Atrophy of spared subcortical nuclei relates to worse post-stroke sensorimotor outcomes across 28 cohorts worldwide

Running title: Post-stroke subcortical atrophy and sensorimotor outcomes

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ABSTRACT

Objective: To identify associations between atrophy of spared subcortical nuclei and sensorimotor behavior at different timepoints after stroke.

Methods: We pooled high-resolution T1-weighted MRI brain scans and behavioral data in 828 individuals with unilateral stroke from 28 cohorts worldwide. Cross-sectional analyses using linear mixed-effects models related post-stroke sensorimotor behavior to non-lesioned subcortical volumes. We analyzed subacute (≤90 days) and chronic (≥180 days) stroke; sub-analyses in chronic stroke were performed on class of sensorimotor deficit (impairment, activity limitations) and side of lesioned hemisphere, with exploratory analyses in early stroke (≤21 days) and across all time (Bonferroni-corrected, $p<0.004$).

Results: Worse sensorimotor behavior was associated with a smaller ipsilesional thalamic volume in both early (n=179; d=0.68) and subacute (n=274, d=0.46) stroke. In chronic stroke (n=404), worse sensorimotor behavior was associated with smaller ipsilesional putamen (d=0.52) and nucleus accumbens (d=0.39) volumes, and a larger ipsilesional lateral ventricle (d=-0.42). Worse chronic sensorimotor impairment specifically (measured by the Fugl-Meyer Assessment; n=256) was associated with smaller ipsilesional putamen (d=0.72) and larger lateral ventricle (d=-0.41) volumes, while several measures of activity limitations (n=116) showed no significant relationships. In the full cohort (n=828), sensorimotor behavior was associated with the volumes of the ipsilesional nucleus accumbens (d=0.23), putamen (d=0.33), thalamus (d=0.33), and lateral ventricle (d=-0.23).

Conclusions: We demonstrate significant relationships between post-stroke sensorimotor behavior and reduced volumes of subcortical gray matter structures that were spared by stroke, which differ by time and class of sensorimotor measure. These findings may provide new targets for improving post-stroke sensorimotor outcomes.

Keywords: stroke, rehabilitation, sensorimotor behavior, MRI, subcortical volumes

INTRODUCTION

Sensorimotor recovery after stroke relies on residual motor architecture.[1] However, the majority of research in this area has focused on the role of cortical networks or regions, which often undergo significant reorganization after stroke, making them challenging targets for stroke rehabilitation. In contrast, spared subcortical nuclei provide a unique opportunity to modulate key nodes of distinct sensorimotor networks across the brain, with clearly defined boundaries, well-mapped inputs and outputs, and known associations with specific neurotransmitters and genetic variants,[2] making them ideal therapeutic targets. Research has shown that lesions to the thalamus and basal ganglia result in poor stroke outcomes, given their roles in sensorimotor control along with learning, motivation, reward, and cognition.[3-7] Atrophy of these structures has been reported after stroke[8] and related to cognitive deficits.[9] However, little is known about whether and how atrophy to spared subcortical regions relates to subsequent sensorimotor behavior.

To address this gap, we conducted a multi-site analysis of high-resolution MRI and post-stroke sensorimotor outcomes in 828 individuals across 28 cohorts worldwide at different times post-stroke. We hypothesized that reduced thalamic volume would relate to worse sensorimotor behavior in early and subacute phases after stroke, given its multiple roles in early cellular repair. Chronically, we hypothesized that atrophy of structures directly associated with sensorimotor control, such as the putamen, and larger ventricles, reflecting general atrophy, would relate to worse long-term sensorimotor behavior. We also examined whether class of sensorimotor deficit (impairment versus activity limitations) and lesioned hemisphere further modulates these relationships with greater granularity.

MATERIALS AND METHODS

Study design

The current cross-sectional pooled analysis used data from the ENIGMA Stroke Recovery Working Group, which was frozen for this analysis on May 22, 2020. A detailed overview of ENIGMA Stroke Recovery procedures and methods are reported elsewhere.[10] The retrospective data were collected across 28 different research studies (i.e., cohorts) at 16 different research institutes in 10 countries. Data were collected in accordance with the Declaration of Helsinki and

in compliance with local ethics review boards at each institute (see *Supplementary Table 1* for details).

ENIGMA Stroke Recovery Dataset

Participants with at least one sensorimotor behavioral outcome measure (see *Behavioral Data Analysis*) and a segmented high-resolution (e.g., 1-mm isotropic) T1-weighted (T1w) structural MRI of the brain (see *MRI Data Analysis*) were included, yielding an initial dataset of 1,285 individuals. Only participants with unilateral ischemic stroke or intracerebral hemorrhage were included, and individuals identified as having bilateral lesions or lesions in the brainstem or cerebellum were excluded from this analysis. For any longitudinal observations, only the first time-point was used; the resulting dataset was therefore cross-sectional. Each brain region was manually inspected for quality and overlap with the lesion (see *MRI Data Analysis).* Any individuals missing covariates of age (n=50) or sex (n=89) were also excluded, yielding a final sample of 828 individuals. As the relationships between brain volume and sensorimotor behavior were expected to change with time after stroke, the data were divided into subacute stroke (≤90 days post-stroke) and chronic stroke (≥180 days post-stroke). Exploratory analyses looking only at early stroke (≤21 days post-stroke) and across all times after stroke are also included.

MRI Data Analysis

To extract subcortical volumes, brain imaging software package FreeSurfer (version 5.3) was used to segment subcortical regions of interest (ROIs) from the T1w MRIs.[11] Twelve ROIs were extracted: the left and right thalamus, caudate, putamen, pallidum, nucleus accumbens, and lateral ventricles. For all analyses, these were characterized as ipsilesional and contralesional based on the lesioned hemisphere. Total intracranial volume (ICV) was also quantified using FreeSurfer outputs. ENIGMA scripts developed in-house were used to extract the volume of each ROI for each individual and to generate quality control (QC) triplanar images of each segmented ROI as done previously (http://enigma.ini.usc.edu/protocols/).[2] Given the variability of post-stroke neuroanatomy following a lesion, trained research team members (A.Z.-P., A.S.) performed visual QC for each ROI in each subject. Any regions intersecting the lesion were marked “lesioned,” and any regions not properly segmented by FreeSurfer were marked “failed.” Regions falling in either category were excluded from further analysis (for the full QC protocol, see Appendix 1 in ref[10]). Sample sizes for each analysis and brain region are reported.

Behavioral Data Analysis

Across cohorts, behavioral data were collected within approximately 72 hours of the MRI. To maximize the utility of the full dataset, a *primary sensorimotor behavior score* was defined for each study cohort using the measure reported in that cohort that was most commonly represented in the dataset overall (see *Supplementary Materials*). From this measure, a fraction of the maximum possible score was calculated, such that 0 represented the worst sensorimotor performance (severe deficits) and 1 represented the best sensorimotor performance (no deficits). The most common measure across cohorts was the Fugl-Meyer Motor Assessment of Upper Extremities (FMA-UE).[12]

In chronic stroke, we also identified behavioral measures that specifically captured impairment and activity limitation. Impairment was measured by the FMA-UE, whereas activity limitation was measured by the Action Research Arm Test (ARAT)[13] and Wolf Motor Function Test (WMFT);[14] data with any of these measures were used. These data were not examined in early stroke due to the limited sample sizes with these measures.

