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Research report

# The structure of arm and hand movements in a spontaneous and food rewarded on-line string-pulling task by the mouse

Ashley A. Blackwell[a], Mark T. Banovetz[a], Qandeel[a,b], Ian Q. Whishaw[b], Douglas G. Wallace[a,*]

[a] *Department of Psychology, Northern Illinois University, De Kalb, Illinois, 60115 USA*
[b] *Canadian Centre for Behavioural Neuroscience, University of Lethbridge, Lethbridge, Alberta, Canada*

A R T I C L E I N F O

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A B S T R A C T

Arm and hand use by the mouse have been studied in a variety of tasks in order to understand the structure of skilled movements and motor learning, the anatomy and function of neural pathways, and to develop animal models of neurological conditions. The present study describes string-pulling by the mouse, a behavior in which a mouse uses hand-over-hand movements to pull down a string that hangs from the top of a test cage. Mice both spontaneously string-pull and also string-pull to obtain cashew nuts tied to the end of the string as food reward. To string-pull, mice sat upright and tracked the string with their nose and then made hand-over-hand movements to reel in the string. A string-pull movement consists of four arm movements (Advance to make purchase, Pull, Push to draw the string down and Lift to return the hand for the next Advance) and four hand movements (Collect to aim the hand, Overgrasp to position the hand, and Grasp to make purchase, and Release). The kinematic profiles of the string-pull movement are distinctive with each hand making similar movements at a rate of 4 cycles per second and with the Lift and Advance movements occurring at a higher speed than Pull and Push movements. The results are discussed in relation to the antecedent repertoire of mouse behavior that lends itself to string-pulling, with respect to the utility of using string-pulling to investigate motor systems and adapting string-pulling to model neurological conditions in mice.

## 1. Introduction

Arm and hand use by the mouse have been studied in a variety of tasks in order to understand the structure of skilled movements and motor learning, the anatomy and function of neural pathways, and to develop animal models of neurological conditions [20]. In the single-pellet reaching task, in which a mouse reaches for an item of food with one hand, proximal arm movements are used to lift/lower, advance/withdraw, and pronate/supinate the hand and distal hand movements are used to open/close the hand for grasping food at a fixed location [40,42]. In the staircase task, an animal reaches for food located on stairs on both sides of an elevated runway, and so is encouraged to reach first with one hand to one side of the staircase and then with the other hand to the other side of the staircase to obtain food [3]. The single-pellet task lends itself to video/kinematic analysis of reach movements whereas the staircase task varies task difficulty and allows the comparative assessment of both hands within each test. Both types of tests and their many variations are used to assess forelimb function in murid models of neurological conditions [18,12,13,29,28,8]. Both reaching tasks, and their many variations, require labor-intensive training of the animals and various degrees of manual behavioral analysis; therefore, investigators have experimented with a variety of methods of automated training and assessment [10,14,15,36,39].

These reaching tasks assess the ability of an animal to advance a hand to a target, purchase the target, and retrieve it, and these same movements can be studied in allied tests, such as string-pulling [6]. String-pulling is a proto-tool use behavior [21] in which an animal pulls in a string in order to obtain a reward attached to its end. String-pulling has been taught to or spontaneously displayed by a wide range of animal species [46,32,22,49,1], and it has been adapted to investigate cognitive processes and social learning [45,24,19,23]. String-pulling falls within the natural repertoire of many animals because it is akin to pulling on nesting material, or pulling on a food object from a branch or a blade of grass that contains food at its end. To date, there has been no investigation of string-pulling or the movements used for string-pulling in the mouse, but methodology that exploits string-pulling could be used to investigate their skilled forelimb movements.

The current study describes qualitative and quantitative techniques to investigate the movement organization associated with spontaneous and food-rewarded string-pulling behavior in mice. The experiments

* Corresponding author.
*E-mail address:* dwallace@niu.edu (D.G. Wallace).

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describe the hand and arm movements used for string-pulling, provide behavioral and kinematic exemplars of string-pulling movement analysis, and describe methods of qualitative and quantitative analysis.

## 2. Materials and methods

### 2.1. Subjects

Subjects were 8 female Swiss mice obtained from Northern Illinois University vivarium at 9 months of age and 6 adult male C57/BL6 mice (2–3 months of age), weighing 20–30 g, raised at the Canadian Centre for Behavioural Neuroscience Vivarium at the University of Lethbridge. Mice were housed in groups of two in opaque plastic cages with wire mesh tops. The colony rooms were maintained at 20–21 degrees Celsius and on a 12-h light/dark cycle. Mice were provided ad libitum access to food and water throughout testing. All experimental protocols were approved by the NIU Institutional Animal Care and Use Committee (IACUC) and by the University of Lethbridge Animal Care Committee.

### 2.2. Apparatus

The habituation apparatus was transparent standard housing cage (46 cm × 26 cm 26 cm). The string-pulling apparatus was a transparent rectangular box (13.3 cm × 7.5 cm × 26 cm) with a plastic top and a transparent barrier restricting access to half the apparatus. The apparatus was positioned on a table (1.5 meters above the floor) in a small room. The string (0.2 cm in diameter 100 cm in length) was 100% cotton. A weight was attached to the end of the string in the cage, preventing the string from falling when the cashew was attached. A JVC HD video camera (Model #: GY-HM100U) was positioned perpendicular to the wall of the apparatus with the string. Additional filming was done with high speed camera that captured video at 240 f/sec. The videos were stored on DVDs for offline analysis.

