BRAINIACS
BRAIN IMAGING AND COMPUTING SCIENCES

2025 Volume 6
Issue 3 Edoc B3D757EF9

From Play to Precision Care: Clinical Telegaming Biomarkers to Evaluate Medication Efficacy for Improving Multiple Sclerosis Patients' Quality of Life*

Kento Shigyo†

Abstract

Multiple sclerosis (MS) is a chronic autoimmune disease that affects motor, sensory, cognitive, and social functioning, often diminishing patients' quality of life. Disease-modifying therapies (DMTs) aim to slow disease progression, yet evaluating their real-world effectiveness remains challenging due to the limitations of brief, clinic-based assessments. This research proposes the use of clinical telegaming as a home-based assessment platform to generate digital biomarkers reflecting motor-sensory and social-behavioral functioning in everyday contexts. By capturing fine-grained gameplay interaction data, the proposed system aims to support precision care by enabling timely, ecologically valid evaluation of medication efficacy and quality-of-life outcomes for individuals living with MS.

Keyphrases

Multiple sclerosis, clinical telegaming, digital biomarkers, precision care, quality of life.

Contents

Introduction

Multiple sclerosis (MS) is a chronic autoimmune disease affecting motor, sensory, social, and cognitive functioning (Friedrich 2023), often diminishing independence and quality of life (Gómez-Melero et al. 2024). Disease-modifying therapies (DMTs) are pharmacologic treatments that aim to slow progression and support functional recovery of MS (Goodin et al. 2002). However, determining which medications work best for individual patients and monitoring their effects over time remains challenging (Pathak 2023). Moreover, current assessments for DMTs, which are typically brief, clinic-based evaluations, provide valuable insights into motor performance but rarely capture the social, affective, and cognitive dimensions that critically shape quality of life, underscoring the importance of evaluating daily functioning holistically. The World Health Organization defines quality of life as "an individual's perception of their position in life in the context of the culture and value systems in which they live, and in relation to their goals, expectations, standards, and concerns" (WHOQOL Group 1994).

DMTs are among the most expensive chronic therapies in medicine, with annual costs often exceeding USD $70,000–$90,000 per patient (Hartung 2021). When a medication is ineffective or discontinued due to adverse effects, continued treatment represents significant financial waste—costs that can accumulate to tens of thousands of dollars within just a few months. Beyond economic burden, prolonged exposure to ineffective drugs increases risks of adverse effects, reduces adherence, and undermines patient trust. These challenges underscore the need for timely, objective, and ecologically valid indicators of treatment efficacy, enabling clinicians to make informed, cost-efficient decisions.

Clinical telegaming (Taswell 2010b; Lockery et al. 2011; Xu et al. 2015) has been recognized as a potential platform to provide such indicators by capturing real-world performance metrics that can support earlier and more accurate risk–benefit analysis. Additionally, it provides a non-stigmatizing, game-based platform that integrates naturally into everyday life, emphasizing quality of life rather than mental health labeling, that is an important consideration in MS care.

To this end, we propose applying the established framework of *clinical telegaming* to evaluate treatment efficacy and quality of life in MS. Clinical telegaming in our study will consists of structured, interactive games delivered at home via augmented displays, mixed-reality systems, or repurposed commercial video games. By capturing motor-sensory and social-interaction metrics during naturalistic, engaging tasks in clinical telegaming, we aim to generate and extract digital biomarkers that complement existing clinical assessments for DMTs. This approach does not replace clinician expertise; rather, it aims to

*Report presented 2025-10-09, Guardians 2025, 4th BHAVI Guardians Conference.
†Correspondence to kshigyo@bhavi.us.

