Stroke

Tracking the dynamics of secondary degeneration after stroke

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Further evidence of diffusion tensor imaging contribution in the characterisation of retrograde and anterograde degeneration after stroke

The advent of diffusion tensor imaging (DTI)–MRI allows direct in vivo visualisation of white matter fibre tracts, opening a window on the important issue of functional connectivity in normal human brain. Furthermore, it provides a tool for measurement of fibre tract integrity in diseases of the central nervous system. Thus it is becoming possible to assess in a single patient whether specific fibre tracts will escape damage and also to relate these changes to clinical outcome. In particular, the application of DTI to the study of retrograde/anterograde degeneration of white matter pathways secondary to focal ischaemia may provide new insights into the mechanisms implicated in loss as well as recovery of function after stroke.

In this issue, two articles have applied DTI to investigate the time course and clinical correlates of secondary degeneration after subcortical stroke involving the motor pathway in patients who were prospectively studied over 3 months (within 1 week, 4 weeks and 12 weeks after stroke). To date, few data were available on this interesting issue.

Liang and colleagues,[1] using a region of interest approach, quantified and monitored the fractional anisotropy (FA) and mean diffusivity (MD) changes along the corticospinal tract in 12 patients with subcortical stroke involving the posterior limb of the internal capsule ***(see p 581)***. They found a progressive significant decrease in FA from week 1 to week 12, not associated with significant changes in MD, in regions located either below or above the site of the infarct, a pattern consistent with progressive fibre tract loss, presumably reflecting wallerian and retrograde degeneration following stroke.

Møller and colleagues[2] propose an original methodological approach that combines a three dimensional fibretracking technique with FA maps to segment the corticospinal tract and to quantify the dynamic changes in FA in the entire corticospinal tract volume ***(see p 587)***. This method appears particularly interesting for the accurate quantification of FA changes in longitudinal studies. As the fibretracking technique is not accurate in regions with crossing fibre boundless (eg, the centrum semiovale and corona radiata), only the distal portion of the pyramidal tract remote from the primary infarct has been considered for quantitative FA analysis. The results obtained in five patients suggest that the method is feasible and also showed a progressive decrease in FA in the pyramidal tract ipsilateral to the infarct, although changes between 1 and 3 months in this small number of patients did not appear to be as sharp.

The results of these studies confirm, in a larger series of patients, that the time course of wallerian degeneration of the distal pyramidal tract may be mapped with DTI after subcortical stroke involving the internal capsule and/or corona radiata, a finding previously reported in two patients.[3] Furthermore, the findings suggest that retrograde degeneration of the proximal portion of the pyramidal tract may also occur, a finding less addressed in vivo with DTI but previously reported in experimental studies, and seems to have a time course similar to that of wallerian degeneration. In this respect it is interesting to note that although the FA of the proximal pyramidal tract was not quantified by Møller and colleagues,[2] a reduction in fibre tracts above the infarct was clearly evident on FA and fibretracking images in one of their patients. These findings are also consistent with previous DTI evidence of retrograde degeneration observed in the thalamus ipsilateral to middle cerebral artery infarcts[4] although the absence of isolated fibre bundles in this structure was translated by an increase in MD without FA changes.

Another major finding is the effort involved in the development of methods that may bring very powerful and sophisticated tools based on fibretracking into clinical practice. Despite some limitations, this type of study appears to be feasible, as shown by Møller and colleagues,[2] opening a window to future mapping of cortico-subcortical connections and study of the functional connectivity after stroke. The ultimate goal of these studies was to assess whether the degree of ongoing secondary degeneration of the corticospinal tract, as quantified with DTI, could predict clinical outcome. The clinical relevance of DTI changes in corticospinal fibres remote from the primary lesion, however, is not evident. Although some association between progressive loss of FA and poor motor outcome is suggested by the results of Møller and colleagues,[2] a finding previously reported in patients studied in the early stage of capsular stroke,[5] a progressive reduction in FA is also associated with progressive clinical recovery, as shown by Liang and colleagues.[1] These discrepancies may be explained in part by differences in the site of lesions, tests used for quantification of motor function and adaptive cortical plastic changes over time.

Clearly this issue warrants further study in a larger cohort of patients. In this respect, a major contribution may come from combined DTI–functional MRI studies. Overall, these studies demonstrate how the DTI technique might be a potential sensitive tool to characterise the time course and clinical correlates of secondary degeneration after stroke and also to monitor the effects of potential therapeutic strategies. In conjunction with positron emission tomography radiotracers of microglial activation,[6] DTI may also provide a way to understand the role of neuroinflammation on axonal degeneration in regions remote from the primary infarct.

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REFERENCES

1 **Liang Z**, Zeng J, Liu S, *et al*. A prospective study of secondary degeneration following subcortical infarction using diffusion tensor imaging. *J Neurol Neurosurg Psychiatry* 2007;**78**:581–6.
2 **Møller M**, Frandsen J, Andersen G, *et al*. Dynamic changes in corticospinal tracts after stroke detected by fibretracking. *J Neurol Neurosurg Psychiatry* 2007;**78**:587–92.
3 **Thomalla G**, Glauche V, Weiller C, *et al*. Time course of wallerian degeneration after ischaemic stroke revealed by diffusion tensor imaging. *J Neurol Neurosurg Psychiatry* 2005;**76**:266–8.
4 **Buffon F**, Molko N, Hervé D, *et al*. Longitudinal diffusion changes in cerebral hemispheres after MCA infarcts. *J Cereb Blood Flow Metab* 2005;**25**:641–50.
5 **Thomalla G**, Glauche V, Koch MA, *et al*. Diffusion tensor imaging detects early Wallerian degeneration of the pyramidal tract after ischemic stroke. *Neuroimage* 2004;**22**:1767–74.
6 **Pappata S**, Levasseur M, Gunn RN, *et al*. Thalamic microglial activation in ischemic stroke detected in vivo by PET and 11C-PK11195. *Neurology* 2000;**55**:1052–4.