**SPECIFIC AIMS**

If you have ever typed an email without actively planning each keystroke, you have experienced motor automaticity. As motor skills are refined through repetition, the brain automates components of the behavior to reduce attentional demands. This phenomenon is vital to a range of behaviors, from mastering a musical instrument to typing on a keyboard. A defining feature of automated behavior is reduced variability across repeated executions, suggesting that reducing motor variationplays a key role in the automation process. *Yet how the brain lessens variability during automation is not understood.* The motor thalamus is a special region of interest for regulating the many sources of variability in the nervous system. The motor thalamus acts as a circuit bottleneck, receiving inhibitory input from a variety of regions before relaying motor plans to cortex. This GABA-ergic inhibition is thought to facilitate action selection by suppressing competing motor representations and neural noise and/or disinhibiting desired motor plans. *However, it is unclear if thalamic inhibition aids in reducing motor variability and/or the transformation of actions from controlled to automated.* Determining if thalamic inhibition facilitates automation in healthy models will be crucial for understanding motor disorders, such as Parkinson’s disease, where thalamic inhibition is abnormal.

The *long-term goal* of this research is to understand how actions become stereotyped through automaticity. The *overall objective* of this proposal is to identify which features of motor behavior exhibit reduced variability with automation and the extent to which thalamic inhibition relates to these reductions of variability. To accomplish this objective, I will measure variability in the timing and kinematics of keyboard typing, a common automated motor skill, and compare individual differences in motor variability against individual differences in thalamic GABA content in healthy participants. I hypothesize thalamic inhibition enables reductions in motor variability to facilitate automaticity. If this hypothesis is correct, I will find that features of variability reduce with increasing motor sequence automation, and individual differences in these same features relate with thalamic GABA concentrations, such that lower variability correlates with higher thalamic GABA. This work will provide novel, crucial insights into the underlying neural mechanisms of motor variability regulation during automation.

**Aim 1: Identify metrics of behavioral and kinematic variability that reduce with increasing motor sequence automation.** By definition, behaviors become stereotyped as they become automated. However, it is unclear whether all facets of motor behavior become more consistent with automation, or if there are some sources of variability that stay constant regardless of automation level. I hypothesize that specific metrics of variability, such as temporal variation between keystrokes and spatial variation across keystroke trajectories, will reduce with increasing levels of sequence of automation. To test this hypothesis, I have developed a novel keyboard typing task to assess diversity in motor variability, given typing is a highly automated, ubiquitous, and naturalistic behavior. Using this task, I will acquire behavioral and kinematic measures of motor variability and assess how these metrics change across sequences with differing levels of familiarity and therefore automation.

**Aim 2: Relate individual differences in keyboard typing variability to individual differences in thalamic inhibition.** People naturally vary in their ability to execute motor skills - our preliminary data show there are differences in motor variability of typed responses across individuals. Additionally, previous experiments have found individual differences in thalamic GABA concentrations to be associated with measurable changes in motor output. However, it is unknown whether higher thalamic GABA content correlates with decreased motor variability. I hypothesize individuals with higher thalamic GABA content will display less temporal and spatial variability in their typed sequences. To test this hypothesis, I will compare motor variability assessed during the keyboard typing task with thalamic GABA content across individuals. Thalamic inhibition cannot be measured directly in humans, so I will use magnetic resonance spectroscopy (MRS) to quantify individual differences in thalamic GABA concentration as a proxy measure.

**Summary:** Aims 1 and 2 will examine relationships of motor variability to motor automation and thalamic GABA, respectively. Together, they will identify a region and process of interest for future work exploring the mechanism of how behaviors become stereotyped through automaticity. Alongside the intellectual merit of this research, these assays will give me the opportunity to receive extensive training in practical skills and theoretical knowledge of MRS and kinematic analysis, which will be crucial for future experimentation in my scientific career.

