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Is Failed Predictive Control a Risk Factor for Focal Dystonia?

Peter Stein, DC, PhD^{1,*}, Elliot Saltzman, PhD^{1,2}, Kenneth Holt, PhD, PT^{1,3}, and Dagmar Sternad, PhD⁴

¹College of Health and Rehabilitation Sciences, Boston University, Boston, Massachusetts, USA

²Haskins Laboratories, New Haven, Connecticut, USA

³Wyss Institute for Biologically Inspired Engineering at Harvard University, Boston, Massachusetts, USA

⁴Departments of Biology, Electrical and Computer Engineering, and Physics, Northeastern University, Boston, Massachusetts, USA

Abstract

Introduction—Task-specific focal dystonia (TSFD) is a disorder marked by degraded coordination in complex and exacting psychomotor tasks, such as musical performance. Its development is associated with prolonged and intensive practice of these tasks, but the etiology of TSFD is still unknown. The prevailing hypothesis was informed by findings in primates following repetitive simple grasping actions. This model implies, however, that complex manual tasks that yield more intricate and subtly varying sensorimotor patterns, as found in musical performance and handwriting, should be unlikely to lead to focal dystonia.

Hypothesis—We propose an alternative, “predictive-control” etiological hypothesis: When an overtaxed performer exhibits poorly controlled variability and errors in motor execution of a well-learned, high-precision task, predictive control processes deteriorate. This includes, in particular, those related to the formation or updating of a forward dynamic model that maps motor commands to predicted end-effector state, e.g. position and velocity of a key-pressing digit.

Conclusion—Based on a critical literature review we argue that this results in the characteristic signs of focal dystonia, such as freezing, halting and inappropriate co-contraction specific to the task. Directions for future research are briefly discussed.

Keywords

focal dystonia; motor control; sensorimotor performance; internal models; musicians

Professional pianists, writers, and typists spend their working day performing highly complex and diversified sequences of precise keyboard actions over extended periods of time. For example, pianists may spend several hours repeating technically demanding

*Correspondence to: Dr. Peter Stein, College of Health and Rehabilitation Sciences, Boston University, 635 Commonwealth Avenue, Boston, MA 02215, USA; pstein@bu.edu.

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passages, continually attempting to refine their motor performance.¹ However, after years of such rigorous practice, some performers experience persistent deterioration of motor coordination specific to the trained tasks. Such localized loss of coordination associated with overtraining these complex motor skills is the defining characteristic of task-specific focal dystonia (TSFD). Evidence indicates that a broad array of somatosensory functions are altered in TSFD,² but the origins of the disorder remain elusive.

A currently influential etiological model of TSFD was motivated by previous reports^{3,4} of sensory cortical dedifferentiation induced in nonhuman primates, whose digits were deprived of the differentiated patterns of mechanical stimulation that typically accompany manipulation and sensing tasks. This subsequent work^{5,6} employed the simple, functional task of repetitive grasping as an experimental model of both repetitive strain injury and TSFD. As with the experimental conditions in the earlier studies,^{3,4} the repetitive grasping task entailed the creation of highly correlated patterns of digital costimulation. After prolonged training on this grasping task, the primate subjects displayed not only sensory cortical dedifferentiation, but also coordinative abnormalities. Even though the coordination deficits were not specific to the repetitive task, these results led the researchers to conclude that it was the sensory costimulation inherent in the grasping task that induced both cortical sensory remapping and the motor deficits that are observed in focal dystonia. This conclusion has served as a key assumption behind current computational models of TSFD.^{7,8} These models have simulated sensory cortical dedifferentiation and reproduced, for example, excessive motor output and/or inappropriate agonist-antagonist cocontraction.

