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Increased cerebral integrity metrics in poliomyelitis survivors: putative adaptation to longstanding lower motor neuron degeneration

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ABSTRACT

Background: Post-polio syndrome (PPS) has been traditionally considered a slowly progressive condition that affects poliomyelitis survivors decades after their initial infection. Cerebral changes in poliomyelitis survivors are poorly characterised and the few existing studies are strikingly conflicting.

Objective: The overarching aim of this study is the comprehensive characterisation of cerebral grey and white matter alterations in poliomyelitis survivors with reference to healthy- and disease-controls using quantitative imaging metrics.

Methods: Thirty-six poliomyelitis survivors, 88 patients with ALS and 117 healthy individuals were recruited in a prospective, single-centre neuroimaging study using uniform MRI acquisition parameters. All participants underwent standardised clinical assessments, T1-weighted structural and diffusion tensor imaging. Whole-brain and region-of-interest morphometric analyses were undertaken to evaluate patterns of grey matter changes. Tract-based spatial statistics were performed to evaluate diffusivity alterations in a study-specific whiter matter skeleton.

Results: In contrast to healthy controls, poliomyelitis survivors exhibited increased grey matter partial volumes in the brainstem, cerebellum and occipital lobe, accompanied by increased FA in the corticospinal tracts, cerebellum, bilateral mesial temporal lobes and inferior frontal tracts. Polio survivors exhibited increased integrity metrics in the same anatomical regions where ALS patients showed degenerative changes.

Conclusions: Our findings indicate considerable cortical and white matter reorganisation in poliomyelitis survivors which may be interpreted as compensatory, adaptive change in response to severe lower motor neuron injury in infancy.

1. Introduction

Poliomyelitis was one of the most debilitating acute viral infectious diseases of the 20th century before the availability of the polio vaccine. [1] It predominantly affected children under 5 years of age, causing flaccid paralysis in less than 1% of those infected and carried a mortality rate of 5–10% due to respiratory failure. [2] Despite being 99% eradicated globally today, there are currently 15–20 million people living with the lasting sequelae of the disease, [3] of which 20–85% are experiencing post-polio syndrome (PPS). [4,5]

Post-polio syndrome was first described by French neurologists Raymond and Jean-Martin Charcot in 1875. [6,7] It is a slowly progressive lower motor neuron condition that can affect polio survivors after a considerable period of functional stability long after the acute poliomyelitis infection. [8,9] PPS typically manifest as new or progressive asymmetrical muscle weakness, atrophy, fatigability, myalgia or fasciculations, [10,11] but also as chronic pain, dysphagia, dysphonia or in some cases as respiratory weakness. [12,13] Despite being traditionally regarded as a pure lower motor neuron syndrome, non-motor symptoms such as generalised fatigue [14], cold intolerance, neuropsychological deficits [15], sensory impairment [16] and sleep disorders [17–20] have also been described, all of which have considerable impact on the patient's well-being and quality of life. [21–23] Research studies in PPS invariably focus on lower motor neuron and muscle pathology utilising quantitative electrophysiology techniques [24,25], muscle biopsies [26,27] and wet biomarkers [28,29]. Despite clinical observations suggestive of cerebral pathology there is a striking paucity of

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Glossary

ALS	amyotrophic lateral sclerosis
ALSFRS-r	revised amyotrophic lateral sclerosis functional rating scale
C9orf72	chromosome 9 open reading frame 72
ANCOVA	analysis of covariance
CC	corpus callosum
CST	corticospinal tract
DTI	Diffusion Tensor Imaging
EMG	electromyogram
EMM	estimated marginal mean
FOV	field of view
FWE	familywise error
GM	grey matter
HC	healthy control
HSP	hereditary spastic paraplegia
IR-SPGR	inversion recovery prepared spoiled gradient recalled echo
IR-TSE	inversion recovery turbo spin echo sequence
Lt	left
LL	Lower limb
LMN	lower motor neuron
MND	motor neuron disease
MNI152	Montreal Neurological Institute 152 standard space
PLS	primary lateral sclerosis
PPS	Post-polio syndrome
Rt	right
ROI	region of interest
SBMA	Spinal-bulbar muscular atrophy
SD	standard deviation
SE-EPI	spin-echo echo planar imaging
SENSE	Sensitivity Encoding
SPIR	spectral presaturation with inversion recovery
T1w	T1-weighted imaging
TE	Echo time
TFCE	threshold-free cluster enhancement
TI	Inversion time
TIV	total intracranial volume
TR	repetition time
UL	Upper limb
UMN	Upper motor neuron

