A Proposed Cause, Mechanism, and Rehabilitation for Focal Task-Specific Dystonia: A Theoretical-Empirical Approach

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Article

A Proposed Cause, Mechanism, and Rehabilitation for Focal Task-Specific Dystonia: A Theoretical-Empirical Approach

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Abstract

Focal task-specific dystonia (FTSD) poses a complex interplay of maladaptive neuroplasticity and motor circuit imbalance. Traditional theories often implicate subcortical nuclei but fail to explain why symptoms remain so tightly bound to a singular, highly practiced skill. Here we propose that the primary driver of FTSD is a newly formed "dystonic synergy" within the primary motor cortex (M1), in which excitatory circuit synapses are adequate relative to under-strengthened inhibitory circuit synapses, triggering involuntary contractions once the skill's intensity demands surpass the functional synergy's excitatory and inhibitory circuit capacity (synaptic strength). In short, we use an extensive single-case observation as the core empirical foundation and chronicle how a decade of stable piano performance deteriorated following a sudden technical change that forced the finger flexion motor synergy to "overreach". The patient's initial phase was dominated by "true weakness," a condition of task-specific paresis where the motor system is physically unable to generate the required excitatory inhibitory (E/I) drive to match the attempted movement speed. Over repetitive attempts to override that limitation, the excitatory circuit strengthened while the inhibitory circuit lagged, culminating in a fully formed dystonic synergy within three weeks. This maladaptive synergy then manifested in both piano playing and typing, a related digit-based skill, greatly disabling normal function in both tasks. We illustrate that once formed, the dystonic synergy remains stable but not spontaneously progressive, consistent with a saturable excitatory capacity. Moreover, a spiking neural network simulation provides proof of concept for the hypothesis and identifies the input strength threshold at which the network shifts from balanced to hyperexcitable output. Finally, we propose and describe a non-invasive motor retraining approach for reversing FTSD, "below or at-threshold retraining" (BATR), in which the inhibitory circuit of the dystonic synergy is methodically strengthened by strict practice at or below the individual symptom threshold. This motor strategy, validated in the single-case longitudinal data and in other published studies using similar methods, reveals that the dysregulated synergy can be rebalanced to restore fully normal motor function and highlights a noninvasive avenue for rehabilitation and prevention in FTSD.

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Introduction

Focal task-specific dystonia (FTSD) is a perplexing motor disorder (Frucht, 2014; Stahl & Frucht, 2017). Affecting individuals who are highly skilled in a specialized movement domain, FTSD typically emerges after years of normal practice, manifesting as abrupt, involuntary contractions and distortions unique to the targeted task (Rozanski et al., 2015). Although FTSD shares some superficial clinical overlap with other primary dystonias, particularly involuntary twisting or posturing, its distinctly "task-bound" nature (i.e., symptoms triggered almost exclusively by a specific skilled activity) underscores a pivotal role for maladaptive neuroplasticity within the cortical circuitry

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subserving that motor subtask (Quartarone et al., 2006). Indeed, multiple electrophysiological findings, notably the characteristic reduction of short-interval intracortical inhibition (SICI), point to an underlying hyperexcitability in the primary motor cortex (M1) (Furuya et al., 2018; Ridding et. al, 1995; Siebner et al., 1999). However, the deep causal chain and precise mechanisms driving these changes have been historically elusive. Most conventional models of dystonia have emphasized basal ganglia (Grossman & Kelly, 1976; Simonyan et al., 2017) or cerebellar dysfunction (Teo et al., 2009), highlighting sensorimotor integration deficits. Yet these explanations do not entirely account for why FTSD can remain confined to a single fine motor skill while leaving nearby tasks, or even adjacent digits, spared.

Hallmark transcranial magnetic stimulation (TMS) findings in "typical" forms of dystonia (as defined in a companion study) show that local cortical inhibitory circuits, presumably $GABA_A$-mediated, are functionally impaired (e.g., Levy & Hallett, 2002; Stinear & Byblow, 2004). In FTSD, these inhibitory deficits appear strongly plasticity-driven: skill repetition at "above-capacity" loads fosters an aberrant reorganization process. Combined, these insights argue for a mechanistic framework in which repeated overreaching of the synergy's excitatory/inhibitory (E/I) capacity gradually sculpts a "dystonic synergy" with excessive excitatory strength relative to its under strengthened inhibitory counterpart. The resulting synergy becomes hyperexcitable, "locking in" involuntary co-contractions or undesired postures whenever that skill is activated. Observations of non-manifesting DYT1 carriers who exhibit partial cortical excitability changes (Edwards et al., 2003), but no clinical dystonia, suggest that genetic predispositions alone are insufficient to produce symptoms for FTSD; environmental triggers appear necessary to amplify a pre-existing E/I imbalance into full-blown dystonic movements (Furuya et al., 2018). Thus, the "cause" of FTSD can be anchored in repeated, maladaptive Hebbian loops that evolve after the synergy's capacity is reduced by major technique changes and is then relentlessly overreached. In this scenario, any concurrency of "genetic predisposition" further lowers the threshold at which overreaching triggers an entrenched dystonic synergy.

Despite the strong emphasis on cortical plasticity, it is critical to recognize that FTSD, much like other forms of dystonia, can present with broad neural alterations outside M1. Numerous imaging and neurophysiological studies have revealed basal ganglia involvement, potentially abnormal cerebellar feedback loops, and sensorimotor smudging in the primary somatosensory cortex (S1), collectively reflecting the entire motor system's capacity to reconfigure in maladaptive ways (Elbert et al. 1998; Kita et al., 2021; Simonyan et al., 2017; Tinazzi et al., 2003). A large body of research, nonetheless, indicates that these changes outside M1 could potentially arise secondarily, through Hebbian adaption from repeated ectopic signals from an M1 circuit locked in chronic hyperexcitability (e.g., Furuya et al., 2018; Hallett, 2011; Tseng et al., 2014). Similarly, spinal inhibitory deficits found in FTSD may represent downstream changes: persistent pathologic input from the affected synergy reshaping inhibitory interneuron networks (Berardelli et al., 1998). Hence, a unifying explanation posits that once the synergy's inhibitory dimension fails to potentiate proportionally to excitatory synaptic strength, excessive excitatory outflow cascades through cortico-subcortical and corticospinal loops, generating new "byproduct" alterations at many levels of the motor hierarchy.

FTSD has been managed symptomatically: botulinum toxin injections aim to reduce excessive muscle over-activity, medications modulate generalized motor excitability, or surgery intervenes on deeper structures (e.g., globus pallidus) (Grigoriu et al., 2015). While these can provide partial relief, none directly tackle the underlying E/I mismatch at its source, nor restore normal synergy function. Over the past two decades, an emerging recognition that FTSD is a problem of maladaptive plasticity has spurred interest in motor retraining approaches, a set of behavioral protocols designed to reshape disordered synergy circuits by carefully controlling practice conditions (Quartarone & Hallett, 2013). Indeed, case studies of "slow-down exercise" (SDE) have documented complete or near-complete resolution of task-specific dystonias (Yoshie et al., 2015). These rehabilitative successes underline the

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principle that, if the synergy can re-strengthen its inhibitory circuit without re-engaging the involuntary synergy's excitatory drive, a rebalancing of synaptic strengths is feasible.

Clinically, practically all forms of FTSD display a characteristic "threshold phenomenon," in which performance remains entirely symptom-free at or below a specific movement intensity for the affected task. Once the attempted movement intensity exceeds this exact level, performance deteriorates abruptly with the onset of involuntary dystonic contractions (Sakai, 2006; Yoshie et al., 2015). We employ the term threshold in two non-interchangeable ways. We use symptom-threshold for the behavioral phenomenon: at or below this task intensity performance is symptom-free; above it involuntary dystonic contractions arise. In contrast, spike threshold (firing threshold) designates the membrane-potential value at which an individual neuron generates an action potential, with subthreshold denoting excursions that do not reach this firing level. To avoid confusion, we hyphenate symptom-threshold for the behavioral phenomenon and leave threshold unmodified for the cellular "spike-threshold" sense. Where both meanings could plausibly be inferred, the appropriate qualifier is repeated explicitly.

Building on these considerations, this paper has four primary aims. First, we propose a concrete cortical mechanism for FTSD, namely that it arises from an imbalance of synaptic strengths between excitatory pyramidal neurons and parvalbumin-expressing interneurons within a task-specific motor synergy (TSMS) in M1. Second, we specify a developmental cause of FTSD by delineating in detail how repeated overreaching in a TSMS whose excitatory and inhibitory capacities have been reduced progressively sculpts this dystonic synergy from an initially balanced TSMS. Third, we develop below- or at-threshold retraining (BATR), a non-invasive motor retraining protocol designed to methodically restore balanced synaptic strengths within the affected synergy, and we propose it as a potentially curative intervention for FTSD, explaining its neurophysiological rationale together with practical considerations for clinical implementation and variability in patient outcomes. Fourth, we present a spiking neural network simulation that provides a quantitative proof-of-concept verification of the hypothesis and pinpoints the input-strength threshold at which the system shifts from balanced to hyperexcitable output. Additionally, a detailed single-case report of the lead author, illustrating the empirical chronology that motivated this framework, is provided in the supplementary material for readers seeking more clinical detail. Ultimately, we propose that, rather than attributing FTSD to a purely genetic origin or a patchwork of co-equal network abnormalities, the M1-centric TSMS framework provides the most direct mechanistic account of both the pathophysiology of FTSD and its behavioral rehabilitation. Thus, this reconceptualization seeks to unify electrophysiological, neuroimaging, computational, and clinical insights within a single synergy-based explanation that is experimentally testable and offers novel rehabilitative possibilities.

