Article title: Clinical Stability and Functional Improvement in Amyotrophic Lateral Sclerosis Following Extended Brain-Gut Photobiomodulation Therapy: A Case Report
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Clinical Stability and Functional Improvement in Amyotrophic Lateral Sclerosis Following Extended Brain-Gut Photobiomodulation Therapy: A Case Report

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Abstract

Background

Amyotrophic lateral sclerosis (ALS) is a form of motor neuron disease (MND), a progressive neurodegenerative disorder with limited therapeutic options. Photobiomodulation (PBM) therapy has demonstrated neuroprotective properties in preclinical models, yet clinical evidence in human ALS patients remains sparse.

Methods

We present a 39-year-old male with bulbar-onset, upper motor neuron-predominant ALS who commenced twice-daily CeraThrive (Light Tree Ventures, Den Haag, Netherlands) red and near-infrared light therapy (630-1070 nm, 40 Hz) in January 2023, applied to the motor cortex, anterior neck, and abdomen.

Results

The clinician-administered ALSFRS-R score improved from 32 at baseline (February 2020) to 37 (February 2025), representing a cumulative 5-point improvement. Peripheral oxygen saturation also improved, rising from 89% (February 2020) to 96% (February 2026). The patient reported subjective improvements in ambulation, spasticity, swallowing, and general wellbeing.

Conclusions

While the case report methodology has limitations, functional improvement in a disease characterised by rapid progressive decline provides rationale for controlled clinical trials investigating PBM in ALS.

Keywords

Motor Neurone Disease, Amyotrophic Lateral Sclerosis, Photobiomodulation

1. Introduction

Motor neurone disease (MND) is a progressive neurodegenerative disorder characterised by the degeneration of both upper and lower motor neurones, typically presenting in middle age (1-3). Its most common form is amyotrophic lateral sclerosis (ALS), which manifests across several phenotypes based on the site and severity of neurological involvement.

1.1 Epidemiology, Pathogenesis, and Current Treatment Limitations

According to 2019 Global Burden of Disease estimates, MND affected approximately 268,673 individuals worldwide, with 63,700 incident cases and 39,081 deaths annually (4). The aetiology of ALS reflects a complex interplay between genetic predisposition and environmental factors (5). Pathogenic processes include mitochondrial dysfunction, oxidative stress, glutamate excitotoxicity, neuroinflammation, neuronal hyperexcitability, and axonal dysfunction (1, 6).

Despite advances in understanding ALS pathophysiology, therapeutic options remain severely limited. Currently, three disease-modifying agents are approved: riluzole, a glutamate antagonist approved for general ALS; tofersen, an antisense oligonucleotide approved for SOD1-mutation ALS; and edaravone, an antioxidant (not approved in UK) (7-9). These agents modestly slow disease progression measured by the revised ALS Functional Rating Scale (ALSFRS-R) but offer only marginal improvements short-term in survival and autonomy (9-14).

Management relies heavily on multidisciplinary supportive care, including respiratory support, nutritional interventions, physical and occupational therapy, and symptomatic management of spasticity, sialorrhea, and pain (15). While these interventions can impact quality of life and may influence disease duration, they do not address the underlying neurodegenerative process. Challenges persist regarding disease definition, appropriate biomarkers of progression, interpretation of genetic heterogeneity, and the transition from promising preclinical findings to effective human therapeutics(15).

1.2 PBM and Infrared Light Therapy

Photobiomodulation (PBM) therapy employs non-ionising light sources in the red to near-infrared spectrum (600-1100 nm) to modulate cellular function through non-thermal mechanisms (16). The therapeutic effects of PBM are mediated through absorption of photon energy by chromophores, primarily cytochrome c oxidase in the mitochondrial respiratory chain and intracellular water molecules (17). This absorption initiates a cascade of cellular events, including modulation of signalling pathways, production of reactive oxygen species (eliciting a preconditioning response and increase in chaperone proteins, eg. Hsp70), ATP synthesis, and alterations in calcium, nitric oxide, and inositol phosphate dynamics (18-20). Secondary effects encompass stress signalling, metabolic regulation, inflammation, cytoskeletal organisation, and modulation of cell proliferation, differentiation, and homeostasis (21, 22).

PBM therapy has demonstrated beneficial effects across diverse medical applications and exhibits a characteristic biphasic dose response (23, 24). Importantly, PBM has generally been reported as well-tolerated in clinical trials (25-27).

Recent preclinical and clinical evidence suggests that PBM possesses significant neuroprotective and anti-inflammatory properties relevant to neurodegenerative diseases(23, 24). In the context of ALS specifically, evidence from preclinical studies demonstrates promise (28-30). However, despite encouraging findings, research on PBM application in human ALS patients remains limited.

1.3 Study Rationale and Significance

Given the limited therapeutic options for ALS and the promising preclinical evidence for PBM therapy, clinical documentation of real-world applications becomes particularly valuable. This case report presents a patient with motor neurone disease who has used a near-infrared light therapy device targeting the gut-brain axis over an extended (over three year) period, with

reported improvements in multiple functional domains. The significance of this case lies in several factors: the extended duration of device use, the comprehensive documentation of functional changes, the novel application of gut-brain axis-targeted PBM in ALS, and the potential to inform future large controlled clinical trials.

