# HOMER-3 Antibodies Were Not Detected in Two German Cohorts of Patients with Multiple System Atrophy

Multiple system atrophy (MSA) is a neurodegenerative disease with progressive disability and reduced life expectancy.[1] Patients suffer from predominant cerebellar or parkinsonian symptoms combined with autonomic failure. In recent years, an increasing number of autoantibodies were detected that can evoke syndromes mimicking neurodegenerative diseases.[2] In this group of newly discovered antibodies, HOMER-3 autoantibodies were reported to mimic an MSA phenotype with cerebellar ataxia, dysautonomia, rapid eye movement (REM) sleep behavior disorder, and a hot cross bun sign on structural MRI in an Asian population.[3] In a cohort of 750 Asian patients suspected for autoimmune cerebellar ataxia, six patients had HOMER-3 antibodies in the serum, and two of these six also in cerebrospinal fluid (CSF).[3] One-third (2/6) of these HOMER-3-positive patients presented with clinical and magnetic resonance imaging (MRI) signs compatible with MSA. Interestingly, these patients presented the HOMER-3 antibody only in serum.[3] Because this HOMER-3-antibody related disease is a potentially treatable condition, our current study aimed to identify the prevalence of HOMER-3 autoantibodies in clinically diagnosed MSA patients.

Therefore, patients of European origin from two German biobank cohorts, diagnosed according to the Gilman criteria for clinical diagnosis of possible or probable MSA[4] were analyzed with a research-grade HOMER-3 antibody assay (Euroimmun, Lübeck, Germany).[3,5] In total, 59 patients (25 female) with a mean age of 61.5 ± 8.4 were included in this study. Of these, 33 presented with a cerebellar (MSA-C) and 26 with a parkinsonian phenotype (MSA-P). The mean disease duration was 3.7 ± 2.3 years. In none of these patients we were able to detect HOMER-3 antibodies in serum.

The preexisting data indicate that HOMER-3 antibody associated cerebellar ataxia may be a rare, but potentially treatable differential diagnosis for MSA.[3,5,6] Based on our data, systematic screening of all patients with clinically suspected MSA cannot be generally recommended. The frequency of HOMER-3 positive patients needs to be determined in larger MSA cohorts of diverse ethnicities, and the specific clinical and imaging phenotype of this autoimmune disease needs to be further elaborated to identify specific features, which would encourage HOMER-3 testing in individual patients not to be missed for individualized therapies.[7]

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## Ethics Statement

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this work is consistent with those guidelines. We obtained approval of the local institutional review boards for this work (MHH: 8666_BO_K_2019; LMU: 18-353). Written informed consent was obtained from every participant.

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## Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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## Author Roles

(1) Research project: A. Conception, B. Organization, C. Execution; (2) Statistical Analysis: A. Design, B. Execution, C. Review and Critique; (3) Manuscript Preparation: A. Writing of the First Draft, B. Review and Critique.: M.K.: 1A, 1B, 1C, 2A, 2B, 3A.: S.K.: 1C, 2C, 3B: J.L.: 1B, 2C, 3B: F.W.: 1B, 2C, 3B: L.K.: 1C, 3B.: M.H.: 1C, 3B.: F.H.: 1C, 3B.: J.H.: 1C, 3B.: T.S.: 1A, 1B, 1C, 2A, 2C, 3B.: G.U.H.: 1A, 1B, 1C, 2A, 2C, 3B

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