

## Publication

### Altered functional adaptation to attention and working memory tasks with increasing complexity in relapsing-remitting multiple sclerosis patients

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**Author(s)** Amann, Michael; Dössegger, Lea Sybil; Penner, Iris-Katharina; Hirsch, Jochen Gunther; Raselli, Carla; Calabrese, Pasquale; Weier, Katrin; Radü, Ernst-Wilhelm; Kappos, Ludwig; Gass, Achim

**Author(s) at UniBasel** [Penner, Iris-Katharina](#) ; [Kappos, Ludwig](#) ;

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As attention, processing speed, and working memory seem to be fundamental for a broad range of cognitive performance, the present study on patients with mild forms of relapsing-remitting multiple sclerosis (RR-MS) focused on these domains. To explore subtle neuropsychological changes in either the clinical or fMRI domain, we applied a multistep experimental design with increasing task complexity to investigate global brain activity, functional adaptation, and behavioral responses to typical cognitive processes related to attention and working memory. Fifteen patients with RR-MS (mean age 38 years, 22-49 years, 9 females, mean disease duration 5.9 years (SD = 3.6 years), mean Expanded Disability Status Scale score, 2.3 (SD = 1.3) but without reported cognitive impairment), and 15 age-matched healthy controls (HC; mean age, 34 years, 23-50 years, 6 women) participated. After a comprehensive neuropsychological assessment, participants performed different fMRI experiments testing attention and working memory. In the neuropsychological assessment, patients showed only subtle reduction in learning and memory abilities. In the fMRI experiments, both groups activated the brain areas typically involved in attention and working memory. HC showed a linear in- or decrease in activation paralleling the changing task complexity. Patients showed stronger activation change at the level of the simple tasks and a subsequent saturation effect of (de-)activation at the highest task load. These group/task interaction differences were found in the right parahippocampal cortex and in the middle and medial frontal regions. Our results indicate that, in MS, functional adaptation patterns can be found which precede clinical evidence of apparent cognitive decline.

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