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Starts and Stops of Rhythmic and Discrete Movements: Modulation in the Excitability of the Corticomotor Tract During Transition to a Different Type of Movement

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Summary

Movement is arguably one of the most important functions that the human brain has control over. Externally, we can divide all movements into rhythmic, continuous movements or discrete, one-time movements. To ensure smooth and purposeful behavior, the motor areas of the brain must have some way of controlling these two types of movements. Recent fMRI (functional magnetic resonance imaging) studies show the preferential activation of contra-lateral M1 (primary motor cortex) in response to rhythmic wrist rotations in the opposite arm, whereas similar discrete wrist movements had much greater activation and in other areas of the brain. To understand the control of these two types of movements, we stimulated the M1 while having the subject perform either a rhythmic, discrete, or transition movement. We found that the motor evoked potentials (MEPs) amplitude increases in degree from regular discrete movement to discrete movement to transition movements (from rhythmic to discrete and vice versa). We anticipated that MEP amplitudes of regular discrete movements will be significantly greater those of regular rhythmic movements, which indicates that discrete movements involve more direct transmission of neurons from the cortical motor system than rhythmic movement due to their physiological nature. We confirmed that fact in our study. However, we were surprised to find out that the MEP amplitude after transition to discrete or rhythmic movements were almost identical, with an average difference of approximately 1%. This similarity between the transition movements suggested that the transition caused by voluntary inhibition operated by the frontal part of the brain, which corresponds to the characteristics of discrete movements. That might explain why the MEP amplitude of transition movements is greater than both rhythmic and discrete movements and why there is no stark distinction within the transition movements.

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Introduction

Humans, like any other animals, perform the movements necessary for survival, such as breathing, walking, running, and grabbing quite effortlessly. We are unaware of the countless transmissions of neurons from the brain to the spinal cord and to the muscles. Regardless, we are able to control our muscles to perform the most complex movements such as fine adjustment of fingers, which involves approximately 34 muscles and 29 individual bones for each hand (1). The primary motor cortex of the brain, known as M1, is responsible for the execution of most types of movements, especially voluntary ones. These complex manipulations of our muscle tissues can be simplified into two basic types of movements in a kinematic sense: discrete and rhythmic movements.

Kinematically, all discrete movements, like grasping, reaching, or throwing, have a distinct start and an end (2). On the other hand, rhythmic movements, such as chewing, walking, or nervously shaking your legs, are repeated and continuous motions. Although rhythmic movements also have a start and an end, they are more characterized by the movement process rather than by the end-goal. On the contrary, discrete movements seem to be directly motivated by the end-goal. Because the terms are defined in a kinematic perspective, there are limitations as to where the exact boundary between the two motions are. For this reason, it is important to ask what is physiologically driving the control of these two types of movements and their differences.

Many groups within the motor science community took note that discrete movements put together resemble a phase of rhythmic movement and that truncated rhythmic movement looks like discrete movements (3). This arose the question as to whether rhythmic and discrete movements are operated under the same motor control areas of our brains. Stephan Schaal, a professor in computer science and neuroscience in the University of Southern California, observed the areas of brain activated during rhythmic and discrete movements (**Fig. 1**). The analysis of the data from the fMRI imaging of the subjects' brain during rhythmic and discrete movements showed that discrete movements involve more higher-planning areas and more cerebral activity than rhythmic

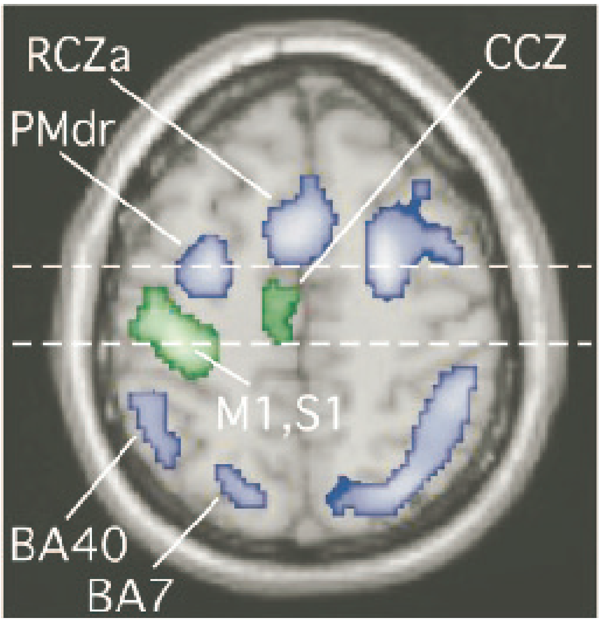


Fig 1. fMRI activation of cortical regions of the brain in response to discrete wrist rotation and rhythmic wrist rotation. The blue areas represent the discrete response subtracted by the rhythmic response and the green areas represent the rhythmic response subtracted by the discrete response. (from Schaal, 2004)

movements, suggesting that discrete movements require more complex motor commands (3). By looking at the different physiological components involved in each of these movement types, we can infer the system of control that is used in both rhythmic and discrete movement generation.