**RESEARCH STRATEGY**

SIGNIFICANCE

Motor skills are considered as chunks of motor output strung into cognitively determined behavioral sequences**1,2**. Conversely, automated action is thought to be controlled by stimulus-response associations that become highly stable over repetition**3**. However, high performance during motor skills requires composite actions to be selected quickly and appropriately, therefore demanding a level of automation. Motor skills exist along a spectrum of cognitive control ranging from fully volitional to automatic. As skills move along this spectrum and become more automated, it is thought the brain caches computations of frequently utilized movements**5**. Yet what features of behavior are cached and the mechanisms of this caching are unclear. Automated behaviors are in part defined by their stereotyped execution over repeated actions manifesting as reduced motor variability**6,7**. While many have examined the cognitive offloading of automated action (CITE), few have studied its characteristic reduction in motor variability. Similarly, motor variability has been well researched in the context of novel skill learning**8, 9, 10** but there is little work examining its function in well-developed skills. Laboratory investigations of both automaticity and motor variability typically use tightly controlled behavioral paradigms**8, 11** and lack external and ethological validity. To elucidate the mechanisms of motor automaticity, it is critical to identify how reductions in motor variability are regulated in naturalistic behaviors.

**Keyboard typing is a useful model for studying automated, naturalistic behavior.** Keyboard typing has been widely studied in the field of cybersecurity**23, 24, 25**. Research has shown frequently typed strings, such as names and passwords, have highly stable and individualized rhythms of motor output, raising the possibility that typed sequences can be used as reliable identifiers**24**. These findings suggest individual differences across typists are measurable and can be utilized. Further, keyboard typing contains highly automated components of behavior at multiple scales – at the level of keystroke, combination of keystrokes, and string (CITE). Keyboard typing allows for the unique opportunity to assess motoric differences between automated and controlled action within the same skill, without hours of training in the laboratory. To leverage this fact, I have designed a task where human participants are asked to produce typed sequences that vary in their amount of prior practice from everyday life. Based on the previous research mentioned, I assume that highly practiced sequences are more automated than seldom practiced sequences. Using typing as a model behavior will allow for detailed assessment of how motor variability is reduced with increasing automation.

**The motor thalamus is involved in regulating motor variability and automaticity.** Prior research has discovered that inactivation of the thalamus has a larger impact on timing variation than other brain regions**28**, and performance-optimizing variation has been associated with thalamic neural activity**11**. While this previous work has implicated the motor thalamus in determining motor variability**11, 12**, relatively little is known about its specific role. Additionally, many studies have implicated the basal ganglia as important brain regions for automation of behavior**37-39**. It is thought that in later stages of motor learning, action sequences become automated by basal ganglia circuitry, with the thalamus being a particular region of interest**40, 41**. One study found silencing striatal-projecting thalamic neurons in mice prevented execution of stereotyped motor sequences (Wolff, et al. 2019). In humans, activity in the thalamus has been correlated with task automaticity**42**, though it is still unclear how the thalamus might be regulating automation. Determining whether thalamic contributions to regulating motor variability and automation are related will be critical to understanding how the brain optimizes behavior in late-stage motor learning.

**Thalamic inhibition plays a role in action selection.** The motor thalamus receives a variety of inhibitory inputs from other brain regions**13, 14**, including the striatum which is known to be critical for producing automated behavior (CITE)**.** The striatum projects strong, GABA-ergic inhibition onto the thalamus via the internal globus pallidus (CITE).Thalamic inhibition is thought to facilitate the selection of motor chunks during behavioral sequencing (Logiaco, et al. 2021).One mechanistic theory is that GABAergic inhibition suppresses undesired motor plans, allowing representations of intended behavior to be sent to cortex**15, 16**. However, it is unknown if this model of thalamic suppression applies past action selection, and reduces variation of desired movement through further paring of non-ideal motor representations and neural noise. Quantified with magnetic resonance spectroscopy (MRS), individual differences in thalamic GABA concentrations are known to have measurable effects on motor output in clinical populations**29, 30**. Little work has quantified thalamic GABA outside clinical studies, but research in the primary motor cortex suggest natural variations in the capacity for inhibition also impact motor function in healthy populations (CITE). Leveraging these individual differences in thalamic GABA content can help us understand whether thalamic inhibition is reducing motor variability and assisting motor automation in healthy models.

