

# Effect of prolonged antibiotic treatment on cognition in patients with Lyme borreliosis

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## Study objective and summary result

This study examined whether prolonging antibiotic treatment improves cognitive performance in patients with persistent symptoms attributed to Lyme borreliosis, but it found that prolonging antibiotic treatment does not improve cognitive performance.

## Classification of evidence

Class II.

## What is known and what this paper adds

Patients with persistent symptoms attributed to Lyme borreliosis often complain of cognitive problems, but it is unclear whether such complaints result from insufficient antibiotic treatment. This study provides evidence against longer antibiotic regimens providing any cognitive benefits.

## Participants and setting

This study analyzed data from 239 patients with persistent symptoms attributed to Lyme borreliosis who participated in the Persistent Lyme Empiric Antibiotic Study Europe (PLEASE) trial, which was performed through 2 centers in Nijmegen, the Netherlands. Enrolment occurred between October 2010 and June 2013.

## Design, size, and duration

All patients received open-label IV ceftriaxone for 2 weeks before continuing into a double-blind period of oral treatment with doxycycline ( $n = 72$ ), clarithromycin–hydroxychloroquine ( $n = 86$ ), or placebo ( $n = 81$ ) for 12 weeks. Computerized randomization was used for group allocations. The PLEASE participants completed neuropsychological test batteries covering the domains of episodic memory, attention/working memory, fluency, speed of information processing, and executive function at a pretreatment baseline timepoint and at 14-, 26-, and 40-week follow-up timepoints. This study used linear mixed models for between-group comparisons of test results.

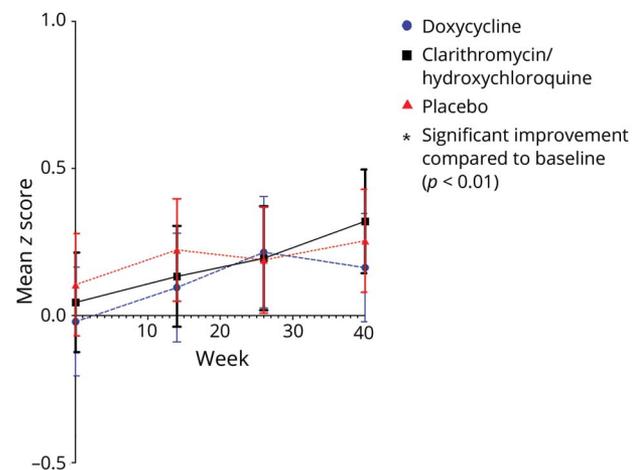
## Primary outcome measures

The primary outcomes were between-group comparisons of domain-specific cognitive function at the posttreatment timepoints.

## Main results and the role of chance

No between-group differences in domain-specific cognitive function were found at any posttreatment timepoint ( $p$  values, 0.37–0.93).

**Figure** Neuropsychological test results in the executive function domain for the doxycycline (blue circles), clarithromycin–hydroxychloroquine (black squares), and placebo (red triangles) groups



## Harms

The treatment groups had similar adverse event frequencies.

## Bias, confounding, and other reasons for caution

This study lacked complete data for all PLEASE participants.

## Generalizability to other populations

The fact that the PLEASE trial was conducted through 2 Dutch centers may limit the international generalizability of this study's results.

## Study funding/potential competing interests

This study was funded by the Netherlands National Organization for Scientific Research. The authors report no competing interests. Go to [Neurology.org/N](http://Neurology.org/N) for full disclosures.

## Trial registration number

NCT01207739 on [ClinicalTrials.gov](http://ClinicalTrials.gov).

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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