

# Apathy is associated with large-scale white matter network disruption in small vessel disease

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## Study objective and summary result

This study tested the hypothesis that white matter (WM) network disruption underlies the pathogenesis of apathy in patients with cerebral small vessel disease (SVD) and found that apathy is associated with WM network disconnection in patients with SVD.

## What is known and what this paper adds

Apathy is prevalent in patients with SVD, and MRI studies have shown that apathy is associated with reduced WM microstructural integrity. This study provides evidence that apathy in SVD is a disconnection syndrome and can be localized to specific networks.

## Participants and setting

This study analyzed data from 331 patients with SVD (58.6% female; 98% Caucasian; mean age,  $68.9 \pm 8.3$  years) who participated in the Radboud University Nijmegen Diffusion Tensor and Magnetic Resonance Cohort (RUN DMC) study, a prospective cohort study that recruited dementia-free individuals with WM hyperintensities (WMH) or lacunar infarcts. The baseline assessment was conducted in 2006, with a follow-up in 2011, which was the data analyzed.

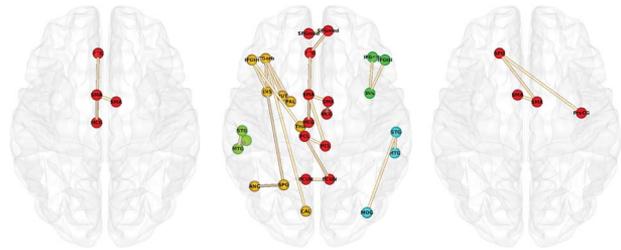
## Design, size, and duration

The Apathy Evaluation Scale was used to assess apathy severity. MRI scans were examined to assess SVD markers (i.e., WMH and lacunar infarcts), and diffusion tensor tractography was used to reconstruct WM pathways. Path analysis was used to determine whether network integrity mediated the relationship between apathy and SVD markers. Network markers were then compared between patient groups.

## Primary outcome measures

The primary outcome was the relevance of network integrity to the relationship between apathy and SVD markers.

**Figure** Topological clusters related to apathy



## Main results and the role of chance

Path analysis showed that network disruption mediated the relationship between apathy and SVD markers. Compared to patients without apathy, those with apathy had worse outcomes for network density and global efficiency ( $p < 0.001$ ). This could be localized to specific WM networks.

## Bias, confounding, and other reasons for caution

Diffusion tractography algorithms cannot easily determine the specific effects of pathologies on WM fibers.

## Generalizability to other populations

The racial homogeneity of the RUN DMC study's participants may limit the interracial generalizability of this study's results.

## Study funding/potential competing interests

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*A draft of the short-form article was written by M. Dalefield, a writer with Editage, a division of Cactus Communications. The authors of the full-length article and the journal editors edited and approved the final version.*

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