Statistical Analysis

To examine the relationships between sensorimotor behavior and non-lesioned subcortical volumes, we performed linear mixed-effects regressions. A separate regression model was run for the volume of each subcortical ROI (outcome) using sensorimotor behavior (e.g., primary sensorimotor behavior score, sensorimotor impairment, or activity limitations) as the primary predictor of interest. After ruling out collinearity (variance inflation factor ≤ 2.5), normalized age, ICV, and sex were included as fixed effects. Research cohort was included as a random effect. In chronic stroke, the effect of lesioned hemisphere was also examined; an interaction term between sensorimotor behavior and side of lesioned hemisphere was added to the model predicting subcortical volume. This was not examined in subacute stroke due to the smaller sample size. A likelihood ratio test (LRT) was performed to compare models with and without random effects and showed that the random effects were always significant. The regression assumptions of linearity, normality of the residuals, and homogeneity of the residual variance were checked via visual inspection of residuals versus fits plots as well as qq-plots for both individual observations and research cohorts. Potential influential values for both observations and cohorts were assessed using Cook's distance with recommended thresholds.[15] As we

detected influential observations in almost all analyses, we re-ran the analyses using robust mixed-effect regression, which reduces the weight of influential observations in the models without excluding data.[16] Results did not differ between original and robust regression models. The results of the robust regression models can be found in *Supplementary Materials*.

For all regression analyses, beta coefficients are presented for the factor of interest (e.g., sensorimotor behavior, sensorimotor impairment, or activity limitations), along with the sample size (n), standard error (SE), degrees of freedom (df), standardized effect size (*d*), t-value, and uncorrected p-value. Statistical significance was adjusted for multiple comparisons across the 12 ROIs using a Bonferroni correction ($p<0.004$). Any significant fixed covariates are also reported.

We also compared sensorimotor behavior scores between left and right hemisphere stroke groups. The data violated the Wilkes-Shapiro test of normality for both groups (LHS: $W=0.89$, $p<0.001$, RHS: $W=0.89$, $p<0.001$). We therefore used a nonparametric Wilcoxon rank sum test to compare independent group samples.

All statistical analyses were conducted in R (version 3.6.3; R Core Team, 2020).[17] The follow R libraries were used for the statistical analyses: the *lme* function from *nmle* was used for the linear mixed-effects regressions,[18] the *rlmer* function from *robustlmm* was used for the robust linear mixed-effects regressions,[19] and the *rstatix* library was used for the Wilcoxon rank sum test.[20] In addition, *influence.ME* was used to detect influential values[15] and *dplyr*[21] and *tidyverse*[22] libraries were used for data organization.

Data Availability Statement

The deidentified summary data and code that support the findings of this study are available upon reasonable request from the corresponding author. The data are not all publicly available in a repository as they may contain information that could compromise the privacy of research participants. There are also data sharing restrictions imposed by some of the (i) ethical review boards of the participating sites, and consent documents; (ii) national and trans-national data sharing laws; and (iii) institutional processes, some of which require a signed DTA for limited and predefined data use. However, we welcome sharing data with researchers, requiring that they become members of the ENIGMA Stroke Recovery working group and submit an analysis plan for a secondary project for group review. Once this analysis plan is approved, access to the

relevant data will be provided contingent on data availability, local PI approval and compliance with all supervening regulatory boards.

RESULTS

Data from 828 individuals from 28 cohorts worldwide were included (see Table 1 for an overview of cohort characteristics). Briefly, the median age was 63 years old (interquartile range (IQR) 19 years), and there were 516 males and 312 females.

In subacute stroke (≤ 90 days; n=274), worse post-stroke sensorimotor behavior was significantly associated with smaller volumes of the ipsilesional thalamus (n=274, d=0.46, p=0.002; Table 2; Figure 1). Analysis of individuals within just the first 21 days post-stroke (n=179, d=0.68, p<0.001) demonstrated the same result (Table 2).

In chronic stroke (≥ 180 days; n=404), worse sensorimotor behavior was related to smaller volumes of the ipsilesional putamen (d=0.52, p<0.001) and ipsilesional nucleus accumbens (d=0.39, p=0.002), and a larger volume of the ipsilesional lateral ventricle (d=-0.42, p<0.001; Table 3; Figure 1).

In chronic stroke, we examined brain-behavior relationships using a measure of impairment (the FMA-UE scale; n=256) and two measures of activity limitation (WMFT, ARAT; n=116). Worse sensorimotor impairment was associated with smaller ipsilesional putamen (d=0.72, p=0.001) and larger ipsilesional lateral ventricle volumes (d=-0.41, p=0.002; Table 4; Figure 1). We found no significant relationships between subcortical nuclei and measures of activity limitations (Table 4).

In chronic stroke, we further analyzed the differences between individuals with left hemisphere stroke (LHS, n=214) versus right hemisphere stroke (RHS, n=190) by including lesioned hemisphere as an interaction term in the model. There were no significant effects of the side of the lesioned hemisphere on the relationship between sensorimotor behavior and subcortical volumes, and no main effects of the lesioned hemisphere (Table 5). Inclusion of the lesioned hemisphere into the model did not change the main effects of sensorimotor behavior. We also examined whether there were differences in behavioral scores for LHS and RHS groups. The median sensorimotor behavior score in LHS was 0.80 (IQR=0.39) and in RHS was 0.74

(IQR=0.49). A Wilcoxon test showed no significant effect of lesioned hemisphere between groups (p=0.29, effect size r=0.053).

Finally, an exploratory analysis of the entire cohort (N=828) demonstrated significant relationships between worse sensorimotor behavior and smaller volumes of the ipsilesional thalamus (*d*=0.33, p=0.001), putamen (*d*=0.33, p<0.001), and nucleus accumbens (*d*=0.23, p=0.004), and a larger lateral ventricle volume (*d*=-0.23, p=0.001; Table 6).

DISCUSSION

We report the first international, multi-site pooled analysis with individual patient data using high-resolution structural brain imaging in stroke rehabilitation research and the largest study to date relating atrophy of residual subcortical brain volumes to post-stroke sensorimotor behavior. We identified novel, significant relationships between worse post-stroke sensorimotor behavior and atrophy of spared deep gray matter structures including the ipsilesional thalamus, putamen, and nucleus accumbens, as well as general atrophy as indexed by enlargement of the ipsilesional lateral ventricle. Notably, all significant relationships were found only in the ipsilesional hemisphere. These findings suggest that, post-stroke, subcortical brain alterations related to sensorimotor behavior occur most prominently in the hemisphere directly affected by the stroke. This was observed despite the fact that, after stroke, atrophy and reorganization has been observed bilaterally.[8] The identification of sensorimotor relationships with these specific ipsilesional subcortical nuclei may provide novel neuromodulatory or pharmacological targets to improve stroke outcomes.

