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Cognitive resilience following paediatric stroke: Biological and environmental predictors

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ABSTRACT

Little is known about resilience after paediatric stroke (PS), or the factors that contribute to better outcomes. Rather, research emphasis has been on impairment, measured through cross-sectional or retrospective designs, often heavily weighted to children presenting for clinical or rehabilitation follow-up. Implementing a resilience framework, this study aimed to investigate cognitive recovery post-stroke and factors that contribute to cognitive resilience at 12 months following PS. In a single site, prospective, longitudinal study (baseline, 1, 6, 12 months post-stroke), 61 children (55.7% male) aged 0–18 years, with a diagnosis of acute arterial ischemic stroke were recruited. Neurological status, lesion and child characteristics were collected at diagnosis. Cognitive, language and motor skills were assessed directly using age-appropriate, standardised tools. Parents rated their mental health, and child social and adaptive abilities. Participants were classified as 'resilient' (74%) or 'vulnerable' based on 12-month cognitive scores. The resilient group demonstrated more intact acute neurological status and higher language and adaptive abilities 1-month post-stroke; 88% of the vulnerable group had strokes involving both cortical and subcortical regions. Neonatal stroke, large lesions, cortical-only lesions, and middle cerebral artery involvement were associated with poorer cognition over the 12 months post-stroke. Absence of seizures and older age at stroke predicted better cognitive outcomes. In summary, most children surviving PS are cognitively resilient at 12 months post-insult. Risk and protective factors identified may guide targeted clinical intervention for more vulnerable children. Future research is needed to explore cognitive resilience trajectories beyond 12 months post-stroke.

1. Introduction

While not usually considered a childhood diagnosis, stroke can occur at any stage across the lifespan. Paediatric stroke (PS) is far less common than adult stroke, and is more often related to co-morbid conditions (congenital heart disease, arteriopathies, prothrombotic disorders, arteriovenous malformation and sickle cell disease) [1]. PS is defined as an acute cerebrovascular event, either arterial ischaemic stroke (AIS) or heamorrhagic stroke (HS). AIS occurs when blood supply to the brain is interrupted by a blockage that disrupts oxygen and nutrient supplies, causing cell death and relatively localised brain pathology. HS refers to the rupture of an

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artery, usually causing diffuse brain damage and global impairment. PS is further classified according to timing. Neonatal stroke (birth – 28 days) is more common (1 in 4000 live births), with child stroke (after 28 days) reported in 1.3–13 cases per 100,000 [1].

Until recently, the majority of PS studies have targeted acute medical treatment, with only a smaller body of research examining functional outcomes (cognitive, physical, language) mostly through a medical lens [2–4]. Many studies report on retrospective or cross-sectional findings from samples derived from outpatient or rehabilitation services [3,5–8]. Such designs risk bias of over-representation of children with persisting deficits who require ongoing care. With a small number of notable exceptions [9–12], very few studies have utilised prospective, longitudinal designs, and so little is known regarding typical recovery trajectories from PS. Even less is known about the likelihood of good outcomes post-PS or factors that may confer resilience on the child post-stroke. Examining PS outcomes through a resilience framework offers the opportunity to identify strengths and guide targeted clinical intervention.

Given these methodological limitations, it is not surprising that findings are inconsistent. Some studies report that more than 50% of survivors of child stroke suffer cognitive impairment, while others document much lower rates (see review) [10]. Similarly, some authors find no associations between brain-related factors, such as *lesion size* or *laterality,* and outcomes [8], while others link intellectual and psychosocial impairments to larger, bilateral infarcts or to bleeds overlapping white and grey matter [13–15]. *Acute functional impairments* have been found to contribute to vulnerability post-stroke, with poorer functional status at 1 month linked to persisting fine and gross motor deficits [16], and poorer cognitive and psychosocial skills [3,17]. Despite evidence that the developing brain is particularly vulnerable to insult due to immature neural networks [18], *age at stroke* effects are inconsistent: neonatal stroke has been associated with better outcomes than later stroke in some studies [15], but worse outcomes in others [4]. A handful of studies have explored *environmental influences* on recovery, supporting a relationship between child behaviour, social skills and family factors (family function, parent mental health, parent education) [6], although these findings require replication.