### 2.3. Procedures

During the habituation day mice were individually placed in standard housing cages without bedding and twenty strings of varying length (30 cm to 100 cm) were hung over the edge of the cage (see panel A of Fig. 1). The strings were placed, such that the portion of the string on the inside of the cage just touched the bottom of the cage. Half of the strings were baited with a piece of cashew (approximately 50 mg) attached with a single overhand knot (see panel B of Fig. 1) to the end of the string outside of the cage. Mice were removed from the apparatus once all of the cashews were retrieved or an hour had elapsed.

Testing began the next day, mice were put in the string-pulling apparatus (13.3 cm × 7.5 cm × 26 cm; see panel C of Fig. 1) and received eight trials with a single 100 cm baited string. A trial started when the mouse was placed in the apparatus and ended after the cashew was retrieved or 20 min had elapsed. If the cashew was not retrieved within 20 min the testing session terminated, the animal was returned to the transport cage, and the apparatus was prepared for the next mouse (e.g., cleaning the apparatus, baiting a new string). If the cashew was retrieved, the mouse was removed from the testing apparatus and placed in a holding cage while the apparatus was prepared for the next trial (e.g., cleaning the apparatus, re-baiting the strings). After the completion of eight trials the mouse was returned to the transport cage and the apparatus was prepared for the next mouse.

### 2.4. Behavioral analysis

The behavioral analysis described multiple aspects of string-pulling behavior.

#### 2.4.1. Spontaneous string-pulling

During habituation (when 10 of the 20 strings were baited with food), a count was made of the number of strings that were fully pulled into the cage.

#### 2.4.2. Motivation to pull

During testing in the string-pulling apparatus, three measures were used to assess motivation to engage in string-pulling behavior during the eight trials with 100 cm string baited pieces of cashew. First, the percent of trials a cashew was successfully retrieved was calculated for each mouse. Next, the latency to the first bout of hand-over-hand string-pulling was recorded for each trial a cashew was successfully retrieved. Finally, the latency to reach the cashew after initiation of the first bout of string-pulling was recorded.

#### 2.4.3. String-pulling movements

The string-pulling movements were inspected by stepping frame-by-frame through the video record in order to describe the arm and hand movements used to reach for and grasp the string to pull on it. The analysis described movements of the upper and lower arm and the hand and fingers. Movement duration was estimated by digitizing reaching sequences in order to match the hand movements used in string-pulling to the kinematic record of pulling.

#### 2.4.4. Sensory guidance of string-pulling

Sensory guidance of string-pulling was determined by noting where/when the mice contacted the string with their hand and how they located the string to obtain contact.

#### 2.4.5. Accuracy in string-pulling

Several measures were used to quantify the accuracy of movement. The first four bouts of hand-over-hand string-pulling were selected from each mouse for further behavioral analysis. The number of left hand, right hand, and mouth contacts were recoded and averaged across the bouts. During the sequence of movements, a hand will occasionally miss contacting the string. Missed string contacts were recorded for each of the four bouts of string-pulling behavior.

### 2.5. Motion capture analysis

Motion capture software (Peak Performance, Vicon, Denver, CO, USA) was used to quantify the kinematic organization of string-pulling behavior. Two bouts of string-pulling behavior were captured at 30 Hz for frame-by-frame analysis. Hand position during string-pulling behavior was digitized by selecting the pixel that corresponded to the center of the left and right hand for each video frame. The resulting x- and y-coordinates were used to quantify multiple aspects of string-pulling behavior.

#### 2.5.1. Bimanual coordination

Strength of bimanual coordination was calculated as the correlation between the distance each hand moved within the y-axis across all of the bouts of digitized string-pulling.

#### 2.5.2. Reach and withdraw phase

Frame-by-frame analysis revealed that mouse string-pulling behavior can be segmented based on functional characteristics of movement (see Fig. 2). Each hand cycled through reach and a withdraw phases of movement. The reach phase was defined as upward movement without string contact; whereas, the withdraw phase was defined as downward movement that involved string contact. These aspects of movement were used to segment hand x- and y-coordinates into reaches and withdraws.

#### 2.5.3. Movement kinematics

Three measures were used to quantify the kinematic characteristics of reach and withdraw phases. First, the peak moment-to-moment speed was recorded and averaged for each set of phases across both

