Upper Limb Recovery After Stroke Is Associated With Ipsilesional Primary Motor Cortical Activity

A Meta-Analysis

Isabelle Favre, MD; Thomas A. Zeffiro, MD, PhD; Olivier Detante, MD, PhD; Alexandre Krainik, MD, PhD; Marc Hommel, MD; Assia Jaillard, MD, PhD

Background and Purpose—Although neuroimaging studies have revealed specific patterns of reorganization in the sensorimotor control network after stroke, their role in recovery remains unsettled. To review the existing evidence systematically, we performed activation likelihood estimation meta-analysis of functional neuroimaging studies investigating upper limb movement-related brain activity after stroke.

Methods—Twenty-four studies using sensorimotor tasks in standardized coordinates were included, totaling 255 patients and 145 healthy controls. Across the entire brain, we compared task-related activity patterns in good and poor recovery and assessed the magnitude of spatial shifts in sensorimotor activity in cortical motor areas after stroke.

Results—When compared with healthy controls, patients showed higher activation likelihood estimation values in contralesional primary motor soon after stroke that abated with time, but were not related to motor outcome. The observed activity changes were consistent with restoration of typical interhemispheric balance. In contrast, activation likelihood estimation values in ipsilesional medial-premotor and primary motor cortex were associated with good outcome, reorganization that may reflect vicarious processes associated with ventral activity shifts from BA4a to 4p. In the anterior cerebellum, a novel finding was the association of poor recovery with increased vermal activity, possibly reflecting behaviorally inadequate compensatory strategies engaging the fastigio-thalamo-cortical and corticoreticulospinal systems.

Conclusions—Activity in ipsilesional primary motor and medial-premotor cortices in chronic stroke signals good motor recovery, whereas cerebellar vermis activity signals poor recovery. Functional MRI may be useful in identifying recovery biomarkers. **(*Stroke*. 2014;45:1077-1083.)**

Key Words: biomarkers ■ functional neuroimaging ■ magnetic resonance imaging ■ motor cortex ■ positron-emission tomography

Sensorimotor deficits after stroke are common and disabling contributors to global functional impairment. Moreover, at the time of the stroke, it is difficult to make accurate prognostic assessments on eventual motor recovery. Although the extent and degree of performance impairment in the subacute period after stroke provide useful information in forming predictions about recovery, the clinical assessment of sensorimotor performance used in forming these predictions is subjective, complex, and time intensive, suggesting that discovery and characterization of biomarkers, predicting either the course of recovery or response to specific therapies, would be of great clinical use.[1] Functional neuroimaging allows rapid assessment of the neural mechanisms associated with stroke recovery,[2,3] suggesting that sensorimotor neural activity measured noninvasively with functional MRI (fMRI) could be used to identify potential surrogate end points predicting recovery.

Although the empirical findings related to neural activity changes after stroke have been complex and sometimes contradictory, 2 related mechanisms have been advanced to explain sensorimotor recovery after stroke. In the first theory, behavioral recovery is supported by a sensorimotor network in the lesioned hemisphere, including medial-premotor (medial-PMC), lateral premotor (lateral-PMC), primary motor (MI), and primary somatosensory (SI) cortices.[4–7] A second hypothesis posits that reorganization in the undamaged contralesional hemisphere supports motor recovery.[8–10] Studies in support of this theory have shown that recovery of motor performance after unilateral stroke is associated with greater activity in contralesional MI and dorsolateral-PMC.[10,11]

Establishing a role of fMRI as a biomarker of motor recovery will require sensitive, specific, and efficient measurement

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From the Unité Neurovasculaire, Pôle Psychiatrie-Neurologie (I.F., O.D.), Unité IRM, Pôle Radiologie (A.K.), Unité IRM 3T Recherche IRMaGe - Inserm US17/CNRS UMS 3552 (A.K., A.J.), and Pôle Recherche (M.H., A.J.), CHU de Grenoble, Grenoble, France; and Neural Systems Group, Massachusetts General Hospital, Charlestown (T.A.Z.).