Transcranial magnetic stimulation (TMS) is a method of stimulating a small region of the brain, such as the motor cortex, by the means of electromagnetic induction that produces small currents (4). This method of stimulation does not involve a physical contact or transmission of direct current to the brain, reducing any discomfort or pain that might have been felt with other methods. Once the stimulation of M1 activates a specific muscle, two electrodes attached to the body part measure the amplitude of the electrical signal transmitted from the brain, a process known as electromyography (EMG) that translates this signal is translated into a graphically displayed motor evoked potential (MEP).

Subject	Gender	Age
1	female	20
2	male	23
3	male	25
4	female	22

Figure 2: Age and gender demographics for all subjects in study

Previous studies of corticomotor excitability using TMS have shown that arm movements, both rhythmic and discrete, show modulation of excitability depending on the phase of movement (5). A study from Lewis, et al. used flexion and extension of wrist to observe a trend in excitability in corticomotor pathways of abductor pollicus brevis (APB) and flexor carpi radialis (FCR) muscles during movement phases. They noticed a marked decrease and increase in MEP amplitude during wrist extension and flexion, respectively, displaying a generally U-shaped graph. In our study, each session of discrete and rhythmic arm movement was also subdivided into phases, but the phases were translated into percentage (0~100%).

Studying the neurological differences between rhythmic and discrete movements motivated us to observe the corticomotor excitability during transition between the two movements, either from rhythmic to discrete or discrete to rhythmic. By observing the boundary between rhythmic and discrete movements, we anticipated a contrast in M1 excitability between regular discrete movement and transition movement, and also between the two different types of transition movements. The goal of this experiment was to observe and compare changes in MEP amplitude during normal rhythmic and discrete movements and during the transition between the two movements.

Results

The subjects

The four subjects that volunteered for this experiment did not have any background information of TMS or rhythmic and discrete movements. All volunteers were undergraduate or graduate students from Northeastern University (**Fig. 2**).

Introduction to the subjects

The subjects were welcomed to the lab and a brief description of the experiment was given with necessary precautions. The experimental set-up is shown in **Fig. 3a.** The subjects were informed about the two movement types, rhythmic and discrete, the effects of TMS, and the desired goal of the experiment. Following the short description, all subjects read and signed a safety and instructional consent form.

A series of questions were posed to each of the subjects in a questionnaire form about anything that could possibly interfere with the results or endanger the subject. Anything that could have affected subjects' excitability was noted. For example: caffeine intake, amount of sleep, any drugs taken, or a recent health problem.

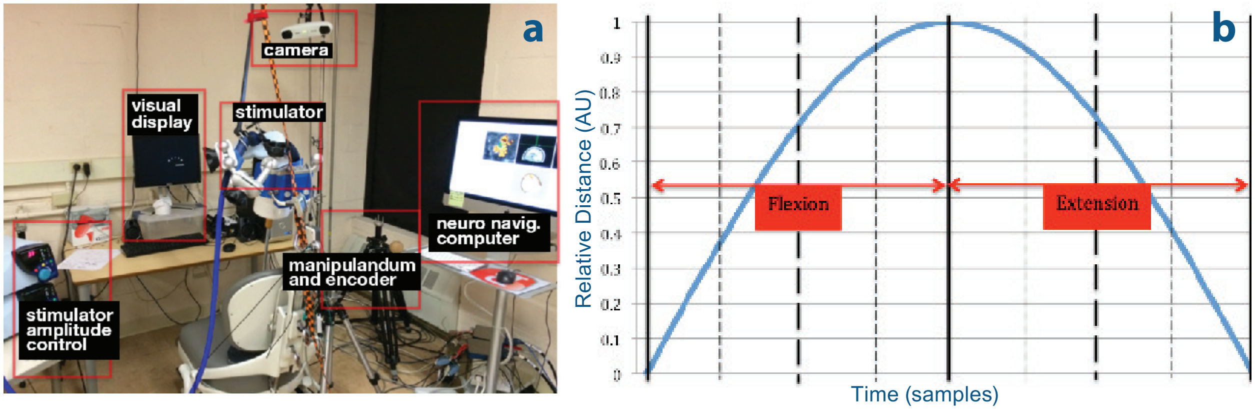


Fig 3. (a) Setup of experiment design with essential components. The Visual Display was turned off for this experiment. (b) A model diagram of one cycle of movement, starting at full flexion, continuing to full extension, and back to full flexion on the manipulandum.