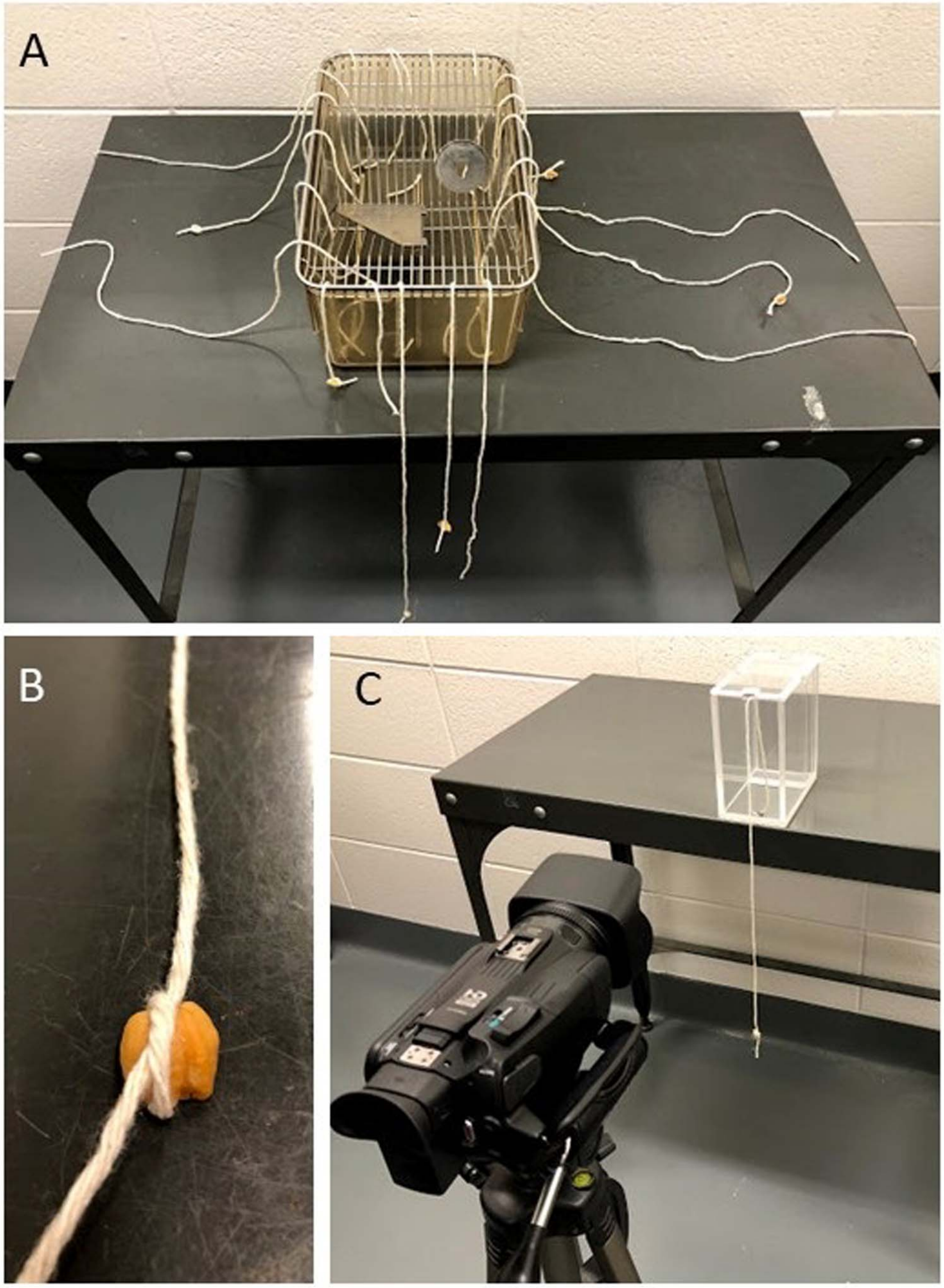


**Fig. 1.** Photographs are provided for the apparatus used during habituation (A), the overhand knot used to secure the cashew piece to the end of the string (B), and camera and apparatus arrangement during string-pulling testing (C).

hands. Next, the Euclidean distance (shortest distance between the start and end of the path) was recorded and averaged for reach and withdraw phases across both hands. Finally, previous research has demonstrated that rats [6] adjust their manipulatory scale peak speeds to the extent of movement. This movement scaling was quantified as the correlation between the set of peak speeds and Euclidean distances obtained from each reach and withdraw phase across both hands.

#### 2.5.4. Movement topography

Three measures were derived from each set of x- and y-coordinates to characterize topographical organization of both phases of movement. First, a phase represents a continuous path through manipulatory space and these paths vary in complexity. Path circuity of a phase was calculated by dividing the Euclidean distance by the total path distance. As values of this ratio increase from 0.0 to 1.0 the paths become more direct.

Next, movements for each reach and withdraw phase are oriented in a specific direction. The heading direction of movement was calculated by transforming the start and end coordinates of the path such that the start of the path is the origin (0,0) and the angle of the end coordinate is calculated relative to a polar coordinate system (0°: right; 90°: up; 180°: left; 270°: down).

