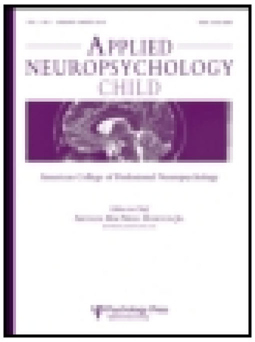

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Relationship between motor abilities and executive functions in patients after pediatric stroke

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ABSTRACT

Patients after pediatric stroke typically experience varying extent of motor and cognitive impairments. During rehabilitation, these impairments are often treated as separate entities. While there is a notion claiming that motor and cognitive functions are interrelated to some degree in healthy children, a minimal amount of evidence exists regarding this issue in patients after pediatric stroke. The purpose of this study was to investigate the association between motor abilities and executive functions in patients after pediatric arterial ischemic stroke. Twenty-seven patients (6 – 23 years) diagnosed with pediatric arterial ischemic stroke in the chronic phase ($\geq$ 2 years after diagnosis, diagnosed $<$ 16 years) and 49 healthy controls (6 – 26 years) were included in this study. Participants completed six tasks from standardized neuropsychological tests assessing the dimensions of executive functions, namely working memory, inhibition, and shifting. Additionally, we assessed hand strength and upper limb performance with two tasks each. In the patient group, the association between upper limb performance and executive functions was stronger than between hand strength and executive functions. Our results point toward the idea of a close interrelation between upper limb performance and executive functions. Training more complex and cognitively engaging motor abilities involving upper limb performance rather than basic motor abilities such as hand strength during a rehabilitation program may have the power to foster executive function development and vice versa in patients after stroke.

KEYWORDS
Childhood stroke; cognition; neonatal stroke; rehabilitation

Introduction

Pediatric arterial ischemic stroke is rare but has a long-term impact on a child's life (Amlie-Lefond et al., 2008; Greenham et al., 2016; Kornfeld et al., 2015). With an incidence between 2 and 13 cases per 100,000 children, it is a significant cause of childhood morbidity and followed by an increased risk for motor and cognitive sequelae (Amlie-Lefond et al., 2008; Steinlin et al., 2005; Studer et al., 2014). Contrary to popular assumptions, children do not necessarily recover better from stroke than adults (Goeggel Simonetti et al., 2015). Early brain damage, such as arterial ischemic stroke, affects the normative development of a child, leading to a lack of accomplishment of developmental milestones and, hence, negative long-term outcomes ("growing into deficits"; Beer & De Scheltens, 2016; Cnossen et al., 2010; Lidzba et al., 2019). However, critical and sensitive periods during brain development offer "windows of opportunities" (Ismail et al., 2017) during which the developing brain can particularly benefit from interventions (Ismail et al., 2017).

Pediatric stroke is often accompanied by alterations in motor abilities varying between mild clumsiness, deficits in finger movements, gross motor function, dystonia, and hemiparesis (Boardman et al., 2005; Everts et al., 2008; Gordon et al., 2015; Greenham et al., 2016). Motor abilities refer to a multidimensional construct including strength, coordination, and gross motor functions (Lämmle et al., 2010). Even mild motor impairment may limit a child's ability to participate in daily activities. In children with cerebral palsy, upper limb functions are often compromised which impedes participation in leisure or scholastic activities (Choudhary et al., 2013). Previous studies show that manual abilities are closely related to quality of life in patients after pediatric stroke (Caspar-Teuscher et al., 2019; Kornfeld et al., 2017), and impairment in bimanual tasks, such as

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eating and dressing, were reported to be a significant concern for parents (Galvin et al., 2010).

Executive functions (EF) mature rather late in the child's development and are prone to the issue of "growing into deficits" (Dinomais et al., 2015; Long et al., 2011). According to one of the many existing EF models (Anderson, 2002), the latent-variable analysis described by Miyake et al. (2000) suggests that EF are higher-order cognitive processes comprising the dimensions of working memory, inhibition, and shifting. Whereas some studies describe worse performance in EF after stroke compared to a normative group (Hajek et al., 2014; Jacomb et al., 2018), other findings suggest that EF remain intact after pediatric stroke (Kolk et al., 2011). Studer et al. (2014) demonstrate their findings in more detail, suggesting that although cognitive performance is often within the lower reference range, performance is significantly worse after pediatric stroke compared to a control group.

