Final version available at: https://www.nature.com/articles/s44220-025-00482-8

Digital Cognitive Twins in mental health

P. Murali Doraiswamy[1] ,

Jon Andoni Duñabeitia[2],

Carlos Rodriguez[3],

Davangere P. Devanand[4]

[1] Neurocognitive Disorders Program, Duke University School of Medicine and Duke Institute for Brain Sciences, Durham, NC, United States

[2] Centro de Investigación Nebrija en Cognición (CINC), Nebrija University, Madrid, Spain

[3] CogniFit Inc., San Francisco, CA, United States

[4] Division of Geriatric Psychiatry, New York State Psychiatric Institute and Department of Psychiatry, Columbia University Irving Medical Center, New York, NY, United States

Correspondence:

Jon Andoni Duñabeitia, PhD

jdunabeitia@nebrija.es

Cognitive health is vital for human success and wellbeing. However, cognitive dysfunction is a common feature across various mental health disorders across the lifespan. Age-related cognitive dysfunction, cognitive impairment associated with mental health conditions, as well as the disorders such as MCI and dementia remain major threats, with no effective preventive treatments available. Epidemiologic studies suggest that up to 40% of the risk for age-related dementias could potentially be prevented or delayed through lifestyle, behavioral and medical risk modification[1]. Consistent with this hypothesis are data showing that age-specific dementia rates have declined over the last several decades in the United States and Europe, likely influenced by factors such as better education and vascular risk reduction[2].

There is enormous public interest in computerized cognitive skills training to enhance one's performance and prevent age-related decline as well as psychopathology-related cognitive dysfunction[3]. While many early interventions yielded only modest, task-specific improvements, there have been an increasing number of rigorous randomized controlled clinical trials in conditions such as MCI and aging showing robust results[4,5]. In addition, computerized brain training-based "digital therapeutics" have been cleared by the US Food and Drug Administration for the treatment of ADHD and major depressive disorder, and similar actions are underway in MCI. Despite such progress, limitations remain such as high attrition rates, low engagement, lack of personalization and suboptimal transfer to everyday functions[6].

Rapid advances in artificial intelligence (AI) and big data, Digital Twins, multimodal interfaces, and wearables are reshaping not only cognitive research, but also how behavioral interventions can be delivered and personalized[7]. For example, a Digital Twin map of a person's cognitive trajectory combined with a simulated 3D model of cortical neurodegeneration may allow a clinician to offer more personalized predictions or prescriptions for a patient at risk for Alzheimer's disease. In this comment, we propose a framework to integrate these developments to improve cognitive training research.

Towards personalized and integrated cognitive training

Historically, brain training was often hyped and marketed as a standalone, failing to integrate the links between cognition, mental health, and physical well-being. Modern computerized cognitive interventions must embrace a broader, more integrative framework to address the full continuum of brain health[5]. This shift leverages real-time user-generated data and synthetic data-generation tools for robust e-health interventions. In a world of stressors and disturbed sleep and rising anxiety, depression, and cognitive decline, new AI-driven systems must be designed to dynamically adapt and personalize protocols to maximize engagement and effectiveness[4].

While some data suggests even unsupervised computerized cognitive training (CCT) can yield meaningful improvements without intensive professional oversight[8], medical oversight is essential for clinical indications. Moreover, meta-analytic findings show personalized interventions produce better outcomes than standardized approaches[9], suggesting sustained improvements in global cognition and daily functioning may be possible with this approach.

The exponential growth in wearables offers an opportunity to embed cognitive training into daily life. Smartwatches, biometric sensors, and trackers feed AI systems that modulate tasks dynamically. If heart rate spikes due to stress, the system could in theory

switch from a demanding working-memory task to a relaxation module, boosting adherence and cognitive impact. Yet true integration goes beyond mere reactivity.
A holistic model would embed cognitive training alongside nutritional guidance, physical activity, and mental health support. Data streams from all these domains would tailor the sequence and complexity of CCT tasks. “Smart scheduling” hinges on AI-driven analytics that link seemingly disparate data, yielding actionable inferences within an integrated framework. Nevertheless, systematic cost-effectiveness evaluations emphasize weighing added interventions (e.g., nutrition or mental health support) against potential benefits, particularly for irregular users requiring additional resources.