However, we are skeptical of the assumption that a simple repetitive grasping task provides a valid exemplar of the complex and highly differentiated real-world tasks that lead to onset of TSFD. For example, performing a classical piano piece or transcribing fast courtroom dialogues using a keyboard involves non-stereotypical, time-varying patterns of cutaneous and proprioceptive stimulation for the involved end-effectors. According to the above hypothesis, such complex activities should not lead to TSFD. Yet, the opposite appears to be the case—complex real-world tasks, such as virtuoso piano performance and professional typing, are those that are most often associated with the onset of TSFD.^{1,8} In addition, somatosensory cortical dedifferentiation does not appear specific to TSFD, but has also been detected in rat models of repetitive motion injury^{9,10} and even in Braille readers who used multiple fingers for reading.¹¹ The latter subjects had no neurological or coordination disorders other than blindness. This suggests that cortical abnormalities in the hand and finger representations may not have a causal role in the motor abnormalities observed in TSFD.

We therefore proceed to reinterpret the genesis of TSFD in terms of the sensorimotor and learning processes underlying the performance of complex tasks. This interpretation yields the following *predictive-control hypothesis*: A highly skilled, strongly motivated performer engages in prolonged, intensive motor task performance. Physical and mental overexposure to such practice diminishes the capacity to meet the demands of the complex task. This creates disruptive patterns of *neuromotor variability*, that is, errors or noise¹² in motor execution. The size and distributions of such errors and noise result in frequent mismatches between expected and actual execution results. A preponderance of such mismatches

eventually overwhelms and distorts the central nervous system's (CNS) adaptive use of a *forward dynamic model* to predict future states (i.e., positions and velocities) of task-relevant end effectors, such as a finger used to strike a piano key. In addition, such deficient predictions impede the CNS's timely selection and activation of the component elements in task-specific movement sequences. The end result is a dysfluency marked by poorly timed, ineffective movement efforts, inappropriate cocontraction and "freezing" or halting of end-effector movements. In the following sections, we lay out both a theoretical rationale and current experimental evidence in support of this hypothesis.

State Estimation and Prediction

To issue accurate, well-timed motor commands in a dexterous task, the CNS must have access to timely information concerning current bodily state. Such information is based, in part, on afferent feedback. However, the peripheral sensory information transmitted to the CNS is both contaminated by noise or uncertainty and subject to significant neural transmission delays.¹³ Therefore, the motor commands issued in rapid, differentiated tasks such as musical performance must be based on accurate computational *estimates* of the current state. This estimation process is hypothesized to entail the use of an internal model,¹⁴ specifically a *forward dynamic model* (see Fig. 1). Given the previous estimated state and previous copy of the motor command (*efference copy*), the output of the model is the predicted current state of the moving system. A discrepancy between this predicted state and the perceived state acts as an error signal that is used to fine tune (optimize) the state estimate in a way that minimizes the uncertainty caused by sensory noise.¹⁵ Because of potentially long neural transmission delays, this rapid central process of optimal state estimation is superior to relying on peripheral feedback to inform rapid action selection and motor command activation.¹⁶

Two key characteristics of internal models are relevant to the present hypothesis. First, they appear to be task-specific: Distinct forward (dynamic) models are thought to mediate predictive control of different tasks, or different types of tasks, each being selectively activated as required.^{17–19} Findings from neuroimaging have supported the assertion that multiple internal models are activated for tasks such as using a computer mouse.^{20,21} Second, such models display plasticity. That is, they adapt to the specific environmental and organismic contexts in which task performances take place, for example, adjusting to the action of keys on an unfamiliar piano, or to growth or injury. Without such adaptation, these context-dependent factors would cause systematic, uncorrected performance errors. A substantial body of research has demonstrated that the CNS continuously updates and adapts internal models, including forward models,^{14,22} when systematic errors are introduced into a previously learned task. These experiments frequently showed that healthy subjects regain consistently accurate performance within a single experimental session.