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Correspondence to Assia Jaillard, MD, PhD, Unité IRM 3T—Recherche CHU Grenoble CS 10217, 38043 Grenoble Cedex 9, France. E-mail Assia.Jaillard@ujf-grenoble.fr

of sensorimotor neural activity.[1] Identifying the specific neuroanatomical targets useful for assessment of stroke recovery involves overcoming the limitations of functional neuroimaging studies with respect to their capacity to include large samples of patients with homogeneous lesions, characteristics that would result in higher and more reliable detection sensitivity.[2] One approach to this problem involves the use of quantitative neuroimaging meta-analysis, a technique that combines results from many studies and thereby has more power to detect subtle effects that may be difficult to identify in individual studies.[12] Meta-analysis offers a principled and efficient procedure for dealing with sometimes inconstant results among studies jointly characterized by small sample sizes, variable times between stroke and study entry, diverse stroke locations, varying degrees of sensorimotor impairment, sensorimotor task variations, and different fMRI acquisition techniques.

A recent quantitative coordinate-based activation likelihood estimation (ALE) meta-analysis suggested that a return to typical task-related activity spatial patterns constitutes a key process in effective functional recovery after stroke. Evidence in support of this conclusion was that less impaired patients showed higher activity not only in ipsilesional-MI and contralesional cerebellum but also in the contralesional hemisphere in the dorsolateral-PMC, anteromedial-PMC, and secondary somatosensory cortex, suggesting that fuller motor recovery might be dependent on contributions from several cortical systems in both hemispheres.[13] However, many of these recovery-related effects were statistically weak not surviving family-wise error critical threshold correction. Furthermore, the meta-analysis included data from duplicate patients from 7 of the 36 included publications, possibly resulting in selection bias as a consequence of overweighting the contributions of the duplicated patients. In addition, between-group effects were estimated using foci computed from between-group contrasts reported in the individual studies rather than performing the between-group contrast at the meta-analysis level in a way that would allow direct group comparisons. Including only studies reporting results of between-group comparisons could introduce a false-positive bias because studies showing between-group differences are much more likely to be reported than those that show no significant differences.[14] Finally, subsequent studies have appeared, including larger numbers of patients and associated outcome data[15,16] and personal communication (A. Jaillard et al, unpublished data, 2014).

The above considerations motivated a re-examination of the existing data on stroke recovery designed to avoid the described limitations. Therefore, we performed an ALE meta-analysis based on a selective and systematic review of the literature, including data from recent studies, with the goal of identifying robust fMRI predictors of motor recovery that might be useful in clinical research and practice.

In our meta-analysis, we sought to (1) characterize sensorimotor system activity changes related to stroke, (2) describe how poststroke delay influences task-related sensorimotor activity patterns in patients with stroke, (3) determine which sensorimotor areas were associated with good or bad behavioral outcome 6 months after stroke, (4) determine if stroke induces spatial shifts in ipsilesional sensorimotor cortical activity, and (5) determine whether these effects are present in a subset of patients with pure subcortical lesions sparing the overlying sensorimotor cortices, as ischemic lesions extending to the cortex could affect accurate identification of cortical activity patterns.[17]

Methods

The experimental methods are described in more detail in the Materials in the online-only Data Supplement. We selected functional neuroimaging studies published from January 1995 to April 2012, investigating upper limb movements and motor recovery after stroke using fMRI or positron-emission tomography. Studies were selected by searching the PubMed database (www.pubmed.org) using 5 keywords: stroke, fMRI, PET, recovery, and motor. Thirty-four studies met our inclusion criteria: (1) patients assessed at acute, subacute, or chronic stages and having motor impairments of the upper limb with partial or complete recovery, (2) a sample size exceeding 5, (3) the use of active or passive sensorimotor tasks involving the upper limb, (4) neuroimaging using positron-emission tomography or fMRI, and (5) voxel-wise whole brain analysis. The time after stroke was divided into 2 categories: 155 subjects were included in the acute group (stroke delay <35 days; first time-point) and 143 in the chronic group (stroke delay >3 months; second time-point). Thirty-two subjects with a delay after stroke between 35 days and 3 months were included only in the global analysis (Figure I in the online-only Data Supplement). Next, duplicate results arising from incorporation of the same fMRI data in multiple studies were excluded, resulting in the 25 remaining studies listed in Table I in the online-only Data Supplement. As we included studies with lesions affecting both right and left hemispheres, when the right hemisphere was affected the x coordinates were flipped about the y axis. Therefore, the left hemisphere corresponded to the affected hemisphere and the right limb corresponded to the affected limb for all contrasts included in the meta-analysis. We then performed a voxel-based ALE meta-analysis using GingerALE 2.1 (http://www.brainmap.org).[12,18]