imaging and post mortem studies, and reports of cerebral involvement are conflicting. While early post mortem studies in the 1940s identified widespread cerebral pathology involving the reticular formation, posterior hypothalamus, thalamus, putamen, caudate, locus coeruleus, substantia nigra as well as preferential involvement of the precentral gyrus and pre-motor areas, [30–32] more recent studies did not confirm these observations [33]. Conversely, recent neurophysiology studies detected changes suggestive of a compensatory functional reorganisation of the motor cortex. [34,35] From a clinical perspective, PPS remains a diagnosis of exclusion and the March of Dimes diagnostic criteriais typically applied. [8,9] Despite coordinated research efforts, the aetiology is not convincingly established, the underlying pathophysiology is not confirmed, [36] and no validated prognostic and monitoring markers currently exist. The mainstay of management in PPS comprises symptomatic relief, [19] prevention of further deterioration through conservative measures, [37] energy conservation strategies, [38,39] muscle training, [40] and improving cardiovascular fitness. [41–43] Past clinical trials for potential disease-modifying drugs have shown disappointing results, [44–48] with the exception of intravenous immunoglobulin (IVIg) therapy which proved promising. [49]

Unlike the imaging profile of other motor neuron diseases [50] such as amyotrophic lateral sclerosis (ALS), [51] primary lateral sclerosis [52] or SBMA [53] the radiological correlates of PPS are woefully understudied. Thanks to advances in magnetic resonance imaging (MRI), phenotype-specific grey matter and white matter alterations can be reliably characterised in vivo. The evaluation of cerebral changes in poliomyelitis survivors not only helps to explore the pathological substrate of common PPS-associated symptoms but more broadly, adds to the existing literature of LMN-predominant MNDs. [54]

Brain imaging in other slowly progressive LMN-predominant MNDs have consistently shown a degree of cerebral reorganisation. Increased grey matter density with underlying neuronal reorganisation was observed in both adult onset spinal muscular atrophy (SMA) [55] and LMN-dominant ALS, [56] which has been interpreted as a compensatory mechanism. Cortical reorganisation and adaptive functional changes were also observed in cases of limb amputation [57] or spinal cord injury [58] after longstanding motor training. [59] The main objective of this study is the comprehensive characterisation of grey and white matter alterations in poliomyelitis survivors in contrast to healthy controls and a cohort of MND patients with ALS.

2. Methods

2.1. Participants

Thirty-six patients with PPS, 88 patients with ALS and 117 healthy controls (HC) were included in a prospective neuroimaging study. The study was approved by the Ethics (Medical Research) Committee - Beaumont Hospital, Dublin, Ireland, and all participants provided informed consent prior to inclusion. Participating PPS patients were diagnosed according to the March of Dimes diagnostic criteria [8,9] and ALS patients had 'probable' or 'definite' ALS according to the El Escorial criteria. Inclusion criteria included the ability to tolerate the duration of MR imaging and exclusion criteria included comorbid neuroinflammatory, neurovascular, neoplastic, psychiatric conditions or prior head or spinal cord injuries. The healthy controls were unrelated to participating patients and had no known neurological or psychiatric diagnoses. Demographic and clinical details were carefully recorded for all PPS patients, including age of acute poliomyelitis, age of PPS onset, handedness, age, education and the relevant demographic variables were used as covariates in the statistical models. PPS and ALS patients also underwent standardised clinical evaluation and the revised ALS functional rating scale (ALSFRS-r) was administered to appraise functional disability. ALSFRS-r subscores were individually recorded to evaluate bulbar, upper limb, lower limb and respiratory dysfunction. Muscle strength was assessed using the Medical Research Council (MRC) scale and composite scores for left and right, upper and lower limbs were individually calculated. Upper limb score comprised of shoulder abduction and adduction, elbow flexion and extension, wrist flexion and extension and finger flexion and extension. Lower limb score was calculated using hip flexion and extension, knee flexion and extension and ankle dorsiflexion and plantarflexion. ALS patients were screened for ALS-associated mutations and the presence of GGGGCC repeat expansions in C9orf72. As described previously, [60] the presence of the *C9orf72* hexanucleotide repeat expansion was determined using repeat-primed polymerase chain reaction (PCR). As the ALS group was included as a motor neuron disease (MND) control group, only C9orf72 negative patients were included to reduce radiological heterogeneity.