The manipulandum and training

Following the introduction, subjects were asked to sit in the experimental chair and undergo several training cycles of rhythmic and discrete movements. One cycle of movement consisted of an inflexion and a flexion (**Fig. 3b**). To start, subjects rested their right forearms on the manipulandum (**Fig 3a**). The manipulandum contains a moveable pivot arm, which is where the forearm rests, and an internal optical encoder that records the angle of the pivot arm.

Electromyography, TMS, and MEPs

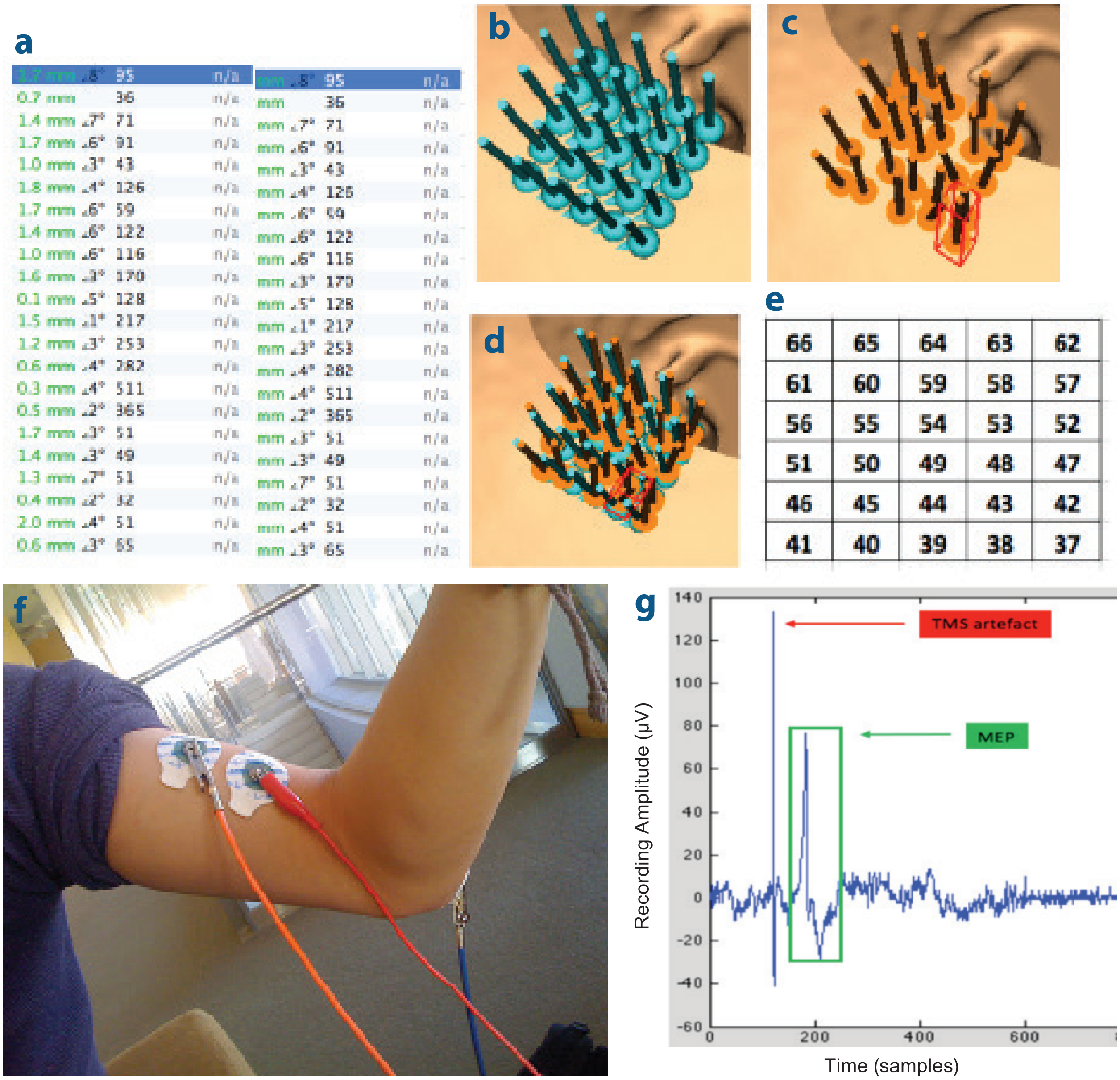
Surface electrodes on the skin were used to measure electrical activity of the biceps muscles. Each subject was asked to flex their biceps muscles on the right arm and an alcohol prep pad was applied to remove any dirt and residue that might cause interference. The first electrode was placed at the point at which the skin bulges out the greatest. The second electrode was placed approximately 3 centimeters down from the first electrode. A third grounding electrode was placed in a neutral location on the elbow (**Fig. 4f**). The electrodes were connected to leads that connected an oscilloscope, a tool that let us visualize the EMG signal.

