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Opinion

Digital Twins in Neurology Care: Evidence, Limitations, and a Path Forward

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Abstract

Digital twins are increasingly promoted in neurology as an advancement beyond conventional artificial intelligence, yet the term is often applied without conceptual or methodological rigor. Strict definitions describe digital twins as dynamically updated, bidirectionally linked models that generate predictive, decision-relevant value, criteria rarely met by current neurological applications. This Opinion critically examines the state of digital twins across major neurological domains, including dementia, multiple sclerosis, Parkinson's disease, epilepsy, stroke, pain, and migraine. We argue that most existing systems are more accurately described as twin-inspired longitudinal decision-support or trial-analytics models rather than true clinical digital twins. While neurology is well-suited to digital twin approaches due to disease heterogeneity, multimodal data, and iterative care pathways, progress is limited by gaps in measurement validity, uncertainty handling, prospective evaluation, and governance. A pragmatic path forward is proposed, emphasizing question-specific, validated neurological digital twins over overgeneralized brain twin narratives, and suggesting that much of the current field is better understood as twin-inspired modeling rather than true clinical digital twin implementation.

Keywords: digital twins; neurology; clinical decision support; personalized medicine; artificial intelligence; longitudinal modeling

Digital twins are increasingly promoted as the next evolutionary step beyond conventional artificial intelligence (AI) models in medicine, yet the term is often used inconsistently and without sufficient conceptual rigor. A widely cited and stringent definition from the US National Academies describes a digital twin as a set of virtual information constructs that mirror the structure, context, and behavior of a system; are dynamically updated through data streams from their physical counterpart; possess predictive capability; and inform decisions that generate real-world value, with a bidirectional link between the virtual and physical systems being central [1,2].

In parallel, healthcare-oriented scholarship has proposed more pragmatic definitions of a "patient digital twin", acknowledging that medical implementations often cannot satisfy all features of industrial digital twins. A recent review [3], for example, defines a patient digital twin as a viewable digital replica containing multidimensional, patient-specific information that supports clinical decision-making, while explicitly aligning its conceptual foundation with the National Academies' framework.

This definitional clarity is not merely academic. A growing body of literature argues that many systems labeled as "digital twins" in healthcare fail to meet these stricter criteria. A 2025 review of "human digital twins" mapped application domains and highlighted that many studies lack dynamic updating, verification or validation procedures, or explicit decision-linked value, and are therefore more accurately described as static models, "digital shadows" or trial-analytics tools [4].

This distinction is particularly consequential in neurology, where clinical decisions are often irreversible or carry long-term consequences, such as surgical interventions, neuromodulation targeting, or the initiation of disease-modifying therapies. If the label "digital twin" implies a level of maturity, reliability, and governance that is not yet achieved, its uncritical use risks misleading clinicians, patients, and regulators alike [4,5]. These concerns highlight the need for a careful examination of how digital twins are currently conceptualized, developed, and applied within neurological care. In this Opinion, it is argued that the main challenge is not simply whether digital twins can be applied to neurology, but whether current neurological applications justify the claim at all. The central view is that most existing systems are better understood as twin-inspired longitudinal decision-support, monitoring, or trial-analytics models rather than true clinical digital twins in the strict sense. From this perspective, the most productive path forward is not to promote broad "brain twin" narratives, but to develop question-specific, validated neurological twins with explicit clinical purpose, uncertainty handling, and decision-linked evaluation.

1. Why Neurology May Be Particularly Suitable for Digital Twin Approaches

Neurology combines several characteristics that make it a compelling domain for considering digital twin–based approaches [6]. First, neurological disorders are marked by substantial heterogeneity in clinical presentation, progression, and treatment response, both across and within diagnostic categories [7]. Second, neurological care increasingly relies on rich, multimodal, and longitudinal data streams spanning complementary domains, including structural neuroimaging (e.g., magnetic resonance imaging (MRI), diffusion imaging), functional recordings (e.g., electroencephalography (EEG)/magnetoencephalography (MEG)), invasive electrophysiology, wearable or mobile sensor-derived measures, and patient-reported outcomes [8,9]. Third, many neurological care pathways are inherently iterative, involving repeated assessment and adjustment over time, such as rehabilitation dosing, medication titration, or neuromodulation programming [10,11]. This temporal dimension is especially important because many neurological disorders are dynamic rather than static, with symptoms, function, and treatment response changing over time. Repeated assessment creates the conditions for model updating, individualized trajectory estimation, and adaptive decision support, which are central to any clinically meaningful digital twin framework.

Together, these features align conceptually with the core premise of digital twins: the continuous integration of heterogeneous data to support individualized inference over time. However, for a neurological digital twin to be clinically meaningful, it must go beyond classification or static prediction. It should support patient-specific inference and, where appropriate, simulation of alternative scenarios; explicitly represent uncertainty; and remain robust under shifts in data quality, clinical workflows, and care contexts. These requirements push the field toward hybrid modeling strategies that integrate mechanistic representations of brain function and disease with data-driven learning approaches, rather than relying solely on black-box predictors.