2.2. Neuroimaging methods

A 3 Tesla Philips Achieva system was used with an 8-channel receive-

only head coil to acquire magnetic resonance (MR) data. A standardised imaging protocol was implemented. A 3D Inversion Recovery prepared Spoiled Gradient Recalled echo (IR-SPGR) sequence was utilised to acquire T_1-weighted images with a spatial resolution of 1 mm^3, field-of-view (FOV) of 256 × 256 × 160 mm, flip angle = 8°, SENSE factor = 1.5, TR/TE = 8.5/3.9 ms, TI =1060 ms. A spin-echo echo planar imaging (SE-EPI) sequence was implemented to acquire diffusion tensor images (DTI) with a 32-direction Stejskal-Tanner diffusion encoding scheme. Spatial resolution = 2.5 mm^3, FOV = 245 × 245 × 150 mm, 60 slices acquired with no interslice gap, TR/TE = 7639 / 59 ms, SENSE factor = 2.5, b-values = 0, 1100 s/mm^2.

2.3. Total intracranial volume estimation

TIV was estimated by linearly aligning each participant's skull-stripped brain to the MNI152 brain image in MNI space, the inverse of the determinant of the affine registration matrix was calculated and multiplied by the size of the template. FSL-FLIRT was used for registration to template and tissue type segmentation was performed using FSL-FAST.

2.4. Whole-brain imaging analyses

Grey matter alterations in PPS were first evaluated by morphometric analyses using the FMRIB's FSL suite. Pre-processing included standard steps such as skull-stripping (BET), motion-corrections and tissue-type segmentation. Using affine registration, individual grey-matter partial volume images were aligned to the MNI152 standard space. A study-specific GM template was created to which the individual grey matter images were non-linearly co-registered. Permutation based non-parametric inference was used for group comparisons, with the threshold-free cluster enhancement (TFCE) method. Comparisons of patient groups and controls were corrected for age and gender and total intracranial volumes (TIV). Tract-based spatial statistics were utilised to assess white matter changes over the entire brain. Subsequent to skull removal and eddy current corrections, a tensor model was fitted to the raw diffusion data to generate maps of fractional anisotropy (FA), radial diffusivity (RD) and axial diffusivity (AD). FMRIB's image analysis suite was utilised for non-linear registration and skeletonisation of each subject's images. [61] FA, AD and RD images were compiled into a single 4D image file and a mean FA mask was created. Similarly to grey matter analyses, permutation-based non-parametric inference was used for the voxelwise analysis of diffusivity parameters using design matrix-defined contrasts which included group membership, age, and gender. The threshold-free cluster enhancement (TFCE) method was implemented and resulting statistical maps were thresholded at $p < .05$ TFCE family-wise error (FWE).

2.5. Region of interest analyses

To further explore the regional grey matter profile of PPS, supplementary morphometric analyses were carried out in the precentral gyrus, brainstem, Broca's area, cerebellum, frontal lobe, occipital lobe, orbitofrontal cortex, parietal lobe, precentral gyrus, temporal lobe, and Wernicke's area. The labels of the Harvard-Oxford cortical probability atlas and the MNI probability atlas were used to define grey matter regions of interest. Average grey partial volume values were retrieved from the above regions and post hoc statistics were performed. The volume profiles of bilateral structures were averaged between left and right. Assumptions of linearity, normality and homogeneity of variances were checked and analyses of covariance (ANCOVAs) were performed with study group membership (PPS, ALS or HC) as the independent variable, regional grey matter volumes as dependent variables. Age, gender, education and TIV were included in the model as covariates. A p-value of <0.05 was considered significant. Estimated marginal means of region grey matter values, standard error, between-group ANCOVA significance and post hoc group contrasts were summarised in a dedicated table.