To date, research in child acquired brain injury, including PS, has mostly adopted a 'pathology' model, with little attention to factors associated with resilience and good outcomes (see Anderson, Northam, & Wrennall, 2019 for review) [19]. Resilience can be broadly defined as achievement of relatively good outcome (e.g., recovery), despite challenging circumstances (e.g., stroke) [20], and may be operationalised as meeting age-appropriate skill maturation despite serious threats to development [21]. An accumulation of risks and stressors, and interactions among these, may inhibit resilience, causing adverse outcomes [22]. Conversely, protective factors support resilience and fall into two categories: (i) *static*: characteristics that cannot be changed through intervention (e.g., age, sex, brain insult characteristics, comorbid conditions); and (ii) *dynamic*: factors providing opportunities for modification (e.g., environment, family function, intervention) [23]. Of relevance for PS, 'cumulative risk factors' refer to the combined effects of multiple risks (e.g., larger lesions, comorbid conditions, social disadvantage), and their impact may be linear or reflect interactions between factors (e.g., double hazard theory) [24,25]. In the field of child health, such cumulative risk models, which capture the impact of exposure to multiple stressors simultaneously, have proven more sensitive than single stressor models in predicting poor developmental outcomes across health and psychosocial domains [26]. To date, in the PS literature few studies have explored the combined impact of such factors.

In summary, factors underpinning resilience and vulnerability after PS are still to be established and cannot be extrapolated directly from adult research due to the potential for greater vulnerability of the developing brain. Nor can they be assumed from findings associated with diffuse childhood brain insults such as traumatic brain injury (TBI), or from PS studies employing cross-sectional designs or biased samples drawn from follow-up clinics. We aimed to contribute to the PS literature by investigating the role of static and dynamic influences on post-stroke recovery and resilience using a biopsychosocial resilience model. First, we explored the relationship between cognitive resilience at 12 months post-stroke and protective factors: static (biologic) and dynamic (psychosocial). We predicted that: cognitive resilience would be associated with both static (older age at stroke, less severe stroke, less acute impairment, and absence of seizures or comorbid conditions) and dynamic factors (higher socioeconomic status [SES], better parent function). Second, we compared recovery trajectories from 1 to 12 months post-stroke across vulnerable and resilient groups, expecting that cognitive abilities across groups would diverge from 1 to 12 months post-stroke.

2. Method

2.1. Design

This study was a single site, prospective, longitudinal (baseline [T0], 1 [T1], 6 [T2], 12 [T3] months post-stroke), observational cohort study. Participants with PS who met eligibility criteria were recruited consecutively from acute presentations to a tertiary paediatric hospital.

2.2. Participants

Children aged between term and 18 years admitted to The Royal Children's Hospital, Melbourne (RCHM), Australia, with a diagnosis of acute AIS were identified and screened between December 2007 and November 2013 [27]. Inclusion criteria were: acute parenchymal ischemic infarct corresponding to one or more arterial territories confirmed on magnetic resonance imaging (MRI: diffusion weighted imaging), referral to the study within one month of stroke, and survival to 1-month post stroke. Exclusions were: previous AIS, co-existing diffuse brain injury, preterm birth (born < 37 weeks gestation), residing out of state, parent/child had insufficient English to complete study requirements.

During the study period, 107 children were admitted to The RCHM and screened for eligibility at 1-month post-stroke: 74 children met eligibility criteria and parents provided written informed consent to participate in the study. Children <13 years who were functionally able, provided assent, in accordance with RCHM Human Research Ethics protocols. Reasons for exclusion were: out of state (n = 6), died acutely (n = 12), referred > 1-month post-stroke (n = 15). Seven families declined participation. Local privacy laws preclude access to information on these children.

Sixty-seven participants completed the study protocol at 1-month post-stroke (90.5% participation). At 12 months, 61 children (82.4%) were assessed. One child had died (non-stroke-related). Five participants were unable to be contacted either by via mail or telephone. The follow up sample comprised 35 boys (55.7%), with a mean (M) age at stroke of 44.0 months (SD = 58.3, range: 0.0–196.5). Thirty-five children (57.4%) had a comorbid diagnosis at time of stroke (Table 1).

