, providing indirect support for the internal modeling hypothesis (Debrabant et al., 2013; Kashiwagi et al., 2009; Zwicker et al., 2010, 2011). The internal modeling deficit hypothesis has implications for occupational therapy intervention. Current evidence suggests that task-specific cognitive approaches are effective for children with DCD (Smits-Engelsman et al., 2013), which implies therapists are using compensatory strategies (explicit motor learning) to work around deficits in forming or updating internal models of movement (implicit motor learning). Future innovations in rehabilitation may find ways to engage brain networks to promote internal modeling, which offers the potential to affect motor skill development beyond task-specific therapy.

Another hypothesis that has gained momentum recently in the DCD literature is the mirror neuron system (MNS; Licari et al., 2015; Reynolds et al., 2015; Werner, Cermak, & Aziz-Zadeh, 2012), which is likely related to the internal modeling hypothesis (Miall, 2003; Kilner, Friston, & Frith, 2007). The MNS comprises a group of neurons that are
activated during observation, motor imagery, execution, and imitation; the MNS circuit includes the pars opercularis in the inferior frontal gyrus, premotor cortex, and the inferior parietal lobule (Reynolds et al., 2015). The MNS hypothesis posits that children with DCD have difficulty with learning motor skills due to MNS dysfunction, and that rehabilitation involving motor imagery may be a promising tool to promotemotor learning in DCD. Preliminary evidence suggests that motor imagery may support development of motor skills in children with DCD (Wilson, Thomas, & Maruff, 2002), but to our knowledge, motor imagery has not been widely adopted in clinical practice.

Another hypothesis is that the motor dysfunction in children with DCD can be explained by impaired executive function. Using fMRI and performance on an attention inhibition task, Querne et al. (2008) reported that children with DCD engaged the attentional network differently (left > right) and less effectively than control children. Licari et al. (2015) also reported fMRI findings that support the theory of suspected deficits in cortical regions associated with working memory and executive functioning in children with DCD. In both of these studies, children with co-occurring ADHD were excluded, which suggests that attentional difficulties are inherent in DCD. Other researchers have compared children with DCD, ADHD, and DCD + ADHD and suggest a shared neurobiological basis for motor and attention deficits. For example, cortical thinness was found in the frontal, parietal and temporal lobes in children with DCD and ADHD (Langevin et al., 2015), reduced connectivity was noted between the primary motor cortex, striatum, and angular gyrus in both the DCD and ADHD groups (McLeod et al., 2014); and the corpus callosum has been implicated in both children with DCD and ADHD. For occupational therapists, knowing whether attentional difficulties are part of DCD or another disorder may have important implications for therapy, as adjunct therapies may need to be considered by the team (e.g., stimulant medication). These studies, as well as an fMRI study by Zwicker et al. (2010), highlight that attention may have a significant impact on motor performance and motor learning in children with DCD. In addition to addressing motor skill development, occupational therapists should also consider grading the attention demands of the task and/or the environment as part of their therapy and recommendations for children with DCD.

In summary, neuroimaging can provide support for different hypothesized mechanisms underlying DCD. Further work will continue to inform our understanding of DCD, which can then be applied to refine current or develop new interventions for DCD.