When we TMS the M1 cortex, we are activating and recruiting neurons from the corticospinal tract that send their signal to a destination muscle. As signals travel from the brain, to the spinal cord, and finally to the muscles, the electrodes will pick up this final signal and record it on the oscilloscope. If the stimulation intensity is high enough, a noticeable involuntary twitch can be visually observed. In addition, the EMG picks up the signal that originated from the motor cortex. This muscle response, triggered by TMS, is called a motor evoked potential (MEP) and can inform us on the relative excitability of the motor cortex at the time of stimulation (**Fig. 4g**). The rationale behind our methods is that when the subject performs a rhythmic or discrete movement, the MEP should reflect the excitability of the M1 as they appear in daily basis. The main difference between rhythmic and discrete movement is the pause between each movement, and the brain differentiates between the two movements through its processing of the pause. We anticipate that the MEPs should reflect the unique way that the brain differentiates the two movements in the primary motor cortex.

When the TMS is fired, a large magnetic field is formed, which is picked up by the electrode leads. This is known as the TMS artifact and occurs instantaneously after the pulse is fired. Although the artifact does not tell us about the muscle activity, it does give us a clear time in which the TMS was fired (**Fig. 4a**). The true MEP onset is triggered between 20-25ms after stimulation and is one way to validate that the observed EMG is not just background muscle activity. Additionally, a true MEP will always have at least a 50 µV potential; anything less will not be considered an MEP.

Data Acquisition

As mentioned previously, kinematic data was collected using an optical encoder that collected angle data from the moveable manipulandum. Every time the TMS pulse was fired, the EMG signal, time of stimulation, and kinematic data (phase) were synchronized and organized in one graph with Matlab data acquisition tool-box. The kinematic data was converted to a position diagram, and velocity and acceleration profiles were calculated. Each time a TMS pulse was generated, a time stamp allowed us to deduce the phase, speed, and acceleration at that moment. A data sheet with these components and TMS stimulus were recorded (**Fig. 5**). Velocity and acceleration profiles were necessary to deduce true stop and true go. In this way, we would retroactively identify when the TMS pulse was fired, what phase it was in, if it contained an MEP, and the size of that MEP.



1.7 mm	∠8°	95	n/a
0.7 mm		36	n/a
1.4 mm	∠7°	71	n/a
1.7 mm	∠6°	91	n/a
1.0 mm	∠3°	43	n/a
1.8 mm	∠4°	126	n/a
1.7 mm	∠6°	59	n/a
1.4 mm	∠6°	122	n/a
1.0 mm	∠6°	116	n/a
1.6 mm	∠3°	170	n/a
0.1 mm	∠5°	128	n/a
1.5 mm	∠1°	217	n/a
1.2 mm	∠3°	253	n/a
0.6 mm	∠4°	282	n/a
0.3 mm	∠4°	511	n/a
0.5 mm	∠2°	365	n/a
1.7 mm	∠3°	51	n/a
1.4 mm	∠3°	49	n/a
1.3 mm	∠7°	51	n/a
0.4 mm	∠2°	32	n/a
2.0 mm	∠4°	51	n/a
0.6 mm	∠3°	65	n/a

mm	∠8°	95	n/a
mm		36	n/a
mm	∠7°	71	n/a
mm	∠6°	91	n/a
mm	∠3°	43	n/a
mm	∠4°	126	n/a
mm	∠6°	59	n/a
mm	∠6°	122	n/a
mm	∠6°	115	n/a
mm	∠3°	179	n/a
mm	∠5°	128	n/a
mm	∠1°	217	n/a
mm	∠3°	253	n/a
mm	∠4°	282	n/a
mm	∠4°	511	n/a
mm	∠2°	365	n/a
mm	∠3°	51	n/a
mm	∠3°	49	n/a
mm	∠7°	51	n/a
mm	∠2°	32	n/a
mm	∠4°	51	n/a
mm	∠3°	65	n/a