Answering the Three Key Questions Regarding Focal Task-Specific Dystonia

The Underlying Mechanism

While synergies are often described at a macro level, using Safavynia et al.'s (2011) definition of motor synergies, we employ the framework of synergy at a micro level in which each TSMS corresponds to the smallest ensemble of muscles co-activated to produce a unidirectional movement (e.g., finger flexion, extension, abduction, adduction, wrist flexion, wrist extension) at an individual effector. Concretely, rather than treating every single muscle as an entirely independent module, we group all prime movers that jointly create the movement force in that one direction, and we define the TSMS as the corresponding population of pyramidal neurons and local inhibitory interneurons in the task-specific subregion of M1 that drives these muscles. Any proximal stabilizers or muscles whose activity merely modulates finger posture indirectly are excluded, leaving only those muscles directly responsible for executing the specific unidirectional motion. In this sense, each TSMS can involve multiple muscles (e.g., intrinsic hand muscles plus certain extrinsic forearm muscles) if they routinely co-activate to produce a single direction of movement in that effector. Crucially, a muscle can also belong to more than one TSMS if it contributes to multiple directions. By focusing on this

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tightly defined "unidirectional synergy," we capture the local population of excitatory and inhibitory neurons that practice together as a functional sub-network for that particular movement. We propose that FTSD can arise in any TSMS when repeated overreaching drives disproportionate potentiation of excitatory synapses relative to inhibitory synapses.

A crucial boundary condition is set by cortical interneuron identity. Across the neocortex, including M1, three non-overlapping molecular families account for virtually all GABAergic cells: parvalbumin-positive (PV), somatostatin-positive (SST), and the ionotropic serotonin receptor 5HT3a (5HT3aR) interneurons (Rudy et al., 2011). Framing FTSD in this canonical tripartite scheme immediately narrows the mechanistic search: any inhibitory deficit in a TSMS must therefore map onto one, or some combination, of these three classes.

Under normal conditions, a TSMS encoding a learned unidirectional movement is represented in M1 by an ensemble of pyramidal neurons that co-fire to produce the intended motor output. These excitatory neurons rely on local inhibitory interneurons, particularly PV fast-spiking cells, which provide short-latency $GABA_A$-mediated inhibition to keep excitatory drive in check. Whenever pyramidal neurons ramp up their firing, the corresponding PV cells receive strong excitatory input and deliver a timely burst of inhibition, preventing runaway activity (a similar mechanism as the pyramidal-interneuron gamma PING described by Keeley et al., 2017). As skill acquisition proceeds through repeated practice, excitatory and inhibitory synapses within the synergy co-strengthen in parallel via Hebbian-like mechanisms: excitatory-excitatory (E-E) connections among frequently co-activated pyramidal cells become more robust, while excitatory-inhibitory (E-I) connections onto PV interneurons also scale up, ensuring balanced inhibitory feedback. The result under healthy circumstances is a balanced synergy, reflected experimentally in normal SICI and moderate intracortical facilitation (ICF) when measured by TMS.

In FTSD, we propose that this balance is disrupted by an imbalance of synaptic strengths between pyramidal neurons and local PV interneurons within the TSMS of the affected effector in M1. Specifically, the pyramidal neurons outpace the inhibitory drive furnished by PV interneurons, the fast-spiking subset of $GABA_A$-mediated cells (Tian & Izumi, 2022) that predominantly govern SICI (Di Lazzaro et al., 2006). In a healthy TSMS, balanced E-I synapses (both E→I and I→E) ensure that pyramidal neurons fire with appropriate spatiotemporal specificity. However, in FTSD, the PV interneuron synapses (E→I and/or I→E) become under-strengthened and disproportionately weak compared to E-E synapses. Regardless of which is more compromised, the net effect is insufficient $GABA_A$ current to hyperpolarize or shunt pyramidal neurons. This weakened short-latency inhibition directly manifests as reduced SICI in TMS studies (Di Lazzaro et al., 2006). Although each TSMS can also contain the two other principal cortical inhibitory interneuron populations, across FTSD subtypes, a substantial body of TMS studies reports markedly reduced SICI (e.g., Furuya et al., 2018; Huang et al., 2010; McDonnell et al., 2007; Ridding et al., 1995; Siebner et al., 1999; Stinear & Byblow, 2004). By contrast, results for long-interval intracortical inhibition (LICI) are heterogeneous: normal in some cohorts (Furuya et al., 2018; Meunier et al., 2012), reduced in others (Chen et al., 1997; Espay et al., 2006), occasionally even increased (Caux-Dedeystère et al., 2021). We contend that by itself, the inconsistency of LICI does not imply methodological noise alone; rather, it offers a clue pointing to the specific interneuron subclass that constitutes the principal locus of dysfunction within the TSMS.

Evidence for this inference comes from the demonstration by Shao and Burkhalter (1999) that slow, metabotropic inhibition gates late polysynaptic activity. In their study, layer-2/3 stimulation (rat V1) evokes an early glutamatergic EPSP followed by a slower $GABA_B$-IPSP. Blocking this IPSP with the GABAB antagonists 2-OH-saclofen or CGP 55845 abolishes it and unveils a train of reverberant EPSPs, indicating that dendrite-targeting SST neurons normally veto late recurrent excitation. The underlying circuit, in which L2/3 pyramids recruit Martinotti cells projecting to distal dendrites in L1, is conserved across the neocortex, including M1 (Jiang et al., 2015). Thus, if one performs the following thought experiment (subtracting SST-mediated GABAB currents while leaving PV-driven GABAA inhibition intact in the context of performing a motor task), the predicted

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motor phenotype diverges sharply from FTSD. Loss of dendrite-targeting SST cells abolishes the ~100–200 ms gain-down window that normally vetoes late polysynaptic reverberation. A brief cortical command should then in theory fragment into a series of low-frequency echo-like bursts of polysynaptic activity, causing a cascade of discrete, clonic after-contractions or phasic tremor-like jerks. FTSD, by contrast, is observed clinically to be a sustained, posture-like involuntary contraction that initiates once the symptom-threshold is crossed and then plateaus for the duration of the action (Sakai, 2006; Yoshie et al., 2015). The absence of involuntary phasic bursting movements in nearly every well-documented case of FTSD therefore argues that dendritic SST gating cannot constitute the primary locus of dysfunction. This empirical result therefore strengthens the inference that PV hypofunction is the critical failure mode in FTSD.

Repeating the same thought experiment with the variables reversed, weakening PV synapses while sparing SST circuits, recapitulates the clinical picture far more faithfully. As PV basket and chandelier cells clamp the perisomatic membrane within 1-5 ms of each pyramidal spike, underpotentiation of their synapses removes the instantaneous brake that normally limits population firing probability. Initial pyramidal discharge therefore rises steeply and, in the face of still-functional SST gain control, settles onto a new, elevated plateau: a hyperexcitable yet largely continuous output drive. Behaviorally, the motor system expresses the excess as a tonic, task-bound spasm, matching the phenomenology of FTSD. That outcome requires no additional failure of SST-mediated inhibition, merely a quantitative mismatch in the E/I ratio at PV synapses.

The same deductive framework further argues against a primary role for 5HT3aR interneurons, many of which are vasoactive-intestinal-peptide (VIP) positive and principally disinhibit SST cells. VIP interneurons normally fire in response to cholinergic or serotonergic drive, transiently silencing SST dendrite-targeting interneurons and permitting brief increases in pyramidal dendritic excitability. If FTSD reflected a loss of VIP interneuron output, SST cells would be over-effective, $GABA_B$ gain control would strengthen, late polysynaptic reverberation would be suppressed, and corticospinal output would tend toward bradykinetic or hypometric movements, opposite to the hyperkinetic, threshold-locked phenotype observed. Conversely, pathological VIP hyperactivity would approximate an SST knock-out and again predict phasic echo bursts rather than the sustained involuntary contractions that define FTSD. These considerations support a working hypothesis in which PV hypofunction is necessary and, at the level of core motor phenomenology, sufficient for FTSD. Whether SST and/or VIP pathways are altered remains an open and empirically testable question; current evidence suggests that their dysfunction is not required and, when present, is smaller and more variable than the PV synaptic-strength deficit.

When an individual attempts a high-intensity movement during a motor skill, insufficient inhibitory "clamping" of pyramidal populations causes them to fire excessively, leading to the characteristic repetitive involuntary movements of FTSD (Furuya et al., 2018; Ridding et al., 1995). PV interneuron synapses still function; inhibition is not completely lost. Nonetheless, their quantitative and qualitative insufficiency adequately explains the loss of surround inhibition that has been repeatedly documented in FTSD (e.g., Beck & Hallett, 2011; Beck et al. 2009; Sohn & Hallett, 2004). Because surround inhibition largely relies on PV interneurons to selectively inhibit neighboring excitatory outputs (Kujirai et al., 1993), weakening these synapses compromises inhibitory "gating," resulting in spillover of excitatory drive into adjacent cortical representations.

Both the excitatory inputs onto PV interneurons (E→I) and the inhibitory outputs from PV interneurons to pyramidal neurons (I→E) could be weakened in FTSD. The reduction of SICI in FTSD directly reflects a weakened $GABA_A$ effect on pyramidal neurons, whether because PV interneurons fire less or have less effective synapses onto these cells. Experimentally, blocking the postsynaptic effect of PV-mediated inhibition in M1 is sufficient to induce dystonic features: in monkey experiments, the focal application of a $GABA_A$ antagonist (bicuculline) to M1 caused excessive excitatory drive and abnormal co-contraction of agonist/antagonist muscles, thus mimicking dystonic movements (Matsumura et al., 1991). This demonstrates how loss of I→E inhibition alone can critically degrade motor control specificity. In a parallel finding, a peripheral afferent stimulus that

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normally elicits cortical inhibition instead produced excitation in FTSD patients, a phenomenon attributable to underactive inhibitory interneuron output (Abbruzzese et al., 2001). Collectively, such data strongly implicate deficient I→E synaptic transmission as a key factor in FTSD pathology.

