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### Can Nutritional Supplements Benefit Patients Receiving Treatment for Neurodegenerative Disorders?

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# Can nutritional supplements benefit patients receiving treatment for neurodegenerative disorders?

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## Background and Significance

- Neurocognitive disorder prevalence is increasing with age, and with an increase in the average age across populations, the overall incidence of neurocognitive disorders is increasing globally<sup>10</sup>
- Uncovering new methods of slowing onset and reducing symptoms of neurocognitive disorders serves as an important task for decreasing disease burden
- Current medications which target neurotransmitter systems carry a myriad of side effects and some serve only to slow down the progression of disease without neuroprotection
- There exists a myriad of cytotoxic and neurotoxic metabolites to target in each disease process<sup>2, 4, 5, 6, 7</sup>
- Nootropics and nutritional supplements have been shown to aid in neuroprotection and act as cognitive aides<sup>2, 4, 5, 6, 7</sup>
- Goal: Determine if concurrent use of nootropics and nutritional supplements with existing medication can promote cognitive health in patients with neurocognitive disorders

## Methods

### Search Strategies

Database Searched	Date of Search	Keyword String	Number of Results
Pubmed	12/16/23	neurocognitive disorders and supplements	123
		neurocognitive disorders and nootropics	71
		neurocognitive disorders and supplements and antioxidants	15
		Parkinson's Disease and vitamin D	4
		Multiple Sclerosis and antioxidants	32
	12/17/23	Multiple Sclerosis and antioxidants and interferon	59
		Alzheimer's Disease and supplements	6
		Amyotrophic Lateral Sclerosis and antioxidants	16
		Amyotrophic Lateral Sclerosis and treatment and vitamin D	1
		Amyotrophic Lateral Sclerosis and treatment and revascular	2
		Cognitive impairment and supplements	114
		Cognitive impairment and supplements and antioxidants	13
Embase	12/18/23	neurocognitive disorders and nootropics	3

### Study Selection

- Inclusion Criteria: All populations were considered. Only primary, peer-reviewed sources were included. Neurodegenerative disorders and supplements included are listed in Table 1. Sources examining both human and murine models were included.
- Exclusion Criteria: Murine-model studies with no tested cell markers were excluded. Human-model studies on only healthy subjects were excluded.

### Data analyses

- No further data analyses were done.