**General Significance.** This proposed study will be the first to examine thalamic GABA content in relation to motor automaticity. My findings would identify the extent to which the thalamus regulates motor variability in naturalistic human behavior and provide insight to how motor skills are automated. Additionally, most research studying thalamic contributions to motor variability and automaticity has been conducted in animal models. Exacting this work in humans will strengthen the connection between human and animal studies as well as our understanding of thalamus function. Many motor impairments in Parkinson’s disease are thought to arise from lack of automation of behavior**17, 18**. The predominant model of Parkinson’s disease suggests there is a pathological increase in thalamic inhibition from the internal globus pallidus (McGregor and Nelson 2019). The proposed research can provide a framework for understanding how physiological changes caused by the disease may impact motor variation and automation of motor output to provide context for future research exploring the role of thalamic GABA in Parkinson’s and other movement disorders.

**Research innovation.** Laboratory experiments exploring motor variability and automaticity typically use highly-trained and non-naturalistic tasks, which can limit the generalizability of research findings to everyday motor behavior. Keyboard typing is globally ubiquitous, making it perfectly situated for examining naturalistic human motor control. However, it has been largely unstudied from a neuroscientific perspective. Generating a novel task with an untapped motor model opens the door for future research to use this experimental paradigm. Additionally, the proposed work includes a robust kinematic analysis of typing. This analysis will be sensitive to multiple features of typing behavior and may expose dimensions of variability unidentified by previous studies using less sensitive techniques and highly trained tasks.

**Goals of the research.** The objective of this research is to determine which features of motor behavior exhibit reductions in variability with increased automation (Aim 1) and whether GABA-ergic inhibition onto the thalamus, a critical brain region for regulating motor variability and automaticity, relates to reduced variability in automated behavior (Aim 2). Together, these aims will determine if this noise-reducing process extends past action selection and further dampens sub-optimal motor plans, aiding motor automation.

APPROACH

**Aim 1: Identify metrics of behavioral and kinematic variability that reduce with increasing motor sequence automation.**

**Rationale:** Late-stage motor learning often involves the automation of sub-behaviors to produce fast and accurate execution. While reduced variability is a defining feature of automated behavior, motor variability research has primarily focused on its role in early-stage learning (CITE). *The objective of this aim* is to determine which aspects of motor behavior reduce in motor variability during motor automation. To achieve this, I will analyze behavioral and kinematic data collected from a carefully crafted typing task, as typing is a highly automated and naturalistic behavior. This task will assess variability of typed sequences across a range of practice, and therefore levels of automation. I hypothesize metrics of both temporal and spatial variability will reduce with increasing sequence automation (ie. standard deviation of interkey interval, keystroke trajectory variation).

**Participants:** 30 healthy, young adults (18-35 years of age, 15 female) from the University of Oregon and surrounding community will be asked to participate in the typing experiment. This sample size was confirmed to be sufficient using G\*Power (CITE). The project is approved by the University of Oregon Institutional Review Board, and all participants will provide written informed consent.

**Task Design:** Participants will complete a typing task during which behavioral keystroke data and high speed (120 FPS) video will be collected. Participants will be seated in front of a stimulus display monitor and QWERTY keyboard. Cameras will be positioned to collect footage from four planes: aerial, frontal, left stereo, and right stereo. During each trial of the task participants will be cued to type 5-letter strings selected from the SUBTLEX corpus**26**. The chosen strings represent a range of bigram (two letter sequence) frequencies and overall word frequencies in American English (Fig. 1). I will also include a category of word-adjacent nonsense strings that serve as entirely unfamiliar word­­s. These nonsense strings are matched to the word stimuli for bigram frequencies to control for effects of intra-word familiarity (Fig. 1). The careful selection of these strings was completed with the help of linguist Dr. Melissa Baese-Berk (one of the supporting collaborators on this grant) and accounts for linguistic effects of familiarity on motor output variability**27**. Strings with higher word and bigram frequencies represent more practiced and therefore automated stimuli, while strings with lower word and bigram frequencies represent less practiced and more cognitively controlled stimuli. Isolating and analyzing typed sequences which have differing levels of practice will allow us to determine how measures of variation change across those conditions.

Fig. 1: A grid plotting selected strings from the keyboard typing task. Strings are placed according to their word frequency and average bigram frequency. Example bigrams are underlined.