Five related model families were run to examine task-related (1) effects related to between-group differences in the healthy and total patient group with stroke, (2) effects of time after stroke, (3) effects of behavioral outcome, (4) spatial shifts in activity compared between stroke and healthy groups, and (5) effect differences with respect to subcortical stroke location. In addition, passive and active sensorimotor tasks were compared among the patient and healthy groups. Time after stroke was divided into 2 categories: an acute group (poststroke delay <35 days) and a chronic group (poststroke delay >3 months). To avoid duplication, data from each patient were assigned to only 1 temporal category. As functional outcome was assessed using a variety of research scales assessing upper limb functional impairment, sensorimotor outcome measures were recoded and then used to split the sample into 2 subgroups, corresponding to good and bad recovery by 2 neurologists with expertise in stroke research. Good outcome or recovery was defined as National Institutes of Health Stroke Scale <3, Fugl-Meyer–Upper-Limb >40, Barthel Index >90, European Stroke Scale ≥85, Motricity Index-Upper-Limb >80, Ashworth Scale ≤2, Upper-Limb-Motor Assessment Scale >13, or modified Rankin Scale ≤2. The relationship between sensorimotor activity and behavioral outcome was only assessed at the chronic stage because outcome is rarely reported in acute stage studies.

We analyzed spatial differences between control and patient groups with stroke in ipsilesional-MI and medial-PMC sensorimotor activity related to active movement tasks. The Montreal Neurological Institute coordinates of task-related activity maxima were obtained for each experimental contrast. Using t tests, we compared MI and medial-PMC maxima locations among the total stroke, subcortical stroke, and healthy groups. In addition, we explored effects of motor recovery in the chronic stroke group using outcome as a factor in an ANOVA with size and number of maxima as nuisance variables. Statistical analyses of spatial shifts in ALE value peaks were performed with SPSS (version 11.5) using a critical threshold of $P<0.05$.

Results

We included 24 studies with 255 patients with stroke: mean age: 60.7±5 years; 68% men versus 32% women; 89% subcortical versus 11% subcortical-cortical damage; 49% right-sided and 51% left-sided lesions. Included studies are listed in Table I and patient characteristics in Table II in the online-only Data Supplement. In addition, 145 healthy subjects were included.

Comparisons Between Patients With Stroke and Healthy Controls

The meta-analysis of task-related activity effects in the total patient group (255 patients; 25 experiments; 193 foci) resulted in ALE peaks in bilateral dorsolateral and medial-PMC, inferior parietal lobule (IPL), the ipsilesional-MI and SI, contralesional insula and anterior cerebellar lobules IV and V (Figure IIA in the online-only Data Supplement). The meta-analysis of effects in the healthy group (145 participants; 11 experiments; 118 foci; Figure IIB in the online-only Data Supplement) showed ALE peaks in left MI and dorsolateral-PMC, and in bilateral medial-PMC, IPL, basal ganglia, and anterior cerebellum (Tables III–VI in the online-only Data Supplement).

The contrast between the total patient versus healthy groups (Figure IIC in the online-only Data Supplement) revealed contralesional MI and dorsolateral-PMC ALE peaks, whereas the reverse contrast showed bilateral peaks in the anterior cerebellum and IPL (Figure IIC in the online-only Data Supplement; Tables V–VI in the online-only Data Supplement).

Effects of Time After Stroke

The analysis of temporal effects in the acute stroke group (103 patients; 9 experiments; 85 foci; Table VII in the online-only Data Supplement) showed a similar pattern to the total stroke group (Figure IIIA in the online-only Data Supplement). In the chronic group (113 patients; 13 experiments; 98 foci), ALE peaks were observed in ipsilesional SI, MI, bilateral dorsolateral-PMC, medial-PMC, thalamus, cerebellar vermis, and contralesional anterior cerebellum (Table VIII in the online-only Data Supplement; Figure IIIB in the online-only Data Supplement). Contrasting patients with acute versus chronic stroke performing an active movement task (Table IX in the online-only Data Supplement; Figure IIIC in the online-only Data Supplement) revealed higher ALE values in the contralesional PMC and ipsilesional IPL, whereas the reverse chronic versus acute contrast showed ipsilesional SI, MI, cerebellar culmen, and contralesional VPL activity (Table X in the online-only Data Supplement).