Against this backdrop, an increasing number of studies have begun to describe or label digital twin-like approaches across different neurological domains [5,12,13]. The following section presents current evidence and illustrative examples, highlighting both progress to date and persistent conceptual and methodological gaps. The examples span a continuum from systems that more closely approach strict digital twin criteria to twin-inspired longitudinal decision-support models; for each, the key question is whether dynamic updating, validation, and decision-linked value are demonstrated.

2. What Has Been Done? Evidence and Examples Across Neurological Domains

2.1 Dementia and Neurodegenerative Diseases

In dementia and related neurodegenerative disorders, the clinical challenge extends beyond diagnosis to longitudinal monitoring, prognosis, and individualized care planning. Disease trajectories vary substantially among individuals, even within the same diagnostic category, and progression reflects the interaction of biological, cognitive, behavioral, and environmental factors. This heterogeneity makes dementia a particularly compelling candidate for digital twin-inspired approaches that model individual trajectories over time rather than rely on static group averages [14].

Recent work increasingly frames dementia-oriented digital twins as longitudinal, patient-specific models that integrate multimodal data to estimate disease state, predict progression, and support clinical decision-making. These models commonly combine neuroimaging, cognitive testing, clinical assessments, and, more recently, digital and wearable data streams capturing real-world function and behavior [15]. In this context, the most clinically relevant "twin-like" utility lies in trajectory-aware decision support: anticipating care needs, tailoring follow-up intensity, detecting deviations from expected progression, and monitoring response to interventions [16].

At the same time, reviews emphasize that many dementia "digital twins" remain at an early developmental stage: uncertainty quantification, missingness, cross-site generalizability, and prospective decision-grade validation are recurring gaps [17]. Ethical challenges are also prominent, given the vulnerability, complexity of consent, and privacy concerns in passive sensing. A realistic near-term pathway is therefore the development of twin-inspired, longitudinal decision-support tools, validated prospectively and embedded in care, rather than full simulation-capable twins deployed at scale [18,19].

2.2 Multiple Sclerosis: Imaging-Driven Trajectories as a Pragmatic "Twin" Entry Point

Multiple sclerosis (MS) is a high-yield addition because it is inherently longitudinal, imaging-rich, and heterogeneous in course and treatment response. Digital twin-style approaches have been proposed to estimate individual-level trajectories and disease-related brain changes from MRI-based models, positioning MS as a pragmatic domain for "twin-inspired" progression forecasting and monitoring [20,21]. These approaches also show a broader point relevant to neurology: the most credible early digital twins may be those anchored in robust, repeatable measurement modalities (e.g., MRI) with well-defined clinical decision points [22]. Their practical usefulness at present lies less in serving as full clinical twins and more in supporting individualized monitoring and progression forecasting in measurement-rich settings.

2.3 Parkinson's Disease: Mechanistic Personalization as a Bridge

A 2025 study describes a "Virtual Parkinsonian patient" that simulates levodopa effects using patient-specific electrophysiological data (including EEG and deep recordings), illustrating mechanistically anchored personalization [23]. This line of work is promising because Parkinson's management often requires iterative parameter tuning (medication regimens and/or stimulation settings). Mechanistic, updateable models could therefore evolve toward twin-like decision support, provided they demonstrate prospective clinical utility, robustness across recording modalities and sites, and safe integration into workflows where model outputs inform real therapeutic adjustments [24]. At present, these systems are best viewed as promising mechanistic personalization tools rather than established routine-care instruments.

2.4 Epilepsy: Virtual Brain Twins for Clinically Actionable Simulation

Drug-resistant focal epilepsy remains one of the most precise near-term neurological targets because the clinical question is specific and actionable: estimating the epileptogenic zone network to guide intervention. A 2024 paper presents a high-resolution "virtual brain twin" workflow designed to estimate the epileptogenic zone network using stimulation paradigms, positioning the approach as a personalized, generative, adaptive model intended for scientific and clinical use [12]. This is important because it moves beyond retrospective classification toward patient-specific modeling capable of "what-if" reasoning, exactly the kind of decision-linked value implied by stricter digital twin definitions. Among current neurological applications, this is one of the clearest examples of potential clinical usefulness because the modeled question is specific, actionable, and linked to intervention planning. Even here, one must look for evidence of prospective validation, verification/validation of the model-to-patient mapping, and clarity about how uncertainty is communicated when outputs may affect irreversible decisions [6].