Letter strings will be presented for 3.5s on each task trial, separated by a 1s intertrial interval. Participants will complete 480 trials in total, comprised of 20 repetitions of each of the 24 strings, administered in two blocks with a short break between blocks. Participants will not be provided with online feedback during typing or allowed to backspace. However, they will be presented with delayed feedback indicating if their response was correct. Alongside the linguistic controls put in place by the word bank, participants will be asked to fill out a short survey regarding their broad motor skill experience (ie. sports, musicianship, video game play) and complete the Edinburgh Handedness Inventory, a standardized survey for determining handedness (CITE). Additionally, participants will perform a short typing skill assessment (CITE) before the task. These supplements will allow us to control for any major differences in individual general motor skill level as well as specifically typing skill level.

**Behavioral and Kinematic Analysis:** From the behavioral data, I will calculate interkey interval (IKI) which is the time between the start of two consecutive key presses. Standard deviation of IKI across trial repetitions will be calculated and assessed at the string and bigram level across all corresponding frequency categories (Fig. 1). When analyzing IKI within words, the average coefficient of variation of each interval based on its position within the string will be calculated to evaluate possible order effects. Results will be grouped across all participants for statistical analysis. I will use a one-way repeated measures ANOVA comparing standard deviation of IKI across each of the three bigram frequency categories and four word frequency categories to determine whether collected metrics differ significantly across levels of automation. To more rigorously test our results, I will also utilize Bayesian analysis with the bayestest R package in R to replicate any findings from the ANOVA analysis.

Kinematic trajectories of keystrokes will be extracted from the video using markerless tracking in DeepLabCut**31**. I will compare hand kinematics across strings and bigrams with differing levels of frequency across individuals. Variation in kinematic trajectories will be calculated by centering around each keystroke in time and overlaying fingertip, distal interphalangeal joint, and proximal interphalangeal joint routes of repeated movements. All fingers except the thumb will be tracked, as the thumb is only used to press the spacebar in standard typing behavior. Euclidean distances from average kinematic paths will be calculated for each trial, and the mean magnitude of these distances will be used as an estimate of variability across trials. Similarly to the behavioral data, ANOVA testing and Bayesian analysis will be employed to determine the extent to which trajectory variation differs across automation level.

**Predicted Results:** Broadly, I hypothesize participants will display higher kinematic variability when producing less automated typing patterns. More specifically, I predict standard deviation of IKI and mean Euclidean magnitude across repeated keystrokes will significantly decrease with increasing bigram and string frequency, representing stereotyped rhythm and of typing with increased automation. This is supported by cybersecurity research**24, 25**. I also suspect unfamiliar or completely novel strings composed of bigrams with high frequencies to exhibit variability similar to higher frequency words. This would indicate often practiced typing sequences produce less motor variability, independent of their context, consistent with more automated motor representations.

**Potential Problems and Alternative Outcomes:** It is possible I do not observe any differences in motor output variation across sequence automation level. Although prior research suggests this outcome is unlikely**24, 25**, it would imply variability reduction plateaus during earlier stages of motor learning and does not reduce with further automation. It is also possible all collected metrics of motor variability are represented equally across string and bigram types, suggesting adjustments in motor variability generalize across multiple performance metrics.

**Aim 2: Relate individual differences in keyboard typing variability to individual differences in thalamic GABA.**

**Rationale:** Differences between people are an inherent feature of all human-subjects work that is often overlooked but can be exploited to probe important scientific questions (Stagg et al. 2011). *The objective of this aim* is to determine whether thalamic inhibition plays a role in motor variability reduction, and if so, which metrics of motor variability does it associate with. To accomplish this, I will compare individual differences in metrics of keyboard typing variability (collected in Aim 1) with individual differences in thalamic GABA content (collected in Aim 2). When all IKIs from a string are combined, they effectively evaluate the typing rhythm of a particular word. This collective IKI measure has been shown to be sensitive to individual differences**24**. I hypothesize individuals with higher thalamic inhibition (ie. higher GABA concentrations) will display lower motor output variability during typing. Further, I predict thalamic GABA will correlate with the same metrics of motor variability that I anticipate will reduce with increasing sequence automation (ie. standard deviation of IKI, keystroke trajectory variation).

**Participants:** The same 30 participants from Aim 1 will be screened for MRI-eligibility prior to performing the typing task and will return for a separate 2.25hr MRI scanning session.

