

Brain Shrinkage (brain volume loss) and Relapsing Multiple Sclerosis

Media Fact Sheet

What is brain shrinkage in neurological diseases?

Brain shrinkage (brain volume loss) refers to the permanent loss of brain tissue (both myelin and axons) and changes in the water containing spaces in and around the brain^{1,2}. Everyone experiences brain shrinkage in their lifetime however this process is accelerated in those with neurological diseases³⁻⁶. It can affect the whole brain or be limited to specific regions, and is associated with the loss of physical (e.g. walking) or cognitive (e.g. memory) function. For example, if some elements of the cerebral hemispheres (the two lobes of the brain that form the cerebrum) are affected, conscious thought and voluntary processes may be impaired². Brain shrinkage can predict a patient's future disability⁷.

How is brain shrinkage measured?

Brain shrinkage is measured by Magnetic Resonance Imaging (MRI). MRI uses a strong magnetic field to create detailed images of pathological changes in the brain including areas of inflammation, damage or scarring in nerve tissue⁸.

How is brain shrinkage linked to relapsing multiple sclerosis (RMS)?

Brain shrinkage occurs three to five times faster in people with RMS compared to those without RMS³⁻⁶. This acceleration starts early in people with relapsing MS, before patients even notice their symptoms⁹⁻¹². Based on growing evidence, damage from lesions and brain shrinkage leads to worsening of the symptoms for RMS^{9,13-15}.

MRI images of the brain demonstrate the extent of brain shrinkage in people with RMS compared to a person without RMS¹⁶. The images show that as the disease progresses the brain itself becomes smaller due to nerve tissue loss, whilst the water containing spaces (in black) within and around the brain increase in size.



Image A: 31-year-old man without MS

Image B: 36-year-old woman with relapsing remitting MS with 2 years disease duration

Image C: 43-year-old woman with secondary progressive MS with 19 years disease duration

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Assessing brain shrinkage is increasingly becoming an important consideration in monitoring RMS treatment effects^{4,17}. Several studies have shown that brain shrinkage is a predictor of long-term disability in RMS^{6,7,9,15}, therefore it is also being measured as an additional endpoint in clinical trials^{4,17}.

There are now disease-modifying therapies (DMTs) that aim to alter the natural course of relapsing MS by modifying the immune response. There are DMTs available that can reduce the frequency of relapses and MRI lesions, delay the accumulation of physical disability and minimize brain shrinkage¹⁸. The differences between the efficacy profiles of DMTs in relation to brain shrinkage may be explained by their mode of action, their overall efficacy and their ability to enter the central nervous system (CNS)^{19,20}.

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References:

1. Simon JH. Brain atrophy in multiple sclerosis: what we know and would like to know. *Mult Scler*. 2006; 12(6):679-87. Review.
2. National Institute of Neurological Disorder and Stroke website http://www.ninds.nih.gov/disorders/cerebral_atrophy/cerebral_atrophy.htm. Accessed March 2015.
3. De Stefano N et al. Proportion of patients with BVL comparable to healthy adults in fingolimod phase 3 MS studies. Abstract presented at: 66th AAN Annual Meeting; April 26 – May 3, 2014; Philadelphia, Pennsylvania. Oral session S13:006.
4. Hedman AM et al. Human Brain Changes Across the Life Span: a review of 56 longitudinal magnetic resonance imaging studies. *Human Brain Mapping* 2012; 33:1987-220.
5. Barkhof F et al. Imaging outcomes for neuroprotection and repair in multiple sclerosis trials. *Nat Rev Neurol*. 2009; 5(5):256-266.
6. Bermel RA & Bakshi R. The measurement and clinical relevance of brain atrophy in multiple sclerosis. *Lancet Neurol*. 2006; 5(2):158-170.
7. Popescu V et al; on behalf of the MAGNIMS Study Group. Brain atrophy and lesion load predict long term disability in multiple sclerosis. *J Neurol Neurosurg Psychiatry*. 2013; 84:1082–1091.
8. <http://www.nationalmssociety.org/about-multiple-sclerosis/what-we-know-about-ms/diagnosing-ms/magnetic-resonance-imaging-mri/index.aspx>. Accessed March 2015.
9. De Stefano N et al. Clinical Relevance of Brain Volume Measures in Multiple Sclerosis. *CNS Drugs*. 2014; 28(2):147-56.
10. Pérez-Miralles F et al. Clinical impact of early brain atrophy in clinically isolated syndromes. *Multiple Sclerosis Journal*. 2013; 19(14):1878–1886.
11. Filippi M et al. Evidence for widespread axonal damage at the earliest clinical stage of multiple sclerosis. *Brain*. 2003; 126(Pt 2):433-437.
12. Filippi M et al. The contribution of MRI in assessing cognitive impairment in multiple sclerosis. *Neurology*. 2010; 75:2121-28
13. Calabrese M et al. Cortical lesions and atrophy associated with cognitive impairment in relapsing-remitting multiple sclerosis. *Arch Neurol*. 2009; 66(9):1144-50.
14. Bakshi R et al. Regional brain atrophy is associated with physical disability in multiple sclerosis: semiquantitative magnetic resonance imaging and relationship to clinical findings. *J Neuroimaging*. 2001; 11(2):129–36.
15. Zivadinov R et al. Evolution of cortical and thalamus atrophy and disability progression early relapsing-remitting MS during 5 years. *AJNR Am J Neuroradiol*. 2013; 34:1931-39.
16. Rudick RA et al. Use of the brain parenchymal fraction to measure whole brain atrophy in relapsing-remitting MS. *Neurology* 1999;53(8):1698–7004.
17. Ge Y. Multiple sclerosis: the role of MR imaging. *AJNR Am J Neuroradiol*. 2006; 27(6):1165–76. Review.
18. <http://www.nationalmssociety.org/Treating-MS/Medications>. Accessed March 2015.
19. Zivadinov R et al. Mechanisms of action of disease-modifying agents and brain volume changes in multiple sclerosis. *Neurology*. 2008; 71:136–144
20. Zivadinov R et al. The place of conventional MRI and newly emerging MRI techniques in monitoring different aspects of treatment outcome. *J Neurol*. 2008; 255 [Suppl 1]:61–74.