2. Case Report

2.1 Patient Presentation

The patient is a 39-year-old male who presented with bulbar-onset, upper motor neurone-predominant amyotrophic lateral sclerosis (ALS). Symptom onset occurred in June 2016 at age 29, with initial manifestations of mild speech slurring. Formal diagnosis was established in February 2019 at age 32, following comprehensive neurological evaluation. Initial prognosis at diagnosis was 2-4 years.

2.2 Clinical History and Disease Progression

The patient, previously healthy with no significant past medical history, first noted subtle speech changes in mid-2016. These were initially dismissed until December 2017, when progressive motor symptoms became apparent. The patient developed left foot drag, difficulty ascending stairs requiring handrail support, impaired balance with multiple falls, upper limb tremor, and generalised bradykinesia predominantly affecting the left side. Concurrent bulbar symptoms included intermittent dysphagia for both solids and liquids. Significant weight loss of approximately 19 kg was documented from 2016, with accelerated decline in the months preceding diagnosis. The patient reported peripheral coldness in the extremities. Notably, cognitive function, sphincter control, and erectile function remained intact throughout.

2.3 Examination Findings (2018-2019, Diagnostic Period)

Neurological examination revealed a spastic gait with pseudobulbar dysarthria, hypermetric saccades, and a positive glabellar tap. Bulbar examination showed slow tongue movement without wasting. Upper limb examination was initially normal but subsequently revealed

bilateral first dorsal interosseous wasting (left greater than right), increased tone, hyperreflexia with spreading reflexes, and positive Hoffman signs bilaterally. Lower limb findings included increased tone (left predominant), mild left foot drop, bilateral sustained ankle clonus, and extensor plantar responses. Sensation was normal across all modalities and systemic examination was unremarkable.

2.4 Examination Findings (February 2024)

Neurological examination in February 2024 demonstrated reduced saccadic eye movements and spastic dysarthria that was slightly slower and more indistinct than previous assessments. Four-limb hypertonicity was present, and a slight decrease in left hand dexterity was noted over the preceding six months. The examination was otherwise relatively stable compared to prior evaluations.

2.5 Laboratory and Diagnostic Investigations

MRI of the brain (2018) demonstrated diffuse, non-specific cerebral volume loss with possible motor cortex atrophy; the cerebellum and pyramidal tracts appeared normal. Spinal MRI was unremarkable. Electromyography (EMG) revealed chronic denervation in both upper limbs, supporting the diagnosis.

Genetic screening for SOD1, FUS, TARDBP, C9orf72, and hereditary spastic paraplegia was negative. Coeliac serology revealed markedly elevated tissue transglutaminase (tTG 1142 U/mL) in October 2018, which normalised following a gluten-free diet.

Forced vital capacity (FVC) was 60% predicted at initial assessment (February 2019), though suboptimal lip seal during testing was noted. Sniff nasal inspiratory pressure (86 cmH_2O) and peak cough flow (340 L/min), assessed in September 2023, were well preserved. The Epworth Sleepiness Score was 13/24 in 2023, with reported morning headaches and daytime somnolence.

2.6 Diagnosis Summary

The primary diagnosis was upper motor neuron-predominant amyotrophic lateral sclerosis with bulbar onset, established in February 2019. Coeliac disease was identified as a secondary diagnosis, with serological markers responsive to a gluten-free diet. The patient is a slow progressor relative to typical ALS. Within-individual progression rates tend to remain relatively stable, making the patient's prior trajectory a useful reference point for interpreting subsequent change.

2.7 Baseline Condition Prior to Intervention (Pre-January 2023)

At the time of intervention initiation, the patient had been non-ambulatory and wheelchair-dependent for over four years. A percutaneous endoscopic gastrostomy (PEG) tube had been inserted for nutritional support, though at the most recent assessment after intervention, the patient was not using the PEG tube for fluid supplementation or nutrition.

2.8 Medications at Baseline

Table 1. Patient Medication regimen at baseline

Medication	Dosage	Notes
Riluzole	50 mg twice daily	Disease-modifying therapy
Baclofen	100 mg daily	For spasticity. 30mg AM, 30mg Afternoon, 40mg PM. (Verified high dose)
Levetiracetam	250 mg daily	For spasticity
Diazepam	5 mg daily	-
Citalopram	40mg daily	For emotionality and mood

Table 1. Patient medication regimen at baseline (January 2023). Medications listed reflect the regimen at initiation of CeraThrive photobiomodulation therapy. All medications were continued throughout the observation period.

2.9 Supplement Regimen

Table 2. Patient daily supplement protocol

Supplement	Dosage
Vitamin B1 (Thiamine HCl)	2 g/day
Vitamin B12 (Methylcobalamin)	As directed
Methylfolate	5 mg/day
B-Complex	As directed
Methylene Blue (tincture)	10 mg/day
Ibudilast	30 mg/day
Saccharomyces boulardii	1 capsule
Akkermansia muciniphila	2 capsules
Curcumin (with Bioperine)	Up to 2 g/day
Milk Thistle	As directed
Vitamin D3	≥5000 IU/day
Vitamin K2	400 mcg/day
Aspirin	300 mg/day

Table 2. Patient daily supplement protocol. Supplements listed reflect the regimen maintained during the observation period.

The patient follows a pre-therapy protocol 30 minutes before each light therapy session, consisting of a minimum of 25 g of carbohydrates, 750 mg of pyruvate, and 500 mg of NAD+.