**NEUROIMAGING CAN HELP IDENTIFY RISK FACTORS FOR DCD**

A significant risk factor associated with DCD is prematurity. Very preterm infants are 6–8 times more likely to develop DCD compared to their full-term peers (Edwards et al., 2011). Unknown factors that lead to prematurity, neonatal illness, medical interventions, infant stress, and altered brain development could also contribute to DCD (Brummelle et al., 2012; Grunau et al., 2009; Ranger et al., 2015; Smith et al., 2011; Tam et al., 2011; Zwicker, Grunau et al., 2013; Zwicker et al., 2015). For example, several risk factors have been identified for DCD, including male sex, low birth weight, and postnatal steroid exposure (Zwicker, Yoon et al., 2013). Postnatal steroids have been associated with reduced cerebellar growth in the neonatal period (Tam et al., 2011), which may be potential mechanism for DCD as the cerebellum and associated networks are implicated in the disorder (Lloyd, Mon-Williams, Waiter, & Williams, 2010; Zwicker, Missiuna, & Boyd, 2009; Zwicker, Missiuna, Harris, & Boyd, 2011). As mentioned previously, the development of the corticospinal tract is altered in children with DCD (Zwicker et al., 2012a). To examine this further in very preterm infants, Zwicker, Grunau et al. (2013) examined antenatal, perinatal, and postnatal risk factors for DCD on the development of the corticospinal tract. They found that illness severity in the first 24 hr of life was associated with poorer maturation of this motor pathway. In addition, higher number of invasive procedures (e.g., heel lances for blood collection, chest tubes) was also independently associated with poorer maturation of the motor pathway. Research is ongoing to determine if these clinical risk factors are associated with DCD in childhood (likely mediated through altered brain development), and if there are brain biomarkers in the neonatal period that may predict DCD in this high-risk population. These neuroimaging studies have the potential to identify modifiable risk factors to prevent DCD in this high-risk population and to inform development of early interventions to improve outcomes of affected children.

**CONTRIBUTION OF NEUROIMAGING RESEARCH TO UNDERSTAND COMORBIDITIES IN DCD**

The issue of comorbidities is an important one because DCD is known to co-occur with other developmental disorders (Visser, 2003; Zwicker et al., 2012b). Children with DCD experience more difficulties with attention compared to typically developing children (Dewey, Cantell, & Crawford, 2002), with up to 50% of children with DCD meeting diagnostic criteria for ADHD (Kadesjo & Gillberg, 1998; Pitcher, Pick, & Hay, 2003). While some authors argue that DCD and ADHD share etiology (Kaplan, Wilson, Dewey, & Crawford, 1998; Langevin et al., 2014; Langevin et al., 2015; MacLeod et al., 2014), others suggest that DCD and ADHD are separate disorders (Goulardins et al., 2015). As mentioned previously, if it is determined that each disorder is distinct rather than sharing a common neural pathway, then different treatment approaches may be required (Goulardins et al., 2015).
Many children diagnosed with DCD also show problems with learning disabilities such as dyslexia (Kaplan, Crawford, Wilson, & Dewey, 1997; Visser, 2003). Neuroimaging studies on reading delay and problems with motor skill acquisition have the potential to contribute support for these relationships. For example, a brain imaging study that used a neuroimaging technique called positron emission tomography (PET), demonstrated an association between motor learning difficulties in adults with dyslexia and abnormal activation of the cerebellum (Nicolson et al., 1999). PET uses radioactive substances injected into the blood stream to provide information about blood flow and metabolic activity in the brain. Interestingly, O’Hare and Khalid (2002) reported behavioral data to suggest an association of abnormal cerebellar function in children with DCD and reading difficulties. Bridging these two lines of evidence, underactivation of the cerebellum was recently reported in children with DCD (Zwicker et al., 2011).

In another study that addresses the underlying neural connections associated with reading performance in children, Beaulieu et al. (2005) investigated the relationship between white matter connectivity and reading performance in typically developing children. Using DTI, these authors reported that regional brain connectivity in the left temporal-parietal white matter was correlated with reading ability in children between 8 and 12 years old. These findings suggest that the posterior limb of the internal capsule is consistent with the location of measures of reading performance. This is a similar region that has been implicated in children with DCD (Debrabant et al., 2016) and highlights the possibility of overlapping etiology of DCD and dyslexia.

With the revisions to the latest edition of the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (American Psychiatric Association, 2013), it is now possible to have a diagnosis of autism spectrum disorder and DCD. Recently, Caeyenberghs et al. (2016) examined distinct neural network parameters in a group of children with DCD, autism spectrum disorder (ASD), and DCD with co-occurring ASD. Using structural MRI and graph theory, they found that children with DCD and children with ASD had a low degree of overlap in abnormalities in brain connectivity networks, and that children with comorbid DCD and ASD showed more widespread differences in connectivity. These results are important for occupational therapists to recognize that the motor difficulties associated with ASD may be comorbid DCD, which will inform intervention for these children. The focus of intervention for children with ASD may be addressing the functional implications of core symptoms of the disorder, such as social communication and sensory processing issues, but the motor issues should not be ignored. Distinct neural networks for DCD and ASD suggest that different treatment approaches are needed to address the needs of children with comorbid diagnoses.