## Results

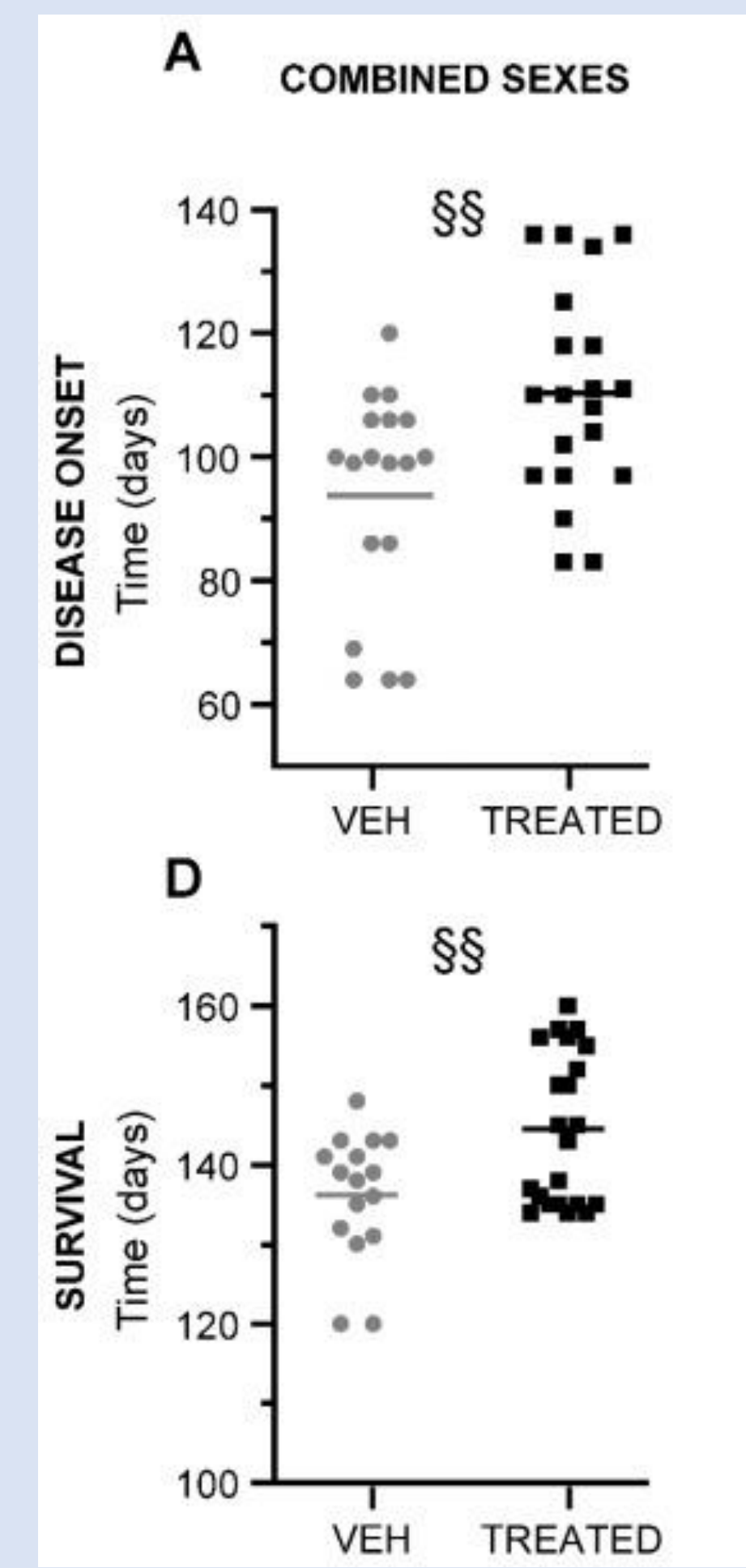


Figure 1: Difference in amyotrophic lateral sclerosis onset and survival in male and female rats with SOD1 mutation. TREATED group received valproate with resveratrol, VEH group received no treatment. A significant delay was observed in the onset and severity of mice receiving treatment with supplement compared to non-treated mice. Significance of  $p < 0.005$  denoted with §§. Modified from Figure 3 (Bankole et al. 2022).