Our results support the hypothesis that non-lesioned deep gray structures serve distinct roles in subacute versus chronic stroke, which is not surprising given the cascade of neurobiological and neuroinflammatory processes that occur early after stroke.[23, 24] Within 90 days after stroke, only the ipsilesional thalamus showed detectable associations with post-stroke sensorimotor behavior, in line with recent research showing marked thalamic atrophy, particularly within the first three months post-stroke.[8] A smaller thalamic volume could reflect cell loss and thalamic dysfunction, thereby limiting resources critical for early recovery.[5, 8] Importantly, in our data, this relationship persists, and is stronger, when looking at only the first 21 days post-stroke. As non-lesioned

brain volumes within six weeks after stroke are assumed to be similar to those before the stroke,[25] this finding suggests that larger thalamic volumes prior to stroke could provide a neuroprotective effect. Thalamic atrophy was recently associated with loss of extrinsic and intrinsic connectivity between the thalamus and the rest of the brain, suggesting that thalamic measures may serve as an index of global brain function.[26] Future research using longitudinal datasets with greater spatial specificity could relate changes in specific thalamic nuclei to sensorimotor recovery to identify targets for neuroprotective or early stroke therapies.

In chronic stroke, reduced volumes of the ipsilesional putamen and nucleus accumbens were consistently associated with worse sensorimotor behavior. General atrophy, as indexed by a larger ipsilesional ventricle volume, was also negatively associated with sensorimotor behavioral measures. This is the first large-scale validation showing atrophy of these specific structures as correlates of sensorimotor behavioral outcomes in chronic stroke. This finding augments existing stroke literature, which has typically examined direct damage to combined subcortical regions, without differentiating roles of the individual basal ganglia nuclei and thalamus. Here, we specifically identify the putamen and nucleus accumbens, which are key components of corticostriatal and mesolimbic circuits, and which both represent key dopaminergic targets in the brain.

Specifically, within the corticostriatal circuit, the putamen receives direct cortical signals from the primary motor, premotor, and sensory cortices and relays them to the thalamus to modulate motor control. Interestingly, although the caudate plays a similar role within this circuit, it receives its inputs from multimodal association cortices and visual regions—not primary motor regions—and was not found to be significant in any of our analyses, suggesting that post-stroke behavior is only associated with atrophy of regions specifically receiving direct sensorimotor input. In line with this, we found that secondary atrophy of the putamen related to both sensorimotor behavior generally and impairment specifically, as evidenced by the association with the FMA-UE in chronic stroke. This is in line with previous work showing that direct damage to the putamen relates to post-stroke gait impairment,[27] upper limb impairment,[28] and spasticity,[29] all deficits which overlap with the behavioral measures used here. In addition, secondary atrophy of the putamen has been reported after cortical stroke and been associated with infarct volume[30] and post-stroke cognitive deficits.[31] The relationship between chronic sensorimotor behavioral deficits and atrophy of the ipsilesional putamen after stroke, however, has not previously been reported. As atrophy of the putamen has been associated with a wide variety of neuropsychiatric and neurodegenerative disorders,[32] including Alzheimer's disease,[33] multiple sclerosis,

attention deficit disorder,[12] and Huntington's disease,[10] it is possible that the integrity of the putamen is required not only for specifically sensorimotor behavior but also, more generally, for overall brain health.

While the ipsilesional nucleus accumbens was significantly related to chronic sensorimotor behavior in general, it was not related to sensorimotor impairment (FMA-UE) alone, nor was it associated with activity limitations (e.g., ARAT, WMFT), as hypothesized. However, the analyses on impairment and activity limitations had less statistical power to detect relationships. As the nucleus accumbens is a key component of the ventral striatum and implicated in dopaminergic modulation of reward-based behaviors,[34] this region may impact more complex aspects of motor performance, such as motivation and participation, compared to impairment or activity. A number of studies show decreases in ventral striatal processes such as reward sensitivity, motivation, and apathy after stroke,[6] and post-stroke hypoactivity in the nucleus accumbens has been identified during reward-based decision-making tasks.[35] This effect was observed despite no direct lesions in the nucleus accumbens, suggesting that secondary dysfunction of this network can impact behavior after stroke. It is likely that the nucleus accumbens impacts sensorimotor behavior by influencing reward and motivation,[36] which could influence use of the affected limb in daily tasks. Although pharmacological methods to modulate the dopaminergic system and promote motor recovery following stroke have been widely studied, there are large individual differences in outcomes.[37] Future research may investigate whether individual differences in the volume and connectivity of the nucleus accumbens, as well as genetics, predict who may benefit from dopaminergic treatment.

Our third important finding in chronic stroke is the association between an enlarged ipsilesional lateral ventricle and poor sensorimotor behavior. This relationship was only significant at the chronic stage and was exclusive to the ipsilesional lateral ventricle, which may be due to hydrocephalus ex vacuo. Ventricular enlargement post-stroke may also be influenced by small vessel disease (i.e., leukoaraiosis), although this is typically observed bilaterally.[38] Enlargement of the bilateral lateral ventricles has also been associated with generalized brain atrophy that occurs during aging and with impaired cognitive function.[39] The contrast between ipsilesional and contralesional ventricles may provide unique insight into the specific impact of the stroke versus general aging on chronic stroke sensorimotor outcomes.

Our results also suggest that there are distinct brain-behavior relationships for different ICF dimensions of sensorimotor behavior. Chronic motor impairment, as measured by the FMA-UE, was associated with a smaller ipsilesional putamen and larger ipsilesional ventricle, which may provide an indication of corticostriatal circuit integrity as well as more general brain functions essential for sensorimotor control. In contrast, there were no subcortical associations with activity limitations in the current study. This could be related to the smaller sample size (n=116 versus n=256 for sensorimotor impairment). Activity limitations may also be more strongly related to the integrity or function of distributed regions across whole brain networks rather than subcortical structures,[40, 41] given that functional performance can be influenced by psychosocial factors to a greater degree than impairment measures.

Findings did not indicate a significant effect of lesioned hemisphere on the relationship between chronic sensorimotor behavior and spared subcortical volumes. These results are surprising, given that the large majority of patients were likely left hemisphere dominant for motor control, and previous research has identified post-stroke hemispheric specializations and roles in sensorimotor control.[42] However, previous research has primarily focused on cortical regions and functional activity, rather than subcortical structures. Side of stroke injury may not directly impact sensorimotor relationships with spared subcortical volumes.

Finally, the current results represent the first large-scale, multi-site analysis utilizing harmonized high-resolution brain imaging and behavioral measures in the field of stroke rehabilitation. Although acute stroke research has successfully utilized pooled approaches with individual patient data to examine acute treatment outcomes,[43] stroke rehabilitation research has been slower to adopt this type of approach due to the complexity of combining elaborate rehabilitation research protocols, diversity of the patient populations recruited, and variety of the stroke neuroimaging and behavioral measures collected, which are not routinely collected as they are in acute settings. To address these challenges, we formed the international ENIGMA Stroke Recovery Working Group to harmonize and combine diverse individual patient data, including high-resolution structural brain MRIs and behavioral outcome measures, across multiple research centers.[10] This combined analysis pools individual patient data across research sites using a harmonized analytical pipeline and includes both published and unpublished data. Compared to traditional single-site analyses or retrospective meta-analyses, this approach allows for greater

statistical rigor, testing of more sophisticated hypotheses (e.g., subgroup analyses), and less bias due to the inclusion of both published and unpublished data across diverse cohorts.[44] Furthermore, pooled analyses with multi-site data increase heterogeneity, which improves generalizability of findings, reduces research inefficiency by leveraging previously collected data to examine novel questions, and advances the field faster than is achievable by prospective studies alone.[45] The fact that the current results, using diverse stroke rehabilitation data, fit with existing literature and reveal new findings is further confirmation that such an approach is not only feasible and effective, but also beneficial for moving the stroke rehabilitation field forward.