3. Intervention: PBM Therapy

3.1 Treatment Method

The patient commenced CeraThrive (Light Tree Ventures, Den Haag, Netherlands) red and near-infrared (NIR) light therapy in January 2023.

3.2 Treatment Parameters

The transcranial device delivered 630-850-1070 nm PBM spanning the red to near-infrared spectrum, pulsed at gamma (40 Hz) frequency. Stimulation was delivered twice daily for 10 minutes, with sessions spaced 12 hours apart.

3.3 Placement Protocol

The patient adopted a modified placement protocol based on his specific symptom profile. The PBM Headband anterior cluster was positioned over the motor cortex rather than the manufacturer's standard prefrontal cortex placement, while the posterior cluster was placed against the anterior neck and throat region rather than the cerebellum. An additional abdominal PBM Body Panel device containing 60 dual-core (630 & 810nm) LEDs was used to modulate the gut microbiome. This treatment strategy sought to primarily stimulate the motor cortex given the patient's upper motor neuron-predominant presentation and to address bulbar symptoms including dysphagia.

3.4 Timeline of key dates in patient history

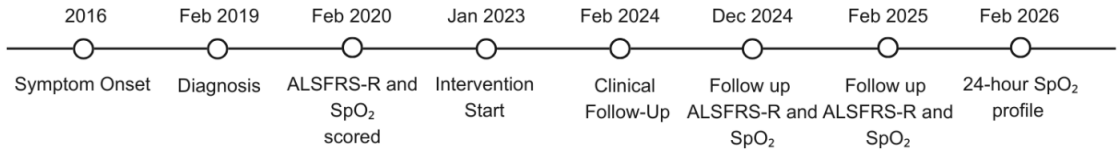


Figure 1. Timeline of key clinical events and assessments from symptom onset to time of report writing.

4. Results

4.1 Functional Outcomes

The primary outcome measure was the Revised Amyotrophic Lateral Sclerosis Functional Rating Scale (ALSFRS-R), a validated 48-point instrument assessing functional status across bulbar, motor, and respiratory domains. Higher scores indicate better functional status.

At baseline (February 2020), the participant's clinician-administered ALSFRS-R score was 32. Following initiation of twice-daily PBM therapy in January 2023, subsequent assessments revealed a score of 33 in December 2023, 35 in December 2024 and 37 in February 2025, representing a cumulative 5-point improvement over the observation period (Figure 2).

Neurological follow-up in February 2024 documented overall clinical stability. Examination showed persistent spastic dysarthria and four-limb hypertonicity, with minor interval change

consisting of slightly reduced left-hand dexterity and somewhat slower, less distinct speech. Respiratory measures remained relatively preserved, including sniff nasal inspiratory pressure of 86 cmH_2O and peak cough flow of 340 L/min.

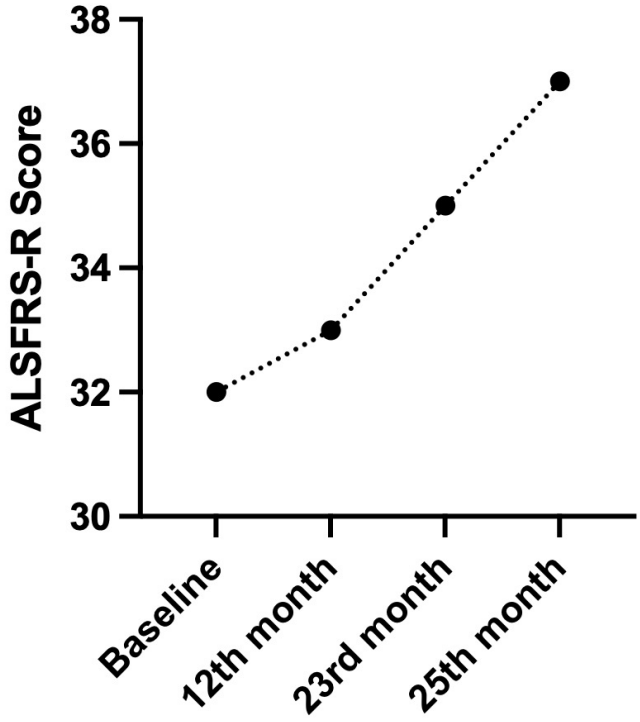
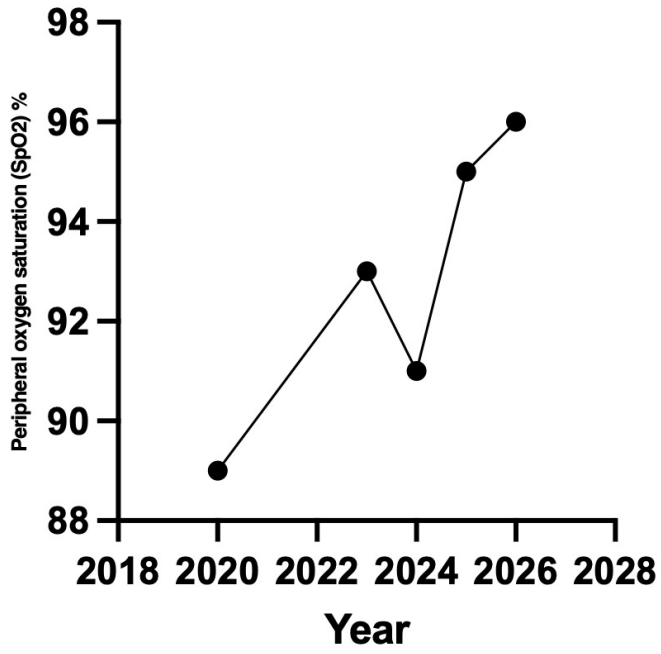


