



Clinician-observed Psychosocial Stress as a Potential Modulator of Functional Durability Following Multidomain Improvement in Progressive Multiple Sclerosis: A Comparative Two-case Report

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Abstract

We report two patients with secondary progressive multiple sclerosis who demonstrated substantial multidomain functional improvement following the Self-organizing Neuro-adaptive Personalized Physiological System, a non-invasive, non-contact, passive-state, hypothesis-generating rehabilitation framework, and subsequently experienced complete functional regression at follow-up. Both patients shared a defining clinical feature: severe, chronic psychosocial stressors that were clinician-observed as persistent and apparently unresolvable throughout and beyond the intervention period. Case 1 (SH, 36F) received 20 sessions, with the Comprehensive Disability and Functional Status Scale (CDFSS) score improving from 26 to 9 before regressing to 18 at the 24-month follow-up. Case 2 (MH, 34M) received 19 sessions, with the CDFSS score improving from 32 to 11 before regressing to 24 at follow-up. In both cases, psychological-behavioral-cognitive domain scores regressed before or concurrently with the decline in physical domain scores. In contrast, four non-relapsing cases from the same observational series did not exhibit similar regression, suggesting that clinician-observed chronic psychosocial burden may be associated with reduced functional durability in progressive multiple sclerosis. This observation is strictly hypothesis-generating.

Keywords: Progressive multiple sclerosis, psychosocial stress; functional durability, psychological-behavioral-cognitive domain, Self-organizing Neuro-adaptive Personalized Physiological System, hypothesis-generating

Introduction

Durable functional improvement in progressive multiple sclerosis (MS) is uncommon, and the factors that determine whether initial rehabilitation gains are sustained or lost remain poorly understood (1,2). Chronic psychosocial stress is a recognized modulator of immune function, autonomic regulation, and neurological outcomes in MS (3,4). Stressful life events have been associated with an increased risk of relapse in relapsing MS (3); however, the relationship between persistent psychosocial burden and the durability of functional

recovery following multidomain rehabilitation has not been systematically investigated.

We present two cases of secondary progressive MS (SPMS) in which substantial multidomain functional improvement was followed by complete functional regression at follow-up. A defining clinical feature observed in both cases was the presence of severe, chronic psychosocial stressors that appeared persistent and apparently unresolvable throughout and beyond the intervention period. In both cases, regression in the psychological-behavioral-cognitive (PBC) domain preceded

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or paralleled the decline in physical domain function. This comparative observation is presented strictly as a hypothesis-generating clinical signal that requires prospective validation.

Case Report

Written informed consent was obtained from both patients for the publication of this case report, including the accompanying clinical data.

SONAPPS Intervention Description

The Self-organizing Neuro-adaptive Personalized Physiological System (SONAPPS) is a non-invasive, non-pharmacological, non-contact, device-free, hypothesis-generating rehabilitation framework. Throughout all sessions, patients remained in a fully passive resting state, either seated or supine, with no volitional movement, physical exercise, or active behavioral participation required at any time. The practitioner was positioned approximately 1-1.5 m from the patient without making physical contact. Sessions were operationally guided by individualized, patient-specific contextual reference materials compiled from available clinical and biographical information, together with practitioner physiological self-monitoring. Each session lasted approximately 90-120 min. Preliminary clinical observations using this framework have been described in three previously published case reports (5-8). A Template for Intervention Description and Replication (TIDieR)-compliant protocol description is in preparation; the present description represents the most detailed operational account currently available. SONAPPS is presented as a hypothesis-generating framework rather than a validated therapeutic modality.