Limitations and Future Directions

A key limitation of pooling multi-site data is inconsistent variables across cohorts, limiting subgroup analyses and reducing the number of included covariates. Models only included the covariates age, sex, and intracranial volume; however, many additional demographic variables, such as duration and type of rehabilitation received, handedness, race, educational level, and comorbidities, may influence these relationships. In addition, larger sample sizes for different sensorimotor outcome measures would provide greater support for the current findings. Related, small high-resolution MRI samples ($n < 50$) at earlier time points of stroke (i.e., ≤ 7 days, defined as acute[46]) with sensorimotor behavioral outcomes limited our ability to specifically examine acute brain-behavior relationships or to examine relationships between impairment versus activity limitations in acute or subacute stroke in the current analysis. The ENIGMA Stroke Recovery Working Group recommends following consensus guidelines for greater harmonization of prospectively-collected data to facilitate more precise pooled analyses across all times after stroke.[10, 47]

Lesion overlap with subcortical regions, and poor segmentation of subcortical regions due to lesion-induced distortions, resulted in a variable sample size for each ROI, potentially limiting the power to detect relationships in regions with smaller samples. Furthermore, excluding individuals with lesioned or incorrectly segmented ROIs may disproportionately exclude individuals with larger lesions, who may be more severely affected. This could have biased the sample towards more mild-to-moderately impaired patients. Future studies using lesion masks for each observation could address these issues and also provide additional information about

lesion location and volume as well as the amount of direct lesion overlap with each subcortical region for each individual.

Finally, many of these subcortical regions are also critical for and related to post-stroke cognition, mood, sleep, learning and other traits of interest. While this analysis was limited to sensorimotor behavioral measures to maximize available data for analysis, these findings may not be unique to sensorimotor behavior. Future studies should assess the relationship between these subcortical volumes and additional stroke outcome measures.

Conclusion

This international collaborative analysis revealed significant relationships between post-stroke sensorimotor behavior and volumetric measures of the residual ipsilesional thalamus, putamen, nucleus accumbens, and lateral ventricle at different times after stroke – brain metrics that may reflect overall brain health and network integrity and could lead to the identification of novel neural targets for pharmacological or behavioral modulation in stroke rehabilitation.

TABLES

Cohort ID	*n*	Females / Males	Median Age (IQR, min-max)	Median Sensorimotor Score (IQR, min-max)
1	39	10 / 29	61 (17, 31-80)	0.65 (0.23, 0.0-0.9)
2	12	06 / 06	70 (12, 39-85)	0.50 (0.41, 0.2-0.7)
3	14	06 / 08	60 (15, 33-85)	0.25 (0.22, 0.1-0.6)
4	19	06 / 13	44 (15, 30-68)	0.14 (0.17, 0.0-0.5)
7	42	14 / 28	56 (14, 18-80)	0.82 (0.35, 0.4-1.0)
8	8	02 / 06	62 (10, 39-75)	0.55 (0.35, 0.0-1.0)
9	93	29 / 64	70 (16, 24-88)	1.00 (0.07, 0.0-1.0)
10	24	05 / 19	59 (13, 42-74)	1.00 (0.02, 0.7-1.0)
11	29	10 / 19	57 (11, 44-71)	1.00 (0.05, 0.1-1.0)
12	57	31 / 26	71 (17, 31-97)	0.65 (0.71, 0.0-1.0)
13	44	22 / 22	72 (18, 33-91)	0.12 (0.32, 0.0-1.0)
15	14	06 / 08	57 (11, 45-74)	0.72 (0.25, 0.4-0.8)
17	16	05 / 11	59 (04, 45-68)	0.55 (0.23, 0.2-0.7)
18	11	05 / 06	59 (07, 46-73)	0.65 (0.22, 0.5-0.9)
19	13	03 / 10	62 (21, 33-74)	0.84 (0.08, 0.8-0.9)
20	22	08 / 14	70 (13, 49-79)	0.91 (0.14, 0.3-1.0)
22	17	04 / 13	59 (30, 25-72)	0.63 (0.50, 0.0-0.8)
23	13	07 / 06	58 (08, 31-90)	0.42 (0.17, 0.3-0.8)
24	21	11 / 10	63 (13, 32-78)	0.95 (0.00, 0.6-1.0)
25	26	10 / 16	65 (18, 37-88)	0.97 (0.20, 0.0-1.0)
26	24	14 / 10	49 (20, 25-71)	0.64 (0.14, 0.3-0.8)
28	26	07 / 19	62 (11, 23-75)	0.75 (0.25, 0.3-1.0)
31	35	09 / 26	58 (12, 21-86)	0.52 (0.31, 0.2-0.9)
32	7	03 / 04	62 (16, 38-72)	0.95 (0.44, 0.2-1.0)
34	15	06 / 09	58 (11, 32-80)	0.82 (0.20, 0.6-1.0)
35	15	06 / 09	64 (18, 31-83)	0.64 (0.52, 0.2-0.9)
38	81	34 / 47	66 (19, 30-89)	0.85 (0.60, 0.0-1.0)
41	91	33 / 58	70 (15, 32-89)	1.00 (0.02, 0.8-1.0)
TOTAL	**828**	**312 / 516**	**63 (19, 18-97)**	**0.82 (0.48, 0-1)**

Table 1. Summary of research cohort characteristics. Age and sensorimotor behavioral score data are shown as median (interquartile range (IQR), minimum-maximum values)

SUBACUTE AND EARLY STROKE

SUBACUTE STROKE (≤ 90 days)

Brain Region	n	beta (CI)	SE	df	t-value	p-value	*d*	Significant covariates
				Ipsilesional				
Caudate	194	-0.01 (-0.51-0.48)	0.25	180	-0.06	0.954	-0.01	ICV
Lateral ventricle	274	0.18 (-0.14-0.51)	0.16	259	1.13	0.258	0.14	Age, ICV
Nucleus accumbens	245	0.24 (-0.14-0.62)	0.19	231	1.26	0.210	0.17	Age
Pallidum	223	0.21 (-0.26-0.67)	0.24	209	0.87	0.387	0.12	ICV
Putamen	201	0.39 (-0.09-0.88)	0.25	187	1.61	0.109	0.24	Age, ICV
Thalamus	**210**	**0.69 (0.27-1.11)**	**0.21**	**197**	**3.21**	**0.002**	**0.46**	**Age, ICV**
				Contralesional				
Caudate	219	0.22 (-0.20-0.64)	0.21	205	1.04	0.298	0.15	ICV
Lateral ventricle	274	0.15 (-0.18-0.49)	0.17	259	0.92	0.361	0.11	Age, ICV
Nucleus accumbens	253	0.15 (-0.23-0.52)	0.19	239	0.77	0.443	0.10	Age, ICV
Pallidum	250	0.50 (0.07-0.92)	0.22	236	2.30	0.022	0.30	ICV
Putamen	229	0.37 (-0.05-0.79)	0.21	215	1.75	0.081	0.24	Age, ICV
Thalamus	217	0.09 (-0.33-0.50)	0.21	204	0.41	0.679	0.06	Age, ICV