2.3. Measures

2.3.1. Primary outcome (12 months)

Cognition was assessed using: (i) Cognition Subscale, Bayley

Table 1
Patient clinical and lesion characteristics.

	Total sample		Resilient		Vulnerable		p	ES
N	61		45	(73.8)	16	(26.2)		
Age at diagnosis (months), M (SD)	43.9	(59.3)	44.8	(54.2)	41.2	(73.6)	0.84	0.06
Age group, n (%)								
Neonatal	28	(45.9)	18	(40.0)	10	(62.5)	0.26	0.22
Pre-school	16	(26.2)	14	(31.1)	2	(12.5)		
School aged	17	(27.9)	13	(28.9)	4	(25.0)		
Sex [female], n (%)	26	(42.6)	18	(40.0)	8	(50.0)	0.56	0.09
Lesion characteristics								
Lesion laterality n (%)								
Left	24	(39.3)	15	(33.3)	9	(56.3)	0.26	0.27
Right	21	(34.4)	17	(37.8)	4	(25.0)		
Bilateral	10	(16.4)	7	(15.6)	3	(18.8)		
Infratentorial only	6	(9.8)	6	(13.3)	0	(0.0)		
Lesion location, n (%)								
Cortical only	1	(1.6)	0	(0.0)	1	(6.3)	0.01	0.41
Subcortical only	16	(26.2)	15	(33.3)	1	(6.3)		
Cortical + subcortical	38	(62.3)	24	(53.3)	14	(87.5)		
N/A	6	(9.8)	6	(13.3)	0	(0.0)		
Lesion size, n (%)								
Small (small perforator and branch)	50	(82.0)	39	(86.7)	11	(68.8)	0.14	0.21
Large (Major vessel)	11	(18.0)	6	(13.3)	5	(31.3)		
Vascular territory, n (%)								
MCA full	3	(4.9)	0	(0.0)	3	(18.8)	0.01	0.48
MCA partial	32	(52.5)	25	(55.60)	7	(43.8)		
PCA	5	(8.2)	5	(11.1)	0	(0.0)		
Vertebrobasilar arteries	6	(9.8)	6	(13.3)	0	(0.0)		
Multiple	15	(24.6)	9	(20.0)	6	(37.5)		
Seizures, n (%)								
No	26	(42.6)	22	(48.9)	4	(25.0)	0.24	0.21
Yes	24	(39.3)	16	(35.6)	8	(50.0)		
Unknown*	11	(18.0)	7	(15.6)	4	(25.0)		
Comorbid diagnosis, n (%)	23		15		8	(50.0)	0.24	0.15
Cardiac								
Congenital heart disease	7	(11.5)	4	(8.9)	3	(18.8)		
Other cardiac condition	7	(11.5)	4	(8.9)	3	(18.8)		
Cardiac surgery	7	(11.5)	3	(6.7)	4	(25.0)		
Arteriopathy								
Focal arteriopathy	5	(8.2)	3	(6.7)	2	(12.5)		
Arterial dissection	5	(8.2)	4	(8.9)	1	(6.3)		
Moyamoya syndrome	4	(6.6)	3	(6.7)	1	(6.3)		
Congenital syndrome	0	(0.0)	0	(0.0)	0	(0.0)		
Sickle cell anemia	0	(0.0)	0	(0.0)	0	(0.0)		
Varicella	0	(0.0)	0	(0.0)	0	(0.0)		
Social Risk Index, n (%)								
≤1	34	(55.7)	24	(53.3)	10	62.5	0.57	−0.08
>1	27	(44.3)	21	(46.7)	6	37.5		

ES = effect size, M = mean, SD = standard deviation, MCA = Middle Cerebral Artery, PCA=Posterior Cerebral Artery.
* children treated at another hospital acutely and transferred to RCH.

Scales of Infant Development III (BSID-III) [28] < 3.5 years; (ii) Full Scale IQ, Wechsler Preschool and Primary Scale of Intelligence-III (WPPSI-III) [29] 3.5–4.0 years; or (iii) IQ composite from the Kaufman Brief Intelligence Test-2 (KBIT-2) [30] > 4 years. All measures are age-standrdised and represent those current at the time of testing, and have a M = 100 and SD = 15.