66	65	64	63	62
61	60	59	58	57
56	55	54	53	52
51	50	49	48	47
46	45	44	43	42
41	40	39	38	37

Fig 4. Neuronavigation interface and muscle recording. List of EMG responses from TMS stimulation to M1 (a). Neuronavigation grid of desired targets on the M1 cortex (b), Actual areas that were stimulated (c), superimposed desired and actual targets (d). Each sample is arranged on a 5x5 grid and randomly stimulated to find the Hot Spot (e). Picture of surface electrode placement on the biceps (orange and red lead) and on the elbow (blue lead) (f). Sample EMG data, displaying TMS artefact and MEP (g).

Data & Analysis

As anticipated and in accordance with previous studies, both binned and non-binned data of all subjects displayed a U-shaped graph. That is, the motor evoked potential of the M1 decreased as the subject extended their arm and increased during flexion. A graph of an un-binned sample rhythmic data had a maximum MEP of 40% (**Fig. 6**). The average maximum MEP of regular rhythmic arm movement was 34.6%, significantly lower than that of regular discrete movement, 50.5%. However, the minimum MEP of discrete arm movement (6.56%) was lower than that of rhythmic movement (17%), reflecting on the more abrupt nature of stopped discrete movement compared to stopped discrete movement. A sample kinematic data of rhythmic and discrete movement from Schaal, Stefan, et al. shows a smoother transition from flexion to extension (3). It seems that the brain is more primed to subsequent movement during rhythmic movement than it is during discrete movement.

Although the raw data indicated an increasing trend in MEP amplitudes during different movement types, it was insufficient to prove any significant difference between the movements (**Fig. 7**). Therefore, using ANOVA with Tukey HSD Test, we compared the four

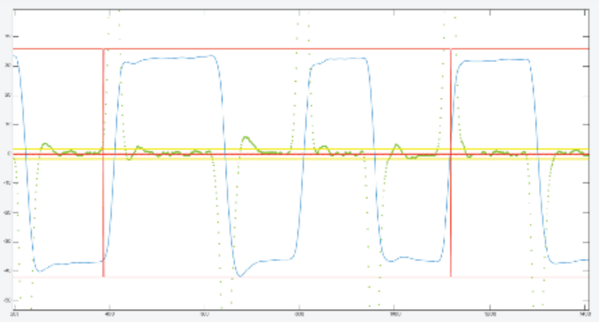


Fig 5. Sample kinematic data. Blue: raw angle data, Red: time of TMS pulse, Green: Instantaneous velocity, Yellow: threshold for 'true stop'

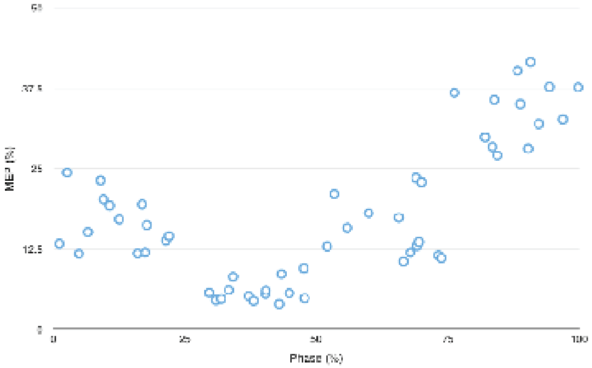


Fig 6. Un-binned sample rhythmic data for one subject. The MEPs generated in the biceps follow a U-shape modulation across phases. Excitability of the M1 is highest when the forearm is flexing.

experimental groups and found out that all pairs of movement types are significantly different for all four phases with the exception between transition to rhythmic movement and transition to discrete movement.

An HSD value (P) less than 0.05 represents a significant difference between two groups. The difference between the four movement conditions (**Fig. 8**) supports the hypothesis that regular discrete and rhythmic movements are under different control. We specifically found that for both transitory movement types, whether from rhythmic to discrete or from discrete to rhythmic, the first cycle elicits MEPs that are on par or higher than steady discrete behavior.