The localization of brain lesion was previously shown to relate to bimanual performance in children with unilateral cerebral palsy (Crichton et al., 2020). In addition to lesion location, age at stroke, time since stroke, lesion laterality, and lesion size are suggested to modulate motor outcome, EF, or both (Allman & Scott, 2013; Dinomais et al., 2015; Everts et al., 2008; Westmacott et al., 2010). Consequently, when investigating motor abilities and EF after stroke, it is important to consider these factors as possible confounding variables.

In healthy children and adolescents, weak evidence exists that certain motor abilities are related to specific cognitive functions (Van der Fels et al., 2015). Particularly fine motor functions, bilateral body coordination, and dexterity somewhat relate to certain cognitive functions such as attention and EF in healthy children and adolescents (Van der Fels et al., 2015; Wassenberg et al., 2005). In contrast, gross motor functions, balance, or strength are suggested to be less associated with cognition. Fine motor functions entail a higher cognitive demand than gross motor functions and can be considered as complex motor abilities requiring higher-order cognitive processes (Van der Fels et al., 2015).

Only a few studies have examined the association between motor abilities and cognitive functions in patients with brain lesions during childhood. For instance, motor imagery is correlated with working memory in children with unilateral cerebral palsy, suggesting that performance in motor imagery depends on working memory performance (Souto et al., 2020). It will remain unknown whether motor and cognitive impairment in children and adolescents after brain lesion are both a consequence of the same problem (i.e., brain lesion entails cognitive and motor impairment) or whether motor and cognitive impairment present two different aspects of the disease (i.e., motor problems entail cognitive problems or vice versa). Despite the notion that certain motor abilities (i.e., complex motor abilities with cognitive demand) and cognition are somehow interrelated in healthy children and adolescents (Roebers & Kauer, 2009; Van der Fels et al., 2015; Wassenberg et al., 2005), the association between these two processes was rarely described in patients after pediatric stroke thus far.

The first aim of the present study was to investigate motor abilities and EF in patients after pediatric arterial ischemic stroke and healthy controls. The second aim was to shed light on the relationship between motor abilities and EF in patients after pediatric stroke. We hypothesize that (1) performance in motor abilities and EF are worse in patients compared to healthy controls. We further hypothesized that (2) motor abilities (hand strength and upper limb performance) correlate positively with EF in patients. Because upper limb performance is more complex and cognitively demanding than hand strength, we hypothesize that (3) a stronger relationship occurs between upper limb performance and EF in patients, rather than hand strength and EF in patients.

A possible relationship between motor abilities and cognitive functions would be of particular interest for neurorehabilitation, given that a training program in one domain could improve performance in the other domain. In post-stroke rehabilitation, motor and cognitive impairments are usually addressed as separate entities, with focus on physical and occupational therapy (Chen et al., 2013). Understanding the relationship between motor and cognitive functions after pediatric stroke might therefore contribute to the development of multimodal therapeutic interventions.

Materials and methods

Participants

This cross-sectional study is part of a clinical trial assessing hemispheric reorganization in patients after pediatric arterial ischemic stroke (HERO research program; Kornfeld et al., 2015), which was approved by the Cantonal Ethics Committee of Bern. Patients were recruited from the Swiss Neuropediatric Stroke Registry (SNPSR; Steinlin et al., 2005). The study was carried out in accordance with the Declaration of Helsinki and written informed consent was obtained from the participant or parent/legal guardian depending on the age of the participant.

Inclusion criteria for the stroke sample were a diagnosis of perinatal/neonatal arterial ischemic stroke (stroke prior to 28 days) or childhood stroke (stroke between 1 month and 16 years; Amlie-Lefond et al., 2008) at least two years prior to recruitment (confirmed by MRI and/or CT) and age older than 6 years at the time of the examination. Due to the rarity of the disease, we included both perinatal/neonatal and childhood arterial ischemic stroke (hereinafter referred to as pediatric stroke, which encompasses perinatal/neonatal and childhood stroke), as well as participants with unilateral and bilateral lesions. Exclusion criteria were: ferrous implants, claustrophobia, active epilepsy, and behavioral problems interfering with the MRI investigation (performed in the HERO research program).

The control sample was recruited through advertisement and flyers in the neighborhood near the University Hospital of Bern. Controls were matched according to age and gender and met the following inclusion criteria, which were determined via a telephone interview with the participant or a parent (if < 16 years): Age at examination ≥ 6 years and absence of neurological diseases or psychiatric disorders (such as depression, autism spectrum disorder, or anxiety disorder). A total of 29 patients after stroke and 50 healthy controls were identified from the HERO-study, of whom 27 patients and 49 healthy controls met the inclusion criteria for the present study (one patient and one control participant were not included as they were under the age of six and one patient was not included due to missing data).