Figure 2. ALSFRS-R scores across the observation period. ALSFRS-R scores were recorded at baseline (February 2020; score 32), approximately 12 months after initiation of twice-daily PBM therapy (December 2023; score 33), 23 months post-initiation (December 2024; score 35), and at 25 months post-initiation (February 2025; score 37), representing a cumulative 5-point improvement. Therapy was initiated in January 2023. n=1.

4.2 Oxygenation and Sleep-Related Measures

Peripheral oxygen saturation (SpO_2) was evaluated as an exploratory physiological measure. Pulse oximetry readings showed SpO_2 of 89% in February 2020, 93% in December 2023, 91% in December 2024, 95% in February 2025 and 96% in February 2026 (Figure 3A). A representative 24-hour SpO_2 profile obtained in February 2026 demonstrated daytime values ranging from 94% to 97%, with overnight values of 92% to 94% and intermittent desaturations below 90% (Figure 3B). By 2025, the Epworth Sleepiness Score had changed from 13/24 (2023) to 15/24 (2024) to 12/24 (Sep 2025).

A



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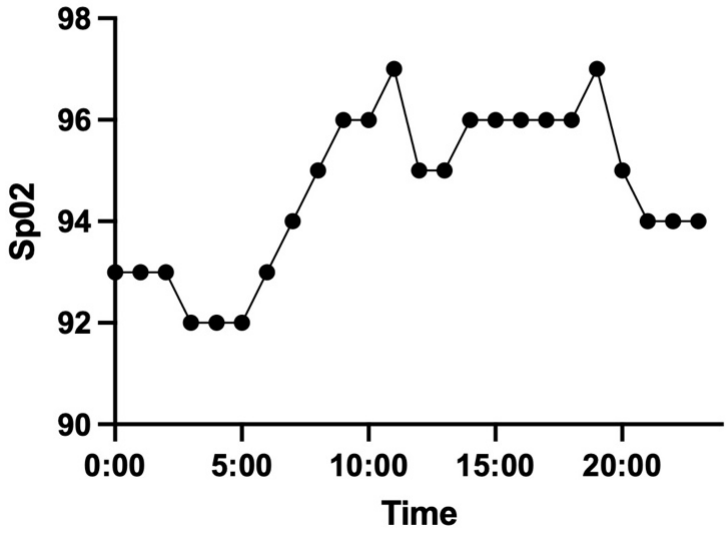

Figure 3A. Peripheral oxygen saturation (SpO_2) across the observation period. Pulse oximetry readings showed SpO_2 of 89% at baseline (February 2020), 93% in December 2023, 91% in December 2024, 95% in February 2025, and a mean daytime value of 96% in February 2026. 3B. Peripheral oxygen saturation (SpO_2) over a 24 hour period (2026). CeraThrive photobiomodulation therapy was initiated in January 2023. n=1.

4.3 Patient-Reported Outcomes

The patient reports several subjective improvements since initiating PBM therapy. In terms of ambulation, after more than four years of complete wheelchair dependence, the patient reported being able to stand and take several steps with assistance. Additionally, the patient reported reduction in spasticity, clonus, and muscle spasms (previously his predominant symptom).

Bulbar function was also reported to improve. The patient described better swallowing and the ability to maintain normal oral intake of food and fluids. He attributed this improvement in part to the NIR application to the anterior neck/throat region.

Additional self-reported benefits included reduced fatigue, improved sense of mental clarity, increased muscle mass, weight gain, and an improved sense of wellbeing, morale, and agency in managing his condition.

5. Discussion

5.1 Principal Findings

This case report documents functional improvement and sustained clinical stability in a patient with upper motor neurone-predominant ALS following extended use of PBM therapy. The principal findings were a five-point improvement in ALSFRS-R score over approximately two years of device use, rising from 32 at baseline to 37 at 25 months post-initiation, as well as an increase in peripheral oxygen saturation from 89% to 96%. This trajectory is notable given that ALS typically follows a course of rapid progressive functional decline. The observed improvements, combined with subjective reports of enhanced motor function, swallowing (eating and drinking normally), and general wellbeing, warrants careful consideration within the context of existing evidence for PBM in neurodegenerative disease.

5.2 Mechanistic Considerations

Several potential mechanisms may underlie the observed clinical effects, drawing on the established biological actions of PBM therapy.

The primary mechanism of PBM involves absorption of near-infrared photons by cytochrome c oxidase, the terminal enzyme of the mitochondrial electron transport chain (31). Mitochondrial dysfunction represents a central pathogenic mechanism in ALS. Therefore, by targeting this directly, PBM may address a fundamental component of ALS pathophysiology that current pharmacological agents do not adequately modulate (32).