Hypothesized Role of Motor Variability in TSFD

Could the task-specific forward model also display *maladaptive* plasticity? Could overexposure to complex, attended tasks negatively influence the formation or updating of the model? Successful updating of the model is predicated on a systematic (i.e., relatively

predictable) pattern of motor error. However, patients with TSFD often report a history of an intensified work or practice schedule, and/or performance-related injury, before onset of symptoms^{23,24}; this indicates prolonged or excessive task exposure. A common consequence of such overexposure is increased motor error and/or noise; therefore, it is possible that the predictability of execution error may be *diminished* in performers who will go on to develop TSFD. That is, such errors may be erratic, unusually frequent, and disruptive to performance quality *before* the emergence of symptoms.

Even in prolonged low-force tasks, neuromuscular fatigue may cause decreased muscular cocontraction,^{25,26} increased force variability,²⁷ and unpredictable momentary “freezing,” or so-called blocking.²⁸ Mental fatigue likewise provokes motor errors,²⁸ likely to an even greater extent during dual-task performance.²⁹ Finally, accuracy in timed force application will also deteriorate in musculotendinous overuse injuries,³⁰ which are pervasive in elite performers such as musicians.³¹ In turn, such noise and errors pose considerable challenges to skillful performance. Indeed, the errors committed during even mild performance deterioration may be intolerable for an elite performer. Note that, unlike fatigue, the symptoms of TSFD are not significantly improved by rest, particularly in later stages of the disorder. Therefore, the following exemplar scenario is presented to illustrate how excessive motor variability could lead to motor dysfluency unrelieved by rest.

Causal Flow in the Predictive-Control Hypothesis

Consider a fatigued pianist whose execution is affected by subtly increasing neuromotor noise or mechanical tendon fatigue, leading to higher motor outcome variability. He or she perseveres under such unfavorable conditions, as has been described for highly motivated performers.²³ To reduce undesired digit motions and thus stabilize performance, he or she may attempt to stiffen the respective joints through agonist-antagonist cocontraction.¹² However, as mentioned previously, fatigue may degrade the ability to do so,^{25,26} and this reduced ability to cocontract may contribute to the amplification of execution errors and noise. As a result, the motor outcome of a given command inherently becomes more difficult to predict. Given that the CNS continues to require updated state estimates to activate the successive sequences comprising a complex action,³² such unreliable estimates impede the proper ordering, timing, and execution of these sequences. For example, if the CNS uses the perceived outcome state of a preceding sequence as a precondition for activating the following sequence,³³ the initiation of the latter sequence may be either delayed or premature. Delayed activation halts execution; premature activation causes excessive temporal overlap of sequences, leading to maladaptive cocontraction of agonist-antagonist muscles associated with adjacent sequences. Such dysfunctional cocontraction results in freezing or blocking of digit motion; halting, freezing, and inappropriate cocontractions are precisely the behavioral hallmarks of TSFD.^{1,34}

As in normal functioning, however, the CNS continues to update the task-specific forward model as errors increase and accumulate. The problem is that the results of motor commands are now unpredictable. Therefore, each of the motor command inputs to this updated model is associated with an overly broad distribution of predicted resulting movements. Such noisy predictions corrupt the error signals that are vital to the model’s own updating, leading to

failure in its role of rapid error monitoring and correction. As a result, the system becomes increasingly vulnerable to mistimings through a maladaptive positive feedback process that gives rise to and perpetuates system instability, freezing, and halting.

Current Evidence of Failure of Predictive Processes in TSFD

Although it has not been proposed previously that disruptive motor noise/error and consequent degradation of state estimation could cause TSFD, a small body of experimental evidence indicates that predictive CNS processes are indeed abnormal in persons with TSFD. Ruiz and colleagues³⁵ measured EEG signals in healthy pianists concomitant with performance errors. They found neural activity in the anterior cingulate cortex that predicted error production in a sequence of tones, and preceded such errors by 70 ms. Furthermore, this predictive neural activity was phase- and frequency-shifted in pianists with focal hand dystonia.³⁶ Given that prediction of motor execution errors relies on the forward dynamic model, these neurophysiological findings are consistent with our arguments of abnormal functioning of a forward model in TSFD.