2.3.2. Predictors

1. Static factors:

Stroke classification and lesion characteristics: MRI scans were conducted at The RCHM on admission, using a standardised clinical protocol. Infarct number and laterality, lesion location and vascular territories were coded by two neuroradiologists and a stroke clinician, using a modified version of the coding system developed by Leventer and colleagues [31,32]. Inter-rater reliability was above 90% for all variables [27].

(i) *lesion laterality:* left, right or bilateral.

(ii) *lesion location*: cortical (grey matter only), subcortical (white matter tracts plus subcortical nuclei), cortical and subcortical or infratentorial.

(iii) *vascular territory*: middle cerebral artery (MCA), full/partial, posterior cerebral artery (PCA), vertibro-basilar or multiple.

(iv) *lesion size*: large (major vessel: e.g., occlusion at M1 or M2 segment of MCA and entire vascular territory damaged; branch = partial territory) or small vessel (e.g., perforator most commonly in the MCA so those serving the basal ganglia).

Acute neurological function and comorbid conditions:

(i) The Pediatric Stroke Outcome Measure (PSOM) [33] provides standardised neurological examination and AIS classification across multiple domains: sensorimotor, language, cognition, behaviour and overall function, based on clinician ratings. Total PSOM score (maximum of 10, higher scores = poorer function) was employed in analyses. The PSOM has good reliability and validity [33].

(ii) Seizure history and relevant comorbid conditions (e.g., moya moya disease, congenital heart disease) were documented (Table 1).

Child characteristics:

(i) Age at stroke was categorised as follows: neonate (0–28 days), preschool (29 days–5 years), school-aged (5 years+), based on literature describing timing of growth spurts in early brain development [31,34–36].
(ii) Sex (male, female).

2. Dynamic factors:

Parent demographics and function:

(i) Social Risk Index (SRI) [37] (1 month [T1]): measures socio-economic status (SES) based on maternal education, occupation, income and ethnicity: higher scores reflect lower social risk. SRI total scores were coded: 1 = low social risk, > 1 = high social risk.
(ii) Short Form Health Survey-version 2 (SF-36 v2) [38] is a measure examining quality of life. Parents completed the Parent Mental Health subscale (6 months [T2]), which scored according to Australian norms. Higher scores indicate better parent function.

3. Child outcomes:

(i) *Expressive and receptive language*: (T1-T3) BSID-III Language Scale [28] (<3.5 years); Expressive Vocabulary Test-2 [39] (>3.5 years) and Peabody Picture Vocabulary Test 4 [40] (>3.5 years), M = 100, SD = 15.
(ii) *Gross and fine motor skills:* (T1-T3) BSID-III Motor Scale [28] (≤42 months), M = 100, SD = 15; Bruininks-Oseretsky Test of Motor Proficiency-2 (BOT-2) [41] (for children 4–21 years), M = 50, SD = 10. Both measures are standardised, norm-referenced motor assessments.
(iii) *Adaptive abilities*: (T1-T3) parents completed the Vineland Adaptive Behavior Scale-2 (VABS) [42], which includes an Adaptive Behavior Composite, and Communication, Daily Living Skills, Socialization and Motor Subscales, M = 100, SD = 15.
(iv) *Social:* (T1-T3) this domain was assessed using: (i) the Social Emotional Scale of the BSID-III [28] (<3.5 years; or ii) Social Skills Improvement System – parent report social skills subscale (SSIS) [43] (>3.5 years), M = 100, SD = 15.

2.4. Procedure

The study was approved by The RCHM Human Research Ethics Committee (HREC #27114). Participants presenting to The RCHM Emergency Department were identified and referred to study staff by physicians once diagnosis of PS was confirmed. Once consent was obtained, and initial eligibility screening was conducted, families provided demographic details and child medical records were reviewed. Acute (1 month), 6 and 12-month child assessments were conducted by trained researchers, and parents completed questionnaires.

Using 12 month cognitive assessment data, participants were classified into two groups: (i) resilient (n = 45) (cognitive function within or above 2/3 SD of the test mean, i.e., ≥ 90); (ii) vulnerable (n = 16) (cognitive function > 2/3 SD below test mean), i.e., <90), consistent with previous research and definitions of clinically significant cut-off scores [44].

