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The Anatomy of Stroke Injury Predicts Extent of Gains from Therapy.

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Introduction: Differences in stroke location might contribute to variability in response to restorative stroke therapies, with some patients sparing and others obliterating key brain substrate. The current study examined this by addressing the hypothesis that anatomical measures of injury to specific white matter tracts predict treatment response, and do so more significantly than behavioral assessments do. **Methods:** Entry criteria included chronic right hemiparetic stroke. Each subject received 24 hrs of robot-based hand/wrist therapy over 2–3 wks. Outcome measures were arm motor Fugl-Meyer (FM, max 66 points), Action Research Arm Test (ARAT, max 57 points), and Box/Blocks (B/B, # blocks moved in 60 sec), scored after therapy and at baseline. Other baseline assessments were MRI, NIHSS, and 3 other motor scales. For each subject, stroke masks were drawn. A previous study in healthy human subjects defined left hemisphere descending white matter tracts from primary motor cortex (M1), dorsal premotor cortex (PMd), ventral premotor cortex (PMv), and supplementary motor area (SMA). These tracts as well as the stroke masks were binarized then transformed into MNI stereotaxic space. The extent to which each tract was injured by stroke was determined for each subject. **Results:** The 23 patients had mean age 59 years, 2.1 years post-stroke, infarct volume 84 cc, and baseline FM score 38. Mean gains at end of treatment were for FM, 4.1 points; B/B, 2.1 blocks; and ARAT, 2 points. Although several baseline behavioral assessments correlated significantly with baseline FM, ARAT, and B/B, none of the baseline behavioral assessments correlated with change in these 3 outcome measures. Total infarct volume correlated with change in FM score; extent of injury to M1, with change in FM and B/B scores; injury to PMd, with change in FM score; injury to PMv, with change in B/B score; and injury to SMA, with change in FM score (all $p<0.05$, and all with larger injury predicting lesser gains). A multivariate linear regression model found that higher change in FM score was predicted by smaller extent of PMd injury ($r2=0.31$, $p=.006$). A model for B/B found that higher change in B/B score was predicted by smaller extent of M1 injury ($r2=0.38$, $p=.02$). **Discussion:** Response to therapy was predicted by extent of injury to motor system white matter tracts, but response was not predicted by baseline behavioral status. Measuring the anatomy of stroke injury might be useful for improving therapeutics, for example, by requiring survival of a minimal amount of key substrate as an entry criterion in clinical trials.