Outcome Measures

The Comprehensive Disability and Functional Status Scale (CDFSS) is a clinician-administered observational scale developed for use within the SONAPPS framework. It is scored from 0 (no disability) to 50 (maximum disability) across three subscales: physical-structural-functional (PSF; 0-25), PBC (0-15), and functional integration (0-10). The CDFSS has not undergone formal psychometric validation, and no established thresholds for the minimal clinically important difference have been determined. In these cases, it was used as a descriptive within-case monitoring instrument rather than as a validated inferential outcome measure. Lower and upper limb strength were assessed using the Medical Research Council (MRC) scale. Bladder dysfunction was evaluated based on patient self-report at each session and follow-up contact; however, no validated bladder-specific instrument was administered. Psychosocial stressors were characterized through structured clinical observation and interviews conducted at each session, and no validated psychometric instrument (e.g., the Perceived Stress Scale) was used. The Expanded Disability Status Scale (EDSS) was not assessed in either case because both patients were

managed retrospectively before the clinic's current prospective assessment protocol was established.

Case 1 (SH) 36-year-old Woman with SPMS

SH first presented in November 2022 with an 18-year history of SPMS diagnosed according to the McDonald criteria. She ambulated with two canes and presented with severe bilateral lower limb weakness (MRC grade 0-1/5), patient-reported bladder dysfunction, fatigue, and a prominent PBC domain burden. She had not received disease-modifying therapy during the preceding year. A defining clinical feature observed by the clinician was the presence of severe, chronic psychosocial stressors that appeared persistent and apparently unresolvable, remaining present at baseline and throughout the intervention and follow-up periods. These stressors were not quantified using validated instruments, and their characterization was based solely on structured clinical observation.

SH underwent 20 SONAPPS sessions between February and June 2023 (approximately 150 days). No changes in medication occurred during the intervention period. The post-intervention assessment was performed after the completion of all 20 sessions.

Outcomes are summarized in Table 1. The CDFSS score improved from 26 to 9 (-65.4%). Lower limb strength improved from MRC grade 0-1/5 to 3/5. The Romberg sign was no longer elicited at the post-intervention assessment. Patient-reported bladder dysfunction resolved according to the patient's report. The PBC domain score improved from 36 to 24. At the 24-month follow-up (June 2025), complete functional regression was documented, with the CDFSS score worsening to 18 and the PBC domain score increasing to 38. Follow-up was conducted through a structured telephone interview, during which the patient reported being unable to return to work and that the psychosocial stressors had persisted.

Case 2 (MH) 34-year-old Man with SPMS

MH first presented in September 2024 with a 14-year history of SPMS. He was wheelchair-dependent and presented with bilateral lower limb paralysis (MRC grade 0/5), severe spasticity, patient-reported bladder dysfunction, prominent compulsive behaviors, and a severe PBC domain burden. He had not received disease-modifying therapy during the preceding period. Clinician-observed psychosocial stressors of considerable magnitude, including major financial litigation, family conflict, and complex personal circumstances, were present throughout and beyond the intervention period. These stressors were not assessed using validated instruments.

MH underwent 19 SONAPPS sessions beginning on December 10, 2024 (approximately 150 days). The post-intervention assessment was performed after completion of the final session. Discontinuation of treatment was attributable not to clinical deterioration but to logistical constraints associated with the ongoing psychosocial burden.

Table 1. Comparative clinical profiles and outcomes of cases SH and MH

Parameter	Case SH (36F)	Case MH (34M)
MS type/duration	SPMS/18 years	SPMS/14 years
First presentation	November 2022	September 2024
Intervention	20 sessions, February–June 2023	19 sessions, December 2024–May 2025
Timing of post-intervention assessment	After session 20 (June 2023)	After session 19 (May 2025)
Baseline CDFSS score	26/50	32/50
Post-intervention CDFSS score	9/50 (-65.4%)	11/50 (-65.6%)
Follow-up CDFSS score	18/50 (regression)	24/50 (regression)
Follow-up assessment method	Structured telephone interview (24-month follow-up)	Structured telephone interview (at follow-up)
Baseline MRC lower limb strength	0-1/5, bilateral	0/5, bilateral
Post-intervention MRC lower limb strength	3/5, bilateral	2-3/5, bilateral
Bladder function (patient-reported)	Resolved according to patient self-report	Partially resolved according to patient self-report
Baseline PBC score	36	43
Post-intervention PBC score	24	22
Follow-up PBC score	38 (regression)	38 (regression)
Psychosocial stressors	Severe; clinician-observed as persistent throughout	Severe; clinician-observed as persistent throughout
Pattern of PBC regression	PBC regression preceded physical regression	PBC regression paralleled physical regression