Effects of Behavioral Outcome

Good behavioral outcome (95 patients; 9 experiments; 59 foci) was associated with ALE peaks in ipsilesional-MI and dorsolateral-PMC, in the contralesional dorsolateral-PMC, anterior cerebellar lobules IV–V, and bilaterally in medial-PMC (Table XI in the online-only Data Supplement; Figure [A]). Poor behavioral outcome (35 patients; 5 experiments; 48 foci) was associated with ALE peaks in the ipsilesional-MI, bilateral dorsolateral-PMC, medial-PMC, bilateral

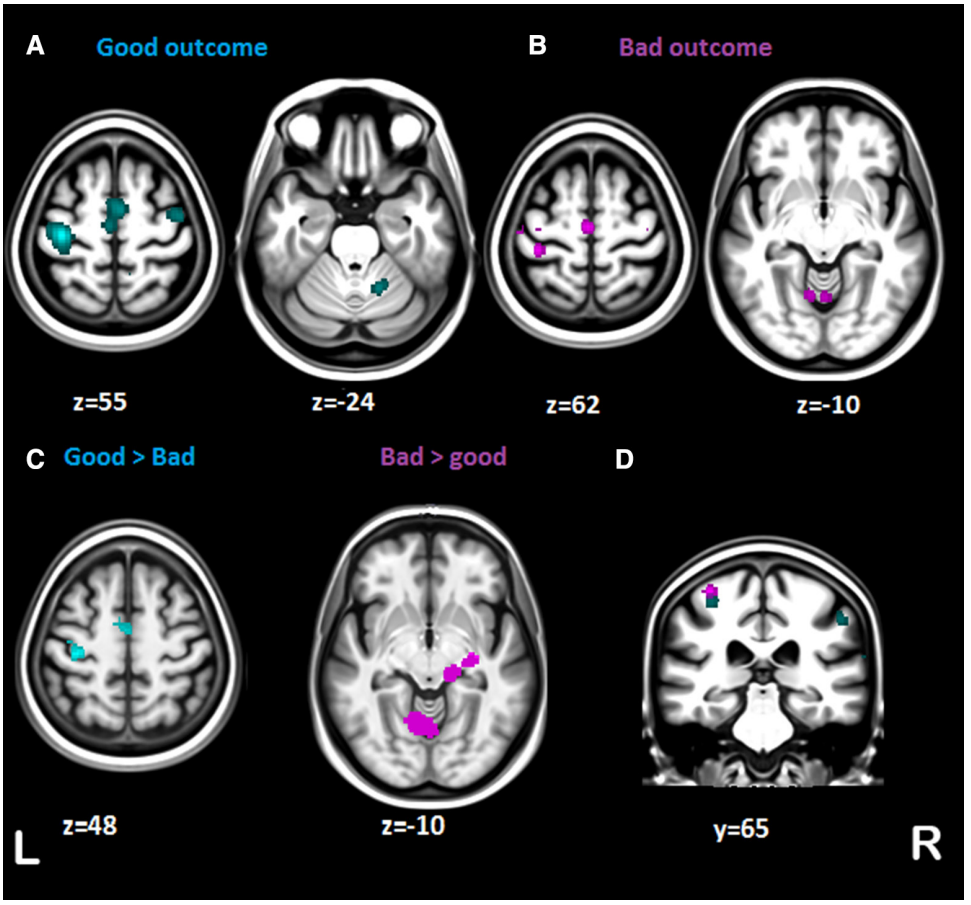

Figure. Different patterns of activity are associated with good vs bad functional outcome in patients during affected upper limb movements. The motor task vs rest contrast is shown for (**A**) good outcome (cyan), (**B**) bad outcome (pink), and (**C**) the contrasts: good vs bad outcome (cyan) and bad vs good outcome (pink). **D**, Overlay maps of good (cyan) and bad (pink) outcome showing ventrocaudal shifts within SIMI associated with good functional outcome.

VPL-thalamus, and anterior cerebellar vermis (Table XII in the online-only Data Supplement; Figure [B]). Contrasting good versus poor behavioral outcome identified higher ALE values in ipsilesional-MI, dorsolateral-PMC, and medial-PMC. The reverse contrast showed higher ALE values in the cerebellum (bilateral culmen), and the contralesional midbrain and thalamic VPL nucleus, potentially reflecting engagement of the fastigio-thalamo-cortical system (Figure [C]; Tables XIII and XIV in the online-only Data Supplement). No contralesional premotor or insular ALE peaks were observed in this contrast.