More direct evidence implicating forward model functioning in TSFD was recently reported by Lee and colleagues.³⁷ It is well established that humans systematically perceive externally applied stimuli more intensely than self-applied stimuli.³⁸ This has been attributed to the ability of forward models to predict—and attenuate—the sensory consequences of self-motion. The experiment by Lee and colleagues showed that this differential sensitivity to the intensity of self-versus experimenter-applied digital stimulation was altered in patients with TSFD. This apparent abnormality in prediction of self-motion is congruent with the findings of Avanzino and colleagues,³⁹ who found that patients with TSFD had diminished ability to predict the moment of completion of *another* person's handwriting gesture seen on a video screen.

Conclusion

According to our predictive-control hypothesis, a disruption in predictive sensorimotor processes occurs in performers with heightened levels of neuromotor noise and insufficient physical and/or cognitive resources attributed to overexposure to a highly specialized task. This disruption results in the dysfunctional behavioral patterns of TSFD. To test this hypothesis, future experimental and modeling research should:

- clarify to what extent sustained performance of high-precision, complex tasks with high cognitive load, such as musical performance, increases variability and thereby threatens motor fluency; and
- specify more fully the role of forward models in TSFD to support our assertion that task specificity of such models underlies the task specificity of TSFD.

These efforts should lead not only to a better understanding of the etiology of TSFD, but also to accelerated progress in the prevention and treatment of TSFD.

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References

1. Altenmüller E. Focal dystonia: advances in brain imaging and understanding of fine motor control in musicians. *Hand Clinics*. 2003; 19:523–538. [PubMed: 12945651]
2. Cheng FP, Grossbach M, Altenmüller EO. Altered sensory feed-backs in pianist's dystonia: the altered auditory feedback paradigm and the glove effect. *Front Hum Neurosci*. 2013; 7:868. [PubMed: 24381552]
3. Allard T, Clark SA, Jenkins WM, Merzenich MM. Reorganization of somatosensory area 3b representations in adult owl monkeys after digital syndactyly. *J Neurophysiol*. 1991; 66:1048–1058. [PubMed: 1753275]
4. Jenkins WM, Merzenich MM, Ochs MT, Allard T, Guic-Robles E. Functional reorganization of primary somatosensory cortex in adult owl monkeys after behaviorally controlled tactile stimulation. *J Neurophysiol*. 1990; 63:82–104. [PubMed: 2299388]
5. Byl N, Wilson F, Merzenich M, et al. Sensory dysfunction associated with repetitive strain injuries of tendinitis and focal hand dystonia: a comparative study. *J Orthop Sports Phys Ther*. 1996; 23:234–244. [PubMed: 8775368]
6. Byl NN, Merzenich MM, Cheung S, Bedenbaugh P, Nagarajan SS, Jenkins WM. A primate model for studying focal dystonia and repetitive strain injury: effects on the primary somatosensory cortex. *Phys Ther*. 1997; 77:269–284. [PubMed: 9062569]
7. Sanger TD, Merzenich MM. Computational model of the role of sensory disorganization in focal task-specific dystonia. *J Neurophysiol*. 2000; 84:2458–2464. [PubMed: 11067988]
8. Altenmüller E, Müller D. A model of task-specific focal dystonia. *Neural Networks*. 2013; 48:25–31. [PubMed: 23892909]
9. Barr AE, Barbe MF, Clark BD. Work-related musculoskeletal disorders of the hand and wrist: epidemiology, pathophysiology, and sensorimotor changes. *J Orthop Sports Phys Ther*. 2004; 34:610–627. [PubMed: 15552707]
10. Coq JO, Barr AE, Strata F, et al. Peripheral and central changes combine to induce motor behavioral deficits in a moderate repetition task. *Exp Neurol*. 2009; 220:234–245. [PubMed: 19686738]
11. Sterr A, Müller MM, Elbert T, Rockstroh B, Pantev C, Taub E. Perceptual correlates of changes in cortical representation of fingers in blind multifinger Braille readers. *J Neurosci*. 1998; 18:4417–4423. [PubMed: 9592118]
12. Van Gemmert AW, Van Galen GP. Stress, neuromotor noise, and human performance: a theoretical perspective. *J Exp Psychol Hum Percept Perform*. 1997; 23:1299–1313. [PubMed: 9336955]
13. Wolpert DM. Probabilistic models in human sensorimotor control. *Hum Mov Sci*. 2007; 26:511–524. [PubMed: 17628731]
14. Wolpert DM, Miall RC, Kawato M. Internal models in the cerebellum. *Trends Cogn Sci*. 1998; 2:338–347. [PubMed: 21227230]
15. Wolpert DM, Ghahramani Z, Jordan MI. An internal model for sensorimotor integration. *Science*. 1995; 269:1880–1882. [PubMed: 7569931]
16. Miall RC, Weir DJ, Wolpert DM, Stein JF. Is the cerebellum a Smith Predictor? *J Mot Behav*. 1993; 25:203–216. [PubMed: 12581990]
17. Haruno M, Wolpert DM, Kawato M. MOSAIC model for sensorimotor learning and control. *Neural Comput*. 2001; 13:2201–2220. [PubMed: 11570996]
18. Lackner JR, DiZio P. Motor control and learning in altered dynamic environments. *Curr Opin Neurobiol*. 2005; 15:653–659. [PubMed: 16271464]