**MRI Acquisition:** To quantify thalamic GABA concentrations in each participant, I will use single-voxel H1 Magnetic Resonance Spectroscopy (MRS). MRS is a technique performed in an MRI scanner to identify concentrations and physical properties of metabolites within a specified region of the brain in live subjects. GABA concentrations will be collected from each participant using a MEGA-PRESS (Mescher et al. 1996) MRS sequence protocol previously established in the lab (TR/TE=2000/68 ms, 320 total averages [160 On; 160 Off resonance], weak water suppression, TA=10:48). All scans will be conducted on a Siemens 3T Prisma MRI scanner at the Lewis Center for Neuroimaging with a 32-channel head coil. Voxels will be placed in five brain regions: the left and right thalamus, left and right primary motor cortex (M1), and bilateral visual cortex as a control**21**. Using an initial T1-weighted anatomical scan as a guide, the measurement voxels (30x35x20mm) for each subject will be manually placed prior to the spectroscopy scans using local anatomical landmarks and minimizing cerebrospinal fluid. Two MEGA-PRESS scans and one water-unsuppressed PRESS scan will be acquired for each voxel. Each of the MEGA-PRESS scans will generate 100 edited at 1.9 ppm (ON) and non-edited (OFF) measurements, while the reference PRESS scan will not have an editing pulse and contain 64 measurements.

**Spectral Analysis:** The MRS data will be processed and analyzed using Gannet, a Matlab toolbox specifically designed to inspect GABA MR spectroscopy data**32**. Gannet will create an amalgamate spectrum of the 200 measurements collected between the two MEGA-PRESS scans. From that spectrum, concentrations of GABA, creatine, and H2O will be calculated from the area under each metabolite’s respective peak. Gannet will then measure the relative quantity of GABA in the voxel through comparisons to the H20 and creatine reference signals. Additionally, each metabolite peak of interest is fit to a model and fit errors are calculated to assess the quality of the collected data. Voxels will be co-registered to the high-resolution anatomical image to calculate grey matter, white matter, and cerebrospinal fluid tissue volumes. This allows for more accurate measurements of voxel-wide GABA content by using estimations of tissue-specific GABA content.

**Regression Analysis and Predicted Results:** Individual differences in standard deviation of IKI and kinematic trajectory variation collected in Aim 1 will be correlated with individual differences in a combined GABA/Cr signal from the right and left thalamus using multiple regression analysis. The same comparisons will be done with a left-right combined GABA/Cr signal from M1 and bilateral GABA/Cr signal from occipital cortex. Comparing behavioral metrics with additional voxels will ensure any correlations are unique to individual differences in thalamic GABA. I hypothesize higher thalamic GABA concentrations will significantly correlate with lower motor variability across all string and bigram categories. Additionally, I predict metrics of variability that correlate with thalamic GABA levels will also decrease with increasing automaticity level in Aim 1 (ie. standard deviation of IKI, variability of kinematic trajectory). This would suggest thalamic inhibition does not only dampen motor noise and competing motor representations in the context of action selection, but also reduces motor variability and assists automation.

**Alternative Outcomes and Potential Problems:** Even if I do not find any variability metrics that reduce with increasing automation level in Aim 1, individual differences in overall typing variability may still associate with thalamic GABA levels. This would indicate thalamic GABA is playing a global role in reducing baseline variability, but its effect is not specific to motor automaticity. It is also possible I observe no significant relationship between individual differences in thalamic GABA concentrations and motor output variability. This would suggest there is another source of variability, such as individual differences in M1 inhibition or linguistic processing, that causes these individual differences in keyboard typing**36**.

MR spectroscopy provides relatively crude spatial resolution. Therefore, it will not be possible to make claims about local GABA content within individual thalamic nuclei. However, previous studies indicate MRS GABA measurements, even in large thalamic voxels, correlate with individual differences in behavior (CITE). Moreover, the Action Control Lab is well established in GABA MR spectroscopy**33, 34**, so the technical implementation of this experiment is not expected to present new challenges. It is possible multiple metabolites correlate with our behavioral and kinematic measurements. To address this, the current protocol will use both creatine and H2O signals as references. Glx (a combined glutamine, glutamate, and glutathione signal) concentrations can be calculated and will provide another comparison to ensure observed correlations are unique to GABA.Additionally, most individual differences in typing variability could be dictated by skill level. I will then use data collected from the pre-task assessments to evaluate differences across individuals in the same skill level (CITE), thus providing higher sensitivity to variation caused by neurochemistry differences.