Notes: EDSS was not assessed because these were retrospective cases managed before implementation of the current prospective assessment protocol. Bladder function was evaluated by patient self-report only. Psychosocial stressors were characterized through structured clinical observation without the use of validated assessment instruments. Red shading indicates regression at follow-up

MS: Multiple sclerosis, CDFSS: Comprehensive Disability and Functional Status Scale (0-50; 0=no disability), PSF: Physical-structural-functional subscale (0-25), SPMS: Secondary progressive multiple sclerosis, PBC: Psychological-behavioral-cognitive subscale (0-15); MRC: Medical research council, EDSS: Expanded Disability Status Scale

Outcomes are summarized in Table 1. The CDFSS score improved from 32 to 11 (-65.6%). Lower limb strength improved bilaterally from MRC grade 0/5 to 2-3/5. Spasticity was assessed by the clinician as markedly reduced. Patient-reported bladder dysfunction partially resolved according to the patient's report. Compulsive behaviors were observed by the clinician to be substantially reduced. The PBC domain score improved from 43 to 22. At follow-up, the CDFSS score worsened to 24, and the PBC domain score increased to 38.

Note on MRC Improvement in a Passive-state Framework

The substantial improvements in MRC lower limb scores observed in both cases are clinically noteworthy because SONAPPS does not incorporate volitional movement or active exercise. The proposed mechanism—that restoration of coherence within the spatiotemporal regulatory network may facilitate neural reorganization without direct motor training—remains hypothetical and has not been established. Alternative explanations, including expectancy effects, assessor expectancy bias, natural fluctuation, and non-specific therapeutic influences, cannot be excluded and are explicitly acknowledged as important limitations of this retrospective, unblinded observational report.

Discussion

These two cases demonstrated a convergent pattern of substantial multidomain improvement followed by complete functional regression at follow-up in the context of clinician-observed, severe, and apparently unresolvable psychosocial stressors. In contrast, four non-relapsing cases showed sustained improvement in the presence of partially resolvable psychosocial stressors (Table 2), generating a specific hypothesis that warrants prospective investigation.

We propose that chronic, persistent psychosocial burden may be associated with reduced functional durability following multidomain improvement in progressive MS, potentially by sustaining dysregulation within the PBC domain, which may in turn undermine gains in the PSF domain through cross-domain regulatory interactions (5). This proposed association is descriptive and observational, and no causal or modulatory relationship can be inferred from this report. The proposed mechanism remains speculative and is consistent with, but not supported by, existing evidence that chronic stress influences autonomic function and neurological outcomes in MS (3,4).

Table 2. Comparison with non-relapsing cases in the same observational series				
Case	CDFSS change	Follow-up CDFSS	Follow-up PBC	Psychosocial stressors (clinician-observed)
Case 1 (HY, 52F), SPMS	29→10 (-65.5%)	6 (stable)	24 (stable)	Partially resolvable
Case 2 (SH, 36F), SPMS	26→9 (-65.4%)	18 (regression)	38 (regression)	Persistent
Case 3 (63M), SPMS	43→22 (-48.8%)	37 (stable)	37 (stable)	Partially resolvable
Case 4 (62M), SPMS	41→14 (-65.9%)	12 (stable)	15 (stable)	Partially resolvable
Case 5 (47F), SPMS	35→12 (-65.7%)	14 (stable)	19 (stable)	Partially resolvable
Case 6 (MH, 34M), SPMS	32→11 (-65.6%)	24 (regression)	38 (regression)	Persistent