Neuropsychological assessment

All tasks were performed in a quiet room by a trained neuropsychologist. To obtain a reliable and valid assessment of EF and its three dimensions (working memory, inhibition, and shifting according to Miyake et al., 2000), every EF dimension was assessed with two different tasks. Additionally, all three EF dimensions were assessed with a task including manual involvement (e.g., pressing a response button, drawing a line) and a task without manual involvement (e.g., verbal answers only). All neuropsychological tests were performed by the patient's dominant hand, which was assessed with the Edinburg handedness inventory (Oldfield, 1971).

Working memory

Working memory was assessed using the subtests Letter-Number-Sequencing and Digit Symbol-Coding (hereinafter referred to as Coding) of the Wechsler Intelligence Scale for Children (WISC-IV; Petermann & Petermann, 2012) or the Wechsler Intelligence Scale for Adults (WAIS-IV; Petermann, 2012) depending on the age of the participant. In the Letter-Number-Sequencing task (WISC-IV reliability $r = .90$; WAIS-IV reliability $r = .86$; validity see test manuals; Williams et al., 2003), participants heard a sequence of letters and numbers and were asked to repeat this sequence beginning with the letters in alphabetical order followed by the numbers in ascending order. Starting with two digits per sequence, the difficulty gradually increased.

For the Coding task (WISC-IV reliability $r = .85$; WAIS-IV reliability $r = .86$; validity see test manuals; Williams et al., 2003), participants saw a code key of numbers (1–9) each with a corresponding symbol. The task included rows with pairs of numbers and blank squares, in which the participants were required to complete the blank squares with the symbol associated to the number as fast as possible. This test is often used to assess processing speed, however storing symbols in the working memory instead of constantly referring to the code key leads to better performance (Pukrop et al., 2003). Hence, this task involves working memory such as suggested in the previous literature (Pukrop et al., 2003).

Inhibition

Inhibition was measured using the Go/NoGo task of the Test of Attentional Performance (TAP) (reliability $r = .73$; validity see test manual; Zimmermann & Fimm, 2012) and the Color Word Interference Test (CWIT) third condition of the Delis-Kaplan Executive Function System (reliability $r = .75$; validity see test manual; Delis et al., 2001). In the Go/NoGo task, participants saw a random sequence of two different crosses (× or +) presented consecutively in the middle of the screen. They were required to press the response button as quickly as possible as soon as the × appeared. According to the manual, the number of errors is an indicator of inhibitory control (Zimmermann & Fimm, 2012). In the CWIT third condition, the participants were presented 50 words each printed in dissonant ink colors. They were asked to name the color of the ink and not to read the word.

Shifting

For the assessment of shifting, the Trail-Making Test (TMT) fourth condition and the CWIT fourth condition of the D-KEFS were performed (Delis et al., 2001). In the TMT fourth condition (reliability $r = .38$; validity see test manual), participants were required to connect the numbers and letters with a pencil on a paper in ascending order as fast as possible. In the CWIT fourth condition (reliability $r = .65$; validity see test manual), participants were presented 50 words, half of them printed in dissonant ink color, half of them presented in a rectangle. The task was the same as in the CWIT third condition, except for the words presented in rectangles; there, the participants were required to read the word and not name the ink color. Hence, the task asks to shift from one rule to the other. Letter-Number-Sequencing and the CWIT were considered as tasks without manual involvement. Coding, Go/NoGo, and the TMT fourth condition were conceptualized as tasks with manual involvement.

Motor assessment

Hand strength

Grip and pinch strength were used to assess maximal hand strength. Grip strength (reliability $r = .82–.99$; Mathiowetz et al., 1984) was measured using a Baseline pneumatic squeeze dynamometer and pinch strength (reliability $r = .75–.99$; Mathiowetz et al., 1984) was tested with a Baseline mechanical pinch gauge, each measured three times for every hand. The maximum trial of both hands was used for further analysis. Due to the inclusion of patients with bilateral lesions ($n = 5$) and to reduce the number of variables, we did not analyze ipsi- and contralesional motor performance separately, but averaged ipsi- and contralesional motor performance to a grip and a pinch strength index such as suggested in a previous study (Auyeung et al., 2008).