**Summary and Future Directions:** Collectively, these aims will elucidate the role of thalamic inhibition in sequence automation and individual differences in the variability of a naturalistic motor skill. My findings will provide critical groundwork and a novel paradigm for future automaticity research, both basic science oriented and clinical. Moving forward, this proposal’s typing task and identified markers of motor variability could offer a new method of diagnosing motor disorders such as Parkinson’s through detecting changes in motor automaticity**22**.

**REFERENCES**

1. Lashley, K. S. The problem of serial order in behavior. Vol. 21, p. 21. Oxford, United Kingdom: Bobbs-Merrill; 1951.
2. Halford GS, Wilson WH, Phillips S. Processing capacity defined by relational complexity: Implications for comparative, developmental, and cognitive psychology. Behavioral and Brain Sciences. Cambridge University Press; 1998 Dec;21(6):803–831.
3. Robbins TW, Costa RM. Habits. Current Biology. 2017 Nov 20;27(22):R1200–R1206.
4. Du Y, Krakauer J, Haith A. The relationship between habits and skills in humans [Internet]. PsyArXiv; 2021 [cited 2021 Sep 29]. Available from: https://psyarxiv.com/9qrgd/
5. Haith AM, Krakauer JW. The multiple effects of practice: skill, habit and reduced cognitive load. Curr Opin Behav Sci. 2018 Apr;20:196–201. PMCID: PMC6443249
6. Shmuelof L, Krakauer JW, Mazzoni P. How is a motor skill learned? Change and invariance at the levels of task success and trajectory control. J Neurophysiol. 2012 Jul;108(2):578–594. PMCID: PMC3404800
7. Müller H, Sternad D. Decomposition of variability in the execution of goal-oriented tasks: three components of skill improvement. J Exp Psychol Hum Percept Perform. 2004 Feb;30(1):212–233. PMID: 14769078
8. Dhawale AK, Miyamoto YR, Smith MA, Ölveczky BP. Adaptive Regulation of Motor Variability. Current Biology. 2019 Nov 4;29(21):3551-3562.e7.
9. Wu HG, Miyamoto YR, Castro LNG, Ölveczky BP, Smith MA. Temporal structure of motor variability is dynamically regulated and predicts motor learning ability. Nat Neurosci. Nature Publishing Group; 2014 Feb;17(2):312–321.
10. Wulf G, Schmidt RA. Variability of practice and implicit motor learning. Journal of Experimental Psychology: Learning, Memory, and Cognition. US: American Psychological Association; 1997;23(4):987–1006.
11. Wang J, Hosseini E, Meirhaeghe N, Akkad A, Jazayeri M. Reinforcement regulates timing variability in thalamus. Wei K, Frank MJ, Wei K, Averbeck BB, editors. eLife. eLife Sciences Publications, Ltd; 2020 Dec 1;9:e55872.
12. Goldberg JH, Fee MS. Vocal babbling in songbirds requires the basal ganglia-recipient motor thalamus but not the basal ganglia. Journal of Neurophysiology. American Physiological Society; 2011 Jun 1;105(6):2729–2739.
13. MacLeod NK, James TA, Kilpatrick IC, Starr MS. Evidence for a GABAergic nigrothalamic pathway in the rat. II. Electrophysiological studies. Exp Brain Res. 1980;40(1):55–61. PMID: 6252030
14. Anderson ME, Postupna N, Ruffo M. Effects of high-frequency stimulation in the internal globus pallidus on the activity of thalamic neurons in the awake monkey. J Neurophysiol. 2003 Feb;89(2):1150–1160. PMID: 12574488
15. Nambu A, Tokuno H, Takada M. Functional significance of the cortico–subthalamo–pallidal ‘hyperdirect’ pathway. Neuroscience Research. 2002 Jun 1;43(2):111–117.
16. Logiaco L, Abbott LF, Escola S. Thalamic control of cortical dynamics in a model of flexible motor sequencing. Cell Reports. 2021 Jun 1;35(9):109090.
