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# **Neuroergonomic Assessment of Developmental Coordination Disorder**

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# **Abstract**

Until recently, neural assessments of gross motor coordination could not reliably handle active tasks, particularly in realistic environments, and offered a narrow understanding of motor-cognition. By applying a comprehensive neuroergonomic approach using optical mobile neuroimaging, we demonstrated the broader capability for ecologically relevant neural evaluations for the "difficult-to-diagnose" Developmental Coordination Disorder (DCD), a motor-learning deficit affecting 5-6% of children with lifelong complications.

We confirmed that DCD is not an intellectual, but a motor-cognitive disability, as gross motor /complex tasks revealed neuro-hemodynamic deficits and dysfunction within the right middle and superior frontal gyri of the Prefrontal Cortex. Furthermore, by incorporating behavioral performance, aberrant patterns of neural efficiency in these regions were revealed in DCD children, specifically during motor tasks. Lastly, we provide a framework, evaluating disorder impact in real-world contexts to identify those for whom interventional approaches are most needed and open the door for precision therapies.

# Introduction

Functional deficits in motor skill acquisition and execution are common concerns regarding child development, and serious impairments can be characterized as Developmental Coordination Disorder (DCD)<sup>1,2</sup>. DCD is a motor-cognitive deficit prevalent among 5–6% of school-aged children (a disorder of high prevalence) often manifested as clumsiness, slowness, and poor motor skill acquisition leading to lifelong impacts within personal, social, academic, and occupational functioning<sup>2,3</sup>. DCD is not a condition that children simply "outgrow," as one in two children diagnosed with DCD retain persistent negative impacts, even upwards of 10 years later<sup>4</sup>. There is currently no cure for DCD, and early pharmacological and non-pharmacological interventions have the potential to reduce the emotional, physical, social and economic consequences that are often associated with this disorder<sup>2,4–6</sup>. However, identifying children with DCD is difficult, as the etiology remains unclear. Diagnosis entails a complex of developmental and medical history, physical examination, school or workplace report, and often the movement assessments, which are a time-consuming assortment of tests that gauge a child's coordination and physical ability <sup>7,8</sup>. Furthermore, skill rating can be subjective where skill deficits can be masked by practice effects and lack of information of the concurrent cognitive effort. As such effective assessment requires highly skilled professionals, training and is inefficient on large and diverse populations. A more broadly applicable and available assessment tool that can capture motor-cognitive deficit directly is needed.

It has been purported that DCD as a neurodevelopmental disorder, may have unique and identifiable neuropathology, and while traditional functional neuroimaging has been critical in understanding the neural mechanisms of a variety of complex disorders<sup>9</sup> including DCD<sup>1,10,11</sup>, their use in motor-cognitive research and understanding has been limited in young people to stationary fine motor tasks and is not reflective of motor disability within active, real world contexts <sup>1,10–13</sup>

Drawing observations from studies exploring every-day walking tasks, in adults exposed to single and dual task conditions in an experiment exploring the impact of age and movement disorder, led us to hypothesize that associated with deficits in motor performance, we would observe higher prefrontal cortical activity in hemodynamic responses as compensation for underlying structural and functional impairment<sup>14,15</sup>. We thus set out to study motor skill acquisition and performance in a novel dynamic task in young people using neuroimaging tools alongside motor performance in order to identify motor-cognitive deficits to inform both diagnosis and understanding of DCD.

Therefore, within this study, we demonstrate the feasibility and importance in determining motor-cognitive disorder impact and extent using an sufficiently replicable, and broadly applicable ecologically-valid neuroergonomic approach, using mobile neuroimaging accounting for motion artifacts with advanced statistical processing techniques, incorporating behavioral and brain-based assessments during active motor tasks<sup>12,16</sup>.

### Results

We challenged both DCD children and those with neurotypical development (TD) in separate cognitive and physical tasks, and a combinatory dual task (as shown in movie S1). Our study is the first of its kind in targeting regions of prefrontal cortical dysfunction for identification of neuropathophysiology for DCD during realistic, active ambulatory motor tasks, and is the largest neuroimaging study (across all modalities) involving DCD<sup>1,10,13</sup>. Therefore, our work is the first to reveal the neural underpinnings of how DCD affects physical activity, and gross motor performance.

## **Behavioral Results**

In first assessing external behavioral performance, results regarding Cognitive Performance (CogP) indicated significant main effects for Group ( $F_{1,505} = 6.42$ ,  $p=0.012^*$ , d=0.34), between TD and DCD, and Task ( $F_{1,505} = 76.13$ ,  $p<0.001^{***}$ , d=0.82), between Single and Dual. However, only a significant main effect for Task ( $F_{1,70.8} = 5.40$ ,  $p=0.023^*$ , d=0.26) was found regarding Physical Performance (PhysP). A statistically significant interaction effect for group and task within CogP ( $F_{1,505} = 6.81$ ,  $p=0.009^{**}$ ), while a nearly significant interaction was present for PhysP ( $F_{1,70.8} = 2.96$ , p=0.090), depicted in Figure 1.

In evaluating the interaction effects of Group and Task for CogP (see Fig. 1A), both groups had worsened performance during dual task conditions (cognitive with simultaneous motor element) compared to single (cognitive only) of 6.96% and 12.89% and respectively (TD:  $F_{1,505}$  = 16.59, p<0.001\*\*\*, d = 0.57 and DCD:  $F_{1,505}$  = 76.63, p<0.001\*\*\*, d = 0.95). TD and DCD groups performed similarly (p > 0.05) on the cognitive only task, however with the addition of the motor element (dual task) the TD group had 5.85% better performance ( $F_{1,505}$  = 13.2, p < 0.001\*\*\*, d = 0.45). This alone suggests that when presented a typical task that is purely cognitive (non-motor), having DCD does not impact performance. But when a motor component is added (dual task), the DCD group is much less capable than neurotypical children.