Note on case selection: Table 2 includes all six consecutive cases managed at the SONAPPS Clinic between 2022 and 2025 for which complete CDFSS and follow-up data were available. No cases were excluded, and case selection was not based on outcomes. The two relapsing cases (SH and MH) and the four non-relapsing cases constitute the complete available dataset for this period

Notes: All six cases represent the complete consecutive dataset from the SONAPPS Clinic for the 2022-2025 study period. Psychosocial stressors were characterized through structured clinical observation without the use of validated assessment instruments. This comparison is strictly observational and hypothesis-generating; therefore, no causal inferences can be drawn

CDFSS: Comprehensive Disability and Functional Status Scale, PBC: Psychological-behavioral-cognitive, SPMS: Secondary progressive multiple sclerosis, SONAPPS: Self-organizing Neuro-adaptive Personalized Physiological System

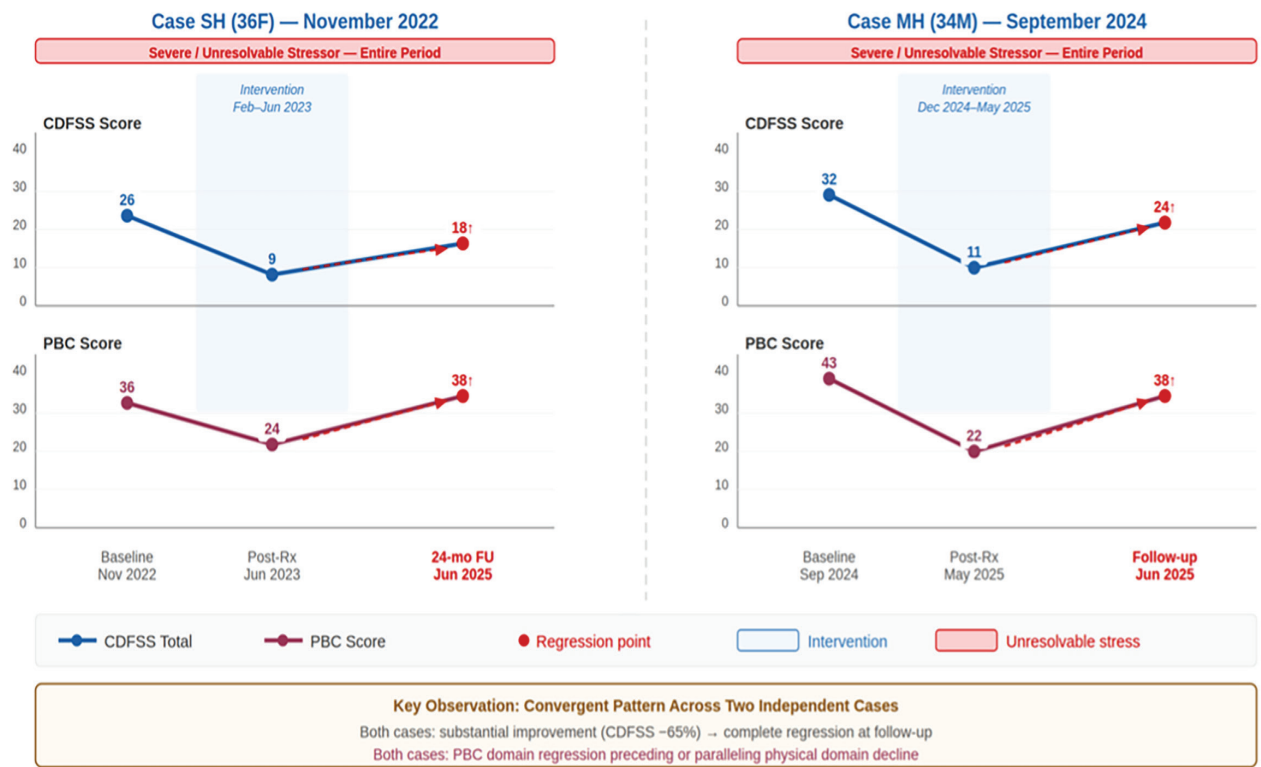


Figure 1. Comparative clinical trajectories of Cases SH and MH. The upper panel shows the CDFSS total score at three time points: baseline (before session 1), post-intervention (performed after completion of the final session—session 20 for SH and session 19 for MH), and follow-up. The lower panel shows the PBC domain total score at the corresponding time points. The orange bar indicates clinician-observed persistent psychosocial stressors throughout the observation period, and the shaded region represents the active intervention period. The post-intervention assessment was performed only after the intervention had been completed, not during the intervention period. Both panels illustrate a convergent observational pattern of substantial improvement followed by regression, with PBC domain regression preceding or paralleling the decline in physical domain function. No causal inference is implied

CDFSS: Comprehensive Disability and Functional Status Scale, PBC: Psychological-behavioral-cognitive

A notable feature in both relapsing cases was that PBC domain scores regressed before or concurrently with the decline in physical domain function (Figure 1). Whether this temporal pattern reflects a causal sequence, a shared response to ongoing psychosocial burden, or coincidence cannot be determined from these observations. Accordingly, the PBC-first regression pattern is presented as a descriptive observation rather than evidence of an underlying mechanism.

The natural progression of SPMS must be considered the primary explanation for the observed regression in both cases. SPMS is characterized by the progressive accumulation of disability (1,2). Without EDSS assessments performed by an independent neurologist, it is not possible to distinguish whether the observed regression was attributable to the natural disease course, the withdrawal of any potential treatment effect, the influence of psychosocial burden, or a combination of these factors. This discussion is not intended to minimize this alternative explanation, which remains at least as plausible as, and potentially more plausible than, the psychosocial stress hypothesis based on the available data.