Discussion

In a physiological perspective, the distinction between the two movements becomes easier to perceive. Although rhythmic movement requires a voluntary start, the process of the movement hardly requires the attention of the mover, thus indicating its instinctual nature (6). This is supported by the observation that habitual activities of more primitive animals demonstrate the involuntary aspect of rhythmic movements. Some common rhythmic movements of animals are running, scratching, and even reproducing. One can view the goal of rhythmic movements as generated from executive top down commands to continue a specific and repeated movement, and not necessarily complete a specific task (i.e. to alleviate an itch). The completion of the task is reached when a threshold triggered (i.e. the scratching has caused enough physical effect to remove the itch). caused by the repetition of the rhythmic behavior (7). In the same manner, winged insects like mosquitos flap their wings continuously in order to fly and keep flying, which involves rhythmic-like movement control, although the direction of their flight is somewhat a higher-level task and involves goal -direction (8). This is distinct from discrete movements, which are always goal -oriented. For instance, the action of grabbing a water bottle involves a more conscious effort, as it can only be stimulated when a person sees the water and desires it, which involves the cerebral activity of the parietal and the frontal lobe (8). Although more complex movements may involve both discrete and rhythmic components, it is necessary to isolate the differences in more simple movements to truly understand the difference in control.

So how does the brain control these movements in space and what are the pathways that transmit these command signals to the muscle cells? Every voluntary movement starts from the primary motor cortex, where neurons are fired through the corticomotor tract. It is known that discrete movements have a preferential activation point in the M1 cortex and descend to lower motor neurons that directly activate their muscles, indicating a direct and voluntary control over the muscles (9). However, the signal executing simple rhythmic movements necessarily must converge on cells in the brainstem before passing on to the same descending corticospinal tract. The variation in corticomotor pathways might account for the movements' characteristics and goal. Although rhythmic movement is best characterized by its involuntary and continuous nature, its start and end are voluntary. And since all voluntary movements must activate the M1, starts and stops of rhythmic movements are discrete, which suggests that the identity of the movement might be determined by the presence of involvement of the brainstem (10). This reflects the fact that our data show MEP amplitudes of post-transition movements more closely resembled MEPs of discrete movement than those of rhythmic. Therefore, in order to understand the anatomical differences between the two movements, it is necessary to understand the function of the brainstem.

The brainstem regulates movements like breathing, heartbeat, blood pressure, and swallowing, which are voluntary movements that require minimal or no conscious effort to execute (11). Breathing and swallowing both involve combinatorial movement of skeletal and smooth muscles, which can also be voluntarily executed or inhibited. However, heartbeat and blood pressure are exclusively involuntary because we have no control over them, and only external stimulations can vary them. Many scientists in the past have hypothesized that movement patterns are generated by alternating activation of agonist and antagonist neurons caused by central pattern generators (CPG), which are circuits that produce a variety of rhythmic patterns without somatosensory inputs (12). By looking at the rhythmic-like functions of the brainstem, we can infer that the brainstem consists of a pattern generator system that is analogous to the CPG that allows continuous and less voluntary motions like walking, and that rhythmic movements are more dependent on the brainstem compared to discrete movements.

Discrete movements are not only responsible for starts and stops of rhythmic movement, but also planning of movement trajectories. Trajectory planning is important when starting an unrehearsed motion, in that it provides muscle tissues a guideline for the motion they are executing (13). However, once one phase of motion is completed, there is no need to recreate the same trajectory, but only to imitate the initial motion according to the same blueprint. In other words, discrete movements are activated under feed-forward control, whereas rhythmic movement, which is highly dependent on the brainstem, repeats the movements already planned during discrete movements (14). This might suggest the brain's ability to rapidly adapt to a new motion, starting from more-discrete and then to less-discrete, when executing rhythmic movement.

The data collected in our experiment suggests a discrete nature of the stops and starts of rhythmic arm movements. We observed that the MEPs of transition movements were, on average, significantly higher than the MEPs of regular rhythmic movements, and also higher than the MEPs of regular discrete movements. We can speculate that it is because transition movements require a higher cognitive demand than regular discrete movements, given that the brain is required to alternate its corticomotor tract during movement (15). The higher MEP of transition movement phase observed in our study might serve to explain the complexity of "multi-tasking" in humans. This fluid alternation between rhythmic and discrete movement is an absolute necessity for humans who are often required to perform complex combinations