Additionally, while evaluating the near significant interaction of Group and Task on PhysP, only the TD group had statistically worse performance for the dual task condition (motor with a simultaneous cognitive task) in comparison to the single (motor only) by 6.74% ( $F_{1,70.8}$ = 7.59, p=0.015\*, d = 0.42), while DCD children had equally impacted PhysP regardless of task condition (see Fig. 1B). This indicates atypical motor-cognition for DCD children, as they found any task (single or dual) with a motor element challenging, while neurotypical children experienced expected dual task reductions in performance measures. This is in contrast to the CogP evaluation, where DCD children had typical reductions in CogP due to dual tasking. Overall, when presented with a physical challenge, DCD children respond with more impaired CogP and find challenge in PhysP regardless of task difficulty, emphasizing the impact of DCD as a motor-cognitive disorder.

# **Neuroimaging Results**

In localizing and evaluating motor-cognitive deficits of DCD during physical activity within the prefrontal cortex (PFC), we quantified the hemodynamic activation as it occurred during the tasks. Neuroimaging results are depicted in Figure 2. Figure 2 depicts brain activity as measured via twenty optode measurement locations covering the PFC, per group and task. The cognitive (non-motor) task elicited increased activity across many regions of the PFC for both TD and DCD children, with no significant regions of difference between the groups. The motor task elicited increased PFC activity for TD children, but significantly less so for DCD children within one particular channel (t(660) = 6.0695, p < 0.001, d = 0.9998) within the right middle frontal gyri (mFG<sub>R</sub>). The dual task led to significantly increased activity for TD children, while the DCD children approached the task with significantly reduced activity. The contrast between the groups highlighted six channels (mFG and sFG) of interest. Complimentary information regarding HbR is depicted in Figure S1 within supplementary information.

These are the first neural activity findings of gross motor tasks for those with DCD as was predicted by the literature<sup>1,6,17</sup>, showing increased neurological deficits for the DCD group as the tasks became more motor oriented, and more difficult. DCD children are explicitly deficient with the introduction of motor tasking, but otherwise cognitively equivalent in non-motor tasks, highlighting the motor-cognitive deficiency found only during real-world whole body motor tasks.

#### Combinatory/Neurobehavioral Results

Neural Efficiency (NE) relates the neurophysiological measures of brain activity to an individual's performance according to the demands of the task and the capability of the individual<sup>18</sup> in a combinatory measure evaluation neurobehavior. The NE for both CogP and PhysP was evaluated for effects on group, task, and the interaction of group and task.

The main effect for group was negligible for both NE of CogP and NE of PhysP in all channels. However, task condition indicated a significant main effect on 18/20 channels for NE of CogP and 6/20 channels for NE of Phys, both metrics indicating that dual tasking reduced NE as detailed in Tables 1 and 2.

# Table 1: Neural Efficiency of Cognitive Performance (Main Effects)

Channel	Source - Detector	Region	MNI Coordinates		Distance	Specificity Mean		F-statistic	р	Effect Size		
			Χ	Υ	Z	(mm)	(%)	Difference		(FDR corrected)	(d)	
Group: Typically Developed > Developmental Coordination Disorder												
Task: Sing	gle > Dual											
1	F3 - F5	$mFG_L$	-45	35	23	29	74.22	0.9096	33.562	<0.001***	0.569	
2	F3 - F1	$mFG_L$	-30	38	39	29	87.01	0.3705	4.09	0.047*	0.227	
3	AF7 – F5	iFG <sub>L</sub>	-47	42	4	34	87.56	0.9203	59.515	<0.001***	0.750	
4	AF7 – Fp1	iFG <sub>L</sub>	-34	56	-4	31	53.57	0.7646	27.200	<0.001***	0.556	
5	AF3 - F1	$mFG_L$	-24	50	30	44	80.24	0.7676	46.854	<0.001***	0.704	
6	AF3 - Fp1	$mFG_L$	-26	60	5	30	90.79	0.6913	18.822	<0.001***	0.393	
7	AF3 - AFz	$mFG_L$	-16	59	21	39	55.88	1.0458	54.451	<0.001***	0.754	
8	Fz - F1	sFG <sub>L</sub>	-11	40	47	30	74.89	0.3706	4.465	0.038*	0.225	
9	Fz - AFz	$sFG_L$	0	48	37	40	48.54	0.67	47.326	<0.001***	0.650	
10	Fz - F2	sFG <sub>R</sub>	11	40	48	28	75.09	0.3892	5.572	0.021*	0.257	
11	Fpz – Fp1	$mFG_L$	-14	64	-3	31	50.16	0.7073	15.908	<0.001***	0.395	
12	Fpz - AFz	sFG <sub>L</sub>	-1	61	11	41	47.28	1.3175	68.787	<0.001***	0.867	
13	Fpz – Fp2	$mFG_R$	14	65	-3	30	51.58	0.7740	42.650	<0.001***	0.656	
14	AF4 - AFz	$mFG_R$	15	59	22	37	52.67	0.9959	49.773	<0.001***	0.727	
15	AF4 – F2	$mFG_R$	23	51	31	43	75.53	0.6090	21.548	<0.001***	0.476	
18	F4 – F6	$mFG_R$	46	38	24	28	87.56	0.9374	21.350	<0.001***	0.515	
19	AF8 - Fp2	$iFG_R$	34	58	-4	30	52.77	0.6259	13.432	<0.001***	0.399	
20	AF8 – F6	iFG <sub>R</sub>	47	45	4	33	88.89	0.9287	59.580	<0.001***	0.755	
	n of Group and Task	=-					71.05			0.0451		
8	Fz - F1	sFG <sub>L</sub>	-11	40	47	30	74.89	-	4.126	0.046*	-	
9	Fz - AFz	sFG <sub>L</sub>	0	48	37	40	48.54	-	4.425	0.039*	-	
12	Fpz - AFz	sFG <sub>L</sub>	-1	61	11	41	47.28	-	5.462	0.022*	-	
14	AF4 - AFz	mFG <sub>R</sub>	15	59	22	37	52.67	-	3.126	0.081 <sup>X</sup>	-	
16	AF4 - Fp2	mFG <sub>R</sub>	26	61	6	30	91.67	-	2.976	0.087 <sup>X</sup>	-	
20	AF8 – F6	iFG <sub>R</sub>	47	45	4	33	88.89	-	4.758	0.032*	-	