In healthy M1, a subthreshold conditioning pulse suppresses late I3-waves but spares the early I1-wave, confirming that I3 activity is gated by intracortical GABA-ergic, likely PV interneuron, inhibition (Hanajima et al., 1998). Current-direction studies provide a second probe: posterior-anterior (PA) stimulation reliably recruits an I1 volley at threshold, whereas anterior-posterior (AP) stimulation can engage later I3-generated circuitry (Di Lazzaro et al., 2001). PA currents therefore mainly interrogate early-wave output, whereas AP currents have access to later, PV-gated I-waves. In FTSD this double probe reveals that SICI tested with PA currents is markedly reduced, yet the same paradigm with AP currents yields normal inhibition (Hanajima et al., 2008). Because PA samples early-wave-dominated output while AP can still engage late-wave pathways, the selective loss of PA-SICI implies that everyday motor output in FTSD relies disproportionately on the fast, direct I1 route and fails to recruit PV-interneuron circuitry that shapes later I-waves. Consistently, Stinear and Byblow (2004) showed that higher conditioning intensities are required to elicit SICI in FTSD, indicating that PV interneurons are present but less excitable. Taken together, these findings indicate that E→I synaptic drive is weakened in FTSD, leaving the inhibitory network under-recruited.

In summary, we propose that the core mechanism in FTSD is a PV-centered synaptic-strength imbalance within a TSMS, in which PV-mediated inhibitory circuits are insufficiently potentiated relative to excitatory circuits, shifting the synergy into a hyperexcitable regime. The hallmark features, repetitive involuntary movements and loss of surround inhibition, result directly from SICI deficiency and the consequent surplus excitatory drive, which functionally locks the TSMS into a maladaptive activity pattern whenever the learned task is engaged.

The Developmental Cause

We propose that when a performer changes technique in a highly trained motor skill, such as piano performance, the new motor pattern recruits a partially overlapping subset of cortical circuitry that previously supported the old technique. In M1, populations of pyramidal neurons and their associated local inhibitory interneurons (acting as modulators) encode elementary movement features (e.g., specific joint angles) that are shared between the old and new techniques. Even when the new technique alters global hand posture or finger movement, it still relies on muscle activations and joint configurations that resemble fragments of the prior motor pattern, such as a characteristic proximal interphalangeal (PIP) flexion angle or a particular wrist alignment. At the level of individual neurons and synapses, this overlap is expressed as a distributed representation in which each pyramidal neuron can potentially participate in multiple TSMSs, rather than adhering to a one-to-one mapping between neuron and movement.

Within M1, pyramidal cells are organized into partially overlapping ensembles that are broadly tuned to movement direction and muscle combinations (Economo et al., 2024 and references therein; Shinotsuka et al., 2023). Consequently, when a pianist adopts a new technique, some movement primitives, for example, distal interphalangeal (DIP) flexion of a particular digit, remain similar enough that the same cortical ensembles are re-engaged. These ensembles already possess strengthened excitatory-excitatory (E-E) synapses and associated inhibitory circuitry arising from prior training, which makes them efficient substrates for the new technique.

At the synaptic scale, each pyramidal neuron forms thousands of E-E connections and receives short-latency inhibition from local interneurons, particularly fast-spiking PV cells. When the performer executes a movement that shares kinematic elements with the old technique, such as depressing a piano key with one digit while stabilizing its neighbors, pyramidal neurons that previously encoded that biomechanical component receive correlated pre- and postsynaptic activity once again. The same PV interneurons, tuned to provide rapid inhibitory control over that movement feature, are co-recruited. The resulting neuronal ensemble, containing pyramidal-interneuron-

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pyramidal loops, is therefore shared between the old and new TSMSs because it encodes a particular fragment of movement output that both techniques happen to employ.

We hypothesize that this architecture arises because M1 is built around semi-redundant, multifunctional neuronal populations rather than from distinct pools that are dedicated to "old-technique" versus "new-technique" commands. Whenever the new technique requires a movement feature close to the preferred tuning of an existing neuron, that neuron is preferentially recruited. Connections that remain behaviorally useful are repeatedly engaged and therefore continue to experience coincident pre- and postsynaptic spiking, which is the fundamental trigger for Hebbian strengthening or maintenance of synaptic efficacy.

By contrast, the subset of neurons and synapses that encode movement features purely unique to the old technique, and not required by the new technique, are no longer reliably recruited. Cortical synaptic plasticity in the cortex is strongly shaped by spike-timing-dependent plasticity (STDP): when a presynaptic axon no longer fires within a favorable time window relative to its postsynaptic target, that synapse tends to undergo long-term depression (LTD) or fails to be stabilized during offline, protein-synthesis-dependent consolidation. Several convergent mechanisms ensure that such unreinforced synapses gradually weaken. First, synaptic tagging and capture mechanisms selectively stabilize reactivated synapses that can capture plasticity-related proteins (PRPs), whereas inactive synapses lack a tag and therefore fail to capture these resources (Bin Ibrahim et al., 2024; Frey & Morris, 1997; Redondo & Morris, 2011). Second, PRPs are limited, so actively firing synapses outcompete inactive synapses for these molecules, which biases maintenance toward the currently used connections (Govindarajan et al., 2011; Sajikumar et al., 2014). Third, homeostatic synaptic scaling prevents unbounded potentiation by downregulating underused inputs relative to network-wide activity levels (Turrigiano et al., 1998; Turrigiano, 2008). Fourth, synaptic occlusion indicates that a local circuit can sustain only a limited amount of long-term potentiation (LTP) at any given time. After sufficient, appropriately targeted practice with the original technique, synapses that support that technique bring the circuit to this ceiling. When the performer adopts a new technique, synapses that encode movement features shared by both techniques remain strongly potentiated because they continue to be recruited. Because of occlusion, potentiation at synapses that encode movement features unique to the new technique can only be expressed if some of the existing potentiation is first reduced to keep total LTP within the circuit's ceiling. Retrograde interference biases this reduction toward synapses that encode movement features unique to the old technique and are no longer consistently recruited, driving them toward LTD. This loss of potentiation frees capacity within the circuit's limited LTP range. Subsequent practice with the new technique can then use this available capacity to potentiate synapses that encode movement features unique to the new technique (Cantarero et al., 2013).

Together, these processes divide the synaptic ensemble of the old technique, comprising excitatory neurons plus their matched inhibitory interneurons, into two functional classes: an overlapping subset that remains active because it contributes to the new TSMS, and a non-overlapping subset that is effectively "abandoned" and allowed to decay. Behaviorally, we describe the resulting reduction in available synaptic strength following a technique change as a partial baseline shift. Early practice with the new technique re-potentiates or stabilizes synapses within the overlapping subset, whereas synapses that encode movement features purely unique to the old technique, belonging to the non-overlapping subset, are no longer engaged and undergo LTD or structural pruning. The performer then experiences a transient performance decrement after each major technique change, because such changes reduce the synaptic strength of the TSMS; with each reconfiguration, only a fraction of its prior strength remains available to support the new motor pattern.

To formalize this idea, it is useful to define the concept of movement intensity at the neural level. For a given TSMS, intensity encompasses the combination of the number of recruited neurons, their mean firing rates, and the degree of spike synchrony. In practice, the speed and force of a keystroke, or the loudness of a note, arise from the net excitatory minus inhibitory drive transmitted to spinal

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motor pools. On the cortical side, this drive is produced by the size of the recruited corticospinal ensemble and its population firing rate; in the spinal cord, it determines how many alpha motoneurons are activated and at what discharge frequencies. Higher intensities correspond to larger populations of pyramidal neurons firing at higher rates, which in turn recruit more and larger motor units and drive muscles to contract more swiftly and forcefully.

Within a digit-specific TSMS, the same muscles and joint movements can be expressed at different intensities by scaling the net excitatory output of the responsible ensemble. A soft, slow keystroke corresponds to modest ensemble recruitment and low firing rates, whereas a loud, rapid keystroke corresponds to extensive recruitment and high rates. The motor system accomplishes this scaling through a combination of rate coding and population coding, orchestrated by premotor and supplementary motor areas, basal ganglia, and cerebellar circuits that shape activity in M1.

We define attempted intensity as the top-down command specifying the intended speed, force, or loudness for a given TSMS. At the cellular level, this command is implemented as preparatory and movement-related activity distributed across premotor and supplementary motor areas, basal ganglia-thalamo-cortical loops, and M1, which together set the net excitatory drive to the relevant pyramidal population. The resulting population activity in corticospinal neurons is transmitted to the spinal cord.

Ideally, the synaptic strengths within a given TSMS are sufficient to convert a chosen attempted intensity into the corresponding pattern of descending drive. Synaptic strengths directly determine how much net excitatory or inhibitory influence the involved neurons can exert, because the degree of potentiation or depression at each synapse sets the amplitude of the excitatory or inhibitory postsynaptic potentials (EPSPs or IPSPs) that shape population firing rates.

On the excitatory side, synaptic strength governs the size of each EPSP. At an excitatory synapse, the density and conductance of AMPA receptors, together with presynaptic release probability and spine structure, determine how much depolarization the postsynaptic neuron receives per presynaptic spike. Strongly potentiated synapses allow each incoming spike volley to generate a large excitatory current, driving higher firing rates and/or recruiting additional neurons. As a result, the corticospinal ensemble can deliver a stronger descending command, engaging more spinal alpha motoneurons at higher discharge frequencies. Robust excitatory strengths, therefore, enable a TSMS to reach higher maximal intensities (faster, more forceful movements) when such intensities are attempted. Conversely, if excitatory synapses are weak or partially depressed, even a strong cortical command cannot produce sufficient postsynaptic spiking, effectively capping the TSMS at a lower maximum speed or force.