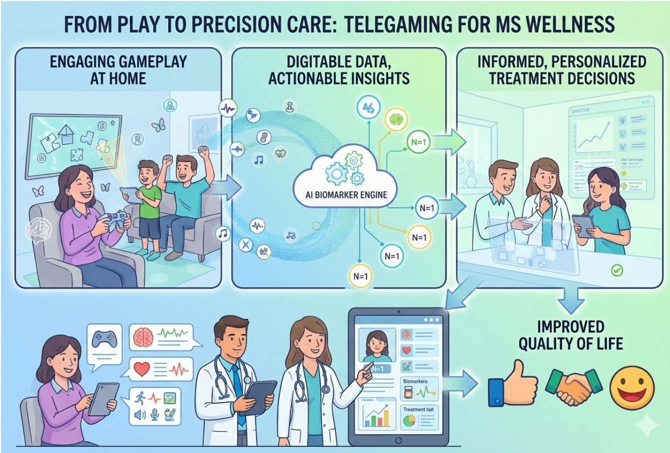

Figure 1: Overview of the proposed clinical telegaming framework for precision care in multiple sclerosis. Home-based gameplay captures motor, sensory, and social interaction data, which are transformed into digital biomarkers to support individualized (N-of-1) treatment decisions and improve quality of life.

provide richer, continuous evidence to support precision care.

Related Work

This section reviews prior work in two domains relevant to our system: (1) digital biomarkers, including their definition, clinical motivations, and methods of collection, and (2) clinical telegaming, a growing approach for remote assessment and rehabilitation. Together, these strands of research highlight opportunities for leveraging game-derived behavioral data as digital biomarkers for monitoring disease progression and treatment response in Multiple Sclerosis (MS).

Digital Biomarker: Food and Drug Administration and the National Institutes of Health define biomarker as "A defined characteristic that is measured as an indicator of normal biological processes, pathogenic processes, or biological responses to an exposure or intervention, including therapeutic interventions" (Group et al. 2016). In addition, a number of categories of biomarkers have defined according to their purposes and applications while some overlaps: 1) diagnostic biomarker, 2) monitoring biomarker, 3) pharmacodynamic/response biomarker, 4) predictive biomarker, 5) prognostic biomarker, 6) safety biomarker and 7) susceptibility/risk biomarker. These biomarkers serve critical functions across diagnosis, disease monitoring, treatment decision-making, and risk stratification, thereby forming the foundation for precision care. This is especially important for complex and multidimensional conditions such as Multiple Sclerosis.

However, collecting these biomarkers can be time-consuming when it requires the direct involvement of physicians or other healthcare professionals (Dillenseger et al. 2021). Moreover, most biomarker assessments are confined to brief clinical visits, offering only snapshot observations that fail to capture patients' daily experiences, fluctuations in symptoms, and social dimensions such as quality of life. A growing body of research has highlighted that clinic-based assessments overlook the lived experiences of patients and often do not reflect their real-world functioning (Shiffman et al. 2008). These limitations have motivated a shift toward digital biomarkers, which enable continuous and ecologically valid data collection in patients' everyday environments.

Digital biomarker refers to "objective, quantifiable physiological and behavioral data that are measured and collected by digital devices" (Dillenseger et al. 2021). Digital biomarkers are typically collected through sensors embedded in smartphones, wearables, and other connected devices, capturing physiological signals (e.g., heart rate, gait characteristics) and behavioral patterns (e.g., mobility, interaction behaviors) in real-world environments (Coravos et al. 2019). These passive and active monitoring approaches allow continuous, longitudinal assessment with low burden on patients or clinicians.

Clinical Telegaming: While most digital biomarkers are derived from sensors or mobile devices, an emerging direction is the use of interactive gameplay data, which is often referred to as clinical telegaming, to capture fine-grained motor, cognitive, and behavioral signals in remote settings. Such game-derived measures offer a promising complementary pathway for developing digital biomarkers that reflect patients' functional abilities in an ecologically valid and engaging format.

Early work on clinical telegaming focused on infrastructure and resource management. Taswell (2010b) integrated telegaming registries into the broader Nexus-PORTAL-DOORS-Scribe (NPDS) framework (Taswell 2007; Taswell 2010a; Dutta et al. 2020), enabling metadata management for telecare and therapeutic interventions. Lockery et al. (2011) extended this effort through the Clinical Telegaming System (CTGS), supporting both clinic-based and home-based telerehabilitation. These systems provide crucial infrastructure but do not address patient-centered outcome evaluation.