The absence of EDSS, the Timed 25-Foot Walk, the Nine Hole Peg Test, the Symbol Digit Modalities Test, and validated psychosocial instruments (e.g., the Perceived Stress Scale) represents the most important methodological limitation of this study. Both cases were managed retrospectively before the establishment of the current prospective assessment protocol, which incorporates these measures from the outset (6-8). Therefore, all clinical observations should be interpreted as descriptive rather than inferential.

Conclusion

We report two patients with SPMS and clinician-observed persistent psychosocial burden who demonstrated nearly identical patterns of multidomain improvement followed by complete functional regression at follow-up. In contrast to four non-relapsing cases from the same observational series, these findings are consistent with the hypothesis that persistent psychosocial burden may be associated with reduced functional durability following rehabilitation in progressive MS. However, this association is observational, uncontrolled, and hypothesis-generating, and it requires prospective validation before any clinical conclusions can be drawn. Prospective studies incorporating validated psychosocial instruments, EDSS assessments performed by independent neurologists, standardized functional outcome measures, and longitudinal follow-up are warranted.

The principal limitations of this report include the following: (1) a retrospective two-case observational design that does not permit causal inference; (2) the absence of EDSS assessments performed by an independent, certified neurologist; (3) the use of a clinician-developed, non-validated outcome measure

(CDFSS) for descriptive tracking; (4) clinician-observed characterization of psychosocial stressors without validated assessment instruments; (5) assessment of bladder dysfunction based solely on patient self-report; (6) the inability to exclude the natural progression of disease; (7) non-blinded outcome assessment; (8) the absence of a TiDieR-compliant protocol description (currently in preparation); and (9) a small sample size, which precludes generalization.

Ethics

Informed Consent: Written informed consent was obtained from both patients for the publication of this case report and the accompanying clinical data.

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During the preparation of this manuscript, the authors used Claude (Anthropic) to assist with drafting and language editing. The authors reviewed and edited all generated content and take full responsibility for the final manuscript.

Footnotes

Authorship Contributions

Surgical and Medical Practices: H.N., Concept: H.N., A.R., Design: H.N., S.N., Data Collection or Processing: H.N., S.N., Analysis or Interpretation: H.N., Literature Search: H.N., A.R., S.N., Writing: H.N., A.R., S.N.

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