Significant Channels (at Source-Detector locations) using MNI coordinates (X, Y, and Z), with the region designation of main effects for Neural Efficiency of Cognitive Performance for Group, Task, and Interaction. Specificity/Coverage of the region per channel is detailed, with the mean difference for the comparison (not applicable in interaction of Group and Task), along with statistical information (F-statistic, p-value, and effect size [not applicable for Interaction of Group and Task]). (p <0.1 $^{\text{X}}$ , p < 0.01 $^{\text{X}}$ , p < 0.001 $^{\text{X}}$ , p < 0.001 $^{\text{X}}$ ).

Table 2: Neural Efficiency of Physical Performance (Main Effects)

Channel	Source - Detector	Region	MNI Coordinates			Distance	Specificity	Mean	F-statistic	р	Effect Size	
			Х	Υ	Z	(mm)	(%)	Difference		(FDR corrected)	(d)	
Group: Ty	Group: Typically Developed > Developmental Coordination Disorder											
Task: Sing	gle > Dual											
4	AF7 - Fp1	$iFG_L$	-34	56	-4	31	53.57	0.386	5.578	0.021*	0.224	
5	AF3 - F1	$mFG_L$	-24	50	30	44	80.24	0.3268	4.779	0.032*	0.218	
9	Fz - AFz	$sFG_L$	0	48	37	40	48.54	0.3038	4.051	0.048*	0.207	
17	17: F4 – F2	$mFG_R$	29	40	40	29	82.62	0.3616	4.308	0.042*	0.195	
18	F4 – F6	$mFG_R$	46	38	24	28	87.56	0.3159	4.502	0.038*	0.228	
19	AF8 - Fp2	iFG <sub>R</sub>	34	58	-4	30	52.77	0.3567	3.974	0.050 <sup>X</sup>	0.165	
Interaction	n of Group and Task											
10	Fz - F2	sFG <sub>R</sub>	28	11	40	28	75.09	-	3.2555	0.076 <sup>X</sup>	-	
13	Fpz – Fp2	$mFG_R$	14	65	-3	30	51.58	-	3.3898	0.070 <sup>X</sup>	-	

Significant Channels (at Source-Detector locations) using MNI coordinates (X, Y, and Z), with the region designation of main effects for Neural Efficiency of Physical Performance for Group, Task, and Interaction. Specificity/Coverage of the region per channel is detailed, with the mean difference for the comparison (not applicable in interaction of Group and Task), along with statistical information (F-statistic, p-value, and effect size [not applicable for Interaction of Group and Task]). (p <0.1 $^{\times}$ , p < 0.05 $^{\times}$ , p < 0.01 $^{\times}$ , p < 0.001 $^{\times}$ ).

Additionally, as detailed within Tables 1 and 2, interaction effects were found in 6/20 channels for NE of CogP and in 2/20 channels for NE of PhysP. Example patterns of the significant interaction between the factors of group and condition are depicted in Figure 3 for both NE of CogP (i.e. channel 9 [most significant channel] found in the sFG<sub>R</sub>) and NE of PhysP (and further detailed in Table 3).

Table 3: Neural Efficiency (Interaction Effects of Group and Tasks)