Finally, the parameter of concentration is a descriptive circular statistic [4] used to quantify the within mouse variability in headings for a set of reaching or grasping phases. Values of the parameter of concentration range from 0.0 (headings are uniformly distributed across 360°) to 1.0 (headings are in the identical direction). Finally, the average directions of movement were calculated for each set of reach

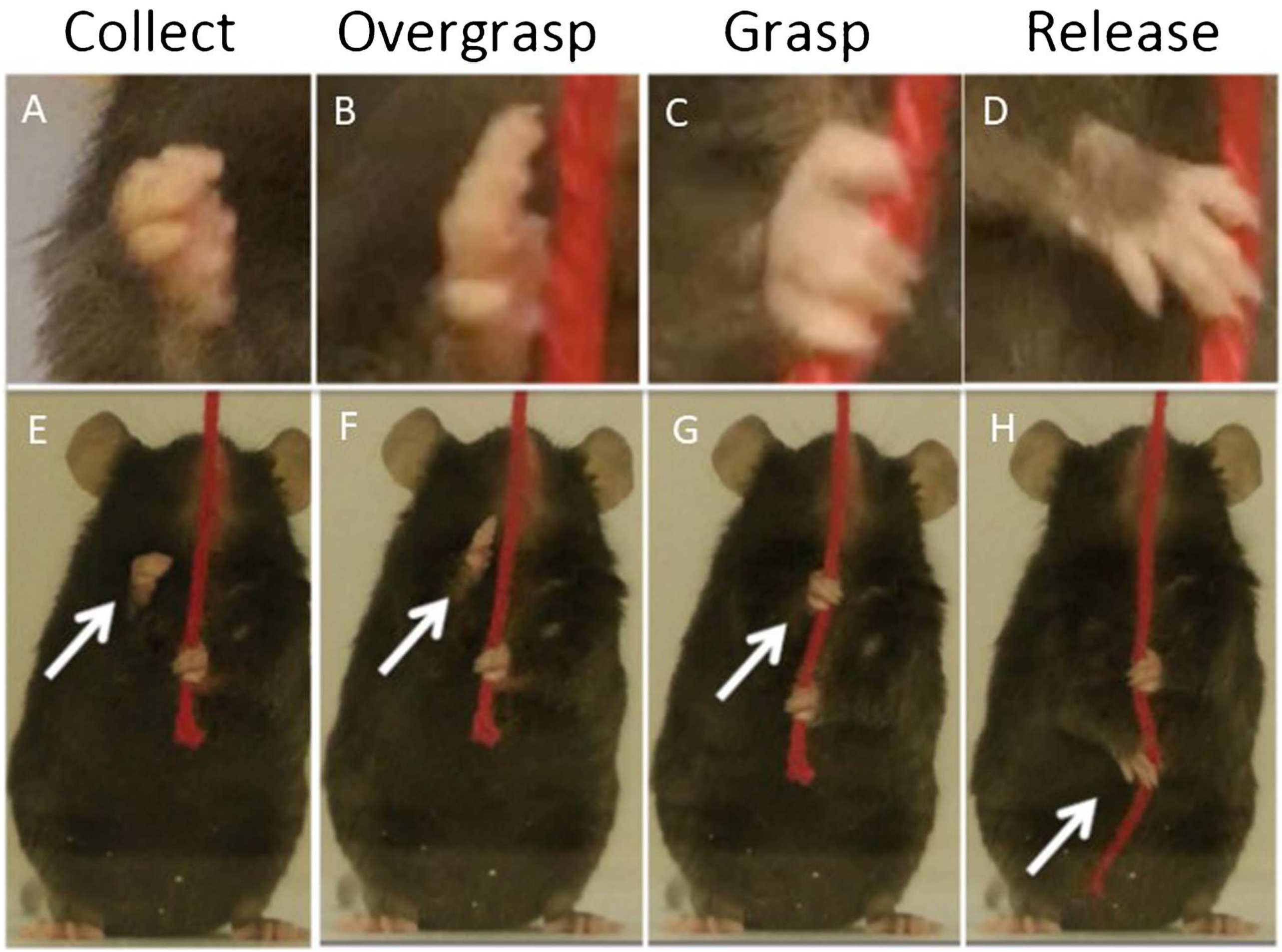


**Fig. 2.** Hand shape (top row) and location (bottom row) are displayed for a single cycle of the right hand during collect (A, E), overgrasp (B, F), grasp (C, G), and release (D, H). Note: different finger configurations are associated with each hand shape.

and withdraw phases across both hands.

### *2.6. Statistical analysis*

Regression analysis was applied to each set of mouse nose and string positions to determine the strength of the relationship during a bout of string-pulling. Single sample *t*-test was applied to characterize whether strength of bi-manual coordination significantly differed from 0.0. Within Subjects ANOVA was used to investigate differences in movement kinematic (peak speed, Euclidean distance, and movement scaling) and topographic (path circuity, parameter of concentration, and average heading) characteristics between hands (right vs. left) and phases (reach vs. withdraw) during bouts of string-pulling behavior.

## 3. Results

The string-pulling movements and behavior displayed by the Swiss and the C57/BL6 were very similar and both groups of mice readily spontaneously engaged in string-pulling and also pulled strings for food reward of a piece of cashew. Thus, both groups of mice were used to describe the movements and kinematic features of pulling; whereas, the formal behavioral, kinematic, and statistical analysis of the movements were obtained from the Swiss mice.

### *3.1. Behavioral analyses*

#### *3.1.1. Spontaneous string-pulling*

A typical bout of string-pulling behavior involves hand-over-hand movements (see video in supplemental resources) and occasional mouth contacts. During habituation, all mice engaged in spontaneous string-pulling. With an average of 17 (SD: 5) strings completely pulled in the apparatus of the 20 strings presented. Almost as soon as mice detected the string by sniffing it, they sat up and engaged in string-pulling movements. These movements were identical to the movements made after a period of reinforcement.