EARLY STROKE (≤ 21 days)

Brain Region	n	beta (CI)	SE	df	t-value	p-value	*d*	Significant covariates
				Ipsilesional				
Caudate	135	-0.09 (-0.67-0.48)	0.29	125	-0.32	0.749	-0.06	ICV
Lateral ventricle	182	0.25 (-0.11-0.61)	0.18	172	1.37	0.173	0.21	Age, ICV
Nucleus accumbens	165	0.19 (-0.23-0.60)	0.21	155	0.90	0.369	0.14	Age
Pallidum	157	0.12 (-0.39-0.63)	0.26	147	0.46	0.644	0.08	ICV
Putamen	143	0.25 (-0.28-0.79)	0.27	133	0.93	0.354	0.16	Age, ICV
Thalamus	**137**	**0.79 (0.38-1.20)**	**0.21**	**128**	**3.82**	**<0.001**	**0.68**	**Age, ICV**
				Contralesional				
Caudate	147	0.17 (-0.29-0.64)	0.24	137	0.74	0.461	0.13	ICV
Lateral ventricle	182	0.19 (-0.20-0.57)	0.19	172	0.96	0.337	0.15	Age, ICV
Nucleus accumbens	170	0.30 (-0.09-0.69)	0.20	160	1.53	0.127	0.24	Age
Pallidum	171	0.65 (0.19-1.11)	0.23	161	2.79	0.006	0.44	ICV
Putamen	158	0.26 (-0.21-0.72)	0.24	148	1.10	0.274	0.18	Age, ICV
Thalamus	150	0.20 (-0.28-0.67)	0.24	141	0.82	0.411	0.14	Age, ICV

Table 2. Relationships between non-lesioned subcortical volumes and sensorimotor behavior in subacute and early stroke. Results from linear mixed-effects models of individuals with subacute stroke (top) and early stroke (bottom). Results in bold indicate significance with a Bonferroni correction for multiple comparisons ($p<0.004$). The beta coefficient for sensorimotor behavior (beta) with 95% confidence interval (CI), along with the sample size (n), standard error (SE), degrees of freedom (df), standardized effect size (*d*), t-value, and uncorrected p-value are reported, in addition to significant fixed covariates including age, sex, and intracranial volume (ICV).

CHRONIC STROKE

CHRONIC STROKE (≥ 180 days)								
Brain Region	**n**	**beta (CI)**	**SE**	**df**	**t-value**	**p-value**	***d***	**Significant covariates**
				Ipsilesional				
Caudate	193	0.27 (-0.28-0.82)	0.28	169	0.98	0.330	0.15	ICV
Lateral ventricle	**404**	**-0.70 (-1.04--0.36)**	**0.17**	**378**	**-4.04**	**<0.001**	**-0.42**	**Age, ICV**
Nucleus accumbens	**289**	**0.72 (0.27-1.18)**	**0.23**	**264**	**3.15**	**0.002**	**0.39**	**Age**
Pallidum	225	0.30 (-0.23-0.84)	0.27	200	1.11	0.267	0.16	ICV
Putamen	**207**	**1.01 (0.45-1.57)**	**0.28**	**183**	**3.54**	**<0.001**	**0.52**	**Age**
Thalamus	169	0.08 (-0.60-0.75)	0.34	146	0.22	0.827	0.04	Age
				Contralesional				
Caudate	345	0.08 (-0.31-0.48)	0.20	320	0.41	0.679	0.05	ICV
Lateral ventricle	404	-0.39 (-0.70--0.07)	0.16	378	-2.42	0.016	-0.25	Age, ICV
Nucleus accumbens	344	0.21 (-0.22-0.65)	0.22	319	0.96	0.339	0.11	Age
Pallidum	359	0.20 (-0.20-0.60)	0.20	334	0.97	0.332	0.11	Sex, ICV
Putamen	355	0.21 (-0.18-0.60)	0.20	330	1.06	0.291	0.12	Age, ICV
Thalamus	329	-0.24 (-0.60-0.12)	0.18	304	-1.29	0.196	-0.15	Age, ICV

Table 3. Relationships between non-lesioned subcortical volumes and sensorimotor behavior in chronic stroke. Results from linear mixed-effects models of individuals with chronic stroke. Results in bold indicate significance with a Bonferroni correction for multiple comparisons ($p<0.004$). The beta coefficient for sensorimotor behavior (beta) with 95% confidence interval (CI), along with the sample size (n), standard error (SE), degrees of freedom (df), standardized effect size (*d*), t-value, and uncorrected p-value are reported, in addition to significant fixed covariates including age, sex, and intracranial volume (ICV).

CHRONIC SENSORIMOTOR IMPAIRMENT AND ACTIVITY LIMITATIONS

SENSORIMOTOR IMPAIRMENT IN CHRONIC STROKE

Brain Region	n	beta (CI)	SE	df	t-value	p-value	*d*	Significant covariates
				Ipsilesional				
Caudate	94	0.92 (-0.06-1.89)	0.49	77	1.87	0.065	0.43	ICV
Lateral ventricle	**256**	**-0.74 (-1.20--0.27)**	**0.24**	**237**	**-3.13**	**0.002**	**-0.41**	**Age, ICV**
Nucleus accumbens	171	0.58 (0.01-1.15)	0.29	153	2.02	0.045	0.33	Age
Pallidum	120	0.76 (0.01-1.51)	0.38	102	2.02	0.046	0.40	-
Putamen	**104**	**1.50 (0.61-2.39)**	**0.45**	**87**	**3.34**	**0.001**	**0.72**	**-**
Thalamus	84	0.33 (-0.72-1.38)	0.53	68	0.62	0.537	0.15	-
				Contralesional				
Caudate	222	0.06 (-0.44-0.57)	0.26	204	0.25	0.806	0.03	ICV
Lateral ventricle	256	-0.51 (-0.88--0.14)	0.19	237	-2.70	0.007	-0.35	Age, ICV
Nucleus accumbens	222	0.21 (-0.31-0.73)	0.26	204	0.80	0.425	0.11	Age
Pallidum	231	0.20 (-0.33-0.73)	0.27	213	0.74	0.459	0.10	Sex
Putamen	229	0.10 (-0.38-0.58)	0.24	211	0.41	0.681	0.06	Age, ICV
Thalamus	211	-0.40 (-0.88-0.07)	0.24	193	-1.67	0.096	-0.24	Age, ICV