Channel	Source - Detector	Region	MNI	Coordin	ates	Distance	Specificity (%)	Mean	F-statistic	р
			Х	Υ	Z	(mm)		Difference		(FDR corrected)
ГурісаІІу	Developed:	Single > Dua	I							
9	Fz – AFz	sFG <sub>L</sub>	0	48	37	40	48.54	0.4651	9.584	0.006**
12	Fpz – AFz	sFG <sub>L</sub>	-1	61	11	41	47.28	0.949	15.2126	<0.001***
14	AF4 – AFz	$mFG_R$	15	59	22	37	52.67	0.7463	11.7451	0.002**
20	AF8 - F6	iFG <sub>R</sub>	47	45	4	33	88.89	0.6663	12.8857	0.001**
Developm	ental Coord	lination Diso	rder: Single	> Dual						
8	Fz - F1	sFG <sub>I</sub>	-11	40	47	30	74.89	0.7269	10.6007	0.003**
9	Fz – AFz	sFG <sub>L</sub>	0	48	37	40	48.54	0.8749	49.8033	<0.001***
12	Fpz – AFz	sFG <sub>L</sub>	-1	61	11	41	47.28	1.6861	70.5415	<0.001***
14	AF4 – AFz	mFG <sub>R</sub>	15	59	22	37	52.67	1.2454	48.0464	<0.001***
			0.6	61	6	30	91.67	0.823	6.9152	0.019*
16	AF4 – Fp2	mFG <sub>R</sub>	26	01						
20	Fp2 AF8 – F6	iFG <sub>R</sub>	47	45	4	33	88.89	1.1912	60.491	<0.001***
20 Single Ta	Fp2 AF8 - F6 sk: Typically	iFG <sub>R</sub>	47 > Developn	45 nental C	4 oordina	33	88.89	1.1912	60.491	<0.001***
20 Single Ta Dual Task	Fp2 AF8 - F6 sk: Typically	iFG <sub>R</sub>	47 > Developn	45 nental C	4 oordina	33 ation Disorder	74.89	0.6817	6.4882	<0.001***
20 Single Ta Dual Task 8	Fp2  AF8 - F6  sk: Typically c: Typically I	iFG <sub>R</sub> Developed >	47 > Developme	45 nental Coental Coental Coe	4 oordina ordinati	33 ation Disorder ion Disorder				
20 Single Ta Dual Task 8 9	Fp2  AF8 - F6  sk: Typically  c: Typically I  Fz - F1  Fz -	iFG <sub>R</sub> Developed >  SFG <sub>L</sub>	47 > Developm  Developme -11	45 nental Coental Coental Coe	4 oordinati 47	33 ation Disorder ion Disorder 30	74.89	0.6817	6.4882	0.024*
20 Single Task Dual Task 8 9	Fp2  AF8 - F6  sk: Typically  c: Typically I  Fz - F1  Fz -  AFz	iFG <sub>R</sub> Developed >  SFG <sub>L</sub> SFG <sub>L</sub>	47  > Developme -11 0	45 mental Comental Co	4  coordination 47 37	ation Disorder ion Disorder 30 40	74.89 48.54	0.6817 0.4487	6.4882 6.2352	0.024*
20 Single Tar Dual Task 8 9 12	Fp2  AF8 - F6  sk: Typically  c: Typically I  Fz - F1  Fz - AFz  Fpz - AFz  AF4 -	iFG <sub>R</sub> Developed >  SFG <sub>L</sub> SFG <sub>L</sub> SFG <sub>L</sub>	27 > Developme -11 0 -1	45  mental Co  40  48  61	oordinati 47 37	ation Disorder ion Disorder 30 40 41	74.89 48.54 47.28	0.6817 0.4487 0.7273	6.4882 6.2352 8.5226	0.024* 0.028* 0.008**
20 Single Task  Bual Task  9 12 14 16	Fp2  AF8 - F6  sk: Typically  c: Typically I  Fz - F1  Fz - AFz  AF2  AF4 - AF2  AF4 - AF4 - AF4 - AF4 -	iFG <sub>R</sub> Developed >  SFG <sub>L</sub> SFG <sub>L</sub> mFG <sub>R</sub>	Developme -11 0 -1 15	45 ental Co 40 48 61 59	4  coordinati 47 37 11 22	33 ation Disorder 30 40 41 37	74.89 48.54 47.28 52.67	0.6817 0.4487 0.7273 0.4906	6.4882 6.2352 8.5226 4.6787	0.024* 0.028* 0.008** 0.064 <sup>X</sup>
Dual Task 8 9 12 14 16 20	Fp2  AF8 - F6  sk: Typically  C: Typically I  Fz - F1  Fz - AFz  Fpz - AFz  AF4 - AFz  AF4 - Fp2  AF8 - F6	iFG <sub>R</sub> **Developed >  **SFG <sub>L</sub> **SFG <sub>L</sub> **SFG <sub>L</sub> **MFG <sub>R</sub> **mFG <sub>R</sub>	47  > Developme -11 0 -1 15 26 47	45  ental Co  40  48  61  59  61	4  coordinati 47 37 11 22 6	33 ation Disorder 30 40 41 37 30	74.89 48.54 47.28 52.67 91.67	0.6817 0.4487 0.7273 0.4906 0.8666	6.4882 6.2352 8.5226 4.6787 6.2113	0.024* 0.028* 0.008** 0.064 <sup>X</sup> 0.028*
20 Single Tail Dual Task 8 9 12 14 16 20 Neural Eff	Fp2  AF8 - F6  sk: Typically  c: Typically I  Fz - F1  Fz - AFz  Fpz - AF2  AF4 - AF2  AF4 - Fp2  AF8 - F6	iFG <sub>R</sub> **Developed >  **SFG <sub>L</sub> **SFG <sub>L</sub> **SFG <sub>L</sub> **MFG <sub>R</sub> **MFG <sub>R</sub> **IFG <sub>R</sub>	47  > Developme -11 0 -1 15 26 47	45  ental Co  40  48  61  59  61	4  coordinati 47 37 11 22 6	33 ation Disorder 30 40 41 37 30	74.89 48.54 47.28 52.67 91.67	0.6817 0.4487 0.7273 0.4906 0.8666	6.4882 6.2352 8.5226 4.6787 6.2113	0.024* 0.028* 0.008** 0.064 <sup>X</sup> 0.028*
20 Single Tai Dual Task 8 9 12 14 16 20 Neural Eff Typically 10	Fp2  AF8 - F6  sk: Typically  c: Typically I  Fz - F1  Fz - AFz  AF4 - AF2  AF4 - Fp2  AF8 - F6  Ciciency of P  Developed:  Fz - F2	iFG <sub>R</sub> Developed >  SFG <sub>L</sub> SFG <sub>L</sub> mFG <sub>R</sub> mFGR  iFG <sub>R</sub> Chysical Performance Single > Dual SFG <sub>R</sub> 2	47  Developme -11 0 -1 15 26 47  Demance	45 ental Co 40 48 61 59 61 45	4  coordinati 47 37 11 22 6 4	33 ation Disorder 30 40 41 37 30 33	74.89 48.54 47.28 52.67 91.67	0.6817 0.4487 0.7273 0.4906 0.8666	6.4882 6.2352 8.5226 4.6787 6.2113 4.6947	0.024* 0.028* 0.008** 0.064 <sup>X</sup> 0.028* 0.064 <sup>X</sup>
20 Single Tail Dual Task 8 9 12 14 16 20 Neural Eff	Fp2  AF8 - F6  sk: Typically  C: Typically I  Fz - F1  Fz - AFz  Fpz - AFz  AF4 - AFz  AF4 - Fp2  AF8 - F6  Ciciency of P	iFG <sub>R</sub> Developed > SFG <sub>L</sub> SFG <sub>L</sub> mFG <sub>R</sub> iFG <sub>R</sub>	47  Developme -11 0 -1 15 26 47  Demance	45 ental Co 40 48 61 59 61 45	4  coordinati 47 37 11 22 6 4	33 ation Disorder 30 40 41 37 30 33	74.89 48.54 47.28 52.67 91.67 88.89	0.6817 0.4487 0.7273 0.4906 0.8666 0.4539	6.4882 6.2352 8.5226 4.6787 6.2113 4.6947	0.024* 0.028* 0.008** 0.064 <sup>X</sup> 0.028*



