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Commentary

The Puzzle of Structural Brain Connectivity Following Traumatic Incidents



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While recent reviews and meta-analyses (e.g. Li et al., 2014) reported structural grey matter reductions in the medial prefrontal cortex in patients suffering from Posttraumatic Stress Disorder (PTSD), it remains unclear if structural changes are also existent within white matter tracts. White matter tracts connect populations of neurons with each other, facilitating the communication between different brain regions.

Childhood trauma is known to result in a cascade of physiological, neurochemical, and hormonal changes (Heim et al., 2010), which in turn can lead to enduring alterations in brain function. It has been suggested that the neurotoxic impact of childhood trauma may also result in deficits in white matter myelination. It is currently unclear if traumatic events during adulthood can have similar effects, although the process of myelination has been completed.

Myelin is an electrically insulating material that forms a layer around the axons of nerve cells and thus increases the speed at which impulses propagate along myelinated fibres. It is essential for the proper functioning of the nervous system. During infancy, myelination occurs quickly and continues through adolescence. With specific brain imaging sequences, the integrity of the white matter fibre tract including its myelin layer can be assessed. A common parameter obtained from DTI measurements is the so-called Fractional Anisotropy (FA) value, which is regarded as a quantitative indicator of white matter integrity, reflecting fibre density, axonal diameter, and myelination.

Recent investigations of white matter integrity in PTSD subjects with traumatization during adulthood identified both increases and decreases in FA values in different brain regions (for a recent metaanalysis see Daniels et al., 2013). However, too few studies have been carried out so far to draw any firm conclusions. Until June 2012, only five investigations had been published which analysed white matter integrity on a whole-brain level in adults with PTSD. The largest one of these five studies (Kim et al., 2005) analysed data from 20 PTSD subjects, which is considered a sufficient, but rather low sample size for neuroimaging data. More importantly, the majority of these five investigations compared adult PTSD patients to healthy subjects not exposed to a traumatic incident. While this is a relevant comparison, it makes it impossible to delineate the effects of the trauma exposure itself from the neural correlates of PTSD development. This is where the study by Li and co-workers published in this issue differs: Not only did Li and co-

workers recruit a large sample of well selected PTSD patients for participation in their study ($n = 88$), they also compared their data to well-matched, healthy subjects ($n = 91$) exposed to the same traumatic stressor, a strong earthquake (Li et al., 2016). This approach allows them to delineate the effect of exposure to a traumatic stressor from the neural correlates of PTSD development. Li and co-workers report increased FA values in the left dorsolateral prefrontal cortex localized beneath the left superior and middle frontal gyri as well as in the posterior part of the corpus callosum after correcting for whole-brain comparisons. These results differ from those of previous studies and need careful interpretation. The authors therefore then traced the fibre tracts passing through the areas with higher FA values to identify their origin. Both clusters in the dorsolateral prefrontal cortex seem to consist mostly of fibres belonging to one tract, the genu of corpus callosum and the thalamic radiation. While this does not provide any hard evidence in itself, it makes it more likely that the reported increases in FA values are not simply an effect of less signal disturbance due to crossing white matter fibres in these regions. To decipher which effects such alterations in white matter volume might have on the overall workings of the brain, a link between structural and functional imaging studies would have to be drawn in future investigations.

It is worth noting that the inclusion of a trauma-exposed comparison group in the study presented here by Li and co-workers, while controlling for exposure to the stressor, also introduces a different potential confounder: resilience. The control subjects might have remained healthy after being exposed to the traumatic incident, because their brains were specifically adapted for dealing with such a stressor. In this sense, they might be a selected sample significantly differing from the average healthy, un-exposed subject. It is thus conceivable that the results of this study should not be phrased as an increase in white matter volume in PTSD subjects, but rather as a decrease in white matter volume in resilient subjects. There is just one way to find out: Future studies should aim to include two control groups; a resilient, trauma-exposed sample as well as a healthy, un-exposed sample. Such a study would allow us to delineate the impact of traumatic stress per se from structural white matter alterations directly related to the development of PTSD. It would also enable us to pinpoint neural correlates of resilience, which might stimulate research into preventive interventions for subjects frequently exposed to traumatic stressors such as first responders.

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