19. Wainscott SK, Donchin O, Shadmehr R. Internal models and contextual cues: encoding serial order and direction of movement. *J Neurophysiol.* 2005; 93:786–800. [PubMed: 15385598]
20. Imamizu H, Kuroda T, Miyauchi S, Yoshioka T, Kawato M. Modular organization of internal models of tools in the human cerebellum. *Proc Natl Acad Sci U S Am.* 2003; 100:5461–5466.
21. Imamizu H, Kuroda T, Yoshioka T, Kawato M. Functional magnetic resonance imaging examination of two modular architectures for switching multiple internal models. *J Neurosci.* 2004; 24:1173–1181. [PubMed: 14762135]
22. Shadmehr R, Smith MA, Krakauer JW. Error correction, sensory prediction, and adaptation in motor control. *Annu Rev Neurosci.* 2010; 33:89–108. [PubMed: 20367317]
23. Leijnse JNAL, Hallett M, Sonneveld GJ. A multifactorial conceptual model of peripheral neuromusculoskeletal predisposing factors in task-specific focal hand dystonia in musicians: etiologic and therapeutic implications. *Biol Cybern.* 2015; 109:109–123. [PubMed: 25323627]
24. Newmark J, Hochberg FH. Isolated painless manual incoordination in 57 musicians. *J Neurol Neurosurg Psychiatry.* 1987; 50:291–295. [PubMed: 3559610]
25. Missenard O, Mottet D, Perrey S. The role of cocontraction in the impairment of movement accuracy with fatigue. *Exp Brain Res.* 2008; 185:151–156. [PubMed: 18205000]
26. Selen LP, Beek PJ, van Dieën JH. Fatigue-induced changes of impedance and performance in target tracking. *Exp Brain Res.* 2007; 181:99–108. [PubMed: 17342476]
27. Missenard O, Mottet D, Perrey S. Muscular fatigue increases signal-dependent noise during isometric force production. *Neurosci Lett.* 2008; 437:154–157. [PubMed: 18440146]
28. Heuer, H. Finger fatigue: blockings and approximate kinematic invariances. In: Schlick, C., editor. *Industrial Engineering and Ergonomics.* Berlin: Springer; 2009. p. 621–629.
29. Lorist MM, Kernell D, Meijman TF, Zijdwind I. Motor fatigue and cognitive task performance in humans. *J Physiol.* 2002; 545:313–319. [PubMed: 12433971]
30. Lin TW, Cardenas L, Soslowsky LJ. Biomechanics of tendon injury and repair. *J Biomech.* 2004; 37:865–877. [PubMed: 15111074]
31. Bejjani FJ, Kaye GM, Benham M. Musculoskeletal and neuromuscular conditions of instrumental musicians. *Arch Phys Med Rehabil.* 1996; 77:406–413. [PubMed: 8607768]
32. Dominey PF. Influences of temporal organization on sequence learning and transfer: Comments on Stadler (1995) and Curran and Keele (1993). *J Exp Psychol Learn Mem Cogn.* 1998; 24:234–248.
33. Saltzman E, Caplan D. A graph-dynamic perspective on coordinative structures, the role of affordance-effectivity relationships in action selection, and the self-organization of complex activities. *Ecol Psychol.* 2015; 27:300–309.
34. Cohen LG, Hallett M. Hand cramps: clinical features and electromyographic patterns in a focal dystonia. *Neurology.* 1988; 38:1005–1005. [PubMed: 3386815]
35. Ruiz, MH., Jabusch, HC., Altenmüller, E. Fast feedforward error-detection mechanisms in highly skilled music performance. Paper presented at: Proceedings of the International Symposium on Performance Science; 15–18 December, 2009; Auckland, New Zealand.
36. Ruiz MH, Strubing F, Jabusch HC, Altenmüller E. EEG oscillatory patterns are associated with error prediction during music performance and are altered in musician's dystonia. *Neuroimage.* 2011; 55:1791–1803. [PubMed: 21195188]
37. Lee A, Furuya S, Karst M, Altenmüller E. Alteration in forward model prediction of sensory outcome of motor action in focal hand dystonia. *Front Hum Neurosci.* 2013; 7:172. [PubMed: 23882198]
38. Blakemore SJ, Wolpert D, Frith C. Why can't you tickle yourself? *Neuroreport.* 2000; 11:R11–R16. [PubMed: 10943682]
39. Avanzino L, Martino D, Martino I, et al. Temporal expectation in focal hand dystonia. *Brain.* 2013; 136(Pt 2):444–454. [PubMed: 23361064]