Significant Channels (at Source-Detector locations) using MNI coordinates (X, Y, and Z), with the region designation of Neural Efficiency of Cognitive Performance and Physical Performance for the Interaction Effect of Group and Task between Typically Developed (TD) and Developmental Coordination Disorder (DCD) children and tasks (Single and Dual). Specificity/Coverage of the region is depicted, with the mean difference for the comparison, along with statistical information (F-statistic, p-value, and effect size). (p <0.1 $^{\text{X}}$ , p < 0.05 $^{\text{X}}$ , p < 0.01 $^{\text{X}}$ , p < 0.001 $^{\text{X}}$ ). No significant channels were implicated during Single Task, comparing TD and DCD children.

Both groups had decreased NE of CogP for the dual task condition compared to single (TD: 4 channels; DCD: 6 channels). Furthermore, during the cognitive only task (single condition), TD and DCD children had similar NE of CogP (p > 0.05), but with the additional simultaneous motor task (dual condition), the DCD group had significantly decreased NE of CogP compared to the TD group (6 channels). This indicates that DCD children were impeded in activating certain regions of the PFC, and therefore resulted in reduced CogP during the dual task. These patterns were evident across six channels within the PFC (mFG and sFG) (see Fig. 3 and Table 3). These findings suggest that children with DCD are neuroergonomically impaired and experience increased difficulty when presented with a physical challenge, due to poor, inefficient approaches in cognitive management for gross motor tasks.

NE of PhysP revealed expected neurotypical behavior for the TD group where only the dual task paradigm significantly decreased NE of PhysP, while the DCD group experienced negative NE of PhysP for both single and dual tasking (but no task distinction). These NE patterns were evident within two channels of the PFC (see Fig. 3 and Table 3). These findings indicate that novel, even simple motor tasks are approached in a neurally inefficient manner for DCD children and warrant intervention and found explicitly through a neuroergonomic approach.

# Discussion

In this study, for the first time we have investigated in a real world setting the neurobehavioral differences in the cognitive and motor capabilities of young people with the developmental motor coordination disorder known as DCD. Through a cross-sectional, within-subjects repeated measures design, with the largest neuroimaging cohort, in which participants engaged in novel solitary cognitive, and motor tasks, and a dual task (where cognitive and motor were combined), we were able to confirm that DCD is a detectable motor-cognitive deficit with hemodynamic dysfunction identified within the right middle and superior frontal gyri of the prefrontal cortex using mobile optical neuroimaging. Further, we were able to confirm that even during simple motor tasks young people with DCD have less neural efficiency and that through testing during dynamic motor activities this deficiency was further exposed during dual tasking conditions furthering our understanding of DCD and creating opportunities for novel interventions uncovered through our neurobehavioral testing paradigm.

As the results indicated, behaviorally, DCD and TD groups showed significant differences during performance of the motor task and more specifically during dual-tasking. While both groups generally had decreased performance in dual task compared to single, it was more significant for individuals with DCD. When evaluating cognitive task performance, DCD children had neurotypical trends regarding task conditions (albeit reduced Cognitive Performance within dual task compared to TD children), but irregular trends within physical gross motor task performance, further detailing the motor-cognitive deficits found within DCD.

Through neuroimaging, we were able to detect a clear difference between tasks, where the number of optodes with significant differences between the groups grew as the task moved from single cognitive task to a single motor task, and finally to a dual task (0, 1, and 6 optodes respectively with increased HbO for the TD group). Contrary to our original hypothesis, during the dual task, individuals with DCD had decreased brain activity, alongside decreased cognitive task performance, and similarly decreased physical task performance. Whilst we expected altered brain activity, the direction of change was different than that observed in adults <sup>1,6,17</sup>, and results here suggest increased task demand for the DCD group as the tasks became more motor oriented, and more difficult.

Furthermore, by combing the task performance and neuroimaging information we were able to show differences in neural efficiency generated for both the Cognitive and Physical Performance. As expected, dual task showed lower neural efficiency compared to single task, and the neural efficiency of Physical Performance specifically showing this difference only for TD individuals, confirming the motor task was already challenging for DCD group. These findings are important as they highlight that combined neuroimaging evaluation is more sensitive at detecting deficits than simple motor task performance measures, and indicates that DCD children approach, even simple novel motor tasks in a neurally inefficient manner. The testing highlights possible causes for deficits, and potential therapeutic strategies for improving motor performance in these children. Our findings also open the door for possible innovative approaches to increase activity in the prefrontal cortex and improve task acquisition and performance. Our data also confirms a mechanism for the enhanced difficulty of performing motor tasks in real world settings for people with DCD that was previously unknown. Our work confirms that DCD is not an intellectual disability, but a motor learning and performance deficit (motor-cognitive disability) through both a neuroimaging and neuroergonomic lens<sup>19</sup>.