Peripheral oxygen saturation improved from 89% at baseline to 96% at most recent assessment (Figure 3). In ALS, SpO_2 typically declines as respiratory muscle weakness progresses, making this trajectory noteworthy (33). PBM has been shown to increase oxygenated haemoglobin concentration in vivo through upregulation of cytochrome c oxidase (34, 35). Photon absorption enhances electron transport efficiency and oxidative phosphorylation, while photodissociation of nitric oxide from cytochrome c oxidase may further support oxygen metabolism and promote microvascular perfusion (36, 37). PBM may therefore influence oxygen physiology through two complementary pathways: improved cellular oxygen utilisation and enhanced oxygen delivery through haemodynamic effects. Studies using broadband near-infrared spectroscopy have demonstrated that 1064 nm laser stimulation increases oxygenated haemoglobin in treated tissues, with effects persisting beyond the stimulation period (38). While the device used in this report operates across a broader wavelength range (630-1070 nm), these findings provide a plausible mechanism through which repeated PBM sessions could contribute to improved tissue oxygenation. However, peripheral SpO_2 is an indirect marker influenced by multiple respiratory and systemic factors, and the observed improvement could reflect changes in respiratory muscle function, posture, or natural variability. These observations should be considered hypothesis-generating rather than evidence of a treatment effect.

Secondly, chronic neuroinflammation, characterised by microglial activation and elevated proinflammatory cytokines, contributes significantly to motor neurone degeneration in ALS

(39, 40). The participant's reported reductions in spasticity and muscle spasms, symptoms with inflammatory components, may partially reflect such anti-inflammatory effects.

Neurotrophic factor upregulation is an additional potential effect of the therapy (41, 42). Given that neurotrophic factor deficiency has been implicated in ALS pathogenesis, enhanced neurotrophic signalling represents a plausible contributor to the observed functional improvements (43).

Gut-brain axis modulation was likely affected by this therapy. Emerging evidence implicates gut microbiome dysbiosis and intestinal barrier dysfunction in ALS pathophysiology, with alterations in gut microbiota composition correlating with disease progression in both animal models and human patients (44, 45). PBM applied to the abdomen may modulate intestinal inflammation, barrier integrity, and vagal afferent signalling, potentially influencing central nervous system function through gut-brain communication pathways (46-48). While speculative, this mechanism aligns with growing recognition of the gut-brain axis as a therapeutic target in neurodegenerative disease.

The device delivers PBM pulsed at 40 Hz, corresponding to the gamma frequency band. This is noteworthy given emerging evidence that 40 Hz sensory stimulation reduces neuroinflammation and modifies microglial activity in neurodegenerative disease models. Pioneering work demonstrated that 40 Hz stimulation in Alzheimer's disease mouse models reduced amyloid-beta levels and shifted microglia toward a phagocytic phenotype, with effects specific to this frequency (49). In human trials, chronic daily 40 Hz stimulation in patients with mild Alzheimer's dementia was associated with reduced brain atrophy and increased functional connectivity (50). While this research has focused predominantly on Alzheimer's disease, the underlying mechanisms are relevant to ALS pathophysiology, and whether the 40 Hz pulsed delivery in this case produced comparable entrainment effects warrants future investigation.

5.3 Relationship to Existing Literature

The findings of this case report align with a growing body of preclinical and clinical evidence supporting PBM in neurodegenerative disease (30). Human studies in related neurodegenerative conditions have demonstrated cognitive improvements in Alzheimer's disease patients receiving transcranial PBM, motor benefits in Parkinson's disease, and mood improvements in major depressive disorder (51-53). The magnitude of improvement observed here, a 5-point ALSFRS-R increase, exceeds what has been reported with approved disease-modifying therapies (9, 12-14).

5.4 Limitations

Several important limitations must be acknowledged. The single-subject design precludes statistical inference and generalisation; effects observed in one individual may not apply to the broader ALS population. The absence of a control condition, whether sham device, no-treatment period, or crossover design, means that observed changes cannot be attributed to the intervention with certainty.

The participant's use of riluzole and an extensive supplement regimen introduces confounding that complicates causal attribution. Interactions between multiple interventions cannot be excluded. Additionally, ibudilast and methylene blue are compounds with independent neuroprotective potential which could affect results. Similarly, the participant's dietary modifications (gluten-free diet for coeliac disease) and lifestyle factors may have contributed to outcomes.

The absence of an ALSFRS-R score at intervention initiation (January 2023) is a further limitation, as the baseline measurement of 32 was recorded approximately three years earlier (February 2020); the patient's functional status immediately before treatment is therefore unknown.

5.5 Future Directions

The observations documented in this case report highlight several priorities for future research. The most pressing need is for well-designed, adequately powered randomised controlled trials comparing PBM to sham treatment in ALS patients.

Mechanistic studies incorporating biomarkers of mitochondrial function, neuroinflammation, oxidative stress, neuronal damage (NF-L) and neurotrophic factors would help elucidate the biological basis of any therapeutic effects of PBM therapy. Finally, given the novel application of gut-brain axis-targeted PBM in this case, studies examining effects on gut microbiome composition, intestinal permeability, and vagal function would help evaluate this proposed mechanism.

6. Conclusion

This case report documents a five-point improvement in ALSFRS-R score, an increase in peripheral oxygen saturation from 89% to 96%, and sustained clinical stability in a patient with ALS following extended use of PBM therapy. This was accompanied by subjective improvements in motor function, swallowing, and general wellbeing, an unexpected trajectory in a disease normally characterised by progressive decline.