17. Marsden CD. The mysterious motor function of the basal ganglia: the Robert Wartenberg Lecture. Neurology. 1982 May;32(5):514–539. PMID: 7200209
18. Hoshiyama M, Kaneoke Y, Koike Y, Takahashi A, Watanabe S. Hypokinesia of associated movement in Parkinson’s disease: a symptom in early stages of the disease. J Neurol. 1994 Aug;241(9):517–521. PMID: 7798998
19. Dharmadhikari S, Ma R, Yeh C-L, Stock A-K, Snyder S, Zauber SE, Dydak U, Beste C. Striatal and thalamic GABA level concentrations play differential roles for the modulation of response selection processes by proprioceptive information. Neuroimage. 2015 Oct 15;120:36–42. PMCID: PMC4589476
20. Gong T, Xiang Y, Saleh MG, Gao F, Chen W, Edden RAE, Wang G. Inhibitory motor dysfunction in parkinson’s disease subtypes. Journal of Magnetic Resonance Imaging. 2018;47(6):1610–1615.
21. van Nuland AJM, den Ouden HEM, Zach H, Dirkx MFM, van Asten JJA, Scheenen TWJ, Toni I, Cools R, Helmich RC. GABAergic changes in the thalamocortical circuit in Parkinson’s disease. Hum Brain Mapp. 2020 Mar;41(4):1017–1029. PMCID: PMC7267977
22. Wu T, Hallett M, Chan P. Motor automaticity in Parkinson’s disease. Neurobiology of Disease. 2015 Oct;82:226–234.
23. Karnan M, Akila M, Krishnaraj N. Biometric personal authentication using keystroke dynamics: A review. Applied Soft Computing. 2011 Mar 1;11(2):1565–1573.
24. Joyce R, Gupta G. Identity authentication based on keystroke latencies. Commun ACM. 1990 Feb;33(2):168–176.
25. Stefan D, Shu X, (Daphne) Yao D. Robustness of keystroke-dynamics based biometrics against synthetic forgeries. Computers & Security. 2012 Feb;31(1):109–121.
26. Brysbaert M, New B. Moving beyond Kučera and Francis: A critical evaluation of current word frequency norms and the introduction of a new and improved word frequency measure for American English. Behavior Research Methods. 2009 Nov 1;41(4):977–990.
27. Jones MN, editor. Crunching Big Data with Fingertips: How Typists Tune Their Performance Toward the Statistics of Natural Language. Big Data in Cognitive Science [Internet]. 0 ed. New York, NY : Routledge, 2016. |: Psychology Press; 2016 [cited 2021 Nov 29]. p. 329–345. Available from: https://www.taylorfrancis.com/books/9781315413563/chapters/10.4324/9781315413570-27
28. Wang J, Narain D, Hosseini EA, Jazayeri M. Flexible timing by temporal scaling of cortical responses. Nat Neurosci. Nature Publishing Group; 2018 Jan;21(1):102–110.
29. Draper A, Stephenson MC, Jackson GM, Pépés S, Morgan PS, Morris PG, Jackson SR. Increased GABA Contributes to Enhanced Control over Motor Excitability in Tourette Syndrome. Current Biology. 2014 Oct 6;24(19):2343–2347.
30. Long Z, Li X-R, Xu J, Edden RAE, Qin W-P, Long L-L, Murdoch JB, Zheng W, Jiang Y-M, Dydak U. Thalamic GABA Predicts Fine Motor Performance in Manganese-Exposed Smelter Workers. PLOS ONE. Public Library of Science; 2014 Feb 4;9(2):e88220.
31. Mathis A, Mamidanna P, Cury KM, Abe T, Murthy VN, Mathis MW, Bethge M. DeepLabCut: markerless pose estimation of user-defined body parts with deep learning. Nat Neurosci. 2018 Sep;21(9):1281–1289.
32. Edden RAE, Puts NAJ, Harris AD, Barker PB, Evans CJ. Gannet: A Batch-Processing Tool for the Quantitative Analysis of Gamma-Aminobutyric Acid–Edited MR Spectroscopy Spectra. J Magn Reson Imaging. 2014 Dec;40(6):1445–1452. PMCID: PMC4280680
33. Greenhouse I, Noah S, Maddock RJ, Ivry RB. Individual differences in GABA content are reliable but are not uniform across the human cortex. NeuroImage. 2016 Oct 1;139:1–7.