ACTIVITY LIMITATIONS IN CHRONIC STROKE

Brain Region	n	beta (CI)	SE	df	t-value	p-value	*d*	Significant covariates
				Ipsilesional				
Caudate	52	-0.63 (-1.80-0.53)	0.58	44	-1.09	0.280	-0.33	-
Lateral ventricle	116	-0.71 (-1.46-0.04)	0.38	108	-1.88	0.062	-0.36	Age, ICV
Nucleus accumbens	86	0.77 (-0.31-1.85)	0.54	78	1.42	0.159	0.32	-
Pallidum	64	0.71 (-0.25-1.67)	0.48	56	1.47	0.146	0.39	-
Putamen	65	0.71 (-0.62-2.04)	0.67	57	1.06	0.292	0.28	-
Thalamus	56	0.94 (-0.36-2.25)	0.65	48	1.45	0.153	0.42	-
				Contralesional				
Caudate	96	-0.07 (-0.98-0.84)	0.46	88	-0.15	0.885	-0.03	-
Lateral ventricle	116	-0.72 (-1.44-0.01)	0.37	108	-1.95	0.054	-0.38	Age, ICV
Nucleus accumbens	107	-0.34 (-1.17-0.49)	0.42	99	-0.81	0.420	-0.16	Age
Pallidum	103	-0.15 (-0.98-0.68)	0.42	95	-0.35	0.728	-0.07	Sex
Putamen	100	0.06 (-0.91-1.03)	0.49	92	0.12	0.903	0.03	Age
Thalamus	92	0.28 (-0.51-1.06)	0.39	84	0.71	0.482	0.15	Age, ICV

Table 4. Relationships between non-lesioned subcortical volumes and two measures of sensorimotor behavior (impairment, activity limitations). Results from linear mixed-effects models in individuals with chronic stroke of sensorimotor impairment (top) compared to activity limitations (bottom). Results in bold indicate significance with a Bonferroni correction for multiple comparisons ($p<0.004$). The beta coefficient for sensorimotor impairment/activity limitations (beta) with 95% confidence interval (CI), along with the sample size (n), standard error (SE), degrees of freedom (df), standardized effect size (*d*), t-value, and uncorrected p-value are reported, in addition to significant fixed covariates including age, sex, and intracranial volume (ICV).

Brain Region	n	df	Interaction between Sensorimotor Behavior & Lesioned Hemisphere			Main Effect Lesioned Hemisphere			Main Effect Sensorimotor Behavior				Significant Covariates
			beta	SE	p-value	beta	SE	p-value	beta	SE	p-value	*d*	
Ipsilesional													
Caudate	193	167	0.14	0.52	0.789	-0.17	0.44	0.693	0.26	0.28	0.365	0.14	ICV
Lateral ventricle	404	376	0.21	0.29	0.487	-0.13	0.23	0.572	**-0.70**	**0.17**	**<0.001**	**-0.42**	Age, ICV
Nucleus accumbens	289	262	0.21	0.39	0.593	-0.13	0.31	0.684	**0.73**	**0.23**	**0.002**	**0.39**	Age
Pallidum	225	198	-0.53	0.48	0.272	0.52	0.39	0.191	0.35	0.27	0.207	0.18	ICV
Putamen	207	181	-0.03	0.53	0.953	-0.28	0.44	0.525	**0.90**	**0.29**	**0.002**	**0.47**	ICV
Thalamus	169	144	0.17	0.63	0.792	-0.95	0.51	0.065	0.05	0.32	0.887	0.02	Age, ICV
Contralesional													
Caudate	345	318	0.12	0.33	0.731	-0.14	0.26	0.583	0.06	0.21	0.760	0.03	ICV
Lateral ventricle	404	376	0.27	0.28	0.343	0.06	0.21	0.789	-0.35	0.16	0.030	-0.22	Age, ICV
Nucleus accumbens	344	317	0.38	0.35	0.282	-0.32	0.27	0.236	0.18	0.22	0.423	0.09	Age
Pallidum	359	332	0.07	0.32	0.819	-0.43	0.25	0.083	0.09	0.20	0.672	0.05	Sex, ICV
Putamen	355	328	-0.08	0.31	0.796	0.14	0.24	0.553	0.23	0.20	0.243	0.13	Age, ICV
Thalamus	329	302	0.25	0.30	0.405	0.47	0.23	0.045	-0.17	0.18	0.353	-0.11	Age, ICV

Table 5. Relationships between non-lesioned subcortical volumes, lesioned hemisphere, and sensorimotor behavior in chronic stroke. Results from linear mixed-effects models including an interaction term between lesioned hemisphere and sensorimotor behavior in people with chronic stroke. There were no significant interactions or main effects of lesioned hemisphere. The significant main effects for sensorimotor behavior remained, similar to those shown in Table 2. Results in bold indicate significance with a Bonferroni correction for multiple comparisons ($p<0.004$). The beta coefficients (beta), standard error (SE), and uncorrected p-value for the interaction between lesioned hemisphere and sensorimotor behavior, as well as main effects for lesioned hemisphere and sensorimotor behavior, are reported, along with the sample size (n), degrees of freedom (df), standardized effectsize (d), and significant fixed covariates including age, sex, and intracranial volume (ICV)

ALL STROKE

Brain Region	n	beta (CI)	SE	df	t-value	p-value	*d*	Significant covariates
				Ipsilesional				
Caudate	482	0.15 (-0.18-0.48)	0.17	451	0.89	0.375	0.08	Sex, ICV
Lateral ventricle	**828**	**-0.39 (-0.63--0.16)**	**0.12**	**796**	**-3.26**	**0.001**	**-0.23**	**Age, ICV**
Nucleus accumbens	**655**	**0.41 (0.13-0.68)**	**0.14**	**624**	**2.91**	**0.004**	**0.23**	**Age**
Pallidum	546	0.29 (-0.04-0.61)	0.16	515	1.75	0.081	0.15	ICV
Putamen	**490**	**0.64 (0.28-1.00)**	**0.18**	**459**	**3.53**	**<0.001**	**0.33**	**Age, ICV**
Thalamus	**462**	**0.58 (0.25-0.91)**	**0.17**	**433**	**3.47**	**0.001**	**0.33**	**Age, ICV**
				Contralesional				
Caudate	689	0.01 (-0.26-0.28)	0.14	658	0.08	0.939	0.01	ICV
Lateral ventricle	828	-0.26 (-0.49--0.03)	0.11	796	-2.27	0.024	-0.16	Age, ICV
Nucleus accumbens	727	0.10 (-0.15-0.36)	0.13	696	0.78	0.436	0.06	Age, ICV
Pallidum	743	0.28 (0.02-0.54)	0.13	712	2.08	0.038	0.16	Age, ICV
Putamen	704	0.19 (-0.07-0.45)	0.13	673	1.45	0.147	0.11	Age, ICV
Thalamus	663	-0.02 (-0.28-0.24)	0.13	633	-0.13	0.898	-0.01	Age, ICV

Table 6. Relationships between non-lesioned subcortical volumes and sensorimotor behavior post-stroke across all times after stroke (N=828). Results from linear mixed-effects models of individuals across all times after stroke. Uncorrected p-values shown. Results in bold indicate significance with a Bonferroni correction for multiple comparisons (p<0.004). The beta coefficient for sensorimotor behavior (beta) with 95% confidence interval (CI), along with the sample size (n), standard error (SE), degrees of freedom (df), standardized effect size (*d*), t-value, and uncorrected p-value are reported, in addition to significant fixed covariates including age, sex, and intracranial volume (ICV).