Upper limb performance

The Melbourne Assessment of Unilateral Upper Limb Function (MUUL; Gilmore et al., 2010; Randall et al., 2001) and the ABILHAND-Kids (Arnould et al., 2004) were performed to assess upper limb performance. The MUUL is a clinician-based functional performance assessment that measures the quality of unilateral upper limb movement such as reach, grasp, manipulation, and release (reliability

$r = .96$; Randall et al., 2001). According to the manual, the child's performance was video-taped and, consequently, the 16 items are scored by a trained physician. For each hand, four subscales are computed (range of movement, accuracy, dexterity, and fluency) varying from 0 to 122, which were converted into a percentage. A MUUL index was calculated using the average of the eight subtests from the left and right hand, resulting in a score for bilateral upper limb performance.

The ABILHAND-Kids is a questionnaire that measures bimanual abilities and was developed for children and adolescents with cerebral palsy (reliability $r = .94$; excellent construct validity; Arnould et al., 2004; Bourke-Taylor, 2003). According to the authors of the questionnaire, manual abilities can be defined as a behavior to perform daily activities using the upper limbs, regardless of the strategies used (Arnould et al., 2004; Penta et al., 2001). Parents rate their child's performance with 21 bimanual items of daily activities (e.g., "zipping up a jacket" or "unwrapping a chocolate bar"). Using the Rasch model, raw scores were converted into the ABILHAND-Kids score according to the manual varying from −6.753 to +6.684 with a higher score indicating better bimanual abilities. Upper limb performance is thus recorded from two perspectives: first, by means of the MUUL as an objective measure to quantify upper limb performance and, second, by means of the ABILHAND-Kids, which records the subjective assessment of the parents.

Baseline variables and lesion characteristics

The nonverbal IQ was included as baseline variable and was assessed by means of the Test of Nonverbal Intelligence, Fourth Edition (TONI-4) designed for individuals aged 6–89 years (reliability $r = .88$; validity see test manual; Brown et al., 2010; Ritter et al., 2011). Participants were asked to complete a stimulus pattern by choosing the correct pattern, which requires abstract reasoning and problem solving. The Pediatric Stroke Outcome Measure (PSOM) was performed to assess the disease-specific outcome (Kitchen et al., 2012). The PSOM (reliability $r = .93$; good construct validity) evaluates neurological deficits and consists of five subscales (right and left sensorimotor functioning, language production, language comprehension, and cognition/behavior) estimating stroke severity (range $0 - 2$ for each subscale). We report the PSOM sensorimotor average of both sides for the patient sample.

Lesion size, lesion laterality, and lesion location were obtained from anatomical images of the HERO MRI protocol (Kornfeld et al., 2015; Wiedemann et al., 2020). High-resolution anatomical T1-weighted images were acquired on a 3 T Magnetom Verio Siemens scanner (Siemens, Erlangen, Germany) using a magnetization-prepared rapid acquisition gradient-echo (MP-RAGE) sequence (repetition time = 2530 ms; echo time = 2.92 ms; inversion time = 1100 ms; 160 sagittal slices; flip angle = 9°; field-of-view = 256 mm × 256 mm; matrix dimension = 256 × 256; isotropic voxel resolution = 1 mm^3). Lesion related characteristics were determined by a board-certified neuroradiologist. To calculate the lesion size, ischemic lesions were manually traced to calculate the volume of affected brain tissue. Lesion size was defined as the affected brain tissue in relation to the total brain volume. Total brain volume was calculated using the MATLAB based toolbox SPM. Lesion laterality was classified depending on the affected hemisphere (left, right, bilateral) and lesion location was divided into three broad categories (cortical, subcortical, combined cortical and subcortical; Everts et al., 2008).

Statistical analysis

Statistical analyses were performed with IBM SPSS Statistics 25.0 (IBM, Armonk, New York). Alpha level was set to .05 and effect sizes were interpreted according to Cohen (1988) with $r = .1$ small effect, $r = .3$ medium effect, and $r = .5$ large effect. Post hoc power analysis (power = .80, $n = 27$, $\alpha = .05$, alternative = one-sided) revealed that the minimum correlation coefficient necessary is .44. Althouse (2016) suggests that in substudies from a larger clinical trial (such as the present study) with predefined hypotheses, adjusting for multiple comparisons is not desirable. We followed these suggestions and did not correct for multiple comparisons but acknowledge that additional studies are required to confirm our findings. We used raw scores for further data analysis (with age as covariate) for all variables, as the tests assessing motor abilities do not provide age-corrected standard scores. For each of the motor and cognitive outcomes, raw scores were transformed into z-scores using the mean and standard deviation of the healthy control group. A positive z-score indicates good performance. To obtain a composite score of EF, the average of the six EF z-scores was calculated (Keefe et al., 2005).

