

From Exposome to Outcome: Personalized Strategies Against Dementia Through Lifestyle Interventions

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Background:

Boosting the autophagy/lysosomal pathway through lifestyle interventions like physical exercise, the Mediterranean diet, and fasting has gained significant popularity in Western societies as a universally effective strategy against dementia. However, how do intrinsic vulnerabilities for dementia—including aging, female sex, and lysosomal gene mutations—influence the efficacy and safety of these interventions remains unexplored.

Methods and Results:

Our research examines the effects of physical exercise training and polyamines—naturally occurring compounds found in foods like durum wheat from the Mediterranean diet—in murine models encompassing both infantile and age-related dementia across various ages and sexes. We discovered that polyamines activate autophagy and mitigate dementia-like symptoms in a sex-specific manner across all genetic backgrounds, while exercise confers benefits universally. These effects correlate with steroid hormone-dependent transcriptional programs that regulate autophagy.

Conclusions and Significance:

Our research underscores the importance of developing targeted therapies for often-overlooked populations rather than relying on "one-size-fits-all" approaches. By personalizing lifestyle interventions based on intrinsic factors of vulnerability, we aim to enhance their efficacy and safety in preventing dementia, which represents a growing public health concern.

Keywords: (max 5) sex-differences, physical exercise, diet, autophagy, rare genetic diseases

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full authors list, title, year, journal, vol.: pages)

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