2.5 Stroke: Rehabilitation-Focused Twins as a Realistic Early Translation

Stroke spans acute decisions and long-term rehabilitation, but the most feasible early "twin-like" value may arise in rehabilitation, where patients generate repeated functional data over time and care is continuously adjusted. A scoping review mapped digital twin objectives, input data, methods, and stakeholder involvement, and proposed "desirable properties", emphasizing that most current efforts remain early-stage and not yet decision-grade twins under strict criteria [25]. This literature supports a realistic translational pathway: rather than aiming immediately for "full brain twins", stroke may benefit first from narrow, task-focused twins that monitor recovery and personalize therapy intensity, targets, and timing, where the bidirectional "twin" loop can be operationalized as data to model, to therapy adjustment, to outcome, and to model update [26]. In this sense, the near-term usefulness of stroke twins may be greatest in rehabilitation optimization rather than in attempting comprehensive whole-brain digital replication.

2.6 Pain and Digital Twin Learning Health Systems: A Systems-Level Blueprint

Pain is a major neurological-care burden and offers a useful systems-level framing. A 2025 article proposes "Digital Twin Learning Health Systems", integrating multimodal biomarkers and adaptive learning loops to personalize pain care, explicitly linking twins to continuous updating and outcome-driven improvement [27]. This perspective is valuable because it connects the digital twin concept to care infrastructure and governance: the twin is not a standalone algorithm, but part of a monitored cycle of data capture, prediction, clinical action, outcome evaluation, and model updating. It also naturally foregrounds issues such as measurement validity, drift, fairness, safety monitoring, and accountability, because the model is explicitly embedded in clinical decision loops [28].

2.7 Migraine and Headache: Digital Phenotyping as the Foundation, With Twins Still Aspirational

Migraine is characterized by fluctuating symptoms and context sensitivity, making it a logical candidate for twin-like models, provided the measurement layer is strong. The medical hypothesis "Intelligent Digital Twins for Personalized Migraine Care" provides a clear rationale for how migraine twins could be constructed around longitudinal, multidimensional patient data streams and decision-support needs [29]. A 2025 perspective on digital phenotyping argues that continuous, real-world measurement could shift the care toward proactive strategies [30]. At the same time, broader reviews of AI in headache medicine describe emerging interest in wearable-based monitoring and personalized simulation while implying that the evidence base remains preliminary for routine clinical adoption [31]. In this domain, the most likely expectation is to emphasize that "twin-like" progress is currently best framed around validated digital biomarkers, prospective care pathways, and transparent uncertainty, rather than overpromised simulation [32–34]. Accordingly, their near-term usefulness is likely to depend on whether digital phenotyping can yield reliable and clinically interpretable biomarkers that genuinely improve monitoring or treatment timing in practice.

3. Where We Are Now: A Field in Rapid Expansion With Uneven Maturity

The current landscape of digital twins in neurology is characterized by rapid conceptual expansion alongside uneven scientific and clinical maturity. Several broad patterns can be identified across domains.

First, the strongest and most defensible twin-like exemplars arise in settings where simulation is clinically meaningful, and data structures are well-defined, most notably in epilepsy, where virtual brain twins are explicitly designed to support intervention planning [12]. In such cases, the clinical question is narrow, decision-relevant, and evaluable, allowing model outputs to be assessed against concrete therapeutic outcomes.

Second, across many other neurological domains, the label "digital twin" is frequently applied to predictive models or trial analytics tools that may be useful but do not meet stricter criteria such as dynamic updating, bidirectional coupling, uncertainty-aware inference, or decision-linked validation. These systems often function as static or periodically updated predictors rather than true twins, despite the terminology used.

Third, limitations in clinical translation are driven less by algorithmic sophistication than by challenges in workflow integration, prospective evaluation, and governance. Even technically advanced models struggle to move beyond proof-of-concept if they are not embedded in clinical decision pathways, aligned with care workflows, or evaluated using outcomes meaningful to patients and clinicians. These observations demonstrate that progress toward functional digital twins depends as much on implementation science and evaluation design as on model development itself.

4. Where We Are Going: A Pragmatic Roadmap and "Gap Map" for Neurological Digital Twins

A realistic roadmap for neurological digital twins requires explicit recognition of several recurring gaps that cut across disease areas.

4.1 Gap 1: Alignment Between Definition and Claim

The first gap concerns clarity and precision in terminology. It should be explicitly stated whether a proposed system represents a static patient-specific model, a periodically updated monitoring tool, a mechanistic simulator, a trial-oriented or prognostic "twin", or a decision-grade clinical digital twin that meets core criteria such as dynamic updating, predictive capability, uncertainty representation, and decision-linked value.

Aligning terminology with actual system capabilities is essential and shapes expectations for validation, regulatory oversight, clinical trust, and ethical accountability.