While case report methodology precludes causal inference, these observations, along with supportive preclinical evidence of PBM's effects, provide rationale for systematic investigation of this therapeutic approach. Controlled clinical trials are needed to determine whether these findings can be replicated and generalised.

List of abbreviations

ALS - Amyotrophic Lateral Sclerosis

ALSFRS-R - Revised Amyotrophic Lateral Sclerosis Functional Rating Scale

ATP - Adenosine Triphosphate

C9orf72 - Chromosome 9 Open Reading Frame 72

EMG - Electromyography

FUS - Fused in Sarcoma

FVC - Forced Vital Capacity

Hsp70 - Heat Shock Protein 70

IRB - Institutional Review Board

LED - Light-Emitting Diode

MND - Motor Neurone Disease

MRI - Magnetic Resonance Imaging

NAD+ - Nicotinamide Adenine Dinucleotide

NF-L - Neurofilament Light Chain

NIR - Near-Infrared

PBM - Photobiomodulation

PEG - Percutaneous Endoscopic Gastrostomy

SOD1 - Superoxide Dismutase 1

SpO_2 - Peripheral Oxygen Saturation

TARDBP - TAR DNA-Binding Protein

tTG - Tissue Transglutaminase

Declarations

Ethics approval and consent to participate

This case report describes the clinical observations and neurophysiological findings of a single participant and does not constitute systematic research involving hypothesis testing or experimental manipulation. As such, formal ethical approval from an Institutional Review Board (IRB) was not required. This determination is consistent with established guidelines for case report publication. CeraThrive is categorized as an FDA Class I medical device for brain wellness. This classification reflects its use in supporting brain health and promoting overall wellness through innovative red-light therapy.

Written informed consent was obtained from the participant for the use of their information in this case report, including all associated clinical data, neurophysiological recordings, and de-identified results.

Consent for publication

The participant was informed of the purpose, scope, and intended audience of the publication prior to data collection and provided consent voluntarily.

Availability of data and materials

Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

Competing Interests

E. Leddy is an independent contractor engaged by CeraThrive Ltd. in the capacity of science communicator and researcher. The author's contractual relationship with CeraThrive represents a potential conflict of interest, which is hereby declared in the interest of full transparency. The analysis, interpretation of findings, and conclusions presented in this report were conducted independently and reflect the author's objective assessment of the available data. CeraThrive did not exert editorial control over the content or conclusions of this manuscript.

The subject independently commenced PBM therapy in January 2023, prior to any engagement with CeraThrive Ltd. The subject of this report is a volunteer engaged by CeraThrive Ltd since 2024. The subject's relationship with CeraThrive represents a potential conflict of interest, which is hereby declared in the interest of full transparency.

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Authors' contributions

E. Leddy conceived the study, analysed the data, created the tables, and drafted the manuscript. P. Chazot FBPhS and J. Zarazua Jiminez created the Figures (GraphPad Prism), provided critical review and editorial input, and contributed to the refinement of key scientific content. All authors reviewed and approved the final manuscript.

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References

1. Hardiman O, Al-Chalabi A, Chio A, Corr EM, Logroscino G, Robberecht W, et al. Amyotrophic lateral sclerosis. Nat Rev Dis Primers. 2017;3:17071.

2. Statland JM, Barohn RJ, McVey AL, Katz JS, Dimachkie MM. Patterns of Weakness, Classification of Motor Neuron Disease, and Clinical Diagnosis of Sporadic Amyotrophic Lateral Sclerosis. Neurol Clin. 2015;33(4):735-48.

3. Ingre C, Roos PM, Piehl F, Kamel F, Fang F. Risk factors for amyotrophic lateral sclerosis. 2015(1179-1349 (Print)).

4. Park J, Kim JE, Song TJ. The Global Burden of Motor Neuron Disease: An Analysis of the 2019 Global Burden of Disease Study. Front Neurol. 2022;13:864339.

5. Chiò A, Mazzini L, D'Alfonso S, Corrado L, Canosa A, Moglia C, et al. The multistep hypothesis of ALS revisited: The role of genetic mutations. Neurology. 2018;91(7):e635-e42.

6. van den Bos MAJ, Geevasinga N, Higashihara M, Menon P, Vucic S. Pathophysiology and Diagnosis of ALS: Insights from Advances in Neurophysiological Techniques. Int J Mol Sci. 2019;20(11).

7. Rammes G, Zieglgänsberger W, Parsons CG. The fraction of activated N-methyl-d-Aspartate receptors during synaptic transmission remains constant in the presence of the glutamate release inhibitor riluzole. Journal of Neural Transmission. 2008;115(8):1119-26.

8. Miller TM, Cudkowicz ME, Genge A, Shaw PJ, Sobue G, Bucelli RC, et al. Trial of Antisense Oligonucleotide Tofersen for SOD1 ALS. N Engl J Med. 2022;387(12):1099-110.

9. Safety and efficacy of edaravone in well defined patients with amyotrophic lateral sclerosis: a randomised, double-blind, placebo-controlled trial. Lancet Neurol. 2017;16(7):505-12.

10. Cedarbaum JM, Stambler N, Malta E, Fuller C, Hilt D, Thurmond B, et al. The ALSFRS-R: a revised ALS functional rating scale that incorporates assessments of respiratory function. BDNF ALS Study Group (Phase III). J Neurol Sci. 1999;169(1-2):13-21.