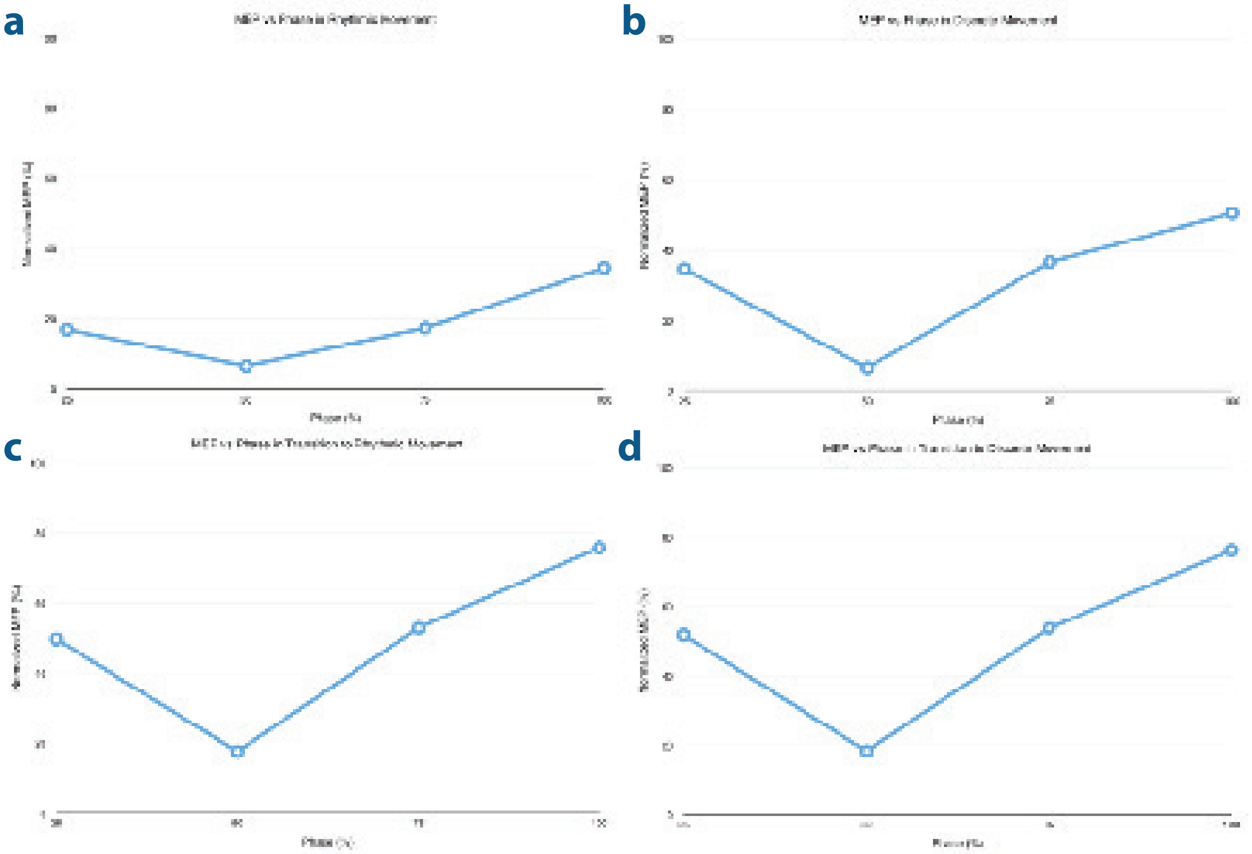


Fig 7. Binned movement data for all subjects. A: The MEPs of regular rhythmic movement had an average maximum of 34.6% and minimum of 17.0%; B: The MEPs of regular discrete movements had an average maximum of 50.5% and minimum of 6.56%; C: The MEPs of transition to rhythmic movement had an average maximum of 75.9% and minimum of 17.5%; D: The MEPs of transition to rhythmic movement had an average maximum of 76.3% and minimum of 18.2%.

of rhythmic and discrete movements, such as eating and walking while talking or searching through a phonebook while driving a car (16). In these situations, one would create a mental priority; in example 1, talking requires the most conscious effort, so the focus shifts to talking, while the other two tasks are kept rhythmic. In the second example, however, neither of the tasks can be operated under rhythmic control; thus, one of the tasks is compromised while the other is prioritized. This is a possible explanation as to why texting while driving will always compromise driving and is normally impossible to do without compromising safety.

Many researchers of this field have observed that the starts and stops of rhythmic movements more resemble discrete movements than do motions during the steady-state of rhythmic movement, during which no start and stop are involved (3). To continue this line of inquiry we can propose a follow up experiment where we observe brainstem activity across different parts of the rhythmic movement. If we record the excitability of the brainstem over one phase of rhythmic movement, we may be able to observe an increase in brainstem activity at the start and decrease in the end of rhythmic movement. Also, incorporating goals into rhythmic movement may isolate brain activity from the kinematic nature that rhythmic movement comprises and provide a deeper insight about goal -orientation in the brain as a whole.