#### *3.1.2. Motivation to pull*

Swiss mice displayed consistent string-pulling behavior to obtain a food reward. On average mice retrieved the cashew on 78% (SD: 26) of the trials. On the first three trials all eight mice retrieved the cashew. During the fourth trial two mice failed to retrieve the cashew and during the seventh trial one mouse failed to retrieve the cashew. Finally, on the eighth trial two mice failed to retrieve the cashew. Of the trials the cashew was retrieved, it took on average 172 (SD: 109) seconds to observe the first bout of string-pulling after a mouse was placed in the string-pulling apparatus. Subsequent to the first bout of string-pulling, it took on average 33 (SD: 16) seconds to reach the cashew. Mice quickly engaged in string-pulling behavior with limited access to the apparatus.

#### *3.1.3. String-pulling movements*

String-pulling movements consisted of two acts: a reach in which a mouse advanced the hand to grasp the string, and a withdraw during which the string was pulled. Overall, string-pulling involved alternating movements of the hands, during which each hand reached and withdrew to advance the string.

**Table 1**
Arm and hand shape used for string-pulling.

| Arm movement | Hand movements |
|---|---|
| Advance – upper arm raised & elbow open | Overgrasp – fingers extended & open |
| Pull – upper arm lowered & elbow closed | Grasp – fingers closed & flexed |
| Push – elbow open | Relase – fingers extended |
| Lift – elbow closed | Collect – fingers lightly closed & flexed |

The shape and movement of the hand changes during each phase of string-pulling behavior. The reach and withdraw movements consisted of four arm movements and four hand movements (Table 1): *(1) Advance*. The advance of the hand toward the string began with the lower arm held at the level of the chest and was produced by extension of the upper arm and opening of the elbow to extend the lower arm. As the hand is extended the fingers extend so that before the string is contacted the hand is fully open. (2). *Pull*. The pull consisted of lowering the arm to the level of the chest with the string held in the hand. Once the string was contacted and grasped, a pull was achieved by lowering of the upper arm and closing of the elbow. (3) *Push*. The push involved extending the arm so that the string was advanced to the level of the abdomen. The push was achieved by the opening of the elbow. At the point that the arm was fully extended the string was released. (4) *Lift*. The lift brought the hand to the starting position while simultaneously closing the fingers.

The four hand movements are illustrated in Fig. 2. (1) *Collect*. The collect posture was a hand shape in which the fingers lightly closed and flexed with the hand held at the level of the chest (Fig. 2 panels A and E). (2) *Overgrasp*. As the advance took place the fingers were fully opened and extended into an overgrasp in preparation to grasp the string (Fig. 2 panels B and F). (3) *Grasp*. As the hand contacted the string and began the pull, the fingers closed around the string to grasp (Fig. 2 panels C and G). Grasps were made with the string held by fingers 2–5 or with the string scissored between two of the fingers. (4) *Release*. At the completion of the push, the fingers fully extended to Release the string (Fig. 2 panels D and H).

### 3.1.4. Sensory guidance of string-pulling

Fig. 3 illustrates the hand contacts with the string on one sequence of string-pulling by a mouse. All contacts were made on the string ipsilateral to the side of the reaching hand, at a point just below the snout. Inspection of the first 10 contacts for eight mice indicated that nearly every contact was in the same approximate location. When the mice released the string, the release point was on the opposite side of the body to the reach hand, approximately at the lower chest and abdomen.

Just before making contact with the string with the reaching hand, the string was invariably aligned with the midpoint of the nose. In order to determine whether the nose was tracking the string, the tip of the nose and the horizontally adjacent point of the string was digitized on successive frames (60 f/sec) through a sequence of string-pulling in four mice in a room with standard lighting and string-pulling in infrared lighting. In both normal and infrared light, the movement of the string and the movement of the mouse's nose were closely coupled (Fig. 4) providing highly significant correlations ($r > 0.80$ for all mice in both normal and infrared testing conditions) between nose movement and string movement.

### 3.1.5. Accuracy in string-pulling

The four sampled bouts of string-pulling revealed that mice on average made 10 (SD: 2) left hand, 10 (SD: 2) right hand, and 3 (SD: 1) mouth contacts with the string. On average mice made 0.1 (SD: 0.2) misses with the left hand and 0.2 (SD: 0.4) misses with the right hand. Mice were accurate in contacting the string during bouts of string-pulling behavior.

## 3.2. Motion capture analysis

### 3.2.1. Bimanual coordination

Bouts of string-pulling behavior were characterized by the bimanual coordination of both hands while pulling the string. Hand position (see panel A of Fig. 5) and distance traveled (see panel B of Fig. 5) on the y-axis revealed that hands alternated through cycles of upward and downward motion. The temporal lag in similar hand movements resulted in an inverse relationship between distances each hand moved in the y-axis during a string-pulling bout (see panel C of Fig. 5). A single sample *t*-test [$t(7) = -7.522$, $p < 0.001$, 95%CI: $-0.53$ to $-0.28$] revealed the average correlation between distance moved on the y-axis was significantly different from 0.0 (see panel of D of Fig. 5).