Effects of Stroke on MI and Medial-PMC Activity Location

Active movement tasks (190 patients; 22 experiments; 175 foci) were associated with a ventral shift of the ALE peak in MI (BA4a/4p) relative to healthy subjects in both the acute (6.4 mm; P=0.022; Figure IV in the online-only Data Supplement) and chronic stages (5.2 mm; P=0.038), suggesting that the spatial reorganization occurred rapidly (Figure IV in the online-only Data Supplement). This displacement was positively correlated with good behavioral outcome (P=0.035). There was also a ventral MI shift in the subcortical group (6.1 mm; P=0.012), which remained significantly related to outcome.

A caudal shift in medial-PMC activity was also observed in patients with stroke relative to healthy subjects for both acute (6.7 mm; P=0.022) and chronic stages (6.2 mm; P=0.038). The shift was not associated with outcome (Figure IV in the online-only Data Supplement).

Activity Patterns in Subcortical Patients

The subcortical group (176 patients; 144 foci; 19 experiments) showed similar effects as the total patient group (Tables XV–XVII in the online-only Data Supplement; Figure V in the online-only Data Supplement). When exploring the effect of poststroke delay (Tables XVIII–IXX in the online-only Data Supplement), the contrast acute (93 patients; 10 experiments; 67 foci) versus chronic (83 patients; 9 experiments; 77 foci) showed ALE peaks in the contralesional dorsolateral-PMC, ipsilesional deep central sulcus (BA4p), somatosensory and posterior parietal regions (BA3/1/2/40; Table XX in the online-only Data Supplement). The reverse contrast revealed ALE peaks in the convexity of the ipsilesional precentral gyrus, the contralesional postcentral gyrus and motor insula, and the bilateral vermis and contralateral lobule V of cerebellum (Table XXI in the online-only Data Supplement; Figure V in the online-only Data Supplement). Ipsilesional central sulcus activity was associated with good outcome (good–poor outcome contrast), whereas poor outcome was related to bilateral ALE peaks in motor insula and vermis (Figure VI in the online-only Data Supplement).

Task-Related Changes

All stroke subjects performing an active task (n=190; 22 experiments; 175 foci) exhibited higher ALE values in ipsilesional SI, MI, medial-PMC, and in contralesional lateral-PMC. Higher ALE values were observed in the posterior parietal cortex (bilateral BA40, ipsilesional BA7) and posterior part of cingulate area when patients performed a passive motor paradigm (n=71; 8 experiments; 54 foci; Tables XXII–XXVII in the online-only Data Supplement).

Discussion

These meta-analyses identified consistently higher ALE values in patients with stroke in ipsilesional-MI, bilateral medial-PMC, dorsolateral-PMC, IPL, insula, and contralesional cerebellar cortex (Figure I in the online-only Data Supplement). This pattern differs from the typical sensorimotor network activity pattern observed in healthy subjects in that patients showed relatively higher contralesional PMC and MI ALE values and lower cerebellar ALE values. The finding that some contralesional motor regions exhibit higher task-related activity after stroke is broadly consistent with previous studies, whereas the observed lower activity in anterior cerebellar cortex has not been previously reported. In comparison with the previous stroke meta-analysis, higher ALE values were not observed in ventrolateral-PMC and contralesional posterior parietal cortex in the stroke versus healthy group contrast.[13] The observed higher ALE values in nonmotor areas observed in the latter study could be related to either inclusion of some experiments using concurrent repetitive transcranial magnetic stimulation that could generate interference with the neural circuits or inclusion of tasks with a high cognitive load.

Temporal Activity Changes After Stroke

It has been suggested that cortical areas showing higher activity after stroke support recovery. Although ALE values were higher in contralesional dorsolateral-PMC at the acute stage, fading with time, ipsilesional SI and MI increased, supporting the idea that time after stroke is associated with restoration of typical interhemispheric activity balance.[7,17,19] However, restoration of this typical activity pattern was not associated with better motor recovery.