This study is the first to reveal neural underpinnings of how DCD affects truly active, and gross motor tasking. Previously, due to constraints in neuroimaging, the literature only discussed DCD with respect to fine motor skills<sup>1,10,11,13</sup>. Using new generation wearable and mobile optical neuroimaging that has been demonstrated to measure similar localized cortical hemodynamic activity as stationary and traditional neuroimaging<sup>20–26</sup>, we were able to localize the functional deficits within the PFC of DCD children, which can allow for more targeted intervention. In addition, this approach provides a new perspective beyond clinical neuroscience, as the first study to use an applied combined human factors technique, to evaluate neural efficiency within this disability cohort. The methods and approach demonstrated can be easily adapted to broader contexts within a host of disabilities that impact motor cognition in and out-of-laboratory settings. The approaches and results may be used in the future for triaging children for DCD, to accelerate diagnosis and assess therapeutic

intervention as suggested in other developmental disorders<sup>27</sup>. We believe that wearable and mobile optical brain imaging and biomechanical information for task performance collectively provides neuroergonomic evaluation of Developmental Coordination Disorders and can help identify children more in need of guided therapeutic intervention during real-world whole-body motor tasks, targeting regions of the Prefrontal Cortex for neural engagement and recovery. We propose this approach can detect mechanisms underlying changes in conditions creating possibilities for personalized and neuroadaptive interventions to transform outcomes for movement and balance disorders.

# Methods

#### Participant Recruitment

Across 3 mainstream schools in Oxfordshire, a total of 1118 children (ages 13-14) screened for Developmental Coordination Disorder (DCD) using the Movement Assessment Battery for Children 2 (MABC-2). Those that scored above the 15<sup>th</sup> percentile of the MABC-2 were identified as Neurotypical or Typically Developed (TD) and those below the 15<sup>th</sup> percentile were identified as DCD resulting in 37 TD and 48 DCD children<sup>28,29</sup>.

Ultimately 85 children (ages  $13.92 \pm 0.33$  yrs) participated in the study (33 male, and 10 left-handed). Fitness was controlled across both groups for using additional fitness parameters including strength, power, and endurance, ensuring all groups were within the lowest quartile of the overall fitness parameters. Therefore, any group differences later found would be less drastic, but more confident, eliminating fitness as a confounding factor assessing specifically motor coordination.

All participants were confirmed to meet the eligibility requirements, and did not have cognitive, neurological, musculoskeletal, behavioral, or non-correctable visual impairments. Control variables were gathered including height, weight, and puberty status (5-stage Tanner scale). Groups showed no significant differences between control variables. Prior to the study, all participants and respective guardians signed informed consent forms, and all methods were performed in accordance with the relevant guidelines and regulations approved by the University Research Ethics Committee (UREC Registration No: 161033) and the trial is registered under ClinicalTrials.gov (NCT03150784) on 12/05/2017.

#### Task Protocol

The experiment consisted of a ten-minute session depicted in Figure 4. Using a within subjects repeated measures design, where participants completed three tasks consisting of a cognitive only task (auditory stroop), a motor only task (rhythmic stepping), and a dual task (simultaneous cognitive and motor task). The tasks had a duration of 42.5s each, with variable 20-30s rest between tasks. These tasks were repeated three times each, and are known as blocks.

The cognitive task utilized was an auditory Stroop test, presented with stimulus at 0.33Hz for approximately 14 prompts as shown in Audio S1 (supplementary file). The task prompts consisted of a voice presenting the words "High" or "Low" in either a high (400Hz) or low (200Hz) pitch for approximately 0.8-1s. Of the 14 prompts, half (seven) were congruent (high pitch along with the word "high" or low pitch along with the word "low") and the other half were incongruent (high pitch along with the word "low" or low pitch along with the word "high"). Participants were instructed to auditorily respond with the categorization of the pitch, and to ignore the word stated as shown in Video S1 (found in supplementary files).

The motor/physical task was a rhythmic stepping task, with instructions displayed visually on a laptop via a customized LabView Program in front of the participant at 0.5Hz. The stepping instructions consisted of the words "left" or "right" displayed on the left or right side of the screen respectively for a duration of 1.5s for a total of twenty stimuli (equally left and right). These stimuli were displayed after a "get ready" cue of a duration of 2.5 s. When instructed "left", participants had to step onto a standardized stepping block with their left foot initially followed by their right, then back down with their left foot followed by their right and vice versa for the "right" prompt.

# **Behavioral Performance Metrics**

Cognitive Performance (CogP) was calculated as a correct percentage of the number of auditory Stroop trials per block and per participant. Auditory Stroop responses were manually recorded by research assistants, and later calculated as CogP. Higher value indicates higher accuracy.

Physical Performance (PhysP) was calculated using information generated from an Inertial Measurement Unit (IMU; LPMS-B2, Life Performance Research, Japan) fitted to lower back of each participant (measuring physical activity at 100Hz). The IMU comprised of tri-axial accelerometers, gyroscopes and magnetometers, synced to the visual stimulus of the motor/physical task, recording physical activity per participant and repetition block. The feature extraction of the IMU data was calculated as adherence to the stimulus frequency (0.5Hz), where perfect in rhythm synchronization was 100%, while any difference to the stimulus would decrease PhysP. Therefore, PhysP was calculates as the percentage of the ratio of Block Frequency to Stimulus Frequency.

Both behavioral measures of CogP and PhysP were calculated per repetition block, per participant and calculated within the respective tasks (cognitive and physical tasks) and within the dual task (combination of both tasks).

#### Neural Activity Acquisition

Each participant was fitted with a portable and battery operated fNIRS sensor (NIRSport, NIRx Medical Technologies LLC, Glen Head, NY, USA) positioned over the forehead. fNIRS channel placement was standardized according to the established international 10-20 system for the eight light source and seven detector placements as depicted in Figure 3B. Cortical regions with landmarks for the experimental configuration were generated using fNIRS Optodes Locator Decider (FOLD) toolbox<sup>30,31</sup> with the Laboratory of Neuroimaging (LONI) Probabilistic Brain Atlas (LPBA40)<sup>32</sup>. Table 4 shows each channel according to source-

detector pair Electroencephalography (EEG) labeling with 'x-y-z' configuration coordinates and brain area/landmark specificity for improved comparability and reproducibility. The inter-channel distance of approximately 3 cm formed 20 channels (measurement areas) sampled at 7.8125Hz.