### 3.2.2. Reach and withdraw

The characteristics of movement changes across a typical reach cycle by one hand are summarized as a set of five phases of movement,

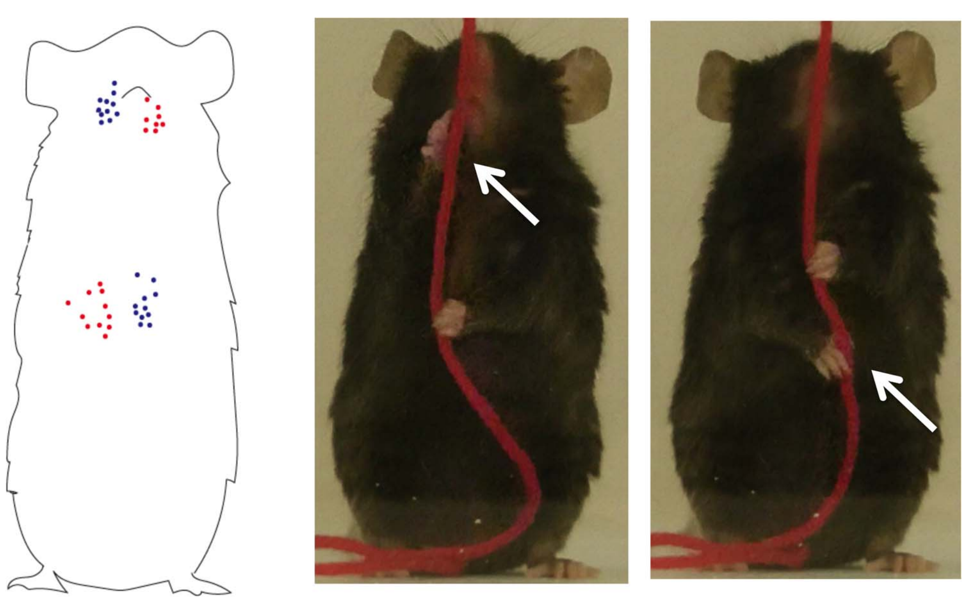

**Fig. 3.** Contact (top) and release (bottom) locations are plotted for the right (red) and left (blue) had during a bout of string-pulling. Note: Contact points for the grasp are adjacent to the snout and within the field of the anterior vibrissae and release points occur contralateral to grasp points. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article).

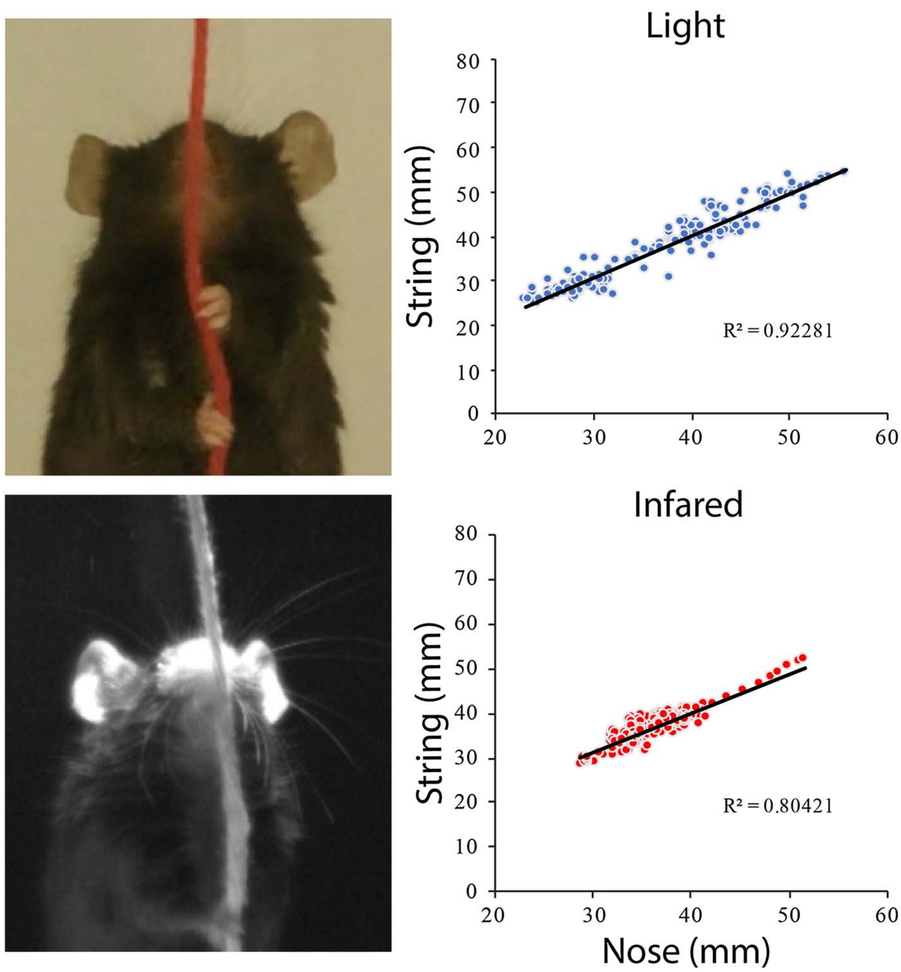


**Fig. 4.** Photographs and scatter plots are presented under normal light (top row) and dark (bottom row) conditions. Scatter plots represent the distance moved by the nose and string between frames observed under both conditions. Note: even though each grasp and pull movement changes the positon of the string, the nose faithfully tracks the string.

beginning with the lift: Lift, Advance, Grasp, Pull, and Push. The movement of the hand through these phases was characterized by digitizing the tip of the third finger from a video record made at 240 f/sec (see Fig. 6, left). The distances the hands moved on each video frame are displayed for a representative trial (see Fig. 6, right). The duration of the reach is approximately 0.25 s, and Fig. 5 illustrates that the movements of Lift and Advance are relatively rapid whereas slower movements characterize Grasp, Pull and Push.