Role of Ipsilesional-MI Activity in Stroke Recovery

We found higher ALE values in ipsilesional-MI and medial-PMC in patients with chronic and good outcome when compared with those in poor outcome. Although in disagreement with some other results, our findings are consistent with many cross-sectional and longitudinal studies, showing that sensorimotor recovery is optimal when typical task-related activity patterns are reestablished.[3,7,15,20,21]

In addition, our meta-analysis demonstrated ventral spatial shifts of ipsilesional task-related MI activity after stroke. The recruitment of sensorimotor representations not typically devoted to hand function may represent a vicarious recovery process,[17] facilitating access to the intact portions of the direct corticospinal pathway.[3] In agreement with reports of MI caudal shifts in patients exhibiting good hand recovery, we showed that good recovery was related to the degree of activity peak shift in MI, suggesting that vicarious process reassignment can reflect successful adaptive reorganization of motor representations.[20,22,23] Indeed, expanded MI finger representations have been observed after motor learning in experimental squirrel monkey studies[24] and after humans learn a piano finger sequence.[25] Such plastic changes may reflect

unmasking of latent connections substituting for damaged corticospinal tract fibers, thereby facilitating recovery. These processes may result from both structural and functional neural changes, such as enlargement of dendritic fields, modification in synaptic weight via long-term depression and long-term potentiation mechanisms.[26,27] The ventral direction of activity shift may reflect processing displacement from dorsal BA4a, located on the upper and anterior bank of the central sulcus, to ventral BA4p in the depth of the sulcus,[28] consistent with previous findings.[29] In addition, better recovery was observed in patients with chronic stroke who showed increased recruitment of BA4p in a motor imagery task.[30]

Role of Ipsilesional Medial-PMC Activity in Recovery

Our meta-analysis showed that medial-PMC activity could support successful sensorimotor processing at the chronic stage, a finding consistent with medial-PMC activity being associated with good recovery both acutely and as long as 6 months after stroke.[5,20] In addition to its possible executive role in voluntary movement control, medial-PMC may support movement integration processing within the damaged motor systems through its role in facilitating motor learning.[31,32] Along these lines, we observed a caudal shift in ipsilesional medial-PMC activity in patients with stroke when compared with healthy controls. Changes in hand somatotopic representations in premotor regions might reflect altered connections with MI subregions, thereby facilitating recruitment of surviving corticospinal fibers emerging from PMC and compensating for impaired monosynaptic projections to the corticospinal tract.[3] Although the medial-PMC shift was not strongly correlated with behavioral outcome, the observed spatial reorganization could reflect the emergence of secondary movement preparation processes acting to assist in the preparation, suppression, and execution of movements.[33]

Contralesional Motor Cortical Activity Changes After Stroke

In contrast with the previous stroke meta-analysis, we did not observe a functional role for contralesional MI and dorsolateral-PMC, as activity there did not differ between good and poor outcomes assessed at the chronic stage.[13] Indeed, the functional relevance of contralesional motor hyperactivity after stroke is still debated.[3,10] Early after stroke, increasing activity in contralesional MI and dorsolateral-PMC is associated with improved functional recovery in severely affected patients.[11] At more chronic stages, enhanced negative coupling between contralesional and ipsilesional-MI is seen in patients with poorer outcome.[34] The higher the activity in those areas, the poorer the associated recovery,[3,7] suggesting that contralesional motor activity might not represent functionally relevant processes. Indeed a recent resting state stroke study using graph theory showed that stronger engagement of the contralesional hemisphere was associated with ineffective motor reorganization.[35]

Cerebellar Cortical Activity Changes After Stroke

We found that activity in contralesional anterior cerebellar lobules decreased early after stroke and remained lower during the chronic stage when compared with healthy subjects. The early cerebellar activity decrease might be expected because the cerebellum has strong and reciprocal functional coupling to MI through corticopontine projections and the dentato-rubro-thalamo-cortical projections, a system that plays an important role in sensorimotor integration.[36] However, there was no association between lobule IV–V activity and functional outcome. Instead, we found an association between chronic stage activity and poor recovery in the vermian culmen, mesencephalon, and VPL-thalamus. This new finding can be interpreted with respect to monkey autoradiographic studies, demonstrating bilateral projections from the fastigial nucleus and the vermis to the VPLO and VLc thalamic nuclei, acting as relays to motor cortex.[37] In contrast to the dentate-thalamo-cortical projections that originate from the cerebellar hemispheres, the fastigial nucleus projects caudally to the vestibular nucleus and the reticulospinal tract, pathways dedicated to control of proximal and axial musculature, in service of locomotion and posture. Culmen activity suggests recruitment of this corticocerebello-fastigio-thalamo-cortical circuit and may reflect compensation for dentato-rubro-thalamo-cortical loop damage, thereby accounting for increased bilateral activity in the VPL-thalamus. The reticulospinal tract is associated with the corticoreticular tract, jointly constituting the multisynaptic corticoreticulospinal pathway. Although typically secondary to the corticospinal tract in support of fine motor control, the functional role of the corticoreticular pathway after corticospinal tract damage has been recently shown in the contralesional hemisphere of patients with chronic stroke.[38] Hence, modifications of the activity balance between the corticospinal tract and these pathways may reflect a compensatory adaptation for motor recovery of the upper limb.