FIGURES

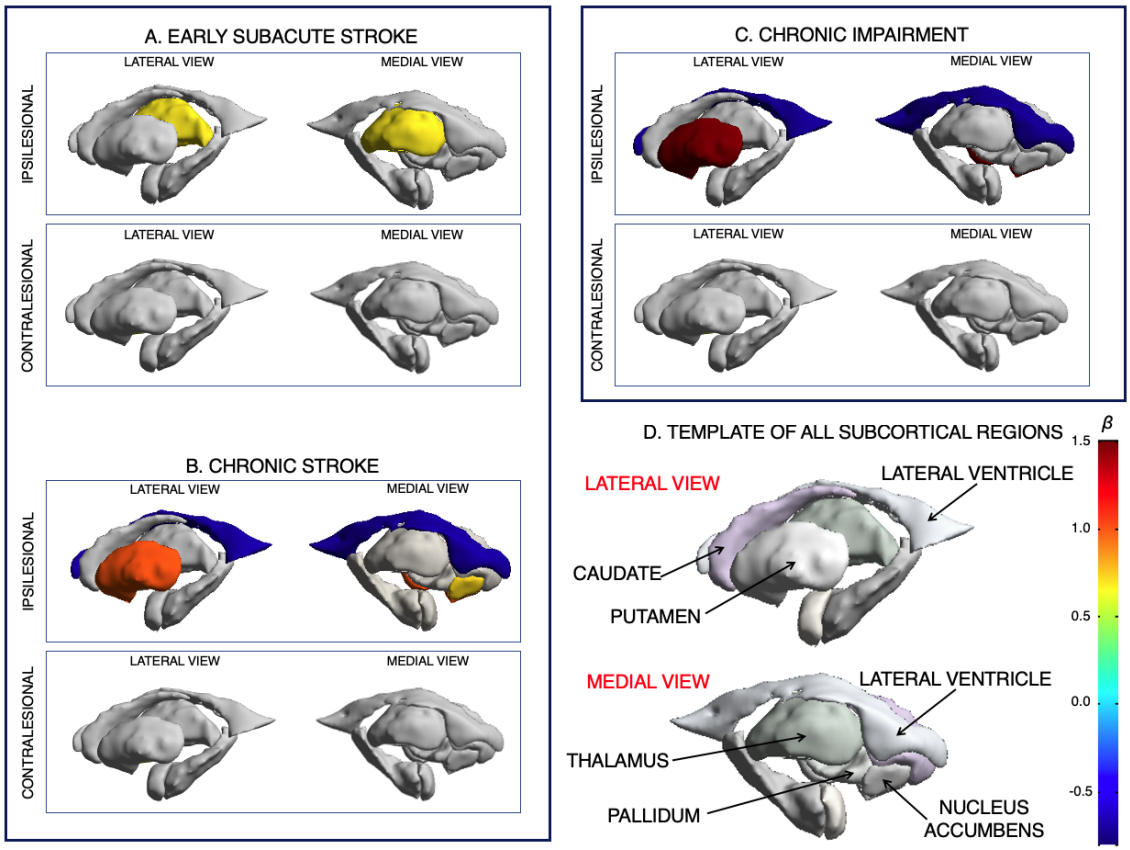

Figure 1. Relationship between post-stroke sensorimotor behavior and non-lesioned subcortical volumes. Non-lesioned subcortical regions (1D, bottom right) that relate to sensorimotor behavior from linear mixed-effects models of people with subacute (1A, top left) and chronic (1B, bottom left) stroke. Non-lesioned subcortical volume relationships with chronic sensorimotor impairment is shown in 1C (top right). There were no significant volume relationships with chronic activity limitations. Colors represent the beta estimate (β) for sensorimotor behavior from each model, with warmer colors representing more positive beta estimates and cooler colors representing more negative beta estimates.

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COMPETING INTERESTS

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SUPPLEMENTARY MATERIALS

COHORT ID	SITE	COUNTRY	N	PRIMARY SENSORIMOTOR MEASURE
1	UNIVERSITY OF SOUTHERN CALIFORNIA	USA	39	FMA-UE
2	UNIVERSITY OF SOUTHERN CALIFORNIA	USA	12	FMA-UE
3	UNIVERSITY OF SOUTHERN CALIFORNIA	USA	14	FMA-UE
4	UNIVERSITY OF TUEBINGEN	GERMANY	19	FMA-UE
7	UNIVERSITY COLLEGE LONDON	UK	42	Action Research Arm Test
8	UNIVERSITY OF SOUTHERN CALIFORNIA	USA	6	Manual Muscle Test
9	UNIVERSITY OF OSLO	NORWAY	93	NIHSS Motor Score
10	TIANJIN MEDICAL UNIVERSITY	CHINA	24	FMA-UE
11	TIANJIN MEDICAL UNIVERSITY	CHINA	29	FMA-UE
12	UNIVERSITY OF AUCKLAND	NEW ZEALAND	57	FMA-UE
13	UNIVERSITY OF AUCKLAND	NEW ZEALAND	44	FMA-UE
15	MEDICAL UNIVERSITY OF SOUTH CAROLINA	USA	14	FMA-UE
17	MEDICAL UNIVERSITY OF SOUTH CAROLINA	USA	16	FMA-UE
18	MEDICAL UNIVERSITY OF SOUTH CAROLINA	USA	10	FMA-UE
19	UNIVERSITY OF GRIEFSWALD	GERMANY	13	Motricity Index
20	UNIVERSITY OF GRIEFSWALD	GERMANY	21	Motricity Index
22	UNIVERSITY OF GRIEFSWALD	GERMANY	17	Bogenhausen Dysphagia Score
23	UNIVERSITY OF THE SCIENCES	USA	13	FMA-UE
24	EMORY UNIVERSITY	USA	21	Manual Muscle Test
25	UNIVERSITY OF TORONTO	CANADA	26	Grip Strength
26	SAO PAOLO UNIVERSITY	BRAZIL	24	FMA-UE
28	UNIVERSITY OF CALIFORNIA, IRVINE	USA	26	FMA-UE
31	UNIVERSITY OF CALIFORNIA, IRVINE	USA	35	FMA-UE
32	UNIVERSITY OF CALIFORNIA, IRVINE	USA	7	FMA-UE
34	UNIVERSITY OF SOUTHERN CALIFORNIA	USA	15	FMA-UE
35	HOSPITAL ISRAELITA ALBERT EINSTEIN	BRAZIL	15	FMA-UE
38	IRCCS SANTA LUCIA FOUNDATION	ITALY	79	Barthel Index
41	FLOREY INSTITUTE OF NEUROSCIENCE AND MENTAL HEALTH	AUSTRALIA	91	NIHSS Total

Supplementary Table 1. Additional cohort details. Research sites (institutions, countries) and primary sensorimotor assessment used are listed for each cohort. FMA-UE = Fugl-Meyer Assesment of Upper Extremities.