### 3.2.3. Movement kinematics

These features in movement kinematics were confirmed in Swiss mice during string-pulling behavior as the hands cycled through the reach and withdraw phases (see Fig. 7). First, the withdraw phase (Pull/Push) elicited slower peak speeds relative to the reach (Lift/Advance) phase (see panel B of Fig. 7). The ANOVA conducted on average peak speeds revealed a significant effect of phase [$F(1,7) = 141.355$, $p < .001$, $\eta_p^2 = 0.953$]; however, neither the main effect of hand [$F(1,7) = 0.038$, $p = 0.851$, $\eta_p^2 = 0.005$] nor the Phase by Hand interaction [$F(1,7) = 2.856$, $p = 0.135$, $\eta_p^2 = 0.290$] were significant.

Next, the withdraw phase elicited shorter Euclidean distances relative to the reach phase (see panel C of Fig. 7). The ANOVA conducted on average Euclidean distance revealed a significant effect of phase [$F(1,7) = 21.678$, $p = 0.002$, $\eta_p^2 = 0.756$]; however, neither the main effect of hand [$F(1,7) = 0.032$, $p = 0.864$, $\eta_p^2 = 0.0.004$] nor the Phase by Hand interaction [$F(1,7) = 3.536$, $p = 0.102$, $\eta_p^2 = 0.336$] were significant.

Finally, scaling of movement extent did not vary as a function of phase of movement or hand (see panel D of Fig. 7). The ANOVA conducted on average movement scaling score failed to reveal a significant effect of phase [$F(1,7) = 5.079$, $p = 0.059$, $\eta_p^2 = 0.421$], hand [$F(1,7) = 2.050$, $p = 0.195$, $\eta_p^2 = 0.227$], and Phase by Hand interaction [$F(1,7) = 0.030$, $p = 0.867$, $\eta_p^2 = 0.004$]. Faster peak speeds and longer Euclidean distances were observed during the reach phase; however, no differences were observed in movement scaling for either phases of string-pulling.

### 3.2.4. Movement topography

Each phase of string-pulling involved a relatively direct path through manipulatory space and was associated with a specific direction of movement (see panel A of Fig. 8). First, the withdraw phase was associated with hands following more circuitous paths relative to the reach phase (see panel B Fig. 8). The ANOVA conducted on average path circuity values revealed a significant effect of phase [$F(1,7) = 6.502$, $p = 0.038$, $\eta_p^2 = 0.482$]; however, neither the main effect of hand [$F(1,7) = 1.814$, $p = 0.220$, $\eta_p^2 = 0.206$] nor the Phase by Hand interaction [$F(1,7) = 0.867$, $p = 0.383$, $\eta_p^2 = 0.110$] were significant.

Next, the withdraw phase was associated less variability in heading relative to the reach phase (see panel C Fig. 8). The ANOVA conducted on average parameter of concentration values revealed a significant effect of phase [$F(1,7) = 19.673$, $p = 0.003$, $\eta_p^2 = 0.738$]; however, neither the main effect of hand [$F(1,7) = 2.012$, $p = 0.199$, $\eta_p^2 = 0.233$] nor the Phase by Hand interaction [$F(1,7) = 1.589$, $p = 0.248$, $\eta_p^2 = 0.185$] were significant.