On the inhibitory side, synaptic strengths determine how effectively local interneurons can clamp or sculpt the TSMS's excitatory output. PV interneurons, among others, receive excitatory E→I input from pyramidal cells, and the strength of these synapses determines how vigorously they fire in response to a given excitatory drive. Their I→E outputs, via GABAA-mediated synapses onto pyramidal somata and proximal dendrites, set how much inhibitory hyperpolarization or shunting each interneuron spike delivers. When both E→I and I→E connections are robust, increased pyramidal firing rapidly recruits a matching interneuron response that provides short-latency feedback inhibition, preventing runaway activity and controlling which neurons remain active. If inhibitory synapses are under-strengthened, the TSMS struggles to curb excessive pyramidal activity, risking unregulated hyperexcitability or overshoot behaviors reminiscent of FTSD.

Taken together, the excitatory circuit sets the upper bound on how large the TSMS's output can become, while the inhibitory circuit determines how precisely that output is gated and shaped. When these circuits are well matched, a performer can translate a chosen attempted intensity into real-world movement up to the TSMS's maximal capacity. When excitatory strengths are insufficient, no amount of attempted intensity achieves the intended high force or speed. When inhibitory strengths are too weak relative to excitation, high attempted intensities can instead produce overshooting or unintended movements.

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We now introduce a central clinical construct. We use the term true weakness to denote a task-specific paresis in which a high-intensity motor command fails to generate the intended movement speed or force, even though performance remains normal at lower intensities and in other tasks. Mechanistically, true weakness arises when the excitatory circuit of a TSMS lacks the synaptic potentiation required to drive the corticospinal system at a specific attempted intensity and above. Strong descending commands then yield only modest increases in pyramidal firing and inadequate recruitment of spinal alpha motoneurons. Subjectively, the performer experiences a pronounced mismatch between the intended intensity and the realized output: keystrokes feel sluggish, feeble, or "paralyzed" within a specific intensity range, despite preserved basic strength and dexterity elsewhere.

At the neural level, true weakness is expressed when pyramidal neurons saturate at relatively low firing frequencies because their synapses have undergone LTD. The EPSPs generated by a strong cortical command are too small to push these neurons into the high-frequency regime needed for that specific high-intensity movement. In the spinal cord, the summed EPSPs arriving at the motor neuron pool fail to bring enough motoneurons to threshold or to sustain high discharge rates. Fewer motor units are engaged, and those that do fire contribute less force. Thus, the TSMS's excitatory circuit lies below the level of synaptic potentiation required to convert a given high attempted intensity above the true-weakness threshold into the corresponding descending spike output.

We define the true-weakness threshold as the highest intensity at which the TSMS can still faithfully implement attempted intensities without producing this task-specific paresis. At or below this threshold, attempted intensity and realized output remain well matched: the TSMS can recruit sufficient excitatory drive to generate the desired speed or force. Above this threshold, strong commands reliably elicit the pattern just described: high subjective effort paired with clearly diminished output. Movements in that band are therefore characterized by true weakness.

Next, we formalize how a second key process can transform a weakened but still functional TSMS/synergy into a dystonic one. We use the term overreaching to refer to situations in which a functional synergy repeatedly attempts intensities (speed, force, or volume) that exceed its current E/I capacity, defined as the level of intensity supportable by the present maximal synaptic strengths of its excitatory and inhibitory circuits. During overreaching, cortical and spinal circuits still generate repeated motor commands in an effort to achieve the desired behavior, but the resulting firing remains fragmented and suboptimal: pyramidal bursts are too small, too brief, or too poorly synchronized to produce the intended movement.

We propose that these repeated partial bursts nevertheless drive a specific pattern of presynaptic activity that can selectively potentiate excitatory circuit synapses while failing to produce parallel potentiation in inhibitory circuit synapses. On a population scale, we posit that this pattern can gradually peel off a subset of excitatory synapses into a new, maladaptive TSMS — a dystonic synergy — that operates above the original functional synergy's capacity. Several features of cortical circuitry bias plasticity toward this outcome.

First, E→I synapses may have higher or more phasic thresholds for LTP induction than E–E synapses. PV interneurons typically require strong, temporally coherent excitatory input to achieve the high-frequency firing that effectively triggers plasticity. During overreaching, pyramidal neurons do fire, but their activity often falls short of the robust, aligned bursts that would optimally drive interneuron spiking. Excitatory bursts are too sporadic or weak to consistently reinforce E→I synapses, even though they may suffice to incrementally potentiate E–E synapses.

Second, PV interneurons exhibit distinctive intrinsic properties, such as short membrane time constants and pronounced afterhyperpolarizations (e.g., related to Ih currents), that favor high-frequency, tightly timed spike trains. When incoming excitation arrives as small, uncoordinated "packets," interneurons may fire only a few scattered spikes instead of sustained, coherent bursts. Because plasticity at E→I synapses is spike-timing-dependent, this sparse, irregular firing fails to provide the consistent pre- and postsynaptic spike relationships needed to consolidate LTP.

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Third, I→E synapses back onto pyramidal neurons are also governed by STDP-like rules. Strengthening these connections requires that interneuron spikes coincide with depolarized states in their pyramidal targets. During overreaching, interneurons may fire only intermittently, and pyramidal cells themselves are not reliably in the appropriate depolarization window when those spikes occur. As a result, I→E synapses do not undergo the strengthening that would normally establish strong, short-latency feedback inhibition.

Fourth, on the molecular side, repeated submaximal pyramidal bursts can still tag and capture PRPs at E–E synapses because at least a subset of the excitatory ensemble fires consistently. Interneurons, by contrast, may fail to capture PRPs if their firing is too irregular or sparse. Consequently, PRP-dependent consolidation is biased toward excitatory connections, which accumulate LTP over time, whereas inhibitory synapses remain relatively unchanged.

Together, these mechanisms indicate that repeated overreaching selectively strengthens the excitatory circuit of a TSMS, while the corresponding inhibitory circuit remains unpotentiated. With continued practice in this regime, this imbalanced subset of the TSMS gradually peels away from the original functional TSMS and consolidates as an excitatory-dominant dystonic synergy that occupies an intensity range just above the functional synergy's current E/I capacity. Once attempted intensity enters this range, the dystonic synergy outcompetes the functional synergy and is preferentially engaged, whereas below it the functional synergy still governs output. This crossover in which synergy dominates is precisely what gives rise to the clinical symptom-threshold phenomenon in FTSD: movements at or below this intensity remain fully voluntary and symptom-free, while movements above it recruit the dystonic synergy and elicit involuntary contractions. Meanwhile, the original functional synergy, which operates comfortably at lower intensities, no longer receives the specific high-intensity co-activation needed to further increase its own E/I synaptic strengths and therefore stagnates.

Importantly, when FTSD first emerges, the dystonic synergy still draws heavily on the same pyramidal neurons and local circuits that support the functional synergy, especially for intensities below the symptom-threshold. Repeated overreaching above the functional synergy's capacity incrementally strengthens E–E synapses within the new dystonic subcircuit, while the corresponding inhibitory synapses fail to track this potentiation. At this early stage, the dystonic synergy functions as an excitatory "extension" of the original synergy, partially overlapping its excitatory and inhibitory resources at lower intensities.

However, we hypothesize and propose that metaplastic processes and continued "use" at higher intensities enable the dystonic synergy's excitatory side to reorganize and add new or re-labeled synapses, effectively building a parallel resource base that was once entirely shared with the functional synergy. Through the tagging and capture of PRPs and the recruitment of additional dendritic spines, the dystonic synergy becomes more autonomous. As repeated high-demand episodes reinforce these excitatory connections above the threshold, the subcircuit does not merely borrow old synergy synapses; it stabilizes its own set of strongly potentiated E-E synapses. Meanwhile, the functional synergy's E/I loops at lower intensities receive fewer co-activations and fewer PRPs, causing them to stagnate at a reduced strength.

Once the dystonic synergy consolidates in this branched-off manner, it no longer relies on the original functional synergy's "below-symptom-threshold" resources. Consequently, technique changes, typically occurring at low or moderate intensities, mainly reshape the functional synergy through partial overlap between the old and new low-intensity motor patterns and retrograde interference. Its unique synapses, which are still being partially engaged during below-symptom-threshold playing, are repeatedly downregulated or pruned. In contrast, the dystonic synergy resides at higher intensities and may be deliberately avoided to minimize symptoms; as a result, its E/I network is not perturbed by these new practice patterns. Moreover, because its excitatory subcircuit has most likely already approached the local LTP ceiling by the time it has consolidated and branched-off, occlusion prevents it from accruing more LTP.

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The functional synergy below the symptom-threshold therefore remains vulnerable to each new technique change, whereas the dystonic synergy is immune to these interference effects. With every technique change, only a subset of the functional synergy's synapses is preserved, and the rest undergo LTD or structural loss. If repeated several times, this process can yield a three-state intensity landscape: (1) a below-threshold zone in which movements are unproblematic, but functionally weak, reflecting the reduced capacity of the functional synergy; (2) a mid-range zone in which attempted intensities exceed this diminished capacity and consistently elicit true weakness; and (3) a higher-intensity zone in which the dystonic synergy is recruited, producing overt dystonic symptoms. In practice, this three-state scenario is most likely to emerge if an individual repeatedly changes technique without allowing each new motor pattern to be fully consolidated.