Table 4. fNIRS Positions and Brain Locations

Channel	Source	Detector	Brain Area	Specificity (%)	MNI Coo	D (mm)		
					X (mm)	Y (mm)	Z (mm)	
1	F3	F5	mFG <sub>L</sub>	74.22	-45	35	23	29
2	F3	F1	mFG <sub>L</sub>	87.01	-30	38	39	29
3	AF7	F5	iFG <sub>L</sub>	87.56	-47	42	4	34
4	AF7	Fp1	iFG <sub>L</sub>	53.57	-34	56	-4	31
5	AF3	F1	mFG <sub>L</sub>	80.24	-24	50	30	44
6	AF3	Fp1	mFG <sub>L</sub>	90.79	-26	60	5	30
7	AF3	AFz	mFG <sub>L</sub>	55.88	-16	59	21	39
8	Fz	F1	sFG <sub>L</sub>	74.89	-11	40	47	30
9	Fz	AFz	sFG <sub>L</sub>	48.54	0	48	37	40
10	Fz	F2	sFG <sub>R</sub>	75.09	11	40	48	28
11	Fpz	Fp1	$mFG_L$	50.16	-14	64	-3	31
12	Fpz	AFz	sFG <sub>L</sub>	47.28	-1	61	11	41
13	Fpz	Fp2	mFG <sub>R</sub>	51.58	14	65	-3	30
14	AF4	AFz	mFG <sub>R</sub>	52.67	15	59	22	37
15	AF4	F2	mFG <sub>R</sub>	75.53	23	51	31	43
16	AF4	Fp2	mFG <sub>R</sub>	91.67	26	61	6	30
17	F4	F2	mFG <sub>R</sub>	82.62	29	40	40	29
18	F4	F6	mFG <sub>R</sub>	87.56	46	38	24	28
19	AF8	Fp2	iFG <sub>R</sub>	52.77	34	58	-4	30
20	AF8	F6	iFG <sub>R</sub>	88.89	47	45	4	33

Channels and Source-Detector locations using Montreal Neurological Institute (MNI) coordinates (X, Y, and Z), with the brain area designation according to International 10-20 system of source-detector location designation. Brain Areas include inferior, middle, and superior (i, m, s) regions of Frontal Gyrus (FG) in either Left or Right hemispheres (L or R). Last column represents distance between source and detector.

fNIRS data was recorded via NIRStar (v14.0) and processed via NIRS AnalyzIR toolbox<sup>33,34</sup>. For each participant, attenuation changes in raw light intensity fNIRS data (two wavelengths of 850nm and 760nm) were transformed to concentration changes of oxygenated (HbO) and deoxygenated (HbR) hemoglobin respectively using the modified Beer-Lambert approach<sup>35</sup>. The data were pre-whitened to resolve high frequency noise, cardiovascular effects, and signal drift using an autoregressive model<sup>33</sup>. A baseline correction algorithm designed to remove motion artifacts/DC shifts was applied<sup>34</sup>, followed by a wavelet filter to remove motion artifacts with a threshold of 5 standard deviations, and a basis function of sym8<sup>36</sup>.

Beta values were calculated from HbO/HbR amplitudes for each block with local baseline (paired t-test: rest vs. circuit) per source-detector pair or channel for each task condition through subject-level autoregressive iteratively reweighted least squares General Linear Modeling. The parameter estimates were derived using a canonical HRF, as previous evidence suggests that tasks of duration longer than ten seconds, such as within this experiment, have better performance for testing hypothesis of difference response amplitudes<sup>37</sup>. The parameters of the canonical (double gamma function) HRF employed included: 1s as the dispersion time constants for the peak and undershoot period, 4s and 16s as the peak and undershoot time respectively, 1:6 as the ratio of main peak height to the undershoot, and 32s as the duration.

# Neural Efficiency Extraction

Neural Efficiency (NE) relates the neurophysiological measures of brain activity to an individual's performance according to the demands of the task and the capability of the individual<sup>18</sup>. NE calculations incorporated the Neural Metrics (HbO) with the Behavioral Performance metrics (Cognitive Performance and Physical Performance) within the formula below resulting in NE of CogP and NE of PhysP respectively.

$$NE = \frac{z(Behavioral\ Performance) - z(Neural\ Metric)}{\sqrt{2}}$$

#### Statistical Approach and Analysis

Statistical analysis of behavioral performance metrics (Cognitive Performance and Physical Performance) during the experimental procedure employed the use of Linear Mixed Modeling (LMM) implemented in NCSS (NCSS, LLC. Kaysville, Utah, USA). The dependent measures were assessed, and parameter estimates derived. Bonferroni p-value adjustments were calculated to indicate significance for interaction effects. Cohen's d values were also calculated to indicate the observed effect size. The subject factor was treated as a random effect drawn from a larger population, while the fixed effects were group (TD vs. DCD) and task condition (single vs. dual).

Within the neuroimaging results, group analysis employed mixed effects with repeated measures across the entire sample allowing for a population inference of the neural measures (HbO and HbR) per channel. The subject factor was treated as a random effect drawn from a larger population, while the fixed effects were group (TD vs. DCD), and task (Auditory Stroop vs. Stepping vs. Dual). Type I Errors were controlled using false detection rate (FDR) Benjamini-Hochberg adjustments<sup>38,39</sup>.

Statistical analysis of NE metrics (NE of CogP and NE of PhysP) per channel following the approach of that of performance metrics. The subject factor was treated as a random effect drawn from a larger population, while the fixed effects were group (TD vs. DCD) and task condition (single vs. dual).