ROBUST REGRESSIONS FOR SUBACUTE AND CHRONIC STROKE

SUBACUTE STROKE (≤ 90 days)

Brain Region	n	beta (CI)	SE	t-value	p-value	Significant covariates
		Ipsilesional				
Caudate	194	0.07 (-0.37 – 0.51)	0.22	0.33	0.742	ICV
Lateral ventricle	274	0.15 (-0.12 – 0.42)	0.14	1.11	0.267	Age, ICV
Nucleus accumbens	245	0.18 (-0.21 – 0.57)	0.20	0.90	0.366	Age
Pallidum	223	0.17 (-0.22 – 0.57)	0.20	0.87	0.387	ICV
Putamen	201	0.40 (-0.06 – 0.86)	0.23	1.72	0.086	Age, ICV
Thalamus	**210**	**0.69 (0.26 – 1.11)**	**0.22**	**3.17**	**0.002**	**Age, ICV**
		Contralesional				
Caudate	219	0.23 (-0.20 – 0.66)	0.22	1.04	0.297	ICV
Lateral ventricle	274	0.06 (-0.24 – 0.36)	0.15	0.37	0.714	Age, ICV
Nucleus accumbens	253	0.19 (-0.17 – 0.55)	0.18	1.05	0.294	Age, ICV
Pallidum	250	0.59 (0.17 – 1.01)	0.22	2.73	0.006	ICV
Putamen	229	0.31 (-0.08 – 0.70)	0.20	1.57	0.116	Age, ICV
Thalamus	217	0.09 (-0.25 – 0.44)	0.18	0.52	0.603	Age, ICV

CHRONIC STROKE (≥ 180 days)

Brain Region	n	beta (CI)	SE	t-value	p-value	Significant covariates
		Ipsilesional				
Caudate	193	0.31 (-0.21 – 0.83)	0.26	1.18	0.240	ICV
Lateral ventricle	**404**	**-0.71 (-1.02 – -0.41)**	**0.16**	**-4.58**	**<0.001**	**Age, ICV**
Nucleus accumbens	**289**	**0.64 (0.20 – 1.07)**	**0.22**	**2.88**	**0.004**	**Age**
Pallidum	225	0.50 (0.04 – 0.97)	0.24	2.13	0.033	ICV
Putamen	**207**	**1.02 (0.48 – 1.55)**	**0.27**	**3.72**	**<0.001**	**Age, ICV**
Thalamus	169	0.11 (-0.53 – 0.75)	0.33	0.33	0.740	Age
		Contralesional				
Caudate	345	0.14 (-0.27 – 0.55)	0.21	0.67	0.501	ICV
Lateral ventricle	404	-0.36 (-0.63 – -0.09)	0.14	-2.62	0.009	Age, ICV
Nucleus accumbens	344	0.22 (-0.19 – 0.63)	0.21	1.07	0.285	Age
Pallidum	359	0.32 (-0.01 – 0.64)	0.17	1.91	0.056	Age, ICV
Putamen	355	0.22 (-0.15 – 0.60)	0.19	1.16	0.244	Age, ICV
Thalamus	329	-0.20 (-0.57 – 0.17)	0.19	-1.06	0.288	Age, ICV

Supplementary Table 2. Robust regressions to examine relationships between non-lesioned subcortical volumes and sensorimotor behavior in subacute and chronic stroke. Results from robust linear mixed-effects models of individuals with subacute stroke (top) and chronic stroke (bottom). Results in bold indicate significance with a Bonferroni correction for multiple comparisons ($p<0.004$). The beta coefficient for sensorimotor behavior (beta) with 95% confidence interval (CI), along with the sample size (n), standard error (SE), t-value, and uncorrected p-value are reported, in addition to significant fixed covariates including age, sex, and intracranial volume (ICV).

ROBUST REGRESSIONS FOR CHRONIC SENSORIMOTOR IMPAIRMENT AND ACTIVITY LIMITATIONS

CHRONIC SENSORIMOTOR IMPAIRMENT

Brain Region	n	beta (CI)	SE	t-value	p-value	Significant covariates
		Ipsilesional				
Caudate	194	0.98 (0.08 – 1.88)	0.46	2.14	0.032	ICV
Lateral ventricle	**274**	**-0.70 (-1.13 – -0.27)**	**0.22**	**-3.2**	**0.001**	**Age, ICV**
Nucleus accumbens	245	0.63 (0.08 – 1.18)	0.28	2.24	0.025	Age
Pallidum	223	0.79 (0.07 – 1.51)	0.37	2.16	0.031	-
Putamen	**201**	**1.54 (0.60 – 2.47)**	**0.48**	**3.23**	**0.001**	**-**
Thalamus	210	0.56 (-0.33 – 1.44)	0.45	1.23	0.22	-
		Contralesional				
Caudate	219	0.02 (-0.52 – 0.56)	0.27	0.08	0.939	ICV
Lateral ventricle	274	-0.46 (-0.80 – -0.13)	0.17	-2.72	0.006	Age, ICV
Nucleus accumbens	253	0.22 (-0.32 – 0.76)	0.28	0.80	0.423	Age
Pallidum	250	0.31 (-0.13 – 0.75)	0.22	1.39	0.166	ICV
Putamen	229	0.02 (-0.46 – 0.51)	0.25	0.09	0.932	Age, ICV
Thalamus	217	-0.34 (-0.84 – 0.15)	0.25	-1.36	0.173	Age, ICV

ACTIVITY LIMITATIONS

Brain Region	n	beta (CI)	SE	t-value	p-value	Significant covariates
		Ipsilesional				
Caudate	193	-0.48 (-1.64 – 0.69)	0.60	-0.80	0.425	-
Lateral ventricle	404	-0.70 (-1.32 – -0.09)	0.31	-2.24	0.025	Age, ICV
Nucleus accumbens	289	0.68 (-0.30 – 1.67)	0.50	1.36	0.172	-
Pallidum	225	0.88 (-0.04 – 1.80)	0.47	1.88	0.060	-
Putamen	207	0.87 (-0.32 – 2.05)	0.60	1.43	0.152	-
Thalamus	169	1.19 (-0.08 – 2.46)	0.65	1.84	0.066	-
		Contralesional				
Caudate	345	0.14 (-0.74 – 1.02)	0.45	0.32	0.750	ICV
Lateral ventricle	404	-0.72 (-1.31 – -0.13)	0.30	-2.38	0.017	Age, ICV
Nucleus accumbens	344	-0.33 (-1.13 – 0.46)	0.41	-0.82	0.413	Age
Pallidum	359	-0.07 (-0.93 – 0.79)	0.44	-0.16	0.874	Sex
Putamen	355	0.33 (-0.54 – 1.20)	0.44	0.75	0.454	Age
Thalamus	329	0.19 (-0.57 – 0.95)	0.39	0.49	0.626	Age, Sex

Supplementary Table 3. Robust regressions to examine relationships between non-lesioned subcortical volumes and two measures of sensorimotor behavior (impairment, activity limitations). Results from robust linear mixed-effects models in individuals with chronic stroke showing sensorimotor impairment (top) compared to activity limitations (bottom). Results in bold indicate significance with a Bonferroni correction for multiple comparisons ($p<0.004$). The beta coefficient for sensorimotor behavior (beta) with 95% confidence interval (CI), along with the sample size (n), standard error (SE), t-value, and uncorrected p-value are reported, in addition to significant fixed covariates including age, sex, and intracranial volume (ICV).