That said, if an individual is already in such a three-state intensity landscape and repeatedly overreaches within the mid-range true-weakness zone, the same partial-burst, E-E-biased plasticity can, in principle, create a second dystonic synergy. In that situation, subthreshold bursts again selectively potentiate E–E synapses in a newly engaged subcircuit while failing to co-develop matching inhibitory circuitry, creating another excitatory-dominant TSMS just above the newly reduced true-weakness threshold.

Because the original dystonic synergy has previously branched off via metaplastic changes and consolidated at a higher intensity domain, it remains insulated from this process. The new dystonic synergy under formation in the mid-range zone no longer draws on the same synaptic resources that stabilized the first dystonic synergy; instead, it reorganizes the remaining E–E synapses of the moderately weakened functional domain into another maladaptive excitatory network. By the principle of occlusion, each dystonic synergy eventually saturates its excitatory circuit once sufficient partial bursts have stabilized those E–E synapses, while the corresponding inhibitory circuits stay under-strengthened due to insufficient synchronous drive.

Theoretically, iterating this cycle, which involves further degrading the functional synergy through repeated, unconsolidated technique changes and then overreaching at each newly lowered capacity, could produce multiple discrete dystonic synergies stacked at progressively lower intensity ranges, each anchored above its own true-weakness threshold. We regard this scenario as extremely rare in practice, as it would require a very specific and persistently maladaptive training pattern. Nonetheless, from a neuroplasticity standpoint, we see no fundamental mechanism that categorically prevents such multi-synergy stacking.

Importantly, when a dystonic synergy first begins to form above the functional synergy's capacity, its excitatory circuit is only partially potentiated. The relevant E–E synapses have acquired LTP via repeated subthreshold bursts, but they have not yet reached the local ceiling imposed by occlusion. If the performer continues to operate in this same high-intensity range, at or slightly beyond the dystonic synergy's current excitatory capacity (i.e., overreaching), each attempt generates further bursts of presynaptic spiking within the same subset of pyramidal neurons. These bursts repeatedly tag those E–E synapses and capture PRPs (e.g., CaMKII, PKMζ, BDNF), pushing the same excitatory circuit closer to its maximal potentiation. Because the firing pattern remains fragmented and suboptimal for recruiting PV interneurons, the inhibitory circuit still fails to undergo parallel LTP. Thus, overreaching within an already dystonic intensity range primarily drives the existing dystonic synergy toward saturation rather than creating a separate additional TSMS.

By contrast, forming a distinct second dystonic synergy requires a different true-weakness zone, as outlined above. The functional synergy must first be degraded through further technique changes, establishing a new mid-range true-weakness threshold. Overreaching in that lower zone, where attempted intensities exceed the newly reduced excitatory capacity but remain below the dystonic threshold of the already formed synergy, can then selectively potentiate a new subset of E–E synapses while again failing to co-develop matching inhibitory circuitry. This process yields a separate excitatory-dominant TSMS anchored above the new true-weakness threshold. In other words, multi-synergy stacking requires cycling through new true-weakness thresholds and overreaching there, not simply pushing harder within an already dystonic intensity range.

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We next consider "counter-motion," which in our framework refers to an intentional effort to produce the antagonist movement of a dystonically driven motion. For example, if a dystonic synergy causes involuntary hyperflexion in the right index finger, counter-motion means attempting extension with that same finger while it simultaneously experiences dystonic hyperflexion. We propose that each digit's representation in M1 comprises multiple partially overlapping TSMSs (e.g., flexion, extension, abduction, adduction), with each unidirectional pattern instantiated as a separate TSMS at the cortical level. Although these synergies share some neuronal populations, each also depends on its own subset of pyramidal neurons and PV interneurons.

In the hyperflexion example, the dystonic flexion synergy has developed just above the functional flexion synergy's excitatory and inhibitory capacities, with abnormally strong E–E synaptic strength and impaired inhibitory feedback via deficient PV interneuron circuits. Once the intended movement intensity crosses the dystonic symptom-threshold, this synergy outcompetes other ensembles for control of the digit, generating involuntary flexor-oriented output. When no counter-motion is attempted, we hypothesize that the dystonic synergy is therefore the dominant TSMS for that digit. Because it is hyperexcitable and insufficiently clamped by inhibition, it saturates a large fraction of the local pyramidal population controlling the finger's prime-mover muscles. In effect, the dystonic ensemble hijacks much of the available motor cortical resource for that digit, overshadowing the functional synergies that would otherwise execute non-dystonic movements at that intensity. This overshadowing is possible because many of the same cortical neurons can, in principle, participate in either synergy; however, the dystonic synergy's strengthened E–E synapses and weak E/I regulation make it disproportionately likely to lock the population into a maladaptive, sustained firing pattern.

When counter-motion is attempted, some pyramidal neurons belonging to the functional extension TSMS still receive descending drive. However, this extension drive is severely constrained because the dystonic flexion synergy has already saturated much of the digit's neuronal pool with high E-E activity. Few recruitable pyramidal neurons remain to support a robust antagonist command, so the extension TSMS cannot scale its excitatory output to the intensity needed to overcome flexion. Behaviorally, the finger produces only a partial, limited extension.

Under these conditions, we propose that the extension TSMS can never overreach during counter-motion, even if its own synaptic strengths have not reached their occlusion maximum. In the presence of an already active dystonic synergy in flexion, most of the excitatory neurons that could, in principle, support high-intensity extension are already substantially depolarized by the dystonic ensemble's E–E activity. As a result, the antagonist TSMS cannot approach its upper excitatory capacity or generate the repeated, moderately high-intensity partial bursts that characterize true overreaching.

Counter-motion, therefore, produces a relatively shallow, low-frequency extension command that merely coexists with the hyperflexion drive. Because the extension TSMS never pushes its excitatory circuit beyond its capacity in isolation, it does not enter the unstable regime in which excitatory plasticity outpaces inhibitory plasticity and does not accumulate the E-E-biased LTP needed to consolidate a new dystonic synergy in the antagonist direction. Instead, the observable behavior is a relatively stable "tug of war" between a hyperexcitable dystonic synergy and a weaker, functional extension synergy.

Therapeutic Translation: Mechanism-Informed Rehabilitation

Once FTSD has arisen, manifesting as a TSMS in which PV-mediated inhibitory synapses are under-strengthened relative to excitatory E-E synapses, we propose a specific motor retraining protocol, below- or at-threshold retraining (BATR). BATR is defined as the systematic practice of the affected skilled movement strictly at or below the intensity that still produces clean, symptom-free performance (the symptom-threshold), and, in a three-state scenario, at or below the true-weakness threshold. We propose that, if applied correctly and for sufficient duration, BATR can serve as a potentially curative intervention for FTSD by engaging STDP mechanisms to restore balance between

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excitation and inhibition within the affected TSMS. Under these conditions, motor retraining is directed to incrementally strengthen E-E, excitatory-inhibitory (E→I), and inhibitory-excitatory (I→E) synapses in the residual functional synergy and, critically, the PV inhibitory synapses (E→I and I→E) of the dystonic synergy itself.

Conceptually, BATR is very similar to the "slow-down exercise" (SDE) first detailed by Sakai (2006) and later replicated by Yoshie et al. (2015). However, both studies focused on the protocol's clinical outcomes and left the underlying neurophysiological mechanisms unexplored. In our framework, BATR functions by constraining every repetition of the skill to an intensity that remains free of dystonic contractions and true weakness and that lies within the current E/I capacity of the functional synergy. At these levels, pyramidal neurons in M1 enter a stable firing regime in which each excitatory burst is strong enough to reliably depolarize local PV interneurons, yet does not overreach the excitatory circuit's current capacity, so firing remains coherent rather than becoming disorganized, partial-burst patterns. Because PV interneurons require well-synchronized excitatory input to undergo LTP at E→I synapses and to deliver precise $GABA_A$-mediated I→E feedback, repeated practice below or at the symptom-threshold provides exactly the presynaptic and postsynaptic timing needed to drive inhibitory plasticity.

From a mechanistic standpoint, repeated co-activation in this clean intensity zone keeps the membrane potentials of pyramidal neurons and PV interneurons within the temporal windows required for STDP. Excitatory-inhibitory connections strengthen when PV cells receive consistent, well-phased EPSPs from presynaptic pyramidal neurons and then fire action potentials that generate IPSCs back onto the same or closely related excitatory targets. Stable, non-fragmented pyramidal spike trains give PV interneurons well-defined, time-locked depolarizations, which in turn produce intracellular calcium transients through NMDA-type glutamate receptors or high-frequency suprathreshold depolarizations. These events are necessary for LTP at E→I synapses. Each short-latency volley of PV-mediated inhibition returning to pyramidal somata further reinforces the tight temporal coupling between excitatory output and inhibitory feedback.

Each correctly timed episode of pyramidal and PV spiking also engages PRPs such as CaMKII, CaMKIV, and PKC in both presynaptic and postsynaptic compartments. Within PV interneurons, these cascades promote $GABA_A$ receptor clustering at their terminals onto pyramidal cells and increase presynaptic release probability at GABAergic synapses, which together enlarge the amplitude and reliability of inhibitory postsynaptic currents. As these changes accumulate, the previously compromised inhibitory loops within the synergy recover the ability to clamp excitatory surges at progressively higher intensities. The symptom-threshold for involuntary dystonic firing is pushed upward as the inhibitory circuit strengthens.