Subsequent research demonstrated telegaming's therapeutic potential for neurological disorders. Xu et al. (2015) developed a web-enabled platform to evaluate multisensory integration and responses to auditory and visual stimuli in Parkinson's disease. Broadly, telerehabilitation studies report improvements in motor and cognitive outcomes (Maggio et al. 2024), enhanced adherence and quality of life (Dhamija et al. 2025; Sharma et al. 2024), and safe long-term use across neurological populations (Peretti et al. 2017).

For MS specifically, emerging work has explored the use of augmented reality–based exercise games for home and clinic-based rehabilitation, with expert workshops identifying design guidelines for safety, patient engagement, and clinical relevance (Adiwangsa et al. 2025).

Collectively, prior studies highlight the feasibility of clinical telegaming for rehabilitation and sensory evaluation. However, no existing work applies telegaming-derived biomarkers to evaluate medication efficacy or to systematically assess quality-of-life dimensions across motor, cognitive, emotional, and social domains. Furthermore, integration of telegaming biomarkers into precision-care frameworks for MS remains unexplored.

Research Plan

Research Goals and Rationale: This project aims to develop a clinically validated, home-based telegaming system capable of generating digital biomarkers that support precision care for individuals living with MS. The planned research will characterize both motor–sensory and social–behavioral functioning through structured gameplay. Motor assessments will examine limb coordination, balance, movement smoothness, and reaction speed, while social–behavioral assessments will focus on cooperative play, turn-taking, and caregiver–patient coordination. These domains are central to daily functioning yet remain difficult to measure in routine clinical visits. A key goal of this research is to link these behavioral signals to individual treatment trajectories, enabling digital biomarkers to serve as indicators of medication effectiveness at the level of 'N-of-1' precision care.

System Design and Co-Design Phase: The first phase of the research will involve a collaborative co-design process with neurologists, MS specialists, patients, and caregivers. This phase will define the clinical requirements, safety considerations, and design constraints necessary for creating gameplay tasks that are both engaging and clinically meaningful. Co-design workshops will guide the creation of early prototypes and interaction concepts, ensuring that the system reflects the needs and lived experiences of its target users. The resulting prototypes will undergo iterative refinement to achieve a stable and usable system architecture suitable for further evaluation.

Biomarker Development and Technical Approach: Following the design phase, the project will focus on transforming gameplay telemetry into interpretable digital biomarkers. This work will include the development of algorithms to extract reaction latencies, coordination measures, temporal movement features, and indicators of cooperative behavior. Special attention will be given to creating features that are robust to variations in home environments and consumer-grade hardware. This technical component will produce the computational foundation required for examining how behavioral patterns relate to medication response and overall patient well-being.

Feasibility and Validation Studies: After the system reaches functional stability, feasibility studies will be conducted in real home environments to assess usability, safety, patient acceptance, and data fidelity. These studies will provide critical insights into the ecological validity of the system and reveal potential barriers to long-term adoption. Building on feasibility results, the project will conduct preliminary validation by comparing telegaming-derived biomarkers with established in-clinic motor assessments and caregiver reports. This phase will evaluate reliability, convergent validity, and responsiveness to treatment-related changes, laying the groundwork for subsequent large-scale clinical evaluation.

Three-Year Development Timeline: The development plan is structured across three years. The first year will focus on co-design activities and the creation of an initial prototype suitable for laboratory testing. The second year will emphasize algorithmic refinement and home-based feasibility testing with MS patients, examining engagement, adherence, and data quality under real-world conditions. The third year will involve preliminary clinical validation, establishing the relationship between biomarker trajectories and treatment outcomes, and producing guidelines for integrating the system into clinical workflows. By the end of the project period, the goal is to deliver a scientifically grounded, clinically meaningful system that advances precision care and supports continuous monitoring in everyday environments.