2.5. Statistical analyses

Sample demographic, clinical and lesion characteristics were compared between resilient and vulnerable groups using independent samples t-tests or Fisher's exact tests. Sizes of effect were described using Cohen's d (small = 0.2; medium = 0.5; large = 0.8) and Cramer's V (small = 0.1; medium = 0.3; large = 0.5). Child and family characteristics were similarly compared between groups.

Generalised Estimating Equation (GEE) models explored trajectories for cognitive recovery adjusting for presence of a comorbid condition, first for the total sample, and then for resilient/vulnerable groups. GEE models allowed for inclusion of available data, without the necessity for cases to be complete for all time points.

Cognitive trajectories were then predicted from static (i.e., non-time-varying) demographic and clinical variables. Categorical predictors were modelled in interaction with a continuous time variable (1, 6 and 12 months), and observed group means and standard deviations presented. For time-varying continuous predictors, models with significant interaction effects were illustrated by plotting estimated marginal means (with 95% confidence intervals).

All GEE models were clustered at the individual level and employed an exchangeable correlation matrix. All analyses were conducted in Stata v15.1 and employed a significance level of $p < 0.05$.

3. Results

3.1. Group demographics

Of the total sample (n = 61), 45 children (74%) were categorised as resilient, with cognitive scores of >90. There were no differences identified between resilient and vulnerable groups for demographic variables including sex (p = 0.09) or age at diagnosis (p = 0.06). As illustrated in Table 1, resilience/vulnerability classifications did not differ significantly across the three age at PS categories (p=.26, ES=.22). However, children with neonatal stroke onset were more highly represented in the vulnerable group, accounting for 62% of this group, compared to children with preschool (12%) and school-aged (25%) stroke onset.

3.2. Predictors of cognitive resilience at 12 months post-stroke

Comparison of child and family characteristics returned no significant results for clinical and lesion variables, with the exception of lesion location (p = 0.01, effect size [ES] = 0.41): 88% of the vulnerable group had lesions involving both cortical and subcortical regions, compared to only 53% of the resilient group (Table 1). No group differences were identified for history of seizures post-stroke (p = 0.24, ES = 0.21) or pre-stroke comorbid diagnosis (p = 0.24, ES = 0.15). Some group differences emerged for child and family characteristics (Table 2). On average, in addition to lower cognitive skills, the vulnerable group showed lower acute language skills (p=<0.001, ES = 1.07), poorer social skills (p=.03, ES = 0.89), and overall adaptive behaviour (p = 0.01, ES = 1.04) at 6 months (Table 2). Neither parent mental health nor SRI (total score) was associated with cognitive outcomes. Further, examination of components of the SRI found no relationship between resilience and any of maternal education, occupation, income and ethnicity.

3.3. Recovery trajectories

Time effects: Longitudinal GEE models explored cognitive resilience trajectories, with no statistically significant results found within the total sample (p = 0.32) or vulnerable (p = 0.33) group,

Table 2
Child and family characteristics.

	Total sample		Resilient		Vulnerable		p	ES
N	61		45		16			
Child neurological function (acute)								
PSOM Total score, M (SD)	1.6	(2.3)	1.3	(1.8)	2.4	(3.4)	0.15	−0.45
PSOM Good outcome, n (%)	28	(50.0)	21	(46.7)	7	(43.8)		
PSOM Poor outcome, n (%)	28	(50.0)	21	(46.7)	7	(43.8)		
Missing, n (%)								
Child function, M (SD)								
Adaptive behaviour (6 mths)	96.7	(15.6)	100.4	(14.1)	85.5	(15.1)	0.01	1.04
Language Skills (1 mth)	101.6	(16.8)	105.9	(14.2)	89.6	(17.9)	<0.001	1.07
Motor Skills (1 mth)	78.6	(31.1)	76.9	(31.38)	83.64	(30.6)	0.49	−0.22
Social Skills (6 mths)	104.2	(15.9)	108.3	(12.1)	95.0	(20.1)	0.03	0.89
Parent function, M (SD)								
Social Risk (acute)	1.7	(1.6)	1.8	(1.7)	1.4	(1.3)	0.48	0.21
Parent Mental Health (6 mths)	45.4	(10.7)	45.2	(10.5)	46.1	(11.6)	0.79	−0.08

ES = effect size, PSOM=Pediatric Stroke Outcome Measure.

but a significant effect of time for the resilient group (β = 0.41, p = 0.003).

