White matter integrity but not BOLD response predicts upper limb motor function in patients after stroke

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Introduction: Stroke remains the leading cause of adult disability in the world with motor deficits, and motor recovery mechanisms remain incompletely understood. It is difficult to choose the type and duration of rehabilitation, and determine whether an individual has reached their full potential for recovery [1]. Functional MRI and diffusion tensor imaging (DTI) may be used as a prognostic indicator, but their role in rehabilitation has yet to be defined [2-3]. The aim of this study was to establish the relationship between upper-extremity motor functional outcomes with the asymmetry of fractional anisotropy (FA) from DTI and with the laterality index (LI) derived from functional MRI.

Subjects and methods: Seventeen patients with moderate upper-extremity impairment after stroke were enrolled into this study. The primary clinical outcome measures were the Wolf Motor Function Test (WMFT) and Fugl-Meyer (FM) assessment. The structural integrity of the posterior limb of the internal capsules (PLIC) were assessed using the FA asymmetry by DTI, and LI of motor cortex activation were measured on the basis of blood oxygenation level-dependent (BOLD) response during finger pinching. A linear regression analysis was performed to predict the relationship between the FA asymmetry and LI with upper-extremity motor functional outcomes (WMFT and FM score). The average activation maps during affected hand pinching were created from the data after flipping the fMRI images of the affected hand to the same direction. Statistical activation maps were obtained using a t- test and an uncorrected threshold of P<0.005.

Results: The data showed a significant relationship between FA asymmetry with FM score (R2 = 0.653, P<0.002), WMFT asymmetry (R2 = 0.649, P<0.002), and with the LOG WMFT score of affected hand (R2 = 0.636, P=0.002), with grip asymmetry (R2 = 0.414, P=0.02). Higher FA asymmetry was associated with greater integrity of PLIC, increasing FA asymmetry predicted lower FM scores and higher WMFT asymmetry. FM score has a significant correlation with the WMFT asymmetry (r= –0.912, P < 0.001) and log WMFT of affected hand (r= – 0.807, P <0.005). BOLD contrasts showed a negative LI of motor cortex activation, M1 LI= – 0.21 (-0.84 ~ +0.72), PMC= – 0.28 (-0.86 ~ +0.65), SMA LI= – 0.14 (-0.63 ~ +0.56), suggesting that the cortical activation lateralize toward the ipsilateral hemisphere (unaffected side) during affected hand movement. Another finding in this study is that posterior parietal cortex (PPC) was more likely activated in patients with lower FA asymmetry. No relationship was found between the LI with the FA asymmetry and clinical motor outcomes.

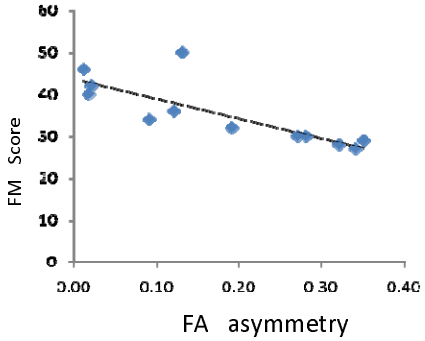

Fig.1: Higher FA asymmetry is associated with lower FM scores (R^2 = 0.653, P<0.002).

Conclusions: The results from this preliminary study reveal that white matter integrity can strongly predict current upper limb motor function in patients with moderate upper-extremity impairment after stroke. The DTI study showed that FA values are decreased in the affected PLIC after stroke, possibly due to local tissue damage or Wallerian degeneration. Reductions in white matter integrity have been shown to give rise to interhemispheric asymmetries in FA values higher FA asymmetry was associated with lower FM scores and higher WMFT asymmetry [3-4]. However, LI can't predict the current clinical motor outcomes; no significant relationship was found between the LI with the FA asymmetry and clinical motor outcomes. Our results also showed negative LI in stroke patients, suggesting more ipsilateral (unaffected side) motor cortex activation during the affected hand pinching, and the cortical activation formed a more bilateral pattern in patients with better performance during affected hand pinching on baseline. Cramer et al found that the degree of ipsilesional primary motor cortex activation during affected hand movement was a significant predictor of behavioral gains, lower motor cortex activity at baseline predicted greater behavioral gains after therapy[5], which is different from Dong et al. who showed that the midpoint (not initial) LI is the best predictor of recovery [6]. In the future study, we will investigate the change of the degree and pattern of motor cortex activation under a specific form of rehabilitation, to discover which pattern of motor cortex activation will get better gains, and to explore whether FA asymmetry and LI measures of brain motor activation can predict the recovery gains and the responsiveness to the treatment.

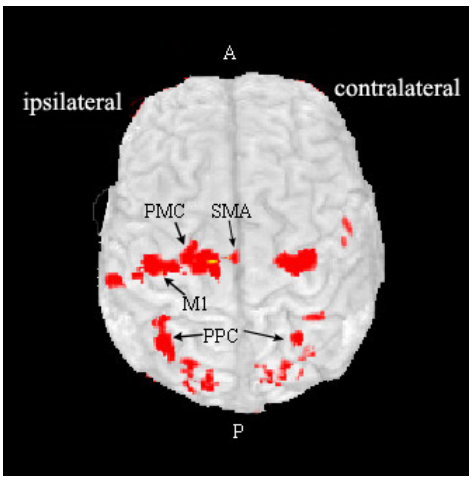

Fig.2 Average activation map of motor cortex, showing more activation in ipsilateral hemisphere during affected hand pinching..

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