Demographic variables were compared between patients and controls using a two-tailed χ^2-test (for categorical data) or a two-tailed independent t-test (for continuous data). Group differences in motor abilities and EF were analyzed using a one-sided independent t-test. To further investigate motor and cognitive impairments (defined as a test score below one standard deviation of the mean score of a control group such as suggested by the Gaussian normal distribution), one-sided χ^2-tests were used to compare the frequency of participants with cognitive impairments (z-score < -1.0) in both groups.

The relationship between motor abilities and EF was only investigated in the patient group due to the small variance of the MUUL and ABILHAND-Kids scores in the control sample. We computed one-sided parametric partial correlations. When potential confounders, such as age at stroke, age at examination, time since stroke, sex, lesion laterality, lesion location, or lesion size were significantly associated with the motor or EF measures, they were entered as covariates in the partial correlation. IQ was not entered as covariate as IQ is a holistic measure of global functional outcome influenced by genes, education, experiences, and environmental factors and thus cannot be separated from the influence of a neurodevelopmental disorder such as stroke (Dennis et al., 2009). Additionally, for comparison reasons, we also computed bivariate correlations between the motor and EF outcomes without controlling for covariates.

To further disentangle the relationship between motor abilities and EF, we performed a series of hierarchical regression analyses to investigate whether motor abilities accounted for significant changes in variance of EF. Covariates were entered into the model in the first step, followed by motor abilities. We calculated ΔR^2, representing the unique amount of variance that the predictor (motor abilities) contributes when added to the model.

Results

Demographics

For demographic characteristics and baseline variables, see Table 1. No significant differences were found in terms of age at assessment and sex. IQ was significantly worse in the patient group compared to the control group.

Motor abilities and executive functions in patients and healthy controls

Patients did not differ significantly in their EF performance when compared to the control group nor was the frequency of impairments higher in patients than controls (*p* values (*ps*) $> .05$; Online Supplementary Table 1). Although not significant, the patient's performance in EF was slightly lower compared to the control group. No group difference was found for hand strength (*ps* $> .05$). Patients showed significant worse performance in both tests assessing upper limb performance (MUUL index: $t = -3.247$, $p = .002$; ABILHAND-Kids: $t = -4.633$, $p < .000$) and higher rates of impairments (MUUL index: $\chi^2 = 4.890$, $p = .014$; ABILHAND-Kids: $\chi^2 = 23.438$, $p < .000$).

Relationship between motor abilities and executive functions

Table 2 presents the correlations between potential confounders and the motor and EF outcomes in patients. Time since stroke and sex were not significantly associated with any of the measures and were therefore not considered in the following partial correlation analysis. Except for shifting (TMT fourth condition), lesion laterality was not associated with the outcome measures. Pinch strength was related to lesion location. Hence, lesion laterality and lesion location were not entered as confounding variables in the partial correlation analysis. Lesion size was significantly associated with some of the outcome measures (see Table 2). Due to the association of age at examination, age at stroke, and lesion size with the motor outcomes and EF, we entered these three variables as covariates in the partial correlation analysis.

Table 1. Demographic and baseline variables of the patients and healthy controls.

	Patients	Controls	$t(df)/\chi^2(df)$	*p*
Sex				
n females (%)	11 (40.7)	27 (55.1)	1.436 (1)	.231
n males (%)	16 (59.3)	22 (44.9)		
Age at exam (years)				
M (*SD*)	14.57 (5.08)	14.29 (5.37)	.220 (74)	.845
range	6.14 – 23.14	6.35 – 25.97		
Nonverbal IQ				
M (*SD*)	97.78 (9.33)	103.71 (9.78)	−2.574 (74)	.012
Range	84–120	89–127		
PSOM				
M (*SD*)	0.44 (0.61)	–	–	–
Range	0–2			
Age at stroke (years)				
M (*SD*)	6.26 (5.24)	–	–	–
range	0–15.63			
Time since stroke (years)				
M (*SD*)	8.31 (3.56)	–	–	–
Range	2.09–15.57			
Type of stroke				
n neonatal (0–28 days)	6 (22.2%)	–	–	–
n childhood (>1 month)	21 (77.8%)			
Lesion size[a]				
M (*SD*)	1.46 (2.69)	–	–	–
Range	.0025–11.68			
Lesion laterality				
n left (%)	17 (63.0)	–	–	–
n right (%)	5 (18.5)			
n bilateral (%)	5 (18.5)			
Lesion location				
n cortical (%)	4 (14.8)	–	–	–
n subcortical (%)	13 (48.1)			
n combined cortical and Subcortical (%)	10 (37.1)			

Note. Patients, $n = 27$ and healthy controls, $n = 49$. M = Mean; SD = Standard Deviation; t = t-test; χ^2 = chi-square; df = degrees of freedom; p = level of significance, two-tailed; PSOM = Pediatric Stroke Outcome Measure (range 0–2).
[a]Lesion size in relation to the total brain volume (cm^3): Lesion volume/total brain volume × 100.