Group effects: As vulnerable and resilient groups were constructed based on cognitive status at 12 months, as expected, the groups differed significantly for cognitive status at all time points post-stroke (p < 0.001) (Fig. 1) Of note, analysis of predictors of cognitive resilience at 12 months identified significant differences for both adaptive (p < 0.001) and language skills (p < 0.001), but not for motor or social skills, social risk or parent mental health.

Time by demographic and clinical characteristics interactions: Longitudinal GEE models explored the cognitive trajectories by demographic and clinical characteristics controlling for comorbid conditions. Of demographic factors, only age group returned a significant interaction effect (p < 0.001), with the neonatal group showing a decreasing trajectory over time, while older age groups were characterised by increasing cognitive ability to 12 months post-stroke. Lesion size, cortical/subcortical classification, and vascular territory all showed significant effects on cognitive trajectories. Those with large lesions (p = 0.03), cortical-only lesions (p = 0.002) and MCA involvement (p = 0.01) had decreasing cognitive trajectories. Additionally, for children with no history of post-stroke seizures, cognitive abilities improved over time when compared to those with a seizure history (p = 0.02).

For continuous child and family characteristics, longitudinal GEE models were again employed to examine cognitive resilience over time. A significant interaction was found for adaptive behaviour, with increases in these skills over time (from 6 to 12 months) related to increased cognitive ability and decreased adaptive behaviour to decreased cognitive ability (p = 0.03, Fig. 2). Significant interaction terms were found for parent mental health (from 6 to 12 months, p = 0.01) and motor skills (over the three time points, p = 0.01). However, in these models, estimated marginal means suggest that over time both higher and lower scores tend toward a central point at 12 months.

4. Discussion

This study examined cognitive recovery over 12 months post-stroke and factors influencing resilience. We employed a bio-psychosocial framework to explore the relationship between resilient and vulnerable children and *static* (e.g., age at stroke, lesion characteristics, acute neurological impairment, seizures, comorbid conditions) and *dynamic factors* (SES, parent function). Results highlight that, when employing a prospective, longitudinal design, which minimises sample bias, and by employing a multi-domain approach to evaluating outcome, the majority of children (74%) have good cognitive outcomes.

Exploration of cognitive ability over time for resilient and vulnerable groups identified surprisingly few group effects. Acute adaptive, language and neurological functions were higher in the resilient group. Over the 12 months post-stroke, neonatal stroke was characterised by decreasing cognitive ability, with subtle improvements noted for preschool and school-aged children, consistent with research reporting early brain injury as a risk factor for

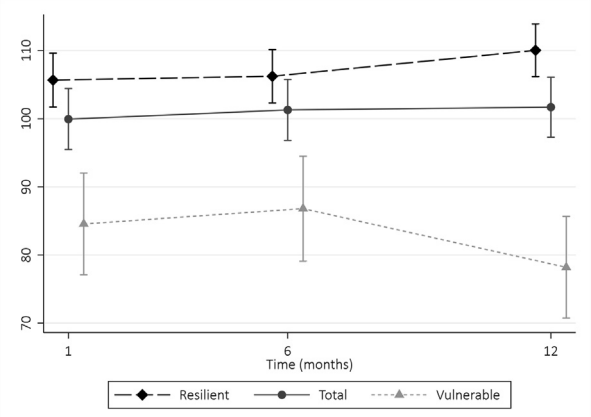

Fig. 1. Cognitive trajectories for Vulnerable and Resilient groups to 12 months post-stroke.