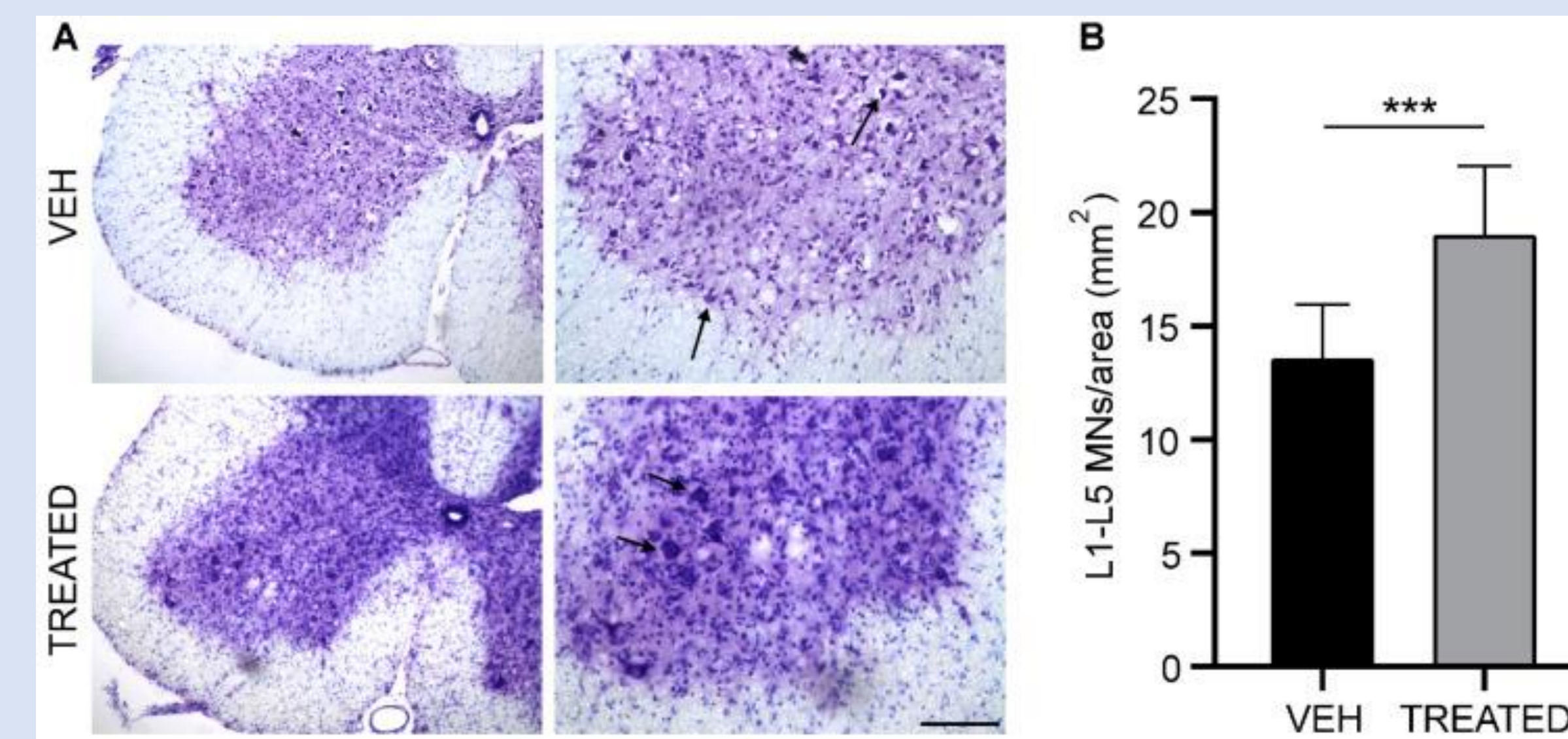


Figure 2: Difference in motor neuron count in the L1-L5 spinal cord region. Mice receiving treatment with supplement displayed significantly higher density of motor neurons and motor neuron survival compared to the non-treated mice group. Significance of  $p < 0.0005$  denoted with \*\*\*. Modified from Figure 4 (Bankole et al. 2022).