Digital Cognitive Twins for predictive cognitive modeling

A Digital Cognitive Twin (DCT) is a real-time computational model of an individual's cognitive state, integrating multimodal data. Through machine learning and AI, the DCT updates to reflect ongoing changes in cognition, enabling personalized predictions, interventions and data-driven insights into cognitive processes and health. We envision a DCT schema that dynamically predicts each user’s daily cognitive needs and state, continuously updating with real-time data. In parallel with the “Medical Digital Twin” concept[10], that is, a dynamic digital replica encapsulating an individual’s biological systems, the DCT integrates wearable metrics and cognitive assessments to enable early detection, personalized interventions, and proactive disease prevention strategies—fully aligning with the goals of preemptive medicine.

Daily interactions would refine predictions, factoring in brain conditions, user preferences, stress levels, or sleep deprivation. Late-day stress might prompt the DCT to shift schedules or introduce calming exercises, while calmer mornings might allow more demanding tasks. This personalization evolves alongside the user’s changing circumstances, continually recalibrating cognitive demands.

From an implementation standpoint, we believe that establishing a baseline over 1-2 weeks is sufficient to let the system capture behavioral, physiological, and cognitive patterns and tailor initial interventions. Afterward, as new data accumulate, the AI-driven DCT continuously refines itself with minimal extra user effort. Clinicians receive succinct, actionable insights via a streamlined dashboard. Yet, practical deployment across heterogeneous healthcare settings requires careful attention to several enabling conditions. These include robust digital infrastructure, secure and interoperable integration with electronic health records, and clearly defined data governance models that address ownership, consent, and cross-provider sharing. Dedicated training programs for healthcare professionals will also be essential to ensure proper interpretation and use of AI-generated cognitive insights. Moreover, to guarantee equitable access, design considerations must proactively accommodate digitally excluded populations (e.g., older adults, individuals with limited digital literacy, persons lacking reliable internet access) through inclusive user interfaces, optional hybrid delivery modes, and embedded support systems. This would ensure that while the DCT might use sophisticated machine learning, front-line workflows remain user-friendly and accessible for providers and individuals.

Validating the clinical efficacy and safety of such dynamically evolving systems will also require novel methodological approaches. While traditional randomized clinical trials and real-world evidence remain foundational, it is equally important to consider adaptive methodologies that capture dynamic intervention effects in real time. Embedded mechanisms like micro-randomized trials (MRTs) and just-in-time adaptive interventions (JITAIs) enable real-time assessment of incremental changes in intervention efficacy[11]. Additionally, digital audit trails that log every model update and its rationale offer a way to maintain transparency and regulatory traceability. This way, outcome metrics must extend beyond prediction accuracy to include algorithmic stability, fairness across subgroups, and longitudinal consistency. Thus, adaptive AI-based Digital Twins must be conceived as complex, self-adjusting systems that require not only socio-ethical robustness but also transparent technical optimization.

Multimodality: expanding the scope of cognitive engagement

Our brains are inherently multimodal, integrating information from vision, hearing, touch, proprioception, and other sensory channels, in addition to intrinsic thoughts, feelings and plans. A critical limitation of many existing cognitive training programs is their narrow approach to interaction with just one screen. Multiple cognitive functions could be targeted within the same training session by including voice devices and leveraging the environment that surrounds the users as a multisensory experience beyond a small screen. Moreover, adding wearable motion sensors and biosensors can make these multimodal environments adaptive. If motion-capture data reveals signs of fatigue, the system can dial down the complexity of tasks. Eye-tracking could detect moments of inattention, prompting brief rest intervals or more straightforward challenges. Such real-time feedback loops would hinge on powerful AI algorithms capable of interpreting data from different modalities and quickly fine-tuning the user's experience.

In line with recent developments in multimodal integration within the medical domain[12], these adaptive platforms could dynamically fuse inputs from imaging, biosensors, and user interactions, creating an intelligent system capable of real-time "sensor fusion" to refine each session's difficulty and focus—ultimately enabling more precise, personalized interventions for the entire spectrum of brain health.

Enhancing adherence through adaptive gamification

Mental health and cognitive enhancement require tools with sustained long-term efficacy. Even the best intervention falters if users abandon it due to boredom or frustration. One of us has previously reported that many marketed digital mental health therapies have large attrition rates once the "honeymoon period" ends[6]. While gamification traditionally uses static point systems or badges, these can quickly lose novelty. Studies on older adults' interaction with AI-driven interventions show that personalization and user-centric features foster sustained engagement, prompting a shift to dynamic, AI-fueled game elements[13]. Over time, the system learns which gamified features spark enthusiasm, keeping the motivational momentum high and bolstering adherence. Promising strategies include adaptive difficulty levels, emotionally responsive feedback, narrative progression mechanics, and rotating micro-challenges tailored to the user's cognitive and affective state. A virtual coach or assistant capable of offering personalized encouragement, guidance, and contextual prompts can further enhance motivation and reduce dropout by fostering a sense of social presence and support. In addition, incorporating short-term goals aligned with user performance trends, regularly generated engagement reports, and surprise-based reinforcement schedules can maintain novelty and emotional investment, while also enabling early intervention to prevent attrition.