3. Results

3.1. Clinical profile

The demographic profile of controls, PPS and ALS patients is presented in Table 1. Even though patients and controls were matched in key demographic variables, statistical models for imaging indices included age, gender and education as covariates.

The mean age at initial acute poliomyelitis infection was 33.50 (SD = 37.867) months old, younger than 3 years of age. At the initial paralytic poliomyelitis infection, all patients were affected in their lower extremities and 27.7% of patients were also affected in the upper limbs. Three PPS patients (8.3%) had bulbar involvement at the initial infection and 2 patients had respiratory weakness spending a period of time in the 'iron lung'. Polio patients spent a mean of 2.68 (SD = 2.757) years in hospital during their childhood and underwent an average of 2 surgeries (Range: 0 to 10) including corrective osteotomies to shorten a leg, leg-lengthening surgeries using the Ilizarov external fixation technique [62], muscle and tendon transfers, arthrodesis, and tendon release surgeries. More than half of the post-polio syndrome patients (61.1%) included in this study had leg length discrepancy ranging from 0.5 cm to 8 cm. The mean age of onset of PPS was 55.08 (SD = 9.075) years and the mean period between the initial infection and PPS onset was 52.29 (SD = 9.917) years. All of the included PPS patients experienced new weakness in their lower limbs; 63% only in their lower limbs while the rest (36.1%) also reported new weakness in their upper limbs. Two-thirds reported weakness in their originally affected body region, while up to 30.6% also reported weakness in previously unaffected limbs. Neurological examination revealed lower limb predominant weakness (LL right: M = 23.528, SD = 7.3959; LL left: M = 24.306, SD = 5.9453, UL right: M = 39.778, SD = 2.4479; UL left: M = 37.958, SD = 3.7690). As expected in a LMN condition, none of the PPS patients had spasticity and the mean total Penn UMN burden score was only 1.81 (SD = 2.424). Consistent with the physical examination, marked disability was noted in the lower limbs (M = 6.78, SD = 1.514) while the upper limbs were less affected. The majority of patients (88.9%) were able to ambulate and only 4 PPS patients were wheelchair bound. Of those able to mobilise, 22.2% did so without any walking aids while the rest used custom-made shoes and orthotics (44.4%), walking stick (41.7%) or 2 crutches or stroller (13.9%). Up to a third of PPS patients experienced a fall in the preceding 12 months period (33.3%). The majority of patients were able to drive, but more than half (52.8%) had to make modifications to their cars and 2 patients had to give up driving due to PPS. Six of the included PPS patients were still working at the time of the study. The majority of patients retired at a mean age of 61.69 years (SD = 6.856) (Range: 43 to 74), and only 4 patients (13.3%) had to retire precociously due to PPS. Bulbar and respiratory function was relatively spared in PPS patients. None of the patients required a feeding tube and only 3 patients used NIV at night. The clinical profile of PPS patients is presented in Table 2.

Table 1
The demographic profile of study participants.

	HC	PPS	ALS C9-	P value
	n = 117	n = 36	n = 88	
Age (years)	63.38 (11.914)	66.97 (5.629)	60.18 (10.311)	0.052
Gender (male)	56 (47.9%)	16 (44.4%)	56 (63.6%)	0.059
Education (years)	13.31 (3.294)	12.56 (3.691)	13.58 (3.169)	0.064
Handedness (right)	109 (93.2%)	34 (94.4%)	81 (92%)	0.855

Table 2
The clinical profile of poliomyelitis survivors and symptoms experienced by PPS patients.