11. Georgoulopoulou E, Fini N, Vinceti M, Monelli M, Vacondio P, Bianconi G, et al. The impact of clinical factors, riluzole and therapeutic interventions on ALS survival: a population based study in Modena, Italy. Amyotroph Lateral Scler Frontotemporal Degener. 2013;14(5-6):338-45.

12. Bensimon G, Lacomblez L, Meininger V. A controlled trial of riluzole in amyotrophic lateral sclerosis. ALS/Riluzole Study Group. N Engl J Med. 1994;330(9):585-91.

13. Lacomblez L, Bensimon G, Leigh PN, Guillet P, Meininger V. Dose-ranging study of riluzole in amyotrophic lateral sclerosis. Amyotrophic Lateral Sclerosis/Riluzole Study Group II. Lancet. 1996;347(9013):1425-31.

14. Miller RG, Mitchell JD, Moore DH. Riluzole for amyotrophic lateral sclerosis (ALS)/motor neuron disease (MND). Cochrane Database Syst Rev. 2012;2012(3):Cd001447.

15. Rosenfeld J, Strong MJ. Challenges in the Understanding and Treatment of Amyotrophic Lateral Sclerosis/Motor Neuron Disease. Neurotherapeutics. 2015;12(2):317-25.

16. Tsai SR, Hamblin MR. Biological effects and medical applications of infrared radiation. J Photochem Photobiol B. 2017;170:197-207.

17. Passarella S, Karu T. Absorption of monochromatic and narrow band radiation in the visible and near IR by both mitochondrial and non-mitochondrial photoacceptors results in photobiomodulation. J Photochem Photobiol B. 2014;140:344-58.

18. Grillo SL, Duggett NA, Ennaceur A, Chazot PL. Non-invasive infra-red therapy (1072 nm) reduces β-amyloid protein levels in the brain of an Alzheimer's disease mouse model, TASTPM. J Photochem Photobiol B. 2013;123:13-22.

19. de Freitas LF, Hamblin MR. Proposed Mechanisms of Photobiomodulation or Low-Level Light Therapy. IEEE J Sel Top Quantum Electron. 2016;22(3).

20. Karu T. Primary and secondary mechanisms of action of visible to near-IR radiation on cells. J Photochem Photobiol B. 1999;49(1):1-17.

21. Rojas JC, Gonzalez-Lima F. Neurological and psychological applications of transcranial lasers and LEDs. Biochem Pharmacol. 2013;86(4):447-57.

22. Calles C, Schneider M, Macaluso F, Benesova T, Krutmann J, Schroeder P. Infrared A radiation influences the skin fibroblast transcriptome: mechanisms and consequences. J Invest Dermatol. 2010;130(6):1524-36.

23. Johnstone DM, Moro C, Stone J, Benabid AL, Mitrofanis J. Turning On Lights to Stop Neurodegeneration: The Potential of Near Infrared Light Therapy in Alzheimer's and Parkinson's Disease. Front Neurosci. 2015;9:500.

24. Huang YY, Sharma SK, Carroll J, Hamblin MR. Biphasic dose response in low level light therapy - an update. Dose Response. 2011;9(4):602-18.

25. Woo K. Photobiomodulation therapy in neurodegenerative diseases: mechanisms, clinical applications, and future directions. Medical Lasers. 2024;13(2):90-7.

26. Bensadoun RJ, Epstein JB, Nair RG, Barasch A, Raber-Durlacher JE, Migliorati C, et al. Safety and efficacy of photobiomodulation therapy in oncology: A systematic review. Cancer Med. 2020;9(22):8279-300.

27. de Pauli Paglioni M, Araújo ALD, Arboleda LPA, Palmier NR, Fonsêca JM, Gomes-Silva W, et al. Tumor safety and side effects of photobiomodulation therapy used for prevention and management of cancer treatment toxicities. A systematic review. Oral Oncol. 2019;93:21-8.

28. Bathini M, Raghushaker CR, Mahato KK. The Molecular Mechanisms of Action of Photobiomodulation Against Neurodegenerative Diseases: A Systematic Review. Cell Mol Neurobiol. 2022;42(4):955-71.

29. Lamptey RNL, Chaulagain B, Trivedi R, Gothwal A, Layek B, Singh J. A Review of the Common Neurodegenerative Disorders: Current Therapeutic Approaches and the Potential Role of Nanotherapeutics. Int J Mol Sci. 2022;23(3).

30. Moges H, Vasconcelos OM, Campbell WW, Borke RC, McCoy JA, Kaczmarczyk L, et al. Light therapy and supplementary Riboflavin in the SOD1 transgenic mouse model of familial amyotrophic lateral sclerosis (FALS). Lasers Surg Med. 2009;41(1):52-9.

31. Wong-Riley MT, Liang HL, Eells JT, Chance B, Henry MM, Buchmann E, et al. Photobiomodulation directly benefits primary neurons functionally inactivated by toxins: role of cytochrome c oxidase. J Biol Chem. 2005;280(6):4761-71.

32. Parvanovova P, Evinova A, Grofik M, Hnilicova P, Tatarkova Z, Turcanova-Koprusakova M. Mitochondrial Dysfunction in Sporadic Amyotrophic Lateral Sclerosis Patients: Insights from High-Resolution Respirometry. Biomedicines. 2024;12(6).