As these technologies converge, one can envision an AI-cognitive ecosystem far beyond current capabilities. Each user's DCT would guide personal training and refine the system via aggregated insights. Patterns discovered across large samples will improve each Twin's predictive accuracy in a feedback loop of refinement. With multimodal engagement, advanced gamification, and attention to digital inclusion for older adults, cognitive training could transform from a niche practice into an integral component of healthcare. Figure 1 illustrates this framework, combining real user data, synthetic data from DCTs, and professional guidance.

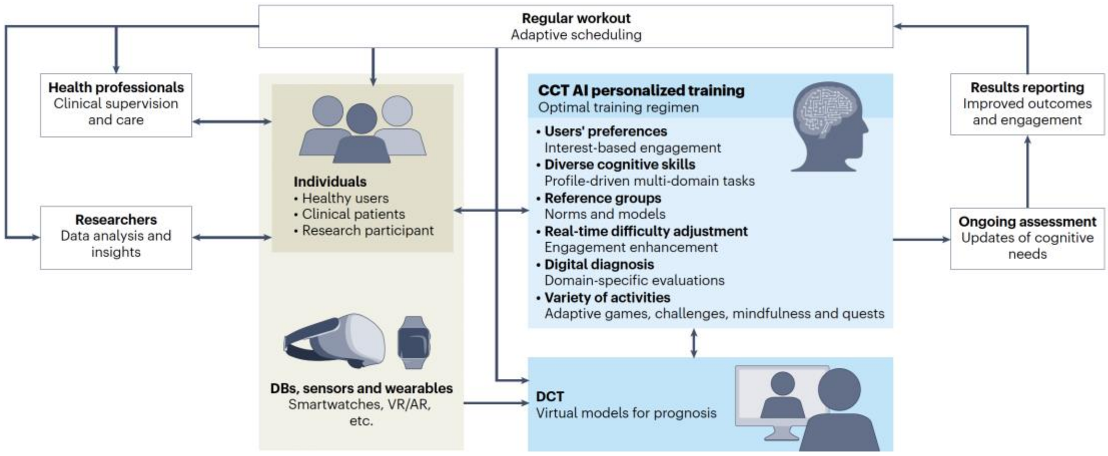

Figure 1. *Illustration of a new framework offering a compelling new standard for preventive brain health.* Jointly proposed by Duke University, Columbia University, and CogniFit Inc., this next-generation cognitive assessment and training platform places each individual and their real-time Digital Cognitive Twin (DCT) at the center of a fully adaptive, AI-driven ecosystem. By continuously integrating data from wearable sensors, clinical inputs, and behavioral insights, the system dynamically adjusts cognitive activities and personalized tasks to meet the user's moment-to-moment cognitive needs.

From an implementation standpoint, a brief initial period of passive/active monitoring calibrates each user's baseline cognitive profile. Once established, a voice assistant can prompt them to engage in whichever challenge best suits their real-time readiness, as indicated by wearable data. Providers can monitor anonymized, aggregated data for early cognitive decline, and policymakers can harness these insights for resource allocation.

Call to action

We believe the field is poised for a transformative shift from static, task-based exercises to a model that integrates real-time physiological adaptation, Digital Cognitive Twins, and multimodal engagement. By leveraging advanced AI/DCT models, our hypothesis is these systems can provide greater prediction, greater personalization, greater engagement and greater efficacy than conventional approaches. Duke University, Columbia University and CogniFit Inc. (San Francisco, US) are jointly designing a cognitive training study using Digital Cognitive Twins to test this hypothesis. It is our hope that others will also conduct similar studies.

The Digital Twin "ethical map"[14] provides a foundational framework for addressing the unique challenges of cognitive and mental health data, including privacy risks, algorithmic opacity, and equity concerns. To operationalize this, safeguards must be embedded by design, integrating robust encryption, federated learning, and dynamic consent frameworks that give users granular control over data access and usage[15].