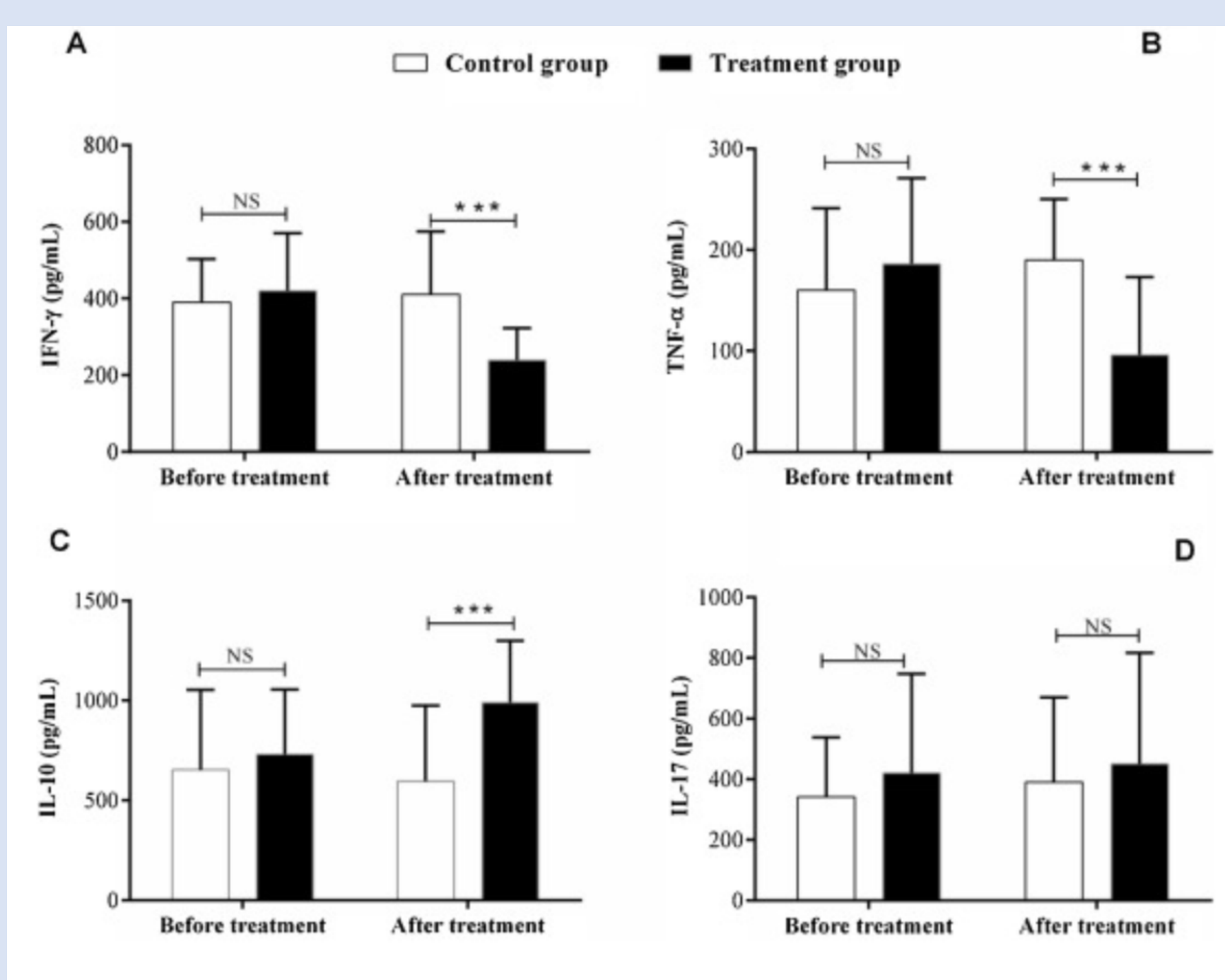


Figure 3: 6-month difference in pro-inflammatory cytokines (IFN- $\gamma$ , TNF- $\alpha$ , IL-17) and anti-inflammatory cytokines (IL-10) between control group (IFN- $\beta$ ) and treatment group (IFN- $\beta$ ) and sesame oil supplement). Significant decreases in TNF- $\alpha$  and IFN- $\gamma$  are seen in the sesame oil treated group and significant increases in IL-10 levels are seen in the sesame oil treated group. Significance of  $p < 0.001-0.0001$  denoted with \*\*\*. Modified from Figure 3 (Faraji et al. 2019).