Conclusion

This work outlines a research agenda for developing a clinically validated telegaming system that captures real-world motor, sensory, and social–behavioral performance to support precision care for people living with MS. By shifting assessment beyond the constraints of brief clinical visits and into patients' daily environments, the proposed approach has the potential to reveal aspects of functioning that are not captured by conventional in-clinic tests. The integration of gameplay-derived digital biomarkers offers a pathway toward earlier identification of treatment response, improved monitoring of quality-of-life outcomes, and more informed decisions regarding the continuation or adjustment of costly disease-modifying therapies.

Importantly, this research aims to bridge clinical neuroscience, rehabilitation, and human–computer interaction by positioning telegaming not simply as a rehabilitation tool, but as an assessment modality with ecological validity and patient-centered design at its core. Through co-design, biomarker development, feasibility testing, and preliminary validation, the project seeks to provide a scientifically grounded foundation for future large-scale clinical evaluation.

This work will contribute to a paradigm in which continuous, context-rich behavioral data can complement traditional clinical measures, empowering clinicians with actionable insights and offering patients engaging, non-stigmatizing ways to participate in their own care. By advancing methods aligned with the *Restore* pathway of the NMSS *Pathways to Cures* roadmap, the proposed system has the potential to enhance therapeutic decision-making, reduce unnecessary healthcare expenditure, and improve long-term quality of life for individuals with MS.

Citation

Brainiacs 2025 Volume 6 Issue 3 Edoc B3D757EF9
Title: "From Play to Precision Care: Clinical Telegaming Biomarkers to Evaluate Medication Efficacy for Improving Multiple Sclerosis Patients' Quality of Life"
Authors: Kento Shigyo
Dates: created 2025-09-16, presented 2025-10-09, updated 2025-12-17, published 2025-12-17

Contact: kshigyo@bhavi.us
NPDS: LINKS/Brainiacs/Shigyo2025FPTPC
DOI: 10.48085/B3D757EF9

Affiliations

Brain Health Alliance Virtual Institute, Ladera Ranch, California, USA.

References

[1] M. Adiwangsa, H. Suominen, and P. Sweetser. "Can Augmented Reality Head-Mounted Display Exergames Support the Management of Multiple Sclerosis at Home? Workshop Discussions with Researchers and Experts with Lived Experience of MS." In: *Proceedings of the Extended Abstracts of the CHI Conference on Human Factors in Computing Systems*. 2025, pp. 1–7 (cited p. 2).

[2] A. Coravos, S. Khozin, and K. D. Mandl. "Developing and adopting safe and effective digital biomarkers to improve patient outcomes." *NPJ digital medicine* 2.1 (2019), p. 14 (cited p. 2).

[3] R. K. Dhamija, A. Saluja, D. Garg, S. Chauhan, et al. "Teleneurorehabilitation and motor and nonmotor symptoms and quality of life in Parkinson disease: the TELEPARK randomized clinical trial." *JAMA neurology* 82.4 (2025), pp. 376–383 (cited p. 2).

[4] A. Dillenseger, M. L. Weidemann, K. Trentzsch, H. Inojosa, et al. "Digital biomarkers in multiple sclerosis." *Brain sciences* 11.11 (2021), p. 1519 (cited p. 2).

[5] S. Dutta, K. Uhegbu, S. Nori, S. Mashkoor, S. K. Taswell, and C. Taswell. "DREAM Principles from the PORTAL-DOORS Project and NPDS Cyberinfrastructure." In: *2020 IEEE 14th International Conference on Semantic Computing (ICSC)*. IEEE, Feb. 4, 2020, pp. 211–216. DOI: 10.1109/ICSC.2020.00044. URL: https://www.portaldoors.org/pub/docs/ICSC2020PDPDREAM191222.pdf (cited p. 2).

[6] A. Friedrich. *The Multiple Sclerosis Companion*. Springer, 2023 (cited p. 1).

[7] S. Gómez-Melero, J. Caballero-Villarraso, B. M. Escribano, A. Galvao-Carmona, I. Túnez, and E. Agüera-Morales. "Impact of Cognitive Impairment on Quality of Life in Multiple Sclerosis Patients—A Comprehensive Review." *Journal of Clinical Medicine* 13.11 (2024), p. 3321 (cited p. 1).