# Declarations

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Author contributions: S. J. planned and performed experiments, was involved in project administration, collected, and analyzed data, drafted the manuscript, and edited and reviewed the manuscript. B. D. W., planned and performed experiments, were involved in project administration, and collected data. P. E. was involved in project conceptualization, funding acquisition, planned and performed experiments, project administration, and editing the manuscript., Y. L., and D. N. S. performed experiments and collected data. A. M. performed experiments and was involved in project administration. M. I. was involved in data analysis. A.D., S. K., and H. I. were involved in project conceptualization and funding acquisition. T. W. was involved in project conceptualization, data analysis, funding acquisition, supervision reviewing and editing the manuscript. H. A. was involved in analytical conceptualization, project administration, data analysis, supervision, and drafting the manuscript, and reviewing/editing the manuscript.

Competing interests: Authors declare no competing interests.

Data and materials availability: All data are available in the main text, or the supplemental material

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# **Figures**

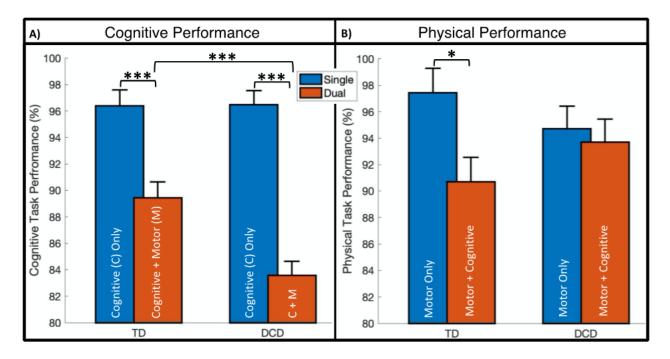


Figure 1

Cognitive Task Performance (%) and Physical Task Performance (%) between group (DCD and TD) per task condition (Single and Dual) for 85 subjects. Increased values indicate better performance. (\*p<0.05; \*\*p<0.01; \*\*\*p<0.001). A) Single task is the cognitive only task, while dual task is with the additional motor task. B) Single task is the motor only task, while the dual task is with the additional cognitive task.

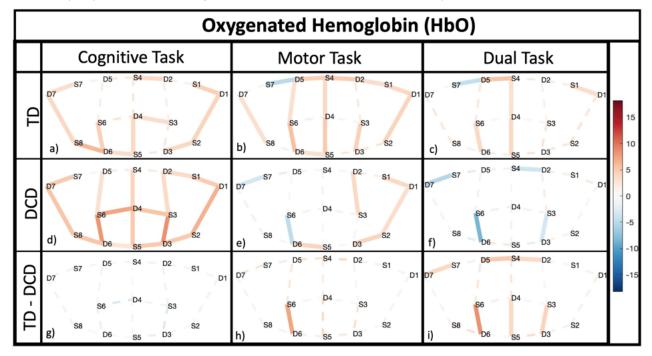


Figure 2

Neuroimaging and Neurobehavioral results for 85 subjects, displaying areas of interest across the PFC comparing differences between groups (TD of DCD) and task (Cognitive, Motor, or Dual Task). A) fNIRS results per group (rows 1&2) and task (columns 1-3), and between group (row 3). Red bars indicated increased HbO (activity), while blue bars represent decreased HbO according to international 10-10 system.

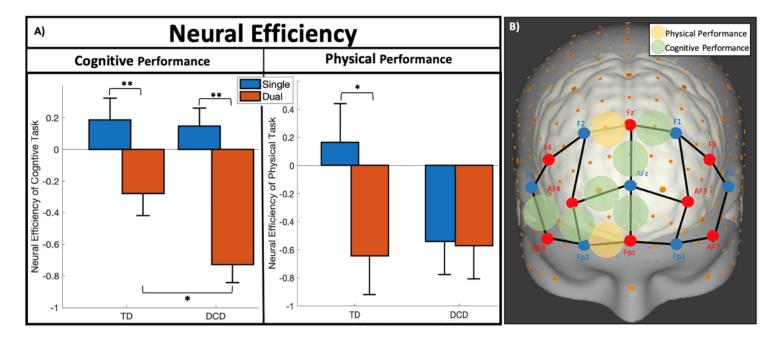


Figure 3

A) Example patterns of Neurobehavioral (Neural Efficiency) results per group and task (\*p<0.05, \*\*p<0.01, \*\*\*p<0.001). Cognitive Performance example pattern is from optode 9, while Physical Performance example pattern is from optode 13. B) Significant regions of the Neural Efficiency patterns found in A, where green circles indicate significant patterns for the NE of Physical Performance.

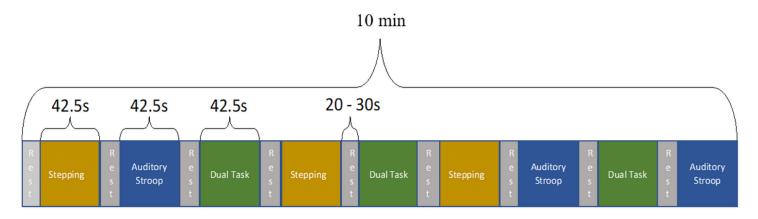


Figure 4

Procedure for Participant Selection and Experimental Protocol Experimental flow, from screening for participants with Developmental Coordination Disorder through running the 10-minute protocol. The 10-minute indicates the three tasks (Stepping, Auditory Stroop and combinatory Dual Task) predicated by variable rests of 20-30s repeated three times each, in a pseudo-random order.

# **Supplementary Files**

This is a list of supplementary files associated with this preprint. Click to download.

- AudioS1.mp3
- DCDAim1SRSupplementalv1.pdf
- VideoS1large.mp4