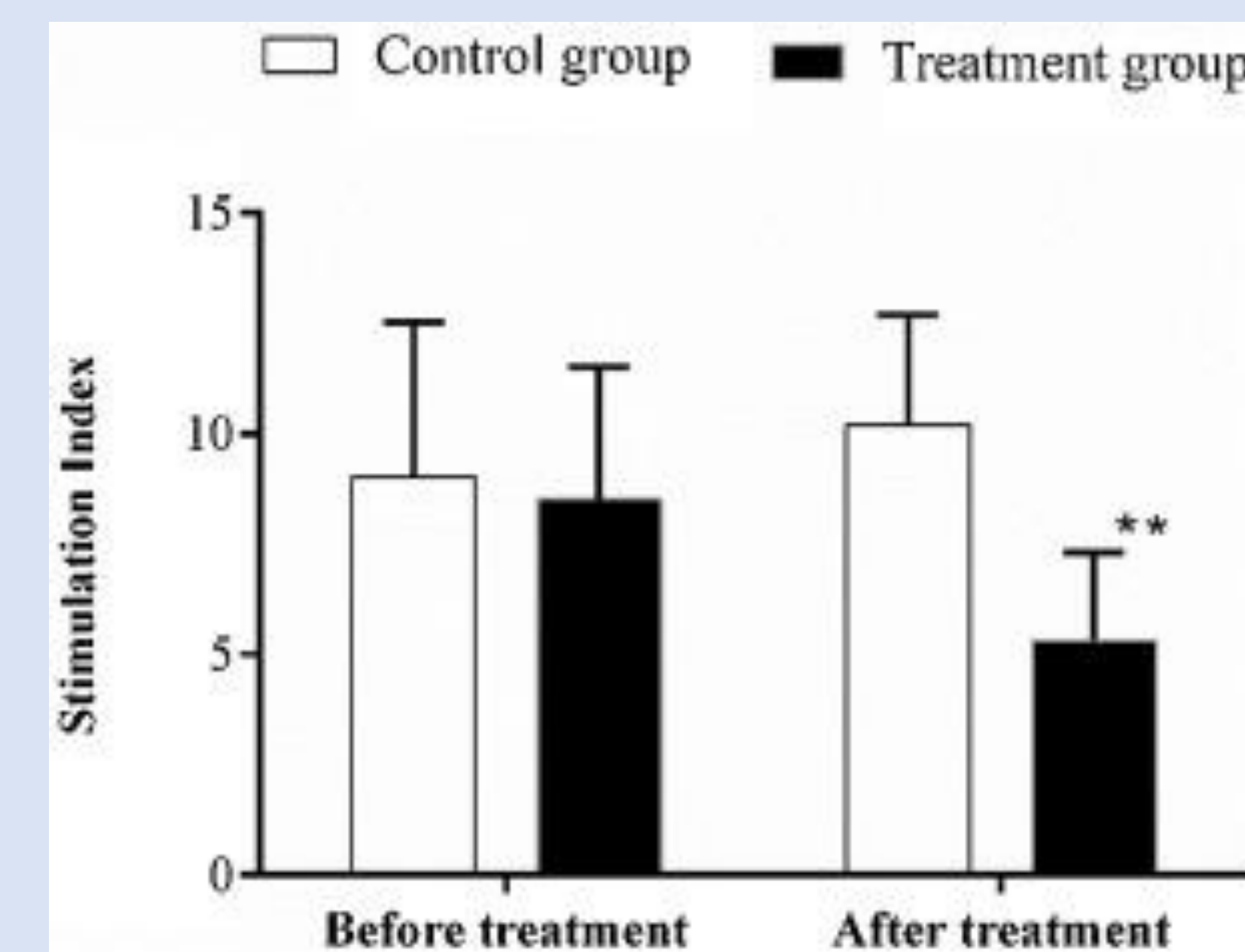


Figure 4: 6-month difference in stimulation index (lymphocyte proliferation) in the untreated and treated groups. Significant decreases in lymphocyte proliferation are seen in the treated group. Significance of  $p < 0.01$  denoted with \*\*. Modified from Figure 2 (Faraji et al. 2019).

## Discussion

- In most disease states examined, the combination of pharmacological treatment with natural supplement provided a supportive effect in reducing disease markers.
- Bankole et al. 2022 show that the use of valproate with the supplement resveratrol decrease the degree of cell death in an ALS model and improve overall survival compared to no supplement use (Figure 1, Figure 2).<sup>1</sup>
- Faraji et al. 2019 examine how the concurrent use of Interferon- $\beta$  and the supplement sesame oil decrease the degree of lymphocytic activity and pro-inflammatory conditions leading to a potential improvement in disease state (Figure 3, Figure 4).<sup>5</sup>
- Bytowska et al. 2023 demonstrate that in Parkinson's disease patients receiving Deep Brain Stimulation, Vitamin D<sub>3</sub> supplementation was associated with improved test performance, reduced inflammation, and a lower fall risk.<sup>2</sup>
- Some natural supplements had no effect on specific damage markers; however, most supplements provided some benefit in symptom progression, amelioration of neurotoxic damage, or in establishing a cytoprotective environment, indicating a net positive effect of their use<sup>1, 2, 5</sup>.