Methods

Training

For rhythmic movements, subjects were asked to rotate their forearms across 100 degrees of movement with any preferred frequency. For discrete movements, subjects were asked to rotate their forearms, but to stop for at least 2 seconds after one cycle. All subjects began with their forearms at the starting point, closest to the mid-line of the body. Subjects would extend the forearm away from the body approximately 100 degrees and then immediately flex back toward the midline of the body. For one cycle, the starting point was the beginning of the phase (0%) at the maximum flexed position and reached the 50% of the phase at maximum extension and finally returned back to max flexed position (100% of phase). In addition to the simple rhythmic and discrete conditions, we introduced two transition conditions, either going from rhythmic to discrete or discrete to rhythmic. The subjects were prompted to switch movement types during the next cycle after feeling a tap on their left shoulder. Subjects performed these simple movements until consistency was achieved.

Locating the Hotspot and Motor Threshold

In order to identify the best location for the magnetic stimulator prior to data collection, we used neuro-navigation software (BrainSight ver 2013) with an attached tracking camera to probe the motor cortex. By applying magnetic pulses and monitoring muscle activity, we were able to locate areas of the brain that evoked an MEP in the biceps. MEPs appear at an invariant time after pulse in the biceps, and any response that had a peak-to-peak voltage value over 50μV in this time window was considered a noticeable MEP (**Fig 4g**). To hone in on the area of interest after finding an initial MEP, we fired pulses on a systematic array of cortical targets using a 5x5 grid with regions of interest randomly distributed (**Fig 4e**). With the aid of the neuro-navigation interface, the targeted area that resulted in maximal bicep activation was termed the “hot spot,” which was used as the stimulator location for all subsequent stimulations (**Fig. 4 b, c, d**).

	0-25%	25-50%	50-75%	75-100%
R vs D	$p < 0.01$	$p < 0.01$	$p < 0.01$	$p < 0.01$
R vs >R	$p < 0.01$	$p < 0.01$	$p < 0.01$	$p < 0.01$
R vs >D	$p < 0.01$	$p < 0.01$	$p < 0.01$	$p < 0.01$
D vs >R	$p < 0.01$	$p < 0.01$	$p < 0.01$	$p < 0.01$
D vs >D	$p < 0.01$	$p < 0.01$	$p < 0.01$	$p < 0.01$
>R vs >D	$p > 0.05$	$p > 0.05$	$p > 0.05$	$p > 0.05$

Fig 8. Quantification of significant differences between each experimental group using HSD Test. $P < 0.05$ indicates significant difference between two groups. R: data for standard rhythmic movement; D: data for standard discrete movement; >R: data for transition to rhythmic movements; >D: data for transition to discrete movements.

For each volunteer, we selected the desired amplitude of stimulation by first finding the amplitude that resulted in a noticeable MEP (above 50 μV) in non-moving biceps 50% of the time, termed the motor threshold (MT). We used an adaptive motor threshold assessment program (AdaptivePEST, MUSC dept. of Psychiatry) to estimate this threshold. As a standard practice in other TMS protocols, we used a supra-threshold stimulation intensity of MT + 20% to excite the motor cortex. **Fig. 5** is a kinematic data sample derived during a subject’s arm movement practice.

Data Normalization & Binning

All of the raw data were normalized for convenience of data analysis. For example, the MEP amplitude, which was measured in μV, were converted into percentage, where 100% represents the maximum MEP amplitude in a session, so that the lower amplitudes could be compared in reference to the maximum. The normalization removes the possibility that the difference of raw MEP amplitude between subjects may interfere with inter-subject comparison, because normalization optimizes each subject's data scale for comparison. This is how the binning of different subjects' data is possible. Additionally, we eliminated each subject's 100% MEP value as these possibly included random twitching of the arm or insignificant outliers, which may unnecessarily enlarge the scale of MEP normalization, and may dwarf lower values that are actually significant for comparison. This process does not compromise the accuracy of our data because even if the removed 100% MEP is significant, the data surrounding the 100% MEP still remains. The phases, which were measured in angles (0º-100º), were also translated into percentage so that we could perceive the MEP in terms of the progress within the phase. Since phases were arranged from 0-100%, we decided to bin the data into four phases: 0-25%, 25-50%, 50-75%, and 75-100%. 0-50 would be all extension and 50-100 would be all flexion. In this way the data analysis would be much more manageable without compromising too much accuracy.

Acknowledgements

The experiments of this research were conducted in Northeastern University's Action Lab.

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