An Atlas for Predicting Stroke Clinical Outcome

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INTRODUCTION

The search for imaging-based surrogates of clinical outcome following human cerebral ischemia have thus far focused on lesion volume. However, lesion volume is only moderately correlated with outcome (r=0.3-0.6, [1]), which is not sufficient for accurate outcome prediction. We hypothesized that the correlation between volume and clinical outcome would be higher if lesion location were also taken into account. Since the brain contains anatomically distinct processing areas, it is likely that lesions in processing areas that are responsible for tasks that are heavily weighted in outcome scores would have a larger impact than lesions in regions that are less weighted. We therefore sought to test our hypothesis by building brain atlases that would indicate the relative importance to outcome scores for lesions in each part of the brain. Specifically, we built 3 atlases: **(1)** a Data-Driven Atlas, **(2)** an Expert Atlas developed by a stroke neurologist and **(3)** a Hybrid Atlas that used patient data to improve upon the Expert Atlas. We then tested these atlases on stroke patients to generate predictions of outcome from both lesion volume and location and compared the result to predictions of outcome based on lesion volume alone.

METHODS

Patients were included in this study if they had diffusion- or T2-weighted MR images and a National Institutes of Health Stroke Scale (NIHSS) score recorded a minimum of 5 days post ictus. Patients with very high NIHSS scores (>30) and very small or large infarcts (<1 or >300 cm^3) were excluded. A total of 47 patients fulfilled the inclusion criteria. For each patient, the lesion was outlined and a binary mask created (1=infarct, 0=no infarct). Data sets were coregistered using FLIRT software (FMRIB, Oxford, UK). The resulting binarized data sets had a resolution of $(2\ mm)^3$. The effect of location was quantified using a Data-Driven Atlas in which each lesion voxel in a given patient's binary data set was multiplied by the corresponding NIHSS score and divided by the lesion volume. Data sets from different patients were then averaged to produce an atlas that was then multiplied by each binarized infarct and the voxels summed to produce a prediction of the NIHSS (Data-Driven Scores). A leave-one-out cross-validation method (jacknifing) was used in which the data-driven atlas applied to a given patient was developed from the remaining 46 patients. In order to gauge the improvement in the prediction of NIHSS by including lesion location, linear regression was used to develop a prediction of NIHSS using lesion volume alone (Volume Scores). Leave-one-out cross validation was also used in developing the volume predictions.

The Data-Driven Atlas was compared to an Expert Atlas in which various anatomical, vascular and functional regions were outlined and scored according to NIHSS by a neurologist using previously established definitions [2,3]. Each voxel in the expert atlas was then divided by the volume of the region it resided it. The resulting set of voxels was then multiplied by each binarized infarct and then summed to come up with a prediction of NIHSS (Expert Scores). A Hybrid Atlas was then created in which the patient data was used to improve upon the scores assigned to the different regions in the expert atlas using least squares regression. The Hybrid Atlas was then applied to patient data to produce outcome predictions (Hybrid Scores) in the same manner as the expert atlas. Correlation analyses were performed comparing each set of predictions to the measured NIHSS scores.

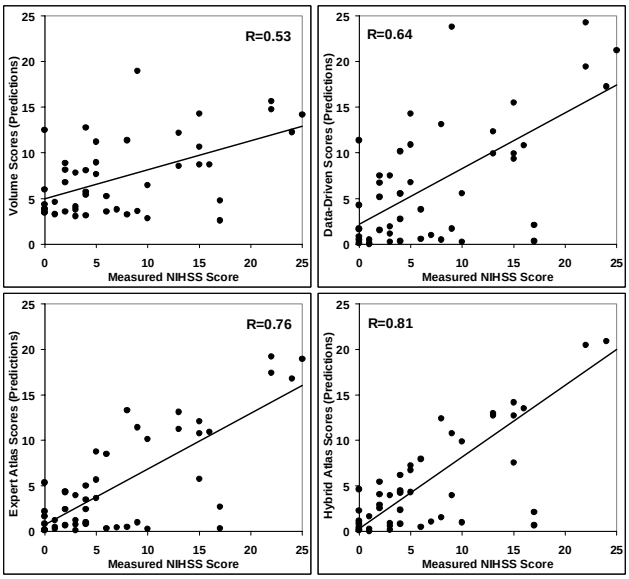

Fig. 1: Scatter plots comparing predictions to measured scores, with their corresponding correlation coefficients. The Hybrid Atlas (lower right) performed best.

RESULTS

The correlation between volume scores and NIHSS scores was r=0.53. The correlation between the data-driven scores and NIHSS scores was r=0.64, an improvement over the volume-based predictions that did not reach statistical significance (p=0.43) for this sample size (n=47). The correlation between the expert scores and NIHSS scores was r=0.76, significantly higher than the correlation with volume (p=0.057). However, the correlation between the hybrid scores and NIHSS scores was the highest, r=0.81 (p=0.012). The 4 correlation plots are shown in Fig. 1. Shown in Fig. 2 are slices of the 3 atlases. The Hybrid Atlas showed substantial asymmetry compared to the Expert Atlas, presumably in an attempt to correct for the fact that left-hemisphere functions are more heavily weighted by NIHSS [4,5].

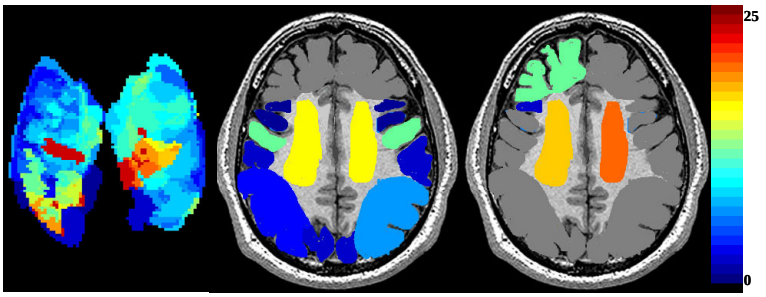

Fig. 2: The same slice of the Data-Driven Atlas (left), Expert Atlas (middle) and Hybrid Atlas (right) are shown for comparison. The scale is in units of NIHSS. The Expert and Hybrid Atlases are shown superimposed on an anatomical image for orientation. The gray-filled regions were assigned a score of 0. Regions that were not outlined or filled in were left unscored.

DISCUSSION

We have demonstrated that the incorporation of lesion location in a volume-based prediction of stroke severity significantly improves the correlation with outcome. To our knowledge, this is the first report of an imaging-based marker that utilizes location to successfully predict a comprehensive measure of clinical outcome in stroke. The atlases developed in the current study and their corresponding predictive scores (in particular the Hybrid Atlas and its predictive score) show great potential as biomarkers of stroke outcome in clinical stroke trials.

Clearly, there is room for improvement in predicting outcome. NIHSS scores for several patients were not well predicted, even with the Hybrid Atlas (as can be seen in the lower right hand plot of Fig. 1). This could be due to the presence of unscored areas (see Fig. 2). However, it is likely that perfect prediction of outcome requires knowledge of the sophisticated networks that connect different brain regions. Nonetheless, the success of our atlas methodology suggests that geography plays a larger role in brain function (or dysfunction) than previously appreciated.

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