Table 2. Relationships between motor and cognitive outcomes and potential confounders in patients.

	Age at exam r	Age at stroke r	Time since stroke r	Lesion size r	Sex[a] r	Lesion location[b] F	Lesion laterality[b] F
Overall EF index	.741**	.461*	.379	−.298	.177	.648	.247
Working memory							
Letter-number-sequencing	.056	−.129	.269	−.458*	−.053	.896	2.041
Coding	.839**	.694**	.119	−.295	.299	1.441	.091
Inhibition							
CWIT 3rd condition	.731**	.485*	.266	−.374	.163	1.757	.115
Go/NoGo	.522*	.362	.212	−.008	.291	.389	1.317
Shifting							
CWIT 4th condition	.590**	.410*	.162	−.185	.128	4.188	.149
TMT 4th condition	.605**	.296	.365	−.048	.260	.138	4.806*
Hand strength							
Grip strength index	.726**	.576**	.189	−.315	−.148	1.247	.348
Pinch strength index	.665**	.661**	−.023	−.336	−.161	17.479**	.674
Upper limb performance							
MUUL index	.295	.255	.045	−.684*	.014	.014	.419
ABILHAND-Kids	.354	.249	.139	−.400*	.351	.843	.007

Note. Patients, $n = 27$. EF = executive functions; CWIT = Color-Word-Interference Test; TMT = Trail-Making Test; MUUL = Melbourne Assessment of Unilateral Upper Limb Function; r = two-sided Pearson's correlation; F = F-Statistics.
[a]A point-biserial correlation was used as sex is a discrete dichotomous variable. [b]The relationships with lesion location (cortical, subcortical, combined cortical and subcortical) and lesion laterality (left, right, bilateral) were computed using a one-way ANOVA as lesion laterality and lesion location are discrete variables.
*$p < .05$. **$p < .01$.

Table 3. Partial correlation coefficients (in bold) and bivariate correlation coefficients (in parentheses) between motor abilities and executive functions in the patient group.

	Hand strength		Upper limb performance	
	Grip strength index	Pinch strength index	MUUL Index	ABILHAND-Kids
Overall EF index	**.071** (.683**)	**.021** (.592**)	**.463*** (.575**)	**.394*** (.603**)
Working memory				
Letter-Number-Sequencing[a]	**.124** (.249)	**.286** (.279)	**.285** (.514**)	**.300** (.409*)
Coding[b]	**−.268** (.641**)	**−.237** (.616**)	**.280** (.530**)	**.226** (.510**)
Inhibition				
CWIT 3rd condition[a]	**.107** (.679**)	**−.116** (.538**)	**.332** (.504**)	**.110** (.446*)
Go/Nogo[b]	**.120** (.433*)	**.093** (.380*)	**.402*** (.433*)	**.311** (.380*)
Shifting				
CWIT 4th condition[a]	**−.027** (.499**)	**−.148** (.388*)	**.453*** (.395*)	**.250** (.430*)
TMT 4th condition[b]	**−.046** (.480**)	**−.220** (.336)	**.215** (.105)	**.351** (.444*)

Note. Bold data represent partial correlation coefficients controlled for age at examination, age at stroke, and lesion size. Data in parentheses represent bivariate correlation coefficients without controlling for confounding variables. Patient group, $n = 27$. EF = executive functions; CWIT = Color-Word Interference Test; TMT = Trail-Making Test; MUUL = Melbourne Assessment of Unilateral Upper Limb Function.
[a]Tasks without manual involvement. [b]Tasks with manual involvement. A positive relationship indicates that better performance in EF is associated with better performance in motor abilities.
*$p < .05$. **$p < .01$.

Results of the partial correlation analysis between motor abilities and EF controlled for age at examination, age at stroke, and lesion size are displayed in Table 3. No significant relationship was found between grip strength index and EF nor between pinch strength index and EF in our patient sample. Concerning upper limb performance, the MUUL index correlated significantly with some of the EF measures and the overall EF index whereas the ABILHAND-Kids correlated significantly with the overall EF index. Correlation coefficients for cognitive tasks with manual involvement (coding, Go/NoGo, TMT) did not differ from correlation coefficients of cognitive tasks without manual involvement (Letter-Number-Sequencing, CWIT). This result presents evidence that cognitive tasks with manual involvement are not more closely related to motor abilities than cognitive task without manual involvement.