Future neuroimaging research can help further identify neural mechanisms associated with DCD and co-occurring conditions; as such, these studies will have the potential to inform rehabilitation intervention practices.

WHAT CAN WE LEARN FROM NEUROIMAGING STUDIES OF ASD AND CEREBRAL PALSY?

Recent results from neuroimaging studies have significantly added to our understanding of neurodevelopmental disorders such as ASD and cerebral palsy (CP). Of interest is how the studies link behavioral outcomes with neuroimaging findings that help to improve diagnosis and rehabilitative techniques. For example, neuroimaging studies have revealed that autism develops early in the process of brain development—which results in atypical brain organization and communication within and between regions of the brain (Minshew & Williams, 2007; Sparks et al., 2002; Williams & Minshew, 2007). Both gray and white matter structures of the brain are affected. Neuroimaging research shows that the association cortex, its neurons, and their projections have been implicated in ASD and further, alterations in patterns of functional brain activation suggest disturbed intracortical connectivity. The implications of these findings suggest that integration of information and coordination of multiple neural systems place greater demand on cognitive resources in children with autism, particularly in language and emotion processing (Minshew & Williams, 2007). Understanding the neurobiological basis of autism has contributed to the critical shift toward early intervention (Williams & Minshew, 2007) and helped inform the development of effective interventions to accommodate how children with autism learn (Williams & Minshew, 2007).

Learning from autism research, the application of neuroimaging research for DCD can inform how children with DCD learn motor skills and may provide insights on how to improve current rehabilitation interventions or develop new treatments grounded in neuroscientific evidence.

Neuroimaging has also played an increasing role in our understanding of CP (Englander et al., 2015). Specifically, neuroimaging techniques such as T2-weighted imaging and DTI have been applied to characterize white matter abnormalities associated with functional deficits in CP (Sheck, Boyd, & Rose, 2012; Yoshida et al., 2010). Other studies have demonstrated that changes in brain structural connectivity are correlated with functional improvements after therapy in children with CP (e.g., Bieyenheuft et al., 2015; Englander et al., 2015; Inguaggiato et al., 2013; Kim, Kwon, & Son, 2015; Trivedi et al., 2008). These studies have provided compelling evidence for neuroplasticity associated with rehabilitation in children with CP. Having a better understanding of neuroplasticity associated with therapy for children with DCD will provide further evidence that therapeutic intervention is beneficial for these children, a group that does not routinely receive occupational therapy as standard of care.
HOW CAN NEUROIMAGING DATA ADVANCE INTERVENTION FOR DCD?