Effects of Lesions Limited to Subcortical Structures

To explore the possible interfering effects of lesions involving cortical sensorimotor structures, we conducted a separate analysis confined to subcortical lesion locations. This subgroup showed the same pattern as the total patient group (Figure V in the online-only Data Supplement), possibly reflecting the degree to which subcortical patients, representing 89% of the total patient group, influenced the outcome. In the subcortical acute group, we also observed lower cerebellar lobule IV ALE values whne compared with both the chronic and the healthy groups. Because lobule IV activity is associated with dentate-thalamo-cortical system integrity, we infer that this circuit was restored in the chronic subcortical group, contrasting with persistent impairment in patients with larger cortico-subcortical ischemic lesions. Although lobule IV was active in patients with good functional outcomes, cerebellar activity was lower in patients with good relative to poor outcomes, questioning its potential as an outcome biomarker.

In contrast with the effects seen in the total stroke group, in the medial-PMC of the subcortical subgroup, higher ALE values were not seen in the good versus poor outcome contrast, suggesting that medial-PMC may be involved in a compensatory role only after more extensive motor system damage.[33] However, there were not enough studies with selective cortical

damage to examine the specific role of medial-PMC in recovery in a cortical subgroup.

Limitations

Consistent with previous findings,[39] passive and active sensorimotor tasks led to similar activity patterns, but higher ALE values were found in motor areas for the active versus the passive tasks. Passive tasks led to more caudal activity in the ipsilesional S1, M1, and BA40, consistent with the role of the posterior parietal cortical areas in sensorimotor integration.[40] Passive movements, referring to the visuospatial description of one's own body, can be associated with IPL activity.[41] There was also possible bias with respect to interpretation of ALE peak locations between healthy participants and patients because most healthy participants performed active movement tasks, whereas half of the patients performed passive ones. The different balance of conditions in the 2 groups could have resulted in a more posterior activation in the patient group. For this reason, participants performing passive tasks were excluded from the analysis focusing on functional outcomes.

Inclusion bias was minimized by a thorough literature review followed by systematic exclusion of studies with duplicate subjects. Similarly, studies with tasks engaging more than basic sensorimotor processes, such as high cognitive load, were also excluded. Only studies with total brain coverage, including the cerebellum, were included to limit false negatives related to incomplete brain sampling.

A limitation of this work stems from study heterogeneity. A meta-analysis can only test factors that can be systemized across experiments. For example, stroke location and hand dominance cannot be easily controlled across studies because it is not possible to select individual participant data from included studies. Stroke location, motor impairment, task complexity, task type, and delay after stroke were principal sources of experimental variability. Even if reported information on those variables was available, performing a separate meta-analysis stratifying for each variable would not be possible in a way that would result in sufficient power. In general, estimation of recovery among the included experiments was limited by the fact that few studies included a complete motor evaluation and those that did were characterized by high variability in the motor scales used to assess motor outcome. In addition, variations in preprocessing and statistical modeling methods could have influenced the patterns of motor-related activity changes seen in the individual studies.

Conclusions

In a series of meta-analyses including data from 24 different studies of stroke recovery, we found a pattern of ipsilesional medial-PMC and MI activity changes characterizing favorable motor recovery. These areas may prove to be excellent potential biomarkers for sensorimotor recovery after sensorimotor system lesions. Neural reorganization within MI may result from vicarious changes, seen as activity shifts from BA4a to BA4p. We also observed stroke-related activity decreases in the anterior medial cerebellar cortex in patients with stroke relative to controls although these activity decreases were not related to motor outcome. In contrast, we found higher cerebellar vermal activity related to poor outcome, possibly reflecting partially effective compensatory strategies engaging the fastigio-thalamo-cortical loop and the corticoreticulospinal pathway. These findings strongly suggest that functional MRI can be used to identify cortical and cerebellar biomarkers efficiently associated with motor outcome that subsequently may be of use in assessing the efficacy of novel therapies designed to enhance recovery in stroke.

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Disclosures

None.

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