## Future Directions

- As most of the current research exists in murine models, expanding the current research into human models would serve to enhance the data available.
- Examining whether combining multiple regimens of natural supplements with existing treatments could provide a greater additive effect.
- Assessing whether tailoring specific natural supplements based on the pharmacological treatments side effect profile and mechanism of action provides a synergistic effect to disease burden and progression.

## References

Study	Neurodegenerative disorder	Supplement utilized	Pro-inflammatory Cytokines (IL-1, IL-6, IL-8, TNF- $\alpha$ )	Glutathione	CRP	Neurofilament Light Chain	Butyrylcholinesterase	Cell viability	Amyloid plaques	Systemic Oxidants	Symptom Progression
Wu et al. 2022, Bytowska et al. 2023	Parkinson's Disease	Vitamin D	Not examined	Not examined	Improved	Not examined	Not examined	Not examined	Not examined	Not examined	Improved
Bahmani et al. 2022, Cortese et al. 2020, Rosjoo et al. 2020, Holmqvist et al. 2019	Multiple Sclerosis	Vitamin D	Improved	Not examined	Not examined	No effect	Not examined	Not examined	Not examined	Not examined	Improved
Orti et al. 2021, Benloch et al. 2020, Platano et al. 2020	Multiple Sclerosis	Epigallocatechin Gallate	Improved	Not examined	No effect	Not examined	Improved	Not examined	Not examined	Improved	Improved
Yulug et al. 2023, More et al. 2018	Alzheimer's Disease	N-Acetyl Cysteine	Not examined	Improved	Not examined	Not examined	Not examined	Not examined	Not examined	Not examined	Improved
Panili-Moser et al. 2021, Jang and Surh 2003	Alzheimer's Disease	Resveratrol	Not examined	Not examined	Not examined	Not examined	Improved	Not examined	Not examined	Improved	Improved
Shao et al. 2023, Thota et al. 2020, Giri et al. 2004	Alzheimer's Disease	Curcumin	Improved	Not examined	Not examined	Not examined	Not examined	Not examined	Improved	Improved	Not examined
Xiao et al. 2022, Quinn et al. 2012, Hashimoto and Hossain 2011	Alzheimer's Disease	Docosahexaenoic Acid	Not examined	Not examined	Not examined	Not examined	Not examined	Improved	Improved	Improved	No effect
Ton et al. 2020	Alzheimer's Disease	Probiotics	Improved	Not examined	Not examined	Not examined	Not examined	Improved	Not examined	Improved	Improved
Kim et al. 2023	Amyotrophic Lateral Sclerosis	Mecasin	Not examined	Not examined	Not examined	Not examined	Not examined	Not examined	Not examined	Not examined	Improved
Troisi et al. 2020	Amyotrophic Lateral Sclerosis	Vitamin D	Not examined	Not examined	Not examined	Not examined	Not examined	Not examined	Not examined	Not examined	No effect
Bankole et al. 2022, Schiaffino et al. 2018	Amyotrophic Lateral Sclerosis	Resveratrol	Not examined	Not examined	Not examined	Not examined	Not examined	Improved	Not examined	Not examined	Improved
Yang et al. 2020	Mild Cognitive Impairment	Vitamin D	Not examined	Not examined	Not examined	Not examined	Not examined	Not examined	Not examined	Improved	Improved

Table 1: Compiled table of the neurodegenerative disorders tested, the corresponding supplement used and the specified marker for determining cell damage and disease progression. Green boxes indicate a positive effect, red boxes indicate either no effect or a negative effect, grey boxes indicate the marker was not tested for. CRP – C-reactive protein.