33. Tsara V, Serasli E, Steiropoulos P, Tsorova A, Antoniadou M, Zisi P. Respiratory function in amyotrophic lateral sclerosis patients. The role of sleep studies. Hippokratia. 2010;14(1):33-6.

34. Wang X, Tian F, Soni SS, Gonzalez-Lima F, Liu H. Interplay between up-regulation of cytochrome-c-oxidase and hemoglobin oxygenation induced by near-infrared laser. Sci Rep. 2016;6:30540.

35. Pruitt T, Carter C, Wang X, Wu A, Liu H. Photobiomodulation at Different Wavelengths Boosts Mitochondrial Redox Metabolism and Hemoglobin Oxygenation: Lasers vs. Light-Emitting Diodes In Vivo. Metabolites. 2022;12(2).

36. Hamblin MR. Mechanisms and Mitochondrial Redox Signaling in Photobiomodulation. Photochem Photobiol. 2018;94(2):199-212.

37. Sarti P, Giuffrè A, Barone MC, Forte E, Mastronicola D, Brunori M. Nitric oxide and cytochrome oxidase: reaction mechanisms from the enzyme to the cell. Free Radic Biol Med. 2003;34(5):509-20.

38. Tian F, Hase SN, Gonzalez-Lima F, Liu H. Transcranial laser stimulation improves human cerebral oxygenation. Lasers Surg Med. 2016;48(4):343-9.

39. Philips T, Robberecht W. Neuroinflammation in amyotrophic lateral sclerosis: role of glial activation in motor neuron disease. Lancet Neurol. 2011;10(3):253-63.

40. Beers DR, Zhao W, Liao B, Kano O, Wang J, Huang A, et al. Neuroinflammation modulates distinct regional and temporal clinical responses in ALS mice. Brain Behav Immun. 2011;25(5):1025-35.

41. de Oliveira BH, Lins EF, Kunde NF, Salgado ASI, Martins LM, Bobinski F, et al. Transcranial photobiomodulation increases cognition and serum BDNF levels in adults over 50 years: A randomized, double-blind, placebo-controlled trial. J Photochem Photobiol B. 2024;260:113041.

42. El Massri N, Lemgruber AP, Rowe IJ, Moro C, Torres N, Reinhart F, et al. Photobiomodulation-induced changes in a monkey model of Parkinson's disease: changes in tyrosine hydroxylase cells and GDNF expression in the striatum. Exp Brain Res. 2017;235(6):1861-74.

43. Tosolini AP, Sleigh JN, Surana S, Rhymes ER, Cahalan SD, Schiavo G. BDNF-dependent modulation of axonal transport is selectively impaired in ALS. Acta Neuropathol Commun. 2022;10(1):121.

44. Blacher E, Bashiardes S, Shapiro H, Rothschild D, Mor U, Dori-Bachash M, et al. Potential roles of gut microbiome and metabolites in modulating ALS in mice. Nature. 2019;572(7770):474-80.

45. Zeng Q, Shen J, Chen K, Zhou J, Liao Q, Lu K, et al. The alteration of gut microbiome and metabolism in amyotrophic lateral sclerosis patients. Sci Rep. 2020;10(1):12998.

46. Bicknell B, Liebert A, Johnstone D, Kiat H. Photobiomodulation of the microbiome: implications for metabolic and inflammatory diseases. Lasers Med Sci. 2019;34(2):317-27.

47. Bicknell B, Liebert A, McLachlan CS, Kiat H. Microbiome Changes in Humans with Parkinson's Disease after Photobiomodulation Therapy: A Retrospective Study. J Pers Med. 2022;12(1).

48. Kang M, Jo J, Shin H, Kang HW. Therapeutic potential of wavelength-dependent photobiomodulation on gut inflammation in an in vitro intestinal model. J Photochem Photobiol B. 2025;269:113201.

49. Iaccarino HF, Singer AC, Martorell AJ, Rudenko A, Gao F, Gillingham TZ, et al. Gamma frequency entrainment attenuates amyloid load and modifies microglia. Nature. 2016;540(7632):230-5.

50. Chan D, Suk HJ, Jackson BL, Milman NP, Stark D, Klerman EB, et al. Gamma frequency sensory stimulation in mild probable Alzheimer's dementia patients: Results of feasibility and pilot studies. PLoS One. 2022;17(12):e0278412.

51. Saltmarche AE, Naeser MA, Ho KF, Hamblin MR, Lim L. Significant Improvement in Cognition in Mild to Moderately Severe Dementia Cases Treated with Transcranial Plus

Intranasal Photobiomodulation: Case Series Report. Photomed Laser Surg. 2017;35(8):432-41.

52. Cassano P, Petrie SR, Mischoulon D, Cusin C, Katnani H, Yeung A, et al. Transcranial Photobiomodulation for the Treatment of Major Depressive Disorder. The ELATED-2 Pilot Trial. Photomed Laser Surg. 2018;36(12):634-46.

53. Liebert A, Bicknell B, Laakso EL, Heller G, Jalilitabaei P, Tilley S, et al. Improvements in clinical signs of Parkinson's disease using photobiomodulation: a prospective proof-of-concept study. BMC Neurol. 2021;21(1):256.