At the network level, inhibitory circuitry in M1 is only partially segregated across synergies. We propose that a subset of PV interneurons participating in the functional synergy also receive input from, and project back to, pyramidal neurons that belong to the dystonic synergy. These shared inhibitory cells link neighboring excitatory ensembles for the same digit. When the functional synergy is repeatedly recruited in a well-timed, high-fidelity manner during BATR, it drives strong E→I input onto these PV interneurons, which then fire robustly and send I→E output not only to the functional pyramidal population but also to overlapping or neighboring pyramidal neurons in the dystonic ensemble. Even though the dystonic synergy's excitatory subcircuit remains silent at below-threshold speeds, every clean practice trial still generates a coincident burst of excitation in shared PV cells and a matched inhibitory volley into the broader M1 region. Over time, this synchronized activity strengthens E→I and I→E synapses in the inhibitory circuit of the dystonic synergy as well.

Thus, the key insight is that this partial overlap in local inhibitory cells allows BATR to act on both synergies at once. Each below-threshold repetition maintains and enhances the functional synergy's E/I balance while simultaneously providing the dormant inhibitory circuit of the dystonic synergy with exactly the frequency and timing of PV co-activation needed to grow its synaptic strength. Because the performer never exceeds the symptom-threshold to engage the dystonic excitatory circuit, those excitatory synapses are not further potentiated. Instead, PV interneurons

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remain strongly and repeatedly engaged within the normal synergy, with ample bursts, calcium signaling, and capture of PRPs, so their $GABA_A$ output onto dystonic pyramidal neurons can gradually catch up.

Across many practice sessions, the inhibitory circuit of the dystonic synergy strengthens until its synaptic strength equals that of the dystonic excitatory circuit, restoring the E-E to E-I ratio toward equilibrium within that maladaptive TSMS. Once local PV interneurons can deliver robust, short-latency inhibition that matches the dystonic excitatory drive, increases in movement intensity no longer produce the runaway bursts characteristic of FTSD, as emerging pyramidal bursts are immediately curtailed and cortical hyperexcitability and involuntary posturing are prevented. Clinically, the symptom-threshold progressively shifts upward, dystonic contractions gradually disappear, and the performer can operate at intensities that previously provoked symptoms without recruiting the involuntary synergy. Through BATR, M1 reestablishes the temporal synchrony between excitation and inhibition: the functional synergy's E/I circuits continue to strengthen through LTP, and, via shared PV interneurons, the dystonic synergy's previously weak inhibitory circuit also undergoes LTP. In principle, this process can reverse the maladaptive plastic changes that define FTSD and allow a complete, lasting recovery.

Clinical Implementation: A Practical Guide for Below- or At-Threshold Retraining

BATR relies on strict adherence to performing the affected motor task while not provoking dystonic symptoms (and true weakness if there is also a true-weakness threshold). Whether the individual is a musician, writer, vocalist, athlete, or any other practitioner whose craft hinges on refined motor skills, the same neuroplastic principles apply: the patient must locate and remain at or below their dystonic or true-weakness threshold while carefully and gradually expanding that threshold once the inhibitory circuit has begun to catch up. In a clinical or self-guided setting, the first step is to identify the highest task intensity at which dystonic symptoms vanish. For a pianist, this means determining the maximal keystroke force; for a laryngeal dystonia patient (also known as spasmodic dysphonia), the maximum speech volume, often when whispering or using very soft phonation; and for a writer, the greatest writing speed or pen pressure. Once that threshold point is determined, the recovery journey begins with long daily practice sessions (with ideally minimal breaks and interruptions) of precisely executing movements at or below this “clean” intensity. The patient should strive for consistently accurate repetitions free of any involuntary contractions, all the while cultivating a sharp sensory awareness of each movement. The goal is to ensure repeated, well-timed co-activation of pyramidal cells and PV interneurons, driving the desired adaptive synaptic potentiation discussed previously.

Clinicians should instruct patients to increment speed or intensity in small, carefully measured steps. The attempted intensity should only be increased if improvement is felt during or after a consistent period, often hours, days or weeks, of symptom-free practice. A musician who experiences improvement at a slow tempo may nudge the metronome up a few beats per minute, provided no dystonic signs appear. A writer might gradually reduce the time taken to physically write a sentence, ensuring no dystonic symptoms creep in. If any dystonic symptoms reemerge, the patient should immediately revert to a lower intensity, ensuring that each successful repetition remains below or at the threshold where no symptoms occur. This cyclical process (discovering the clean range, reinforcing it through repetitive practice, and then gently expanding it) systematically coaxes the inhibitory circuit of the dystonic synergy and both excitatory and inhibitory circuits of the functional synergy to strengthen, a process necessitating weeks to potentially months of continuous daily training (ideally lasting several uninterrupted hours every day).

Additionally, clinicians must emphasize patience to patients: rebalancing the E/I interplay in FTSD demands high repetition counts, distributed over consistent daily practice. In the early stages, patients may often find that progress remains slow or negligible for days or weeks. It is important that the clinician or therapist helps sustain morale and ensures the therapy adheres to core

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neuroplastic principles. Relapses into dystonic firing may occur momentarily if the chosen intensity increase after experienced improvement is more than what the recent improvement can provide, serving as a barometer to step back and reconsolidate inhibitory strength at slightly lower intensities. By carefully following BATR, the performer incrementally shrinks the E/I gap that underlies the dystonia. Over time, the thresholds at which dystonic activity or true weakness intrudes move higher, gradually matching or surpassing normal functional demands and eventually resolving.

Addressing Variability in Patient Outcomes

A vital point for both clinicians and patients to understand is that BATR should, in theory, be universally applicable to all FTSDs, so long as a symptom-free range of movement intensities at or below a given movement-intensity threshold can be identified. The fundamental mechanism, properly and regularly engaging shared PV interneurons without reinforcing high-excitability loops, should not vary among different individuals with FTSD. Thus, when a patient reports slow or insufficient progress, it does not indicate that the method "does not work" for that particular case of FTSD. Rather, such variability most often reflects a breakdown in practice protocols or an insufficient duration of training. If the patient increases speed or force too rapidly, inadvertently activating or potentially reinforcing the dystonic synergy, the inhibitory side never engages robustly enough to induce the necessary synaptic strengthening. Similarly, if practice sessions are too brief or too inconsistent, then the neural circuits have not received enough of the consistent E/I co-activation needed to recalibrate its balance.

From the clinician's perspective, monitoring adherence is paramount. Detailed logs of daily practice, recording the exact speed (e.g., metronome markings), duration of below-threshold performance, and any lapses into dystonic firing, help pinpoint whether the patient is genuinely meeting the criteria for correct execution and implementation of BATR. Crucially, the published SDE protocols (Sakai, 2006; Yoshie et al., 2015) and other below-threshold retraining approaches (e.g., van Vugt et al., 2014, Video S1) have demonstrated objective success in carefully documented cases, indicating that the method is robust across the spectrum of FTSD. The key is that any BATR practice must be truly dystonia-free, repeated adequately to induce synaptic potentiation (both E→I and I→E), and carried out with unwavering consistency to allow Hebbian plasticity to accumulate.

In practical terms, clinicians can reassure patients that the BATR protocol works on a solid neurophysiological foundation, backed by empirical data, scientific reasoning, and direct clinical observation. Hence, persistent use of BATR remains the recommended route to lasting resolution, regardless of individual variation in short-term outcomes.

Hypothesis Verification via Computational Modeling

While much of the evidence for the synergy-based explanation of FTSD comes from clinical observation and electrophysiological findings, computational modeling offers a powerful complementary approach to test and refine these hypotheses. Specifically, by simulating a neural architecture underlying excitatory/inhibitory (E/I) balance, one can systematically manipulate synaptic strengths, plasticity rates, and network connectivity to observe whether, and under what conditions, a "maladaptive synergy" emerges. This strategy allows a more rigorous, iterative cycle of hypothesis generation (from clinical observation to modeling) and hypothesis verification (from modeling back to empirical testing), without actually accessing human patients which is oftentimes not possible. In this section, we present findings from a simulated spiking neural network we used to verify some of the hypotheses described above.

Network Model

We simulated a spiking neural network composed of two interconnected populations: an excitatory population (E) and an inhibitory population (I). Each population consisted of N_{ex} excitatory

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and N_{inh} inhibitory neurons, following a leaky integrate-and-fire (LIF) neuron model with synaptic interactions.

The neurons evolved according to the following membrane potential equation:

$$\tau_m dV/dt = (V_{rest} - V) + I_{syn}$$

where V is the membrane potential, V_{rest} is the resting potential, τ_m is the membrane time constant, and I_{syn} represents synaptic input.

Spiking events were generated when V exceeded a threshold Vth, after which the membrane potential was reset to V_{reset}.

Synaptic Connectivity

Synaptic interactions were implemented with conductance-based synapses, where synaptic current was given by:

$$I_{syn} = g_{syn}(V - E_{syn})$$

where g_{syn} is the synaptic conductance, and E_{syn} is the reversal potential of the synapse. Excitatory-to-inhibitory (E→I) and inhibitory-to-excitatory (I→E) connections were defined with a probability of connection p.

Input Drive and External Stimuli

External inputs were applied to neurons via a Poisson-distributed spike train, simulating background noise and task-related input. Input amplitude to the excitatory populations was systematically varied to examine the network's response to different stimulation intensities. The external drive followed:

$$I_{ext} = A \times Poisson(r)$$

where A was the input amplitude and r the baseline firing rate of the Poisson process.

Simulation of Overreaching and Dystonia

To simulate maladaptive plasticity leading to dystonia, we introduced a functional synergy (FS) and a dystonic synergy (DS) within the excitatory population. FS was modeled with balanced excitatory/inhibitory drive (EF, IF), while DS was introduced as an imbalance where excitatory synapses (ED) increased without a corresponding increase in inhibitory synapses (ID). Overreaching was induced by systematically increasing external drive beyond the functional synergy's limit.

Firing Rate Analysis

Network activity was analyzed by computing population-averaged firing rates for both excitatory populations. The firing rate was calculated as:

$$r = \frac{total\ spikes}{number\ of\ neurons \times simulation\ time}.$$

For systematic variation of input amplitude to the second population, firing rates of both populations were measured and plotted as a function of the input strength.