Transparent algorithmic pipelines, auditable logs, and explainable AI models are essential for maintaining clinical trust and accountability.

With the aging of the population, cognitive fitness will only grow in priority worldwide, not only for maintaining cognitive abilities but also for supporting mental health and emotional wellbeing. We call on the field to rigorously examine if the current limitations of cognitive training can be overcome using these newer personalization methods. If successful, such studies could pave the way to better integrate cognitive training as a cornerstone of preventive brain and mental health strategies, based on trustworthy AI consistently aligned with ethical principles of justice, autonomy, and non-maleficence.

References

1 **Yaffe, K. et al.** Effect of Personalized Risk-Reduction Strategies on Cognition and Dementia Risk Profile Among Older Adults: The SMARRT Randomized Clinical Trial. *JAMA Intern. Med.* **184**, 54–62 (2024). doi: 10.1001/jamainternmed.2023.6279

2 **Stallard, P.J.E., Ukraintseva, S.V. & Doraiswamy, P.M.** Changing Story of the Dementia Epidemic. *JAMA* (2025). doi: 10.1001/jama.2025.1897

3 **Hallion, L.S., Hsu, K.J. & Schleider, J.L.** Cognitive training for mental health problems. *Nat. Mental Health* **2**, 17–24 (2024). doi: 10.1038/s44220-023-00185-y

4 **Bodner, K.A., Goldberg, T.E., Devanand, D.P. & Doraiswamy, P.M.** Advancing Computerized Cognitive Training for MCI and Alzheimer's Disease in a Pandemic and Post-pandemic World. *Front. Psychiatry* **11**, 557571 (2020). doi: 10.3389/fpsyt.2020.557571

5 **Devanand DP, Goldberg TE, Qian M et al**. Computerized games versus crosswords training in mild cognitive impairment. *NEJM Evidence* 2022. doi: 10.1056/EVIDoa2200121

6 **Nwosu, A., Boardman, S., Husain, M. M., & Doraiswamy, P. M.** Digital therapeutics for mental health: Is attrition the Achilles heel?. *Frontiers in psychiatry*, **13**, 900615 (2022). doi: 10.3389/fpsyt.2022.900615

7 **Doraiswamy, P.M., Narayan, V.A. & Manji, H.K.** Mobile and pervasive computing technologies and the future of Alzheimer's clinical trials. *npj Digital Med* **1**, 1 (2018). doi: 10.1038/s41746-017-0008-y

8 **Chan, A.T.C., Ip, R.T.F., Tran, J.Y.S. et al.** Computerized cognitive training for memory functions in mild cognitive impairment or dementia: a systematic review and meta-analysis. *npj Digit. Med.* **7**, 1 (2024). doi: 10.1038/s41746-023-00987-5

9 **Richter, T., Shani, R., Tal, S. et al.** Machine learning meta-analysis identifies individual characteristics moderating cognitive intervention efficacy for anxiety and depression symptoms. *npj Digit. Med.* **8**, 65 (2025). doi: 10.1038/s41746-025-01449-w

10 **Ooka, T.** The Era of Preemptive Medicine: Developing Medical Digital Twins through Omics, IoT, and AI Integration. *JMA J.* **8**, 1–10 (2025). doi: 10.31662/jmaj.2024-0213

11 **Nahum-Shani, I., et al.** Just-in-time adaptive interventions (JITAIs) in mobile health: Key components and design principles for ongoing health behavior support. *Ann Behav Med* **52**(6), 446-462 (2018). doi:10.1007/s12160-016-9830-8

12 **Ibrahim, M. et al.** Generative AI for synthetic data across multiple medical modalities: A systematic review of recent developments and challenges. *Comput. Biol. Med.* **189**, 109834 (2025). doi: 10.1016/j.compbiomed.2025.109834

13 **Shade, M., Yan, C., Jones, V.K. & Boron, J.** Evaluating Older Adults' Engagement and Usability With AI-Driven Interventions: Randomized Pilot Study. *JMIR Form. Res.* **9**, e64763 (2025). doi: 10.2196/64763

14 **Huang, P. H., Kim, K. H., & Schermer, M.** Ethical Issues of Digital Twins for Personalized Health Care Service: Preliminary Mapping Study. *Journal of medical Internet research*, ***24***(1), e33081 (2022). doi: 10.2196/33081

15 **Li, X. et al.** Digital twins as global learning health and disease models for preventive and personalized medicine. *Genome Med.***17**(1), 11 (2025). doi: 10.1186/s13073-025-01435-7