	Mean (SD)
Bulbar (max 12)	11.36 (1.199)
Upper limb (max 12)	10.50 (1.732)
Lower limb (max 12)	6.78 (1.514)
Respiratory (max 12)	11.36 (1.313)
Total ALSFRS-R score	40.00 (3.986)
MRC – Right upper limb (max. 40)	39.778 (2.4479)
MRC – Left upper limb (max. 40)	37.958 (3.7690)
MRC – Right lower limb (max. 30)	23.528 (7.3959)
MRC – Left lower limb (max. 30)	24.306 (5.9453)
Symptom duration (months)	148.11 (100.354)
Age at acute poliomyelitis (months)	33.50 (37.867)
Age at PPS onset (years)	55.08 (9.075)
Time between acute poliomyelitis to PPS onset (years)	52.29 (9.917)
New symptoms suggestive of PPS	Proportion of patients (%)
Weakness	36 (100%)
Decreased endurance	29 (80.6%)
Pain	28 (77.8%)
Cold intolerance	33 (91.7%)
Fatigue	29 (80.6%)
Hypersensitivity	2 (5.6%)
Bulbar involvement	12 (33.3%)
Respiratory difficulties	8 (22.2%)
Poor sleep	19 (52.8%)
Breathing related sleeping disorders	5 (13.9%)

3.2. Grey matter findings

On grey matter morphometric analyses increased regional volumes were identified in the PPS cohort in lingual, peri-calcarine, cerebellar and brainstem regions compared to healthy controls at $p < .05$ FWE TFCE. In comparison to ALS patients, PPS patients exhibited higher partial volumes values in the bilateral motor cortex, mesial temporal lobes, cerebellum and occipital lobe. (Fig. 1.)

Our whole-brain VBM-type analyses were complemented by ROI analyses. Increased grey matter density was noted within the brainstem ($p = .001$), cerebellum ($p = .033$) and occipital lobe ($p = .028$) compared to healthy individuals, but no differences were observed in primary motor cortex. No cerebral grey matter changes were noted in the PSP cohort in frontotemporal regions including the orbitofrontal cortex, Brocas's or Wernicke's areas. Compared to the ALS group, increased grey matter volumes were noted in the brainstem, frontal lobe, occipital lobe and precentral gyrus. (Table 3.)

3.3. White matter findings

Three diffusivity metrics were evaluated, fractional anisotropy (FA), axial diffusivity (AD) and radial diffusivity (RD). Increase FA was noted in PPS compared to healthy controls along the entire cerebral course of the corticospinal tracts from the precentral gyrus, through the internal capsule to the mesencephalic crura. Additionally, higher FA was noted in the cerebellum, bilateral mesial temporal lobes and inferior frontal brain regions. The contrast to the ALS group was even more striking capturing higher FA in nearly all major commissural bundles and association tracts, including the corpus callosum and the fornix. (Fig. 2.)

Higher AD was identified in the PPS cohort compared to healthy controls along the entire cerebral course of the corticospinal tracts, fornix, corpus callosum, mesial temporal lobes and brainstem. (Fig. 3.A) Significantly higher AD was detected in nearly the entire white matter skeleton in PPS patients compared to ALS patients. (Fig. 3.B) Lower radial diffusivity (RD) was observed in the PPS group compared to healthy controls in cerebellum and external capsule. (Fig. 3.C) Lower RD was detected in PPS in contrast to ALS along the bilateral pyramidal tracts, corpus callosum, cerebellum and mesial temporal lobes. (Fig. 3. D).

4. Discussion

The overarching objective of this study was to characterise cerebral changes in post-polio syndrome, which has been previously debated in the literature. [30,33,34] Our imaging findings revealed no evidence of cortical and subcortical grey matter atrophy, but conversely, revealed focal areas of grey matter hypertrophy compared to controls involving the brainstem, cerebellar and occipital regions. This pattern of cortical reorganisation was accompanied by increased white matter integrity in the corticospinal tracts, cerebellum, bilateral mesial temporal lobes and inferior frontal tracts. The very same anatomical regions which showed degeneration in ALS, revealed increased integrity in the PPS cohort.