[8] D. S. Goodin, E. Frohman, G. Garmany, J. Halper, W. Likosky, F. Lublin, et al. "Disease modifying therapies in multiple sclerosis." *Neurology* 58.2 (2002), pp. 169–178 (cited p. 1).

[9] F.-N. B. W. Group et al. "BEST (biomarkers, EndpointS, and other tools) resource [internet]" (2016) (cited p. 2).

[10] D. M. Hartung. "Economics of multiple sclerosis disease-modifying therapies in the USA." *Current Neurology and Neuroscience Reports* 21.7 (2021), p. 28 (cited p. 1).

[11] D. Lockery, J. F. Peters, and C. Taswell. "CTGaming: A Problem-Oriented Registry for Clinical TeleGaming Rehabilitation and Intervention." *Journal of Emerging Technologies in Web Intelligence* 3.1 (Feb. 2011), pp. 28–37. DOI: 10.4304/JETWI.3.1.28-37 (cited pp. 1, 2).

[12] M. G. Maggio, F. Baglio, F. Arcuri, F. Borgnis, et al. "Cognitive telerehabilitation: An expert consensus paper on current evidence and future perspective." *Frontiers in Neurology* 15 (2024), p. 1338873 (cited p. 2).

[13] L. Pathak. "Personalized treatment for multiple sclerosis: the role of precision medicine." *Neurology Letters* 2.1 (2023), pp. 30–34 (cited p. 1).

[14] A. Peretti, F. Amenta, S. K. Tayebati, G. Nittari, and S. S. Mahdi. "Telerehabilitation: review of the state-of-the-art and areas of application." *JMIR rehabilitation and assistive technologies* 4.2 (2017), e7511 (cited p. 2).

[15] N. Sharma, A. Yadav, M. Kaur, P. Kumar, S. Kaur, G. Kapoor, and M. Verma. "Group tele-rehabilitation improves quality of life among subjects with Parkinson's disease: A two arm non-parallel non-randomized clinical trial." *Parkinsonism & Related Disorders* 121 (2024) (cited p. 2).

[16] S. Shiffman, A. A. Stone, and M. R. Hufford. "Ecological momentary assessment." *Annu. Rev. Clin. Psychol.* 4.1 (2008), pp. 1–32 (cited p. 2).

[17] C. Taswell. "DOORS to the Semantic Web and Grid with a PORTAL for Biomedical Computing." *IEEE Transactions on Information Technology in Biomedicine* 12.2 (2 Mar. 2007). In the Special Section on Bio-Grid published online 3 Aug. 2007, pp. 191–204. ISSN: 1089-7771. DOI: 10.1109/TITB.2007.905861 (cited p. 2).

[18] C. Taswell. "A Distributed Infrastructure for Metadata about Metadata: The HDMM Architectural Style and PORTAL-DOORS System." *Future Internet* 2.2 (2010), pp. 156–189. ISSN: 1999-5903. DOI: 10.3390/FI2020156. URL: https://www.mdpi.com/1999-5903/2/2/156/ (cited p. 2).

[19] C. Taswell. "A New PDS PORTAL for Clinical TeleGaming Rehabilitation and Intervention." In: *2010 IEEE International Conference on Bioinformatics and Biomedicine Workshops (BIBMW)*. IEEE, Dec. 2010. DOI: 10.1109/BIBMW.2010.5703953 (cited pp. 1, 2).

[20] WHOQOL Group. "Development of the WHOQOL: Rationale and current status." *International Journal of Mental Health* 23.3 (1994), pp. 24–56. ISSN: 1557-9328. DOI: 10.1080/00207411.1994.11449286 (cited p. 1).

[21] L. Xu, S. Loh, and C. Taswell. "Web-Enabled Software for Clinical Telegaming Evaluation of Multisensory Integration and Response to Auditory and Visual Stimuli." In: *Neural Engineering (NER), 2015 7th International IEEE/EMBS Conference on*. IEEE, Apr. 2015, pp. 739–742. DOI: 10.1109/NER.2015.7146729 (cited pp. 1, 2).