Additionally, bivariate correlations (without entering any covariates) are presented in parentheses in Table 3. Almost all correlations are significant with large effect sizes. After adjusting for age at examination, age at stroke, and lesion size, the correlation coefficients between hand strength and EF decreased largely. In contrast, the correlations coefficients between upper limb performance and EF also decreased, but some remained significant, indicating that the relationship between upper limb performance, notably between the MUUL index and EF, is stronger than between hand strength and EF.

Results of the hierarchical multiple regression analyses revealed that after controlling for age at examination, age at stroke, and lesion size, neither grip strength ($\Delta R^2 = .002$; $p = .749$) nor pinch strength ($\Delta R^2 = .000$; $p = .926$) accounted for a significant amount of variance in EF. The ABILHAND-Kids explained no significant additional amount of variance in EF, but a trend can be reported ($\Delta R^2 = .052$; $p = .063$). The MUUL was a significant predictor ($p = .026$), explaining 7.2% of variance in overall EF after controlling for the covariates.

Discussion

This cross-sectional study investigated motor abilities and EF in patients after arterial ischemic stroke and healthy controls and examined whether motor abilities and EF are interrelated in patients after stroke. The patient's performance in EF and hand strength did not significantly differ compared to the control group whereas upper limb performance was significantly worse in patients than controls. Neither time since stroke, sex, lesion laterality, nor lesion location were related to motor or cognitive performance. However, age at examination, age at stroke, and lesion size correlated significantly with some of the motor or cognitive outcomes. After adjusting for age at examination, age at stroke, and lesion size, our data suggest that upper limb performance, but not hand strength, is closely related to EF in patients after pediatric stroke. Cognitive tasks with manual involvement did not relate to motor abilities differently than cognitive tasks without manual involvement. Our findings further support the notion that specific motor abilities are related to EF in patients after pediatric arterial ischemic stroke.

In terms of EF, our patient sample did not differ in their mean performance nor did they display a higher frequency of impairments than the control sample. These findings further confirm results by Kolk et al. (2011), suggesting that EF remain intact after stroke, whereas attention, memory, and sensorimotor functions are worse compared to healthy controls. In contrast, several studies reveal that pediatric stroke entails alterations in cognitive functions (Hajek et al., 2014; Jacomb et al., 2018; Studer et al., 2014). In addition, we did not find group differences in hand strength, which is surprising as several studies suggest that stroke is followed by weaknesses in finger and hand movements (Everts et al., 2008; Guzzetta et al., 2010). One reason might be that we included only patients in the chronic phase of stroke (≥ 2 years after diagnosis), whereas previous studies focused on patients in earlier stages after stroke (Guzzetta et al., 2010: three months after stroke) or on a mixed sample (Everts et al., 2008: 1 month to 14 years after stroke). Furthermore, our patient's cognitive and motor performance may be biased as our rather heterogeneous and small sample does not account for patients that are lost to follow up (due to comorbidities or adverse long-term outcomes).

Compared to the control sample, the mean group performance in upper limb performance was worse and the prevalence of impairments was higher in the patient sample. The ABILHAND-Kids and the MUUL are both designed to assess upper limb performance in children and adolescents with neurological impairments and are thus particularly sensitive to alterations in motor abilities. However, our results are in line with previous findings showing that patients after neonatal stroke spend less time with bilateral toy manipulation suggesting a reduction of bimanual performance after stroke (Chen et al., 2013).

Motor and cognitive functions are often studied separately and are generally viewed as independent phenomena. However, there are several possible notions explaining the relationship between motor and cognitive functions in our patient sample.

First, the link between motor and cognitive functions might occur because both, motor and cognitive functions, have several common underlying processes, such as sequencing, monitoring, and planning of task demands (Roebers & Kauer, 2009). Bilateral upper limb performance such as bimanual activities includes the coordinated use of both hands, the integration of motion sequences, and the fine-tuning of movements and hence contains cognitive demands (Davis et al., 2010). Because of this interrelation, a disruption in one functional domain (i.e., EF) may entail consequences in the associated domain (i.e., upper limb performance).