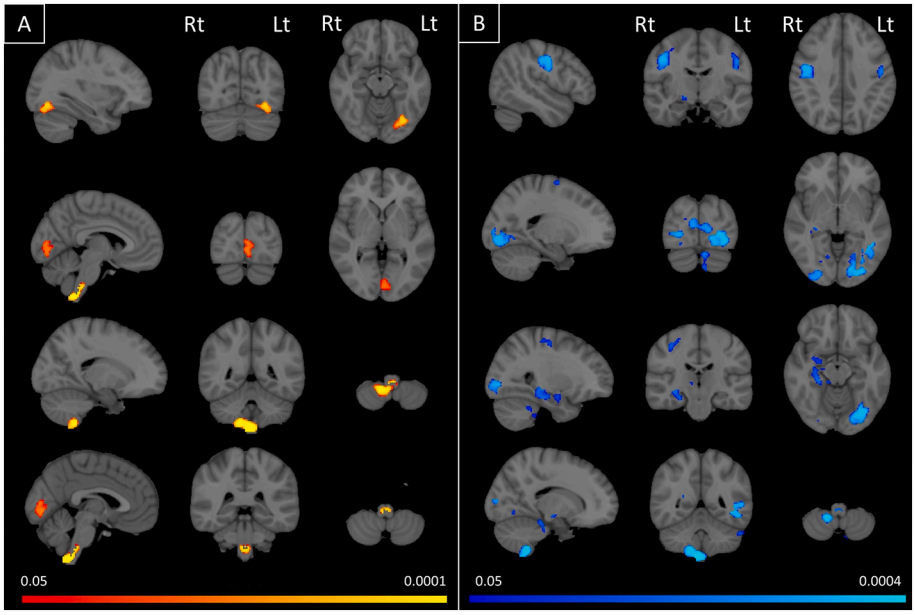

Fig. 1. Increased grey matter density in PPS compared to healthy controls (A) and ALS patients (B). Contrasts are corrected for age, gender, education and total intracranial volumes, statistical maps shown with corresponding colour bars using p values corrected for FWE. Radiological convention used.

Table 3
The regional grey matte profile of post-polio patients (PPS), healthy controls (HC) and patients with amyotrophic lateral sclerosis (ALS). Group comparisons are corrected for age, gender, education and total intracranial volumes and are Bonferroni corrected. Statistically significant *p*-values are marked with asterisk* and trends with a 't'.

Grey matter ROIs	Study group	Estimated Marginal Mean	Standard error	MANCOVA Sig. (*p*)	PPS vs HC	PPS vs ALS C9-	ALS C9- vs HC
Brainstem	HC	0.080640	0.000660	0.001*	0.001*	0.024*	0.547
	PPS	0.085831	0.001215				
	ALS	0.081990	0.000754				
Cerebellum	HC	0.490554	0.004158	0.033*	0.033*	.069[t]	1.000
	PPS	0.513279	0.007659				
	ALS	0.492599	0.004754				
Frontal lobe	HC	0.454041	0.002223	0.001*	1.000	0.020*	0.002*
	PPS	0.455585	0.004094				
	ALS	0.442407	0.002541				
Occipital lobe	HC	0.448231	0.002770	0.002*	0.028*	0.001*	0.507
	PPS	0.463694	0.005103				
	ALS	0.442380	0.003167				
Orbitofrontal cortex	HC	0.494966	0.003729	0.107	1.000	0.811	0.112
	PPS	0.491949	0.006868				
	ALS	0.483008	0.004263				
Parietal lobe	HC	0.429299	0.002259	0.082	0.918	0.112	0.373
	PPS	0.434240	0.004161				
	ALS	0.423963	0.002583				
Precentral gyrus	HC	0.465694	0.002848	<0.001*	1.000	0.004*	<0.001*
	PPS	0.460406	0.005245				
	ALS	0.440441	0.003256				
Temporal Lobe	HC	0.505666	0.002767	0.008*	1.000	0.287	0.007*
	PPS	0.502658	0.005096				
	ALS	0.492612	0.003163				