34. Považan M, Mikkelsen M, Berrington A, Bhattacharyya PK, Brix MK, Buur PF, Cecil KM, Chan KL, Chen DYT, Craven AR, Cuypers K, Dacko M, Duncan NW, Dydak U, Edmondson DA, Ende G, Ersland L, Forbes MA, Gao F, Greenhouse I, Harris AD, He N, Heba S, Hoggard N, Hsu T-W, Jansen JFA, Kangarlu A, Lange T, Lebel RM, Li Y, Lin C-YE, Liou J-K, Lirng J-F, Liu F, Long JR, Ma R, Maes C, Moreno-Ortega M, Murray SO, Noah S, Noeske R, Noseworthy MD, Oeltzschner G, Porges EC, Prisciandaro JJ, Puts NAJ, Roberts TPL, Sack M, Sailasuta N, Saleh MG, Schallmo M-P, Simard N, Stoffers D, Swinnen SP, Tegenthoff M, Truong P, Wang G, Wilkinson ID, Wittsack H-J, Woods AJ, Xu H, Yan F, Zhang C, Zipunnikov V, Zöllner HJ, Edden RAE, Barker PB. Comparison of Multivendor Single-Voxel MR Spectroscopy Data Acquired in Healthy Brain at 26 Sites. Radiology. Radiological Society of North America; 2020 Apr;295(1):171–180.
35. Maes C, Cuypers K, Heise K-F, Edden RAE, Gooijers J, Swinnen SP. GABA levels are differentially associated with bimanual motor performance in older as compared to young adults. Neuroimage. 2021 May 1;231:117871. PMCID: PMC8275071
36. Gordon CL, Spivey MJ, Balasubramaniam R. Corticospinal excitability during the processing of handwritten and typed words and non-words. Neuroscience Letters. 2017 Jun;651:232–236.
37. Ashby FG, Turner BO, Horvitz JC. Cortical and basal ganglia contributions to habit learning and automaticity. Trends in Cognitive Sciences. Elsevier; 2010 May 1;14(5):208–215. PMID: 20207189
38. Lerner TN. Interfacing behavioral and neural circuit models for habit formation. Journal of Neuroscience Research. 2020;98(6):1031–1045.
39. Yin HH, Ostlund SB, Balleine BW. Reward-guided learning beyond dopamine in the nucleus accumbens: The integrative functions of cortico-basal ganglia networks. Eur J Neurosci. 2008 Oct;28(8):1437–1448. PMCID: PMC2756656
40. Wolff SBE, Ko R, Ölveczky BP. Distinct roles for motor cortical and thalamic inputs to striatum during motor learning and execution [Internet]. bioRxiv; 2019 [cited 2022 Feb 17]. p. 825810. Available from: https://www.biorxiv.org/content/10.1101/825810v2
41. Floyer-Lea A, Matthews PM. Distinguishable Brain Activation Networks for Short- and Long-Term Motor Skill Learning. Journal of Neurophysiology. American Physiological Society; 2005 Jul 1;94(1):512–518.
42. Floyer-Lea A, Matthews PM. Changing Brain Networks for Visuomotor Control With Increased Movement Automaticity. Journal of Neurophysiology. 2004 Oct;92(4):2405–2412.
43. Logan GD, Etherton JL. What is learned during automatization? The role of attention in constructing an instance. Journal of Experimental Psychology: Learning, Memory, and Cognition. US: American Psychological Association; 19950201;20(5):1022.
44. Smits-Bandstra S, De Nil L, Rochon E. The transition to increased automaticity during finger sequence learning in adult males who stutter. Journal of Fluency Disorders. 2006 Jan 1;31(1):22–42.
45. Graybiel AM, Grafton ST. The Striatum: Where Skills and Habits Meet. Cold Spring Harb Perspect Biol [Internet]. 2015 Aug [cited 2020 Nov 11];7(8). Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4526748/> PMCID: PMC4526748
46. Quetscher C, Yildiz A, Dharmadhikari S, Glaubitz B, Schmidt-Wilcke T, Dydak U, Beste C. Striatal GABA-MRS predicts response inhibition performance and its cortical electrophysiological correlates. Brain Struct Funct. 2015 Nov;220(6):3555–3564. PMCID: PMC4447607