During the past decade, cross-sectional and longitudinal studies of healthy individuals have supported the notion that morphological changes in the structure of the brain, usually named as “structural plasticity”, might occur during the entire lifespan, and not only during the developmental and aging periods, or in course of disease. Learning motor skills is associated with an increased spatial and temporal accuracy of movements with practice and a reduction of attention to execute actions (Doyon and Benali, 2005, Doyon et al., 2002). Several functional neuroimaging studies have identified a set of brain regions showing dynamic changes in their profiles of activations during different stages of motor learning (Doyon and Benali, 2005, Doyon et al., 2002). More recently, several techniques have been applied to track the regional modifications of gray matter (GM) volumes and white matter (WM) architecture following motor learning. These techniques include voxel-based morphometry (VBM), tensor-based morphometry (TBM) and tract-based spatial statistics (TBSS). Although the neurobiological substrates underlying these brain structural changes are largely unknown, exercise-induced increases in hippocampal cerebral blood flow, measured with MRI, were found to correlate with postmortem measurements of neurogenesis (Pereira et al., 2007). In addition, sprouting of new connections, dendritic spine growth, and modification in the strength of existing connections are all likely to explain at least part of the observed structural MRI changes (Sur and Rubenstein, 2005, Trachtenberg et al., 2002).

Longitudinal VBM studies have shown that structural changes of the GM do occur following motor learning in healthy adult subjects (Draganski and May, 2008), independently of their age (Boyke et al., 2008). Such structural modifications are supposed to occur relatively early during the learning process of new motor skills, since they have been observed even after seven days of daily training (Driemeyer et al., 2008).

Using TBM, a method that infers volume modifications from the non-linear deformation field required to warp two serial MRI scans (Leow et al., 2006), GM volume increases of several areas of the temporal, occipital, parietal and frontal lobes have been found in young healthy individuals following a two-week daily training of fine motor skills with the dominant right hand (Filippi et al., 2010). Notably, contrary to the results of the previous VBM studies (Boyke et al., 2008, Draganski et al., 2004), which suggested that the observed GM changes were reversible after cessation of training, this latter study demonstrated that GM volume increases were still detectable at least three months after training was stopped. This is in agreement with the results of a recent study (Scholz et al., 2009), which showed persistent changes of GM and WM architecture in healthy individuals 4 weeks after juggling was terminated. Additionally, different patterns of structural GM changes were found according to the scheme applied during the learning phase.

Short-term structural GM changes of neuronal networks in healthy individuals have also been described following cognitive learning (Ceccarelli et al., 2009).

All of this may have important implications for the development of rehabilitation strategies in patients with neurological diseases. At present, only a few studies have evaluated structural modifications of the GM and WM in diseased subjects following specific interventions.
A VBM study in patients with chronic stroke receiving constraint-induced movement therapy showed that treated patients exhibited greater improvement in use of the more affected arm in the life situation than the comparison therapy group. Structural brain changes paralleled these improvements in spontaneous use of the more impaired arm for activities of daily living (Gauthier et al., 2008). There were increases of GM volumes in bilateral sensory and motor areas as well as in the hippocampus. In contrast, the comparison therapy group failed to show GM increases. The magnitude of the observed GM increases was significantly increased and was significantly correlated with amount of improvement in real-world arm use.

A combined fMRI, TBM and TBSS study assessing the effects of cognitive rehabilitation in multiple sclerosis (MS) showed that after 12 weeks of cognitive rehabilitation, MS patients experienced a change of recruitment of several regions mainly located in the fronto-parietal lobes (Filippi et al., 2012). These results suggest that rehabilitation of attention/information processing and executive functions in RRMS may be effected through enhanced recruitment of brain networks subserving the trained functions. Notably, this study found no structural changes in the GM and NAWM over the follow up. Such a negative finding might reflect an impairment of structural plasticity in these patients, which is likely to be caused by the MS pathological process. Indeed, axonal and myelin damage, which can be quantified reliably using DT MRI, and neuronal loss, which can be estimated using volumetry, are among the pathological hallmarks of the disease.

**Possible areas of improvements**

Possible areas of improvement are the following:

1) definition of the best strategy to evaluate longitudinal modifications of GM/WM volume and WM architecture (e.g., use of standard space registration, application of atlases, registration algorithms, statistical issues, etc.),

2) definition of the temporal dynamics of brain structural changes (time required for their occurrence, persistence after cessation of training),

3) application of the above techniques to various neurological diseases to evaluate structural plasticity in chronic vs. acute conditions and the effects of therapeutic interventions (disease-related effect of global CNS response independent from etiology?)

4) comparisons of the effects of different therapeutic and rehabilitative strategies on brain WM and GM plasticity in order to develop specific treatment strategies (disease specific or system specific?)

**Suggested reading:**