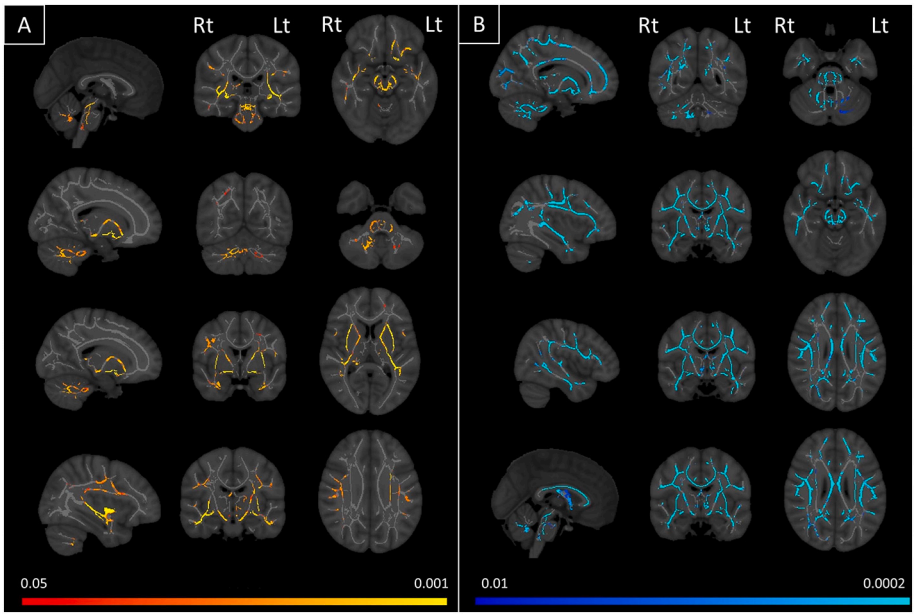

Fig. 2. Regions of increased fractional anisotropy in PPS compared to healthy controls (A) and ALS patients (B). Contrasts are corrected for age, gender and education. Radiological convention used.

The structural and diffusion profile observed in PPS can be best interpreted from a neuroplasticity perspective, as a compensatory mechanism in response to anterior horn injury early in life. Attempted cerebral adaptation to slowly progressive LMN degeneration has been observed in other neurological conditions such as SMA [55] and lower-motor neuron predominant ALS. [56,63] Similarly to our findings, the absence of cerebral pathology was noted in spinal-bulbar muscular atrophy (SBMA) [64] and other lower-motor neuron predominant motor neuron disease cohorts. [54]

Neuroplasticity is a broad term which refers to the malleable properties of the brain to rewire and reorganise its structure, function and connections throughout life in response to experience and injury. [65] The biological processes underpinning this phenomenon are thought to be particularly effective in children, especially in the first few years of life when neurogenesis, synaptogenesis, synaptic pruning and myelination occurs physiologically. [66,67] The efficiency of the cerebral adaptation is supported by variety of paediatric examples including early brain injury, [68] brain tumour survivors, [59] or surgical hemispherectomy [69,70] in the management of intractable seizures. The biological process of neuroplasticity, although less efficient, is thought to continue throughout adolescence into adulthood. [71,72] Structural brain plasticity has also been recognized in animal studies [73] and also observed in healthy adult populations such as professional athletes, [74] highly skilled musicians [75,76] or even in non-expert populations