4.2 Gap 2: Measurement Validity and Robustness in Real-World Neurology

A second significant gap concerns the validity and robustness of measurement, particularly in ambulatory and real-world neurological settings. Many proposed digital twins depend on wearable sensors, smartphones, or patient-reported data streams. Without well-validated digital biomarkers that perform reliably across devices, contexts, and populations, model updating risks amplifying noise rather than improving inference. Migraine digital phenotyping illustrates both the opportunity and the challenge of this paradigm. Continuous data streams may enable earlier detection of change and more adaptive care, but only when signals are clinically interpretable, reproducible, and meaningfully linked to outcomes [29,35]. Similar measurement challenges apply across movement disorders, rehabilitation, and chronic neurological disease, where variability and context sensitivity remain significant obstacles to robust modeling.

4.3 Gap 3: Uncertainty, Verification, and Safety

A third gap concerns the explicit handling of uncertainty. Neurological digital twins must not only generate predictions but also communicate confidence, limitations, and failure modes. In high-stakes neurological decisions, a clinically useful twin is one that supports reasoning under uncertainty rather than obscuring it. Verification, validation, and uncertainty quantification are increasingly recognized as foundational scientific requirements for digital twins in precision medicine [36]. This includes evaluating model behavior across populations, over time, and under distributional shift. Without these safeguards, even technically advanced systems risk overconfidence, misinterpretation, and unsafe deployment.

4.4 Gap 4: Prospective Evaluation and Implementation Science

The fourth gap lies in evaluation design and real-world deployment. Future studies must move beyond retrospective performance metrics to assess whether digital twins improve clinically meaningful outcomes, such as time to appropriate treatment, functional recovery, quality of life, adverse event rates, or healthcare utilization. Experience from trial-analytics twins in Alzheimer's disease [37] illustrates that "value" may emerge through multiple pathways, including improved evidence generation, patient stratification, and trial efficiency, not solely through bedside decision support. Evaluation frameworks must therefore be matched to the intended function of each twin type and embedded within realistic clinical workflows.

4.5 Gap 5: Governance, Equity, and Accountability

Finally, governance represents a central and unresolved challenge. Neurological digital twins may integrate highly sensitive longitudinal data and influence high-stakes clinical decisions. Robust frameworks are needed for data stewardship, transparency, auditing, and accountability. Equally important is demonstrating performance across diverse populations to avoid reinforcing existing inequities in neurological care. Governance mechanisms must evolve alongside technical development rather than being treated as an afterthought.

Cost and implementation feasibility must also be considered explicitly. Routine clinical use of neurological dig-

ital twins may require substantial investment in multimodal data acquisition, computational infrastructure, interoperability, technical support, and clinician training. These demands may be manageable in highly resourced academic centers but remain challenging for many routine care settings. From a global health perspective, there is a real risk that digital twin technologies could deepen existing inequities in neurological care if they are developed primarily around high-resource infrastructures, proprietary systems, or narrowly represented populations. A realistic translational pathway therefore requires not only technical sophistication, but also scalable, equitable, and context-sensitive implementation models.

5. Toward a Realistic Vision of Neurological Digital Twins

Taken together, these considerations argue against a single, monolithic "brain twin for everything". Instead, a more realistic and scientifically defensible trajectory is the development of a family of question-specific neurological twins: narrow enough to be validated, yet connected enough to learn and improve over time. At one end of this spectrum lie epilepsy virtual brain twins, where mechanistic simulation is tightly coupled to intervention planning [12]. At the other end are dementia-oriented trial twins that function as analytics infrastructures for evidence generation and longitudinal modeling [37]. Between these poles lie rehabilitation and chronic neurological conditions, such as stroke, Parkinson's disease, migraine, and pain, where continuous monitoring and adaptive decision support may gradually evolve into true twin loops as measurement quality, validation frameworks, and governance mature. In this broader context, digital twins should also be understood as one possible component of the future neurological examination and consultation, complementing rather than replacing traditional clinical assessment. As neurological care becomes increasingly data-enriched, continuous, and digitally supported, digital twins may serve as integrative frameworks that combine multimodal observations, longitudinal trajectories, and scenario-based inference within the consultation process [38].

If digital twins in neurology are to deliver on their promise, the term must be treated as a scientific claim rather than a marketing label. This requires explicit definitions, clinically meaningful endpoints, robust validation strategies, transparent handling of uncertainty, and responsible implementation pathways. When grounded in clear clinical questions, rigorous evaluation, and responsible implementation, digital twins may move from conceptual appeal toward genuinely impactful tools for neurological care.

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PG wrote the opinion piece, reviewed and approved the final version after revisions, and is accountable for all aspects of the work.

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Conflicts of Interest

Parisa Gazerani is serving as one of the Editorial Board members and Guest editors of this journal. We declare that Parisa Gazerani had no involvement in the peer review of this article and has no access to information regarding its peer review. Full responsibility for the editorial process for this article was delegated to Bettina Platt.

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