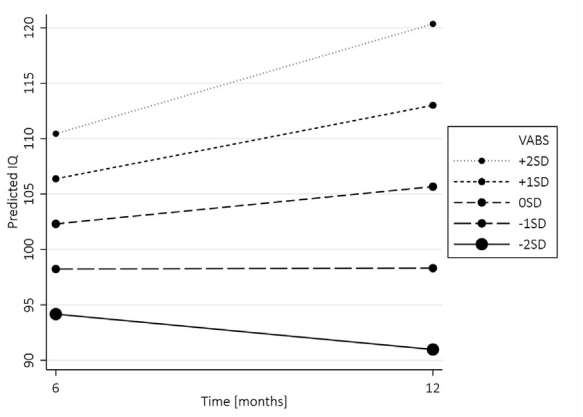

Fig. 2. Relationship between children's adaptive abilities and Iq across time post-stroke.

poor outcome [3,15,27]. Children with MCA stroke also showed a reduction in cognitive ability from acute to 12-month assessments (20 IQ point decrease), as did those with cortical stroke (30 point decrease) and larger lesion size. Absence of seizures was associated with significant gains in cognitive ability, which is commonly reported in the context of other child brain insults [15]. Those with lower acute adaptive skills showed a decrease in IQ to 12 months, while those with higher adaptive skills recorded higher IQ. SES did not impact cognitive trajectories, and parent mental health effects on IQ attenuated over time, raising the possibility that deteriorating function reported in the more widely studied child TBI may be due to the well-established pre-injury parent vulnerability in this group [15], and not characteristic of early brain insult more generally.

Findings support the importance of *static factors* having a greater impact on outcomes, with *dynamic factors* playing a less significant role. Those children with good outcomes were significantly less likely to have stroke impacting both cortical and subcortical brain regions, tended to show evidence of more focal brain pathology and better acute function across neurological, adaptive and language domains. Other *static factors*, including sex and lesion laterality, did not differentiate the groups. With respect to *dynamic factors*, social risk, parent function and post-stroke seizures did not differ across groups, contrary to findings from studies describing the importance of environment, and quality of family environment in particular, to resilience following childhood brain insult. Of note, this literature argues that environmental factors increase in impact with time since brain insult, and even overtake the influence of insult factors. It may be that such effects have not yet emerged by 12 months post-stroke, and further follow-up is warranted.

To date, knowledge gain regarding functional outcomes from PS has been limited by studies with small samples, retrospective designs and limited use of standardised measures. We prospectively recruited a relatively large, representative sample of PS survivors and followed them for 12 months (82.4% retention), enabling a comparatively unbiased exploration of risk and protective factors. However, our results must be interpreted in the context of several limitations. While our sample is relatively large in the context of the child stroke literature, we did not have sufficient power to consider interactions among variables, such as MCA stroke and lesion size, or to conduct a detailed exploration of an extensive set of variables, for example, the nature and reliability of cognitive assessment across developmental levels, which is likely to differ across neonates and older children. In addition, given the age distribution of PS, age at insult was necessarily treated as a categorical variable (i.e., no variability within the neonatal group). We chose to focus on cognitive outcome, as this provided comparable metrics across the age range of our sample, but also limited the applicability of results to specific neurocognitive domains (e.g., attention), or to academic or socio-emotional function. There may also be limitations in employing a resilience model to PS: given that many children sustain stroke in the neonatal period, it is not possible to measure key variables associated with resilience such as pre-insult temperament or cognitive ability. Further, despite potential to modify outcomes, we did not address the complex issue of impact of post-stroke intervention, due to limited sample size and variations in availability of intervention across the study age range. Future research should consider this domain.

Our results are relevant to clinical practice. In a representative sample, the majority of children are resilient in the context of PS, which is reassuring. This information may be particularly valuable to convey to parents and families in the acute stages post-stroke, when concerns around medical status and future are paramount. Our findings guide identification of vulnerable children in greatest need of clinical intervention: those younger at stroke onset, with more diffuse pathology positive seizure history, and poorer neurological function. Similarly, better acute function across language, motor and adaptive abilities indicate greater likelihood of cognitive recovery.

5. Conclusions

The majority of PS survivors demonstrate age appropriate cognitive skills at 12 months post-injury, providing support for a resilience model of recovery and cautioning against over-emphasis of poor outcomes. Risk and protective factors identified in the present study provide a guide for targeting clinical follow-up and intervention. Future research is needed to explore cognitive resilience trajectories beyond 12 months post-stroke.

Data availability statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Declaration of competing interest

There are no conflicts of interest to declare.

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