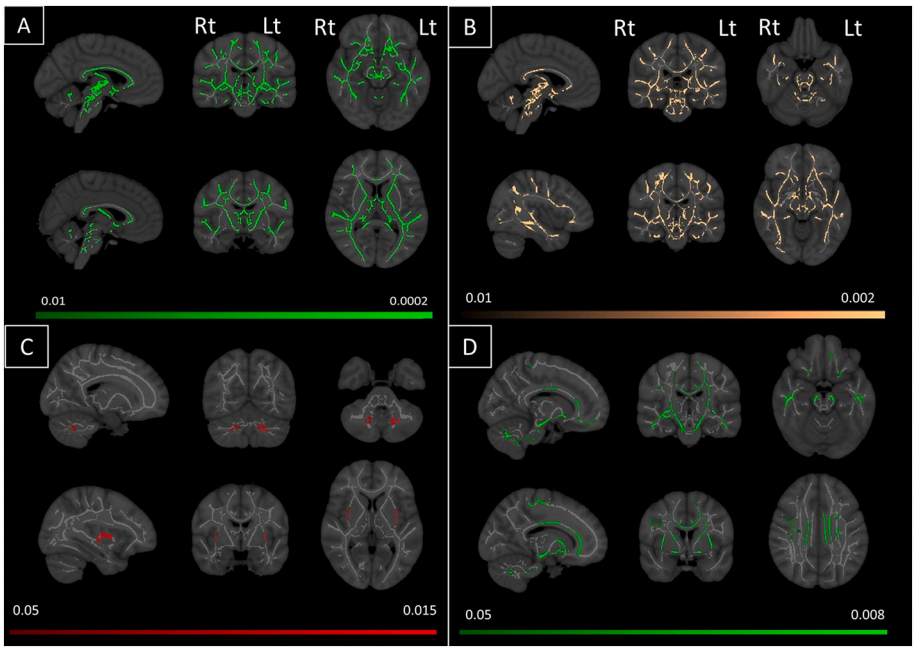

Fig. 3. The axial diffusivity profile of PPS in comparison to healthy controls (A) and ALS patients (B). The radial diffusivity profile of the PPS cohort in contrast to healthy controls (C) and ALS patients (D). Statistical maps are shown according the colour bars. *P*-values are corrected for age and gender. Radiological convention used.

following targeted motor and cognitive training. [77] Successful compensatory adaptation has been also noted in adults following rehabilitation and locomotor training after serious neurological events such as traumatic brain injury, [78] spinal cord injury, [79] or stroke. [80] Children with spinal cord injuries were consistently found to have better functional outcomes than those suffering spinal cord injuries in adulthood. [81] Given the young age at which our polio cohort sustained anterior horn damage due to the virus, we can speculate that considerable cortical reorganisation ensued.

Congruent to recent neurophysiology reports in adult polio patients [34,35], we also detected changes in the motor pathways of PPS patients. These changes were evident along the entire cerebral course of the corticospinal tracts from the corona radiata through the internal capsule to the mesencephalic crura. (Figs. 2, 3) The higher FA and lower RD in PPS compared to controls suggest well organised and well myelinated tracts, [82] the opposite of what is observed in motor neuron conditions with upper motor neuron involvement. [52,83,84] Increased brainstem density values and brainstem signal intensity was evident on whole-brain morphometry as well as region-of-interest analyses in the PPS cohort which are regions where preferential degeneration is known to occur in MND. [85–88] The cerebellum has long been implicated in adaptation to primary motor system injuries and compensatory processes have been detected by structural and functional studies [56,86]. The cerebellum plays a key role in motor learning [89], and the coordination of a variety of functions including posture, balance, speech integrating inputs from the spinal cord and cortex. [90] Many polio patients acquired considerable physical disabilities such as leg length discrepancy, muscle atrophy, foot deformations and joint misalignments after the acute infection resulting in altered gait patterns. [91] Given the longstanding physical disability experienced by polio survivors, increased cerebellar grey matter volume and superior cerebellar white matter fibre organisation may represent an adaptive process to maintain gait and posture in face of lower extremity deformities, leg length discrepancies and lower motor neuron degeneration.

This study is not without limitations. One of the drawbacks of a single-centre study design is the relatively small sample size of poliomyelitis survivors which risks the over-interpretation of findings and precludes subgroup analyses. We only report group-level observations in this study and don't explore approaches to categorise individual subjects into diagnostic or prognostic groups. [92,93] The additional inclusion of a pure UMN group, such as PLS, may have been desirable to contrast the cerebral changes observed in PPS. [94] Lastly, we acknowledge that cross-sectional imaging studies merely offer a snapshot of pathology and provide limited insights compared to longitudinal studies. [95] Notwithstanding these limitations, this neuroimaging study suggest that adult polio survivors who had their initial infection in their infancy, exhibit cerebral and cerebellar adaptation and corticospinal tract reorganisation. Larger studies are needed to validate our observations in independent cohorts and verify if the cerebral compensatory processes noted herein are analogous to other lower motor neuron conditions or unique to patients who have sustained spinal cord insults in their infancy.

5. Conclusions

Contrary to previous reports, we found no evidence of cerebral grey or white matter degeneration in a cohort of polio survivors using a validated quantitative neuroimaging protocol. The brainstem, corticospinal tracts and the cerebellum exhibit superior integrity in poliomyelitis survivors compared to healthy controls.

Potential conflicts of interest

None declared.

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