Findings from neuroimaging studies can be applied clinically to help quantify which behavioral intervention is associated with brain indices associated with learning. This is a growing field as the neural mechanisms involved in the relationship between brain function, behavior, and motor learning are currently not well understood in children with DCD. Drawing from what we have learned from neuroimaging studies of ASD and CP, we can apply similar methodology to advance our understanding of DCD and interventions that help children with DCD learn motor skills. Current best-practice for children with DCD is a task-specific treatment approach called Cognitive Orientation to Occupational Performance (CO-OP; Armstrong, 2012; Polatajko & Cantin, 2006; Smits-Engelsman et al., 2013; Blank et al., 2012) CO-OP is designed for 7–12-year-old children with DCD and is an individualized treatment approach designed to improve motor-based skills that a child needs or wants to master (Polatajko et al., 2001b). CO-OP has been effective in helping children achieve functional motor goals (Miller, Polatajko, Missiuna, Mandich, & Macnab, 2001; Zwicker et al., 2015), but the neurological mechanisms underlying the approach are unknown. The theory of neuroplasticity has been proposed to explain the benefits of rehabilitation. Neuroplasticity is defined as the ability of the brain to change in response to external stimuli, experience, or damage (Boyd, Vidoni, & Daly, 2007). Data from this research would provide rehabilitation scientists and clinical practitioners with a better understanding of how interventions change the neural network that lead to motor learning (Zatorre, Fields, & Johansen-Berg, 2012). Studies are underway by Zwicker et al. to examine changes in brain structure and function after CO-OP intervention, which will inform if and how this rehabilitation approach leads to neuroplastic change associated with improved motor function. We hope and hypothesize that this study will provide compelling neurobiological evidence for rehabilitation for children with DCD. Based on other imaging studies examining brain changes with intervention in children (e.g., Gebauer et al., 2012; Keller & Just, 2009; Krafft et al., 2014; Sterling et al., 2013), we expect that children with DCD who receive CO-OP intervention (compared to a waitlist control group) will show: (a) strengthened functional connectivity in resting state, sensorimotor, frontal, and cerebellar networks; (b) higher FA in the cerebello-thalamo-cortical and cortico-ponto-cerebellar pathways; (c) increased gray matter volume in the dorsolateral prefrontal, motor, and cerebellar cortices; and (d) improved motor function, as measured by performance and satisfaction ratings of child-chosen functional motor goals, standardized motor assessment, and movement quality. If we find differences in brain structure or function with intervention, this study will provide neurobiological evidence for CO-OP intervention for children with DCD. If we do not find any brain changes, then the intervention dose may need to be increased and/or the follow-up time lengthened. Alternatively, a different type of intervention may be warranted. We suspect that children with DCD show relative underactivation of the cerebellar-frontal pathway during motor learning compared to typically developing children, as brain regions in this pathway have previously been associated with poor motor learning (Zwicker et al., 2011); perhaps if we can activate this pathway in children with DCD with novel rehabilitation approaches, they will show increased motor learning and functional motor performance.

LIMITATIONS TO MRI AND INTERPRETING MRI STUDIES

There are a number of neuroimaging studies that have contributed to our understanding of DCD; however, interpretation of these and future findings should be made with caution. A major limitation to interpreting neuroimaging studies is that MRI scans are not a direct measure of brain activity or connective pathways. With the current technology and software capabilities, MRI scans are an indirect measure of the structure, function and connectivity of the brain. Further, these studies are limited by small sample sizes and lack of uniformity in diagnostic cutoff scores to define DCD. Despite these limitations, studies have found significant differences compared to typically developing children. Larger studies with uniform cutoff scores and similar study designs would help advance the significance of these findings. Last, because most of the neuroimaging findings in DCD are related to differences in brain activation or are at the microstructural level, using MRI for diagnosis is not practical at this time. Despite these limitations, neuroimaging research has been critical to help build our understanding of the neural basis of DCD.

CONCLUSION

While neuroimaging seems far removed from the clinical practice of occupational therapy, we aimed to bridge the gap from neuroscience to rehabilitation sciences and how information from these fields of research can be applied to occupational therapy. In particular, we discussed the clinical implications of neuroimaging findings as a way to better understand the etiology and risk factors of DCD and the application of brain imaging to evaluate rehabilitation interventions for children with this disorder. While brain imaging may provide evidence for neuroplastic changes associated with current best-practice for children with DCD, a better understanding of the neural basis of DCD may also lead to refinement or development of new interventions that will ultimately help inform clinical practice for this population. The integration of brain imaging and occupational therapy has the potential to significantly
advance the field by grounding interventions in neuroscience, improve our understanding of and outcomes for children with DCD, and apply this knowledge to other populations seen by occupational therapists, such as children with neurodevelopmental disabilities and adults with neurological impairment.

**FUNDING**

Meisan Brown-Lum is funded by the BC Children’s Hospital Research Institute. Dr. Zwicker is funded by the Michael Smith Foundation for Health Research, Canadian Child Health Clinician Scientist Program, Sunny Hill Foundation, BC Children’s Hospital Research Institute, and Canadian Institutes of Health Research.

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