Second, our data point toward the idea that motor and cognitive functions are only interrelated in regard to specific sub-functions in patients after pediatric stroke (Diamond, 2000; Roebers & Kauer, 2009; Van der Fels et al., 2015). We did not find a link between hand strength and EF in our small and heterogeneous patient sample but our results suggest a link between upper limb performance and EF, independent on whether EF tasks included manual involvement or not. Van der Fels et al. (2015) show in their review including healthy children and adolescents that closer associations between motor and cognitive domains occur when fine motor functions are the focus of research (opposed to gross motor functions such as balance, strength, or agility). Fine motor functions and upper limb performance that involve functional movements (i.e. grasping, object manipulation, or reaching) are suggested to hold more cognitive demand than gross motor functions and hence might present a stronger link to cognitive performance (Hooyman et al., 2021; Wassenberg et al., 2005; Ziereis & Jansen, 2016). Together, our data follow the idea that only specific motor abilities entailing a certain extent of cognitive demand are significantly interrelated with EFs in patients after pediatric stroke.

Third, neuroimaging studies point out, that motor and cognitive functions exhibit overlapping neural mechanisms and share common neural resources (Desmond et al., 1997; Diamond, 2000; Hanakawa et al., 2008; Rigoli et al., 2012). During motor and cognitive tasks, co-activation occurs between the prefrontal cortex, the cerebellum, and connecting structures (including the basal ganglia; Hanakawa et al., 2008; Rigoli et al., 2012). Particular regions of the cerebellum have been shown to be important not only for motor but also for cognitive functions (Davis et al., 2010; Diamond, 2000; Stoodley, 2012). The link between motor and cognitive functions might occur due to a neural co-activation that is likely based on a common developmental trajectory of the prefrontal cortex and the cerebellum. Both of these brain structures reach maturity late and both show development up to the prepubertal age (Anderson et al., 2001; Stargatt et al., 2002; Tiemeier et al., 2010). In contrast, maximal force production such as hand strength, primarily relies on sensorimotor cortical regions (Hooyman et al., 2021) and therefore likely relates to cognitive functions differently.

Age at stroke, age at exam, and lesion size were closely associated with cognitive and motor outcome.

Neuroimaging studies trying to explain the influence of lesion characteristics on outcome suggest that although frontal regions may play a vital role in the mediation of EF, the integrity of the entire brain is necessary for efficient cognitive functioning (Anderson et al., 2001; Stuss & Alexander, 2000). In our previous research, we showed that pediatric stroke is associated with functional network disruption with connectivity strength being related to cognitive outcome (Kornfeld et al., 2018) and cerebral blood flow being associated with bimanual abilities in patients after pediatric stroke (Leistner et al., 2019). To summarize, functional network disruption and cerebral blood flow alterations are both issues likely affecting the association between motor and cognitive performance in our study sample.

Despite the manifold investigation on the link between motor abilities and EF, very little research exists about the effects of motor intervention programs on EF (Benzing et al., 2020). There is first promising evidence of beneficial effects of motor coordination training suggesting that movement games may impact on children's EF (Chang et al., 2013; Koutsandréou et al., 2016; Pesce et al., 2016). Benefits in EF are most likely achieved if a motor intervention includes cognitive challenges in a playful setting. Furthermore, activities with novelty, diversity, adaptive effort, feeling of successfulness, and enjoyment might be essential ingredients for a successful transfer on EF (Diamond, 2013; Pesce et al., 2016). Based on the results of the present study, interventions targeting upper limb functions such as functional movements and bimanual abilities may not only improve motor abilities, but executive functions could benefit as well.

Limitations of the study include first the small sample size and the wide age range and heterogeneity of the patients, which is an inherent circumstance when investigating pediatric stroke. Second, comparability with other studies is limited as motor abilities and EF are broad concepts and are defined and assessed in a number of different ways across studies. Third, the MUUL and ABILHAND-Kids are pediatric scales and are indirect measures prone to perception bias, beliefs, and expectations of the rating physician and the rating parents. Furthermore, power analysis should ideally be performed a priori. Finally, yet importantly, the relationship between motor and cognitive functions is only controlled for the extent of the lesion rather than for the functional brain area affected. Including the ASPECT-Score as a quantitative measure referring to the localization of the lesion (Mackay et al., 2020) sheds a different light on the association between motor and cognitive functions.

Conclusion

The present study found no significant group differences in terms of executive functions and hand strength. However, upper limb performance was worse in patients than healthy controls. Our study further supports the notion of a close coupling between upper limb performance and executive functions, whereas hand strength was rather unrelated to executive functions. Future work should focus on the development of training programs targeting upper limb performance and executive functions and evaluate whether training in one domain could optimize motor or cognitive functions or both, in patients after pediatric arterial ischemic stroke.

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