FIG. 1.

Under normal conditions, motor command u elicits movement (kinematic) outcome state x with a predictable pattern of variability (error). This, in turn, yields a predictable sensory outcome state y . An efference copy of u is sent to a forward model, which includes both forward-dynamic state prediction and a corresponding kinematic-to-sensory state mapping. This yields sensory prediction $\hat{y}$. The actual outcome y is compared to $\hat{y}$, and the resulting sensory error signal y is submitted to an optimization process. The resulting corrected estimate $\hat{x}^+$ minimizes error variability. $\hat{x}^+$ not only informs ongoing motor planning and execution through the system's controller, but also may be used to update or revise the forward model. Note that some mechanism must ensure synchrony of comparisons of sensory predictions to sensory outcomes, given that the loop delay through the periphery is longer than that through the forward model. Such a mechanism, using an explicit delay model in series with the forward model, has been proposed,¹⁶ but is omitted here to limit complexity. In the pathological case, (1) unwanted motor variability or motor noise enters the system. The resulting perturbed movement outcome creates (2) discrepancy between predicted (intended) and actual (unintended) outcomes. (3) This discrepancy reduces the certainty of the optimized estimate of biomechanical state. (4) Given an ambiguous state estimate, it becomes similarly uncertain which motor command (among a competing set) the controller should next issue. (5) The corresponding inputs to the forward model, and hence the next sensory prediction, become likewise uncertain. Over prolonged training periods, repeated cycles of ambiguous state predictions and corrections yield a revised (task-specific) forward model that issues increasingly worse estimates of bodily state. (6) Future outputs of this corrupted model contribute to unacceptably noisy error signals in a maladaptive positive feedback process.