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Simulation and Implementation

All simulations were implemented in Python using custom-built neuron models. The integration of differential equations was performed using the fourth-order Runge-Kutta method with a time step of dt=0.1ms. The network was simulated for T=2000, and results were analyzed with Matplotlib and Pandas for statistical processing and visualization.

Computational Model Demonstrates the Emergency of Dystonic Synergy in E/I Network

This section analyzes the spiking neural network results under different conditions to understand the transition from normal motor control to dystonia. Three different scenarios are examined: the healthy network representing baseline functional synergy, the mixed functional and dystonic population, and the loss of balance leading to dystonia. The comparison of firing frequencies across these conditions provides insights into how dystonic circuits emerge and disrupt normal motor function.

In Figure 1B we show the spiking activity of a healthy network, where excitatory and inhibitory functional synergies maintain a stable balance. The firing activity remains regular and within a physiological range, ensuring proper motor control. This serves as a baseline reference, illustrating a scenario where neurons fire without abnormal synchrony or instability. Also, the experiment where input strength is increased (simulating speed/intensity), demonstrates that for this case the firing rate follows a linear increase with the input strength. The inset shows the activity of inhibitory cells, typical of PV cells in that brain area that follows a similar linear increase.

This pattern is not always the case, and although in a 2D excitatory/inhibitory (E/I) neuron network model, increasing the amplitude of the external stimulus typically leads to an increase in the firing rate of the neurons a low-pass pattern is expected and could come earlier depending on the balance. This is because a stronger external stimulus can drive the excitatory neurons to fire more frequently but, as the excitatory neurons become more active, they can, in turn, increase the activity of inhibitory neurons due to the network's connectivity (Figure 1D).

The overall effect on the network's firing rate can depend on several factors, including the balance between excitation and inhibition, the network's connectivity, and the specific dynamics of the neurons involved. If the inhibitory feedback is strong enough, it might counteract the increase in excitatory activity, potentially stabilizing the firing rate or even reducing it after an initial increase.

In summary, while you can generally expect an increase in firing rate with a stronger external stimulus, the precise outcome will depend on the specific parameters and dynamics of your E/I network model.

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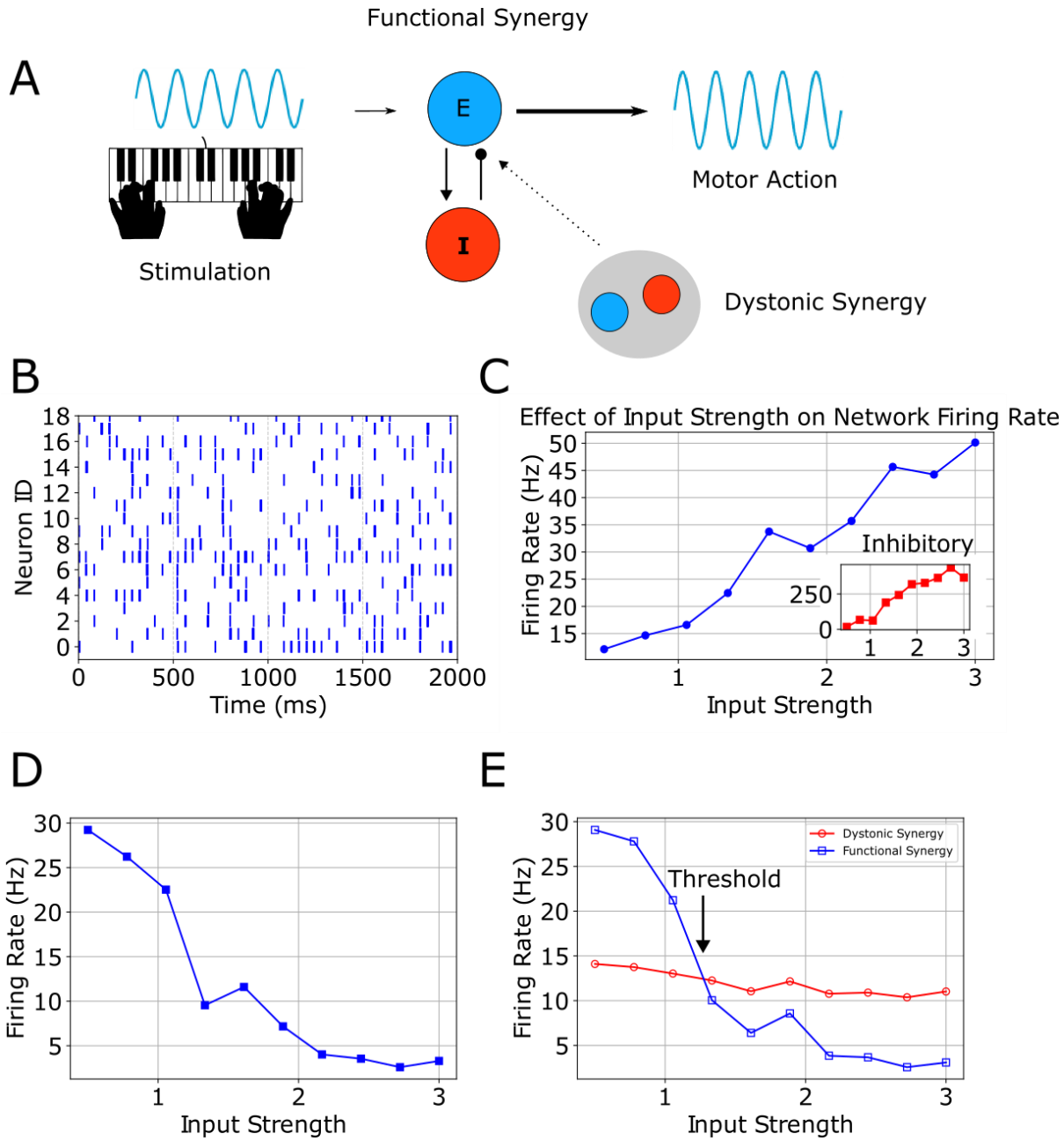

Figure 1. A. Schematic representation of the experimental setup. Stimulation (depicted by a piano keyboard) leads to motor action through functional synergy involving excitatory (E) and inhibitory (I) neurons. Dystonic synergy is indicated by the overlapping circles. The latter could be present or absent depending on the situation (see text) **B.** Raster plot showing neuronal firing activity over time for healthy state. Each row represents a different neuron, and each tick mark indicates a spike. **C.** Graph illustrating the effect of input strength on network firing rate (same as in B). The main plot shows the firing rate increasing with input strength. The inset highlights the inhibitory effect at a specific input strength. **D.** Graph showing the decrease in firing rate with increasing input strength, indicating a different network response. Different E/I balance and input strengths change the response pattern of the network. **E.** Comparison of firing rates between dystonic and functional synergies across varying input strengths. A threshold is marked where the firing rate diverges between the two conditions.

As the dystonic synergy emerges alongside the existing functional synergy (Figure 1E), a firing rate competition becomes apparent. Thus, the network consists of two interacting populations. Notice that the dystonic synergy has low firing rate for smaller input strengths and does not affect

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considerably the functional, but after a certain threshold, it is firing at higher rates than the functional. In other words, the distinct firing rates indicate that both populations coexist and interference is apparent after the threshold, suggesting that dystonic neurons are active but not dominating motor function unless higher input strengths, here associated with speeds, are attempted.

This result is significant because it is associated to unbalanced networks and how dystonia allows excessive synchronization and hyper-excitability in motor circuits. The dystonic synergy overshadows the functional synergy, leading to involuntary contractions due to the loss of independent motor control, pathological co-activation of neurons, and a shift in motor circuit dynamics that reinforces maladaptive plasticity.

Discussion

High-Level Synthesis

This work advances a unified, M1-centric account of FTSD that links clinical phenomenology, cortical circuitry, and computational modeling. We propose that FTSD arises within a TSMS in M1, in which excitatory synapses are disproportionately strengthened relative to PV synapses. This PV-centered imbalance produces a hyperexcitable, "dystonic synergy" that is recruited only when movement intensity exceeds a well-defined symptom-threshold.

The developmental account specifies how such a dystonic synergy can emerge insidiously. Technique changes create partial baseline shifts that reduce the synaptic capacity of the original functional synergy. Attempts to perform above this reduced capacity generate true weakness, a task-specific paresis in which strong motor commands fail to produce the intended movement intensity. Repeated overreaching in this state favors LTP of excitatory synapses while leaving inhibitory synapses understrengthened, gradually peeling off an excitatory-dominant subcircuit that becomes the dystonic synergy.

Building on this mechanism, we introduce BATR as a mechanism-based motor retraining protocol. By practicing strictly at intensities that do not elicit dystonia or true weakness, patients repeatedly co-activate pyramidal neurons and shared PV interneurons in a stable regime. This practice pattern is predicted to strengthen both excitatory and inhibitory synapses in the functional synergy and to restore inhibitory strength in the dystonic synergy until excitation and inhibition are again balanced, consistent with the observed resolution of symptoms under BATR in our case, under SDE (Sakai, 2006; Yoshie et al., 2015), and under an operationally equivalent below- or at-threshold retraining protocol implemented by van Vugt et al. (2014, Video S1).

Finally, a spiking E/I network model demonstrates that, under plausible parameters, a maladaptive "dystonic" population can indeed emerge and dominate output above a critical input strength, recapitulating the clinical threshold phenomenon. Together, these elements outline a coherent framework in which FTSD is understood as a plastic, synergy-level imbalance that can, at least in principle, be behaviorally reversed.

Relation to Existing Models and Literature

A natural question is how this TSMS and PV-centered model relates to existing basal ganglia, cerebellar, and network-level models of FTSD. Classical basal ganglia centric views of FTSD build on the canonical model in which the direct, D1 receptor-expressing pathway and the indirect, D2 receptor-expressing pathway within cortico-striato-pallido-thalamo-cortical loops jointly regulate facilitation of intended movements and suppression of competing ones (Alexander & Crutcher, 1990; Calabresi et al., 2014; Gerfen, 1992; Wichmann & DeLong, 1996). Within this framework, FTSD is proposed to arise when this pathway balance is shifted, typically through reduced function of the D2-mediated indirect pathway and/or excessive D1-mediated direct pathway drive, leading to disinhibition of thalamo-cortical outputs and, downstream, to reduced intracortical inhibition and motor cortical hyperexcitability (Berman et al., 2013; Chen et al., 1997; Hallett, 2006; Perlmutter et al., 1997; Simonyan et al., 2017). Cerebellar-centric accounts propose that FTSD arises when abnormal

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cerebellar activity and plasticity, especially dysregulated Purkinje cell firing and altered cerebello-thalamo-cortical connectivity, corrupt the calibration of motor output and sensorimotor integration, leading to maladaptive motor cortical plasticity and the emergence of symptoms (Bologna & Berardelli, 2017; Hubsch et al., 2013; Morigaki et al., 2021). Network-centric models, in turn, conceptualize FTSD as a disorder of a distributed motor network, in which abnormal connectivity and interactions among cortical, basal ganglia, thalamic, and cerebellar components of motor circuits disturb normal sensorimotor processing and the control of highly learned movements, without positing a single privileged site of origin (Fuertinger & Simonyan, 2018; Jinnah et al., 2017; Schirinzi et al., 2018). These three perspectives have been highly influential and successfully organized a large corpus of imaging and neurophysiological data, yet they leave several core phenomenological features of FTSD only partially explained.

In particular, they offer little explanation for several defining features of FTSD, including the confinement of symptoms to a single, highly practiced skill with sparing of other skills and even adjacent digits, the robust symptom-threshold at a specific movement intensity, and the observation that purely behavioral, threshold-based retraining can abolish symptoms. If the primary defect resided in basal ganglia or cerebellar circuitry that broadly modulates motor output, one would reasonably expect a wider spread of abnormal movements across tasks and effectors, rather than a syndrome that remains restricted for years to a single skilled movement such as rapid right-hand piano playing. Similarly, the symptom-threshold phenomenon, in which performance of the affected task is completely normal at or below a specific movement intensity but deteriorates abruptly above it, is most parsimoniously explained by treating it as a property of a circuit that directly generates the task-specific motor command, rather than as the consequence of a diffuse state change in a global gating structure. A model that privileges basal ganglia or cerebellum as the primary lesion site therefore requires additional, often implicit, assumptions about how such sharply task-specific and intensity-dependent expression arises from a relatively global perturbation.

The present TSMS framework addresses these gaps by locating the decisive plastic changes in a narrowly defined synergy in M1 that drives a unidirectional movement of a specific digit or other effector. Within this view, basal ganglia and cerebellar alterations remain important components of the syndrome, but they are driven by repeated activation of a hyperexcitable cortical synergy rather than initiating it. Task specificity follows directly from the fact that only the TSMS responsible for that exact motor task is repeatedly overreached and pushed into an excitatory-dominated, maladaptive regime, whereas synergies for other tasks remain balanced. The symptom-threshold reflects the intensity range at which the dystonic synergy, with its strengthened excitatory subcircuit and lagging inhibition, begins to outcompete the residual functional synergy for control of the same muscles. The developmental sequence from stable performance, through true weakness, to overt dystonia emerges naturally once partial baseline shifts and overreaching are taken into account, without the need to invoke qualitatively different mechanisms at each stage. In this sense, M1 is not simply another node in a distributed network, but a privileged locus where the plasticity rules of a specific TSMS determine whether FTSD arises at all and which movement it will affect.

At the same time, the TSMS account is compatible with and helps organize network-level observations. It predicts that chronic hyperexcitable output from a dystonic synergy will induce plastic changes throughout the motor hierarchy, including basal ganglia reinforcement of the overactive pattern, cerebellar adaptation to persistent error-like input, sensory map smudging in S1, and reduced spinal reciprocal inhibition. These adaptations are treated in detail in a companion study, but conceptually they can all be viewed as consequences of M1 repeatedly broadcasting an abnormal, task-bound motor command. From this perspective, basal ganglia and cerebellar abnormalities in FTSD do not compete with an M1-centric explanation; instead, they reflect the brain's attempt to stabilize and compensate for a maladaptive cortical synergy that has already shifted into an excitatory-dominated state. The TSMS and PV-based framework thus preserves the empirical richness of prior models while supplying a specific cortical circuit in which the key pathogenic imbalance is instantiated and a clear route by which that imbalance can be reversed.

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Future Directions and Testable Predictions

The TSMS and PV-centered framework yields a set of concrete predictions that can be evaluated in both human and animal studies. The most immediate prediction is that successful BATR should rebalance excitation and inhibition within the affected TSMS. At the level of human physiology, this implies that patients who regain normal skilled performance after sustained BATR should show a restoration of SICI in M1, together with the normalization of surround inhibition. Longitudinal TMS studies that track standard measures of intracortical excitability and inhibition before, during, and after BATR would directly test this claim.

Because the framework views basal ganglia, cerebellar, somatosensory, and spinal changes as secondary to chronic hyperexcitable M1 output, it also predicts that these "downstream" alterations should gradually normalize as the cortical TSMS is rebalanced. Multimodal neuroimaging and neurophysiological measures can be combined with BATR interventions to examine how these adaptations unwind over time.

Prospective clinical trials should test BATR in a way that could justify its integration into standard care. Future randomized studies should enroll a broad sample of newly diagnosed FTSD patients and assign them either to a standardized, manualized BATR program or to current usual care, which typically includes botulinum toxin injections, oral agents, and conventional physiotherapy. Trial designs should use blinded assessors, and should rely on validated dystonia severity scales together with quantitative task performance measures as the main outcomes, with follow up of at least six to twelve months to assess durability and relapse. Investigators should also systematically record adverse events and basic health economic indices, including number of procedures, clinic visits, and direct treatment costs. If such studies demonstrate that BATR is superior or clearly noninferior to standard care on these clinical outcomes, while remaining safer and less resource intensive, they would provide the level of evidence needed to support BATR as a first line treatment in clinical guidelines and hospital practice.

Complementary mechanistic tests will require animal models. For causally probing a PV centered E/I imbalance within M1, rodent forelimb motor cortex is likely the most practical starting point, because PV-Cre lines, viral tools and chronic imaging already permit selective manipulation and readout of excitatory and PV mediated inhibitory synapses in defined forelimb modules during skilled tasks. Future experiments could target the M1 ensemble controlling a learned reach to grasp or lever press and bias PV mediated inhibition relative to local excitatory connectivity, for example by weakening excitatory input to PV cells or their output synapses, or by chemogenetically attenuating PV activity during training while leaving pyramidal circuitry largely intact. The present framework predicts that a chronic PV centered synaptic strength imbalance in such a module should be sufficient to produce a task bound motor disturbance that is normal at low movement demands but becomes abnormal once movement intensity exceeds a clear symptom-threshold, with relative sparing of other behaviors, and that restoring PV function or allowing PV synapses to re potentiate would normalize intracortical E/I measures and behavior. Demonstrating this causal chain in rodents, and ultimately in non human primates once adequate cell type specific tools are available, would directly test the claim that FTSD can originate from plastic PV dominated changes within M1 itself rather than from a purely upstream source.

Related animal work should address the proposed developmental sequence that links stable skill performance to technique change, overreaching, consolidation of a dystonic synergy, and eventual recovery under BATR like conditions. In rodents, skilled reach to grasp paradigms and other automated forelimb tasks already support detailed analysis of how new task demands and repetitive practice reshape M1 circuits, and similar logic can be extended to non human primate hand and digit tasks that more closely resemble human musicianship. A representative design would first train animals to criterion on a dexterous forelimb skill performed with a well defined initial technique, then introduce a modified posture or kinematic requirement that reduces effective capacity. After this technique change, experimenters would explicitly shape behavior so that animals perform the task at speeds or forces above this reduced capacity, leading them to repeatedly overreach the

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available E/I capacity, while excitatory and PV interneuron activity and synaptic efficacy within the relevant M1 ensemble are tracked over time. The model predicts a transition from true weakness to a task-specific, intensity-dependent movement abnormality as excitatory synapses outpace inhibitory strengthening, and further predicts that imposing BATR in the same animals should gradually restore E/I balance and abolish the threshold phenomenon. Longitudinal studies of this sort would provide a direct experimental test of the TSMS based developmental account in a way that is ethically and technically inaccessible in humans.

Taken together, these future directions are not purely technical. They bear directly on how FTSD is managed in clinical practice. At present, many patients are steered immediately toward symptom focused pharmacologic, injectable, or invasive treatments, including deep brain stimulation, that aim to dampen motor output rather than address the underlying M1 circuitry that generates the dystonic symptoms. These methods can be valuable, but they do not directly target the cortical synaptic imbalance within M1 that constitutes the dystonic synergy. If the framework outlined here withstands rigorous testing, BATR could eventually be integrated early in the treatment pathway, in analogy to pelvic floor dysfunction, where motor retraining and biofeedback based protocols are now standard initial therapies. Because BATR is noninvasive, mechanism based, scalable, associated with minimal direct financial cost, and essentially free of serious adverse effects, it has the potential to serve as a truly curative intervention for FTSD, rather than a purely palliative one.

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