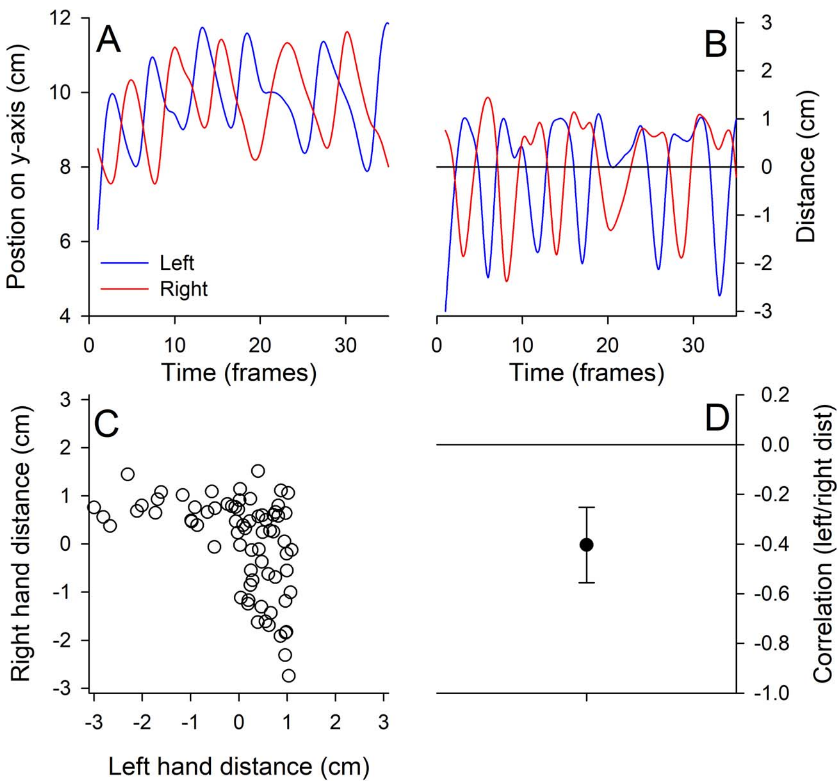


**Fig. 5.** Left and right hand position on the y-axis is plotted for a single bout of string-pulling behavior (A). The distance moved within the y-axis is plotted for the same bout of string-pulling behavior, negative values representing downward movements (B). A scatter plot represents the relationship between distance moved for each hand (C). The average correlation between left and right hand distance moved is plotted for the eight Swiss mice (D).

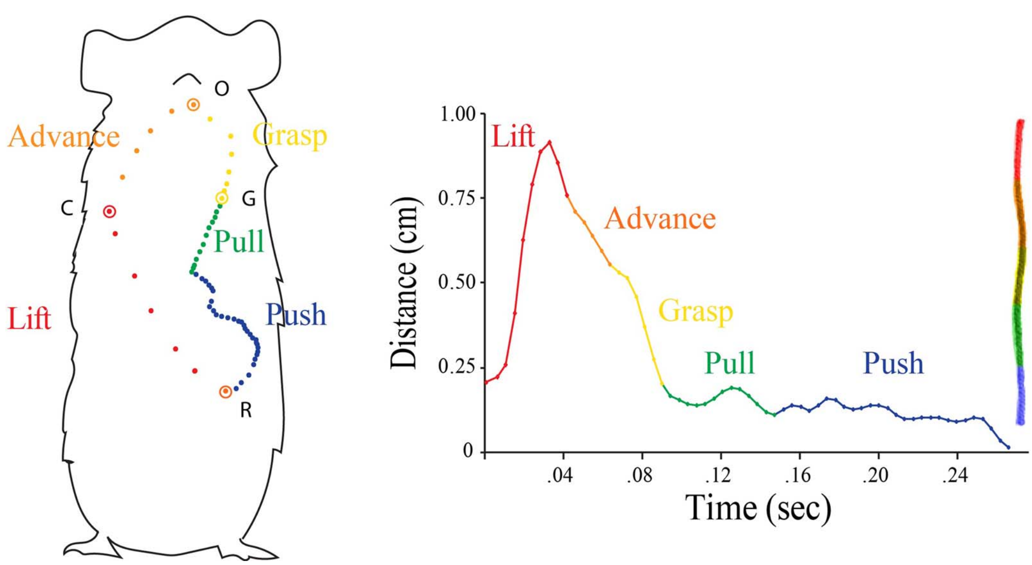


**Fig. 6.** Topographic (left panel) and kinematic (right panel) characteristics are plotted for a single cycle of string-pulling behavior. The location of the Collect (C), Overgrasp (O), Grasp (G), and Release (R) hand shapes are indicated in the topography of movement. Note: there is a fast phase and a slow phase with the fast phase occurring on the ipsilateral side of the body with the hand open and the slow phase occurring on the contralateral side of the body with the hand closed. The horizontal directional change at the Pull/Push transition is largely produced by body rotation as the contralateral hand engages in the Advance.

Average heading direction was observed to be influenced by both phase of string-pulling and hand (see panel D of Fig. 8). The ANOVA conducted on average heading direction revealed a significant effect of phase [$F(1,7) = 18{,}670.823$, $p < 0.001$, $\eta_p^2 = 1.000$], hand [$F(1,7) = 51.710$, $p < 0.001$, $\eta_p^2 = 0.881$], and Phase by Hand interaction [$F(1,7) = 11.950$, $p = 0.011$, $\eta_p^2 = 0.631$]. The reach phase was associated with more direct paths that were more variable in heading direction, relative to the withdraw phase. In addition, average heading direction of each phase varied as function of hand, with both phases crossing the midline.

## 4. Discussion

Male and female mice of two different strains were similarly found to pull down strings that protruded into their cage from above. The behavior quickly occurred spontaneously when a string was presented and continued to occur when food reinforcement was tied to the end of the string. The string retrieval method was a hand-over-hand movement achieved with the mouse sitting/standing with an upright posture. Mice identified and tracked the string with the snout/vibrissae and reached to grasp the string at a point just below the snout. The rapid acquisition and performance of string-pulling may be related to the online nature of the behavior; the mice can put their hand where their nose is on each reach. Retrieval consisted of four arm movements and four hand shape changes that alternated between hands with each reach/withdraw movement occurring in about 0.25 s. The utility of the behavior is that it allows a large number of reach and withdraw movements by both hands to be collected using procedures that involve minimal training. The behavior should prove useful for investigating the neural basis of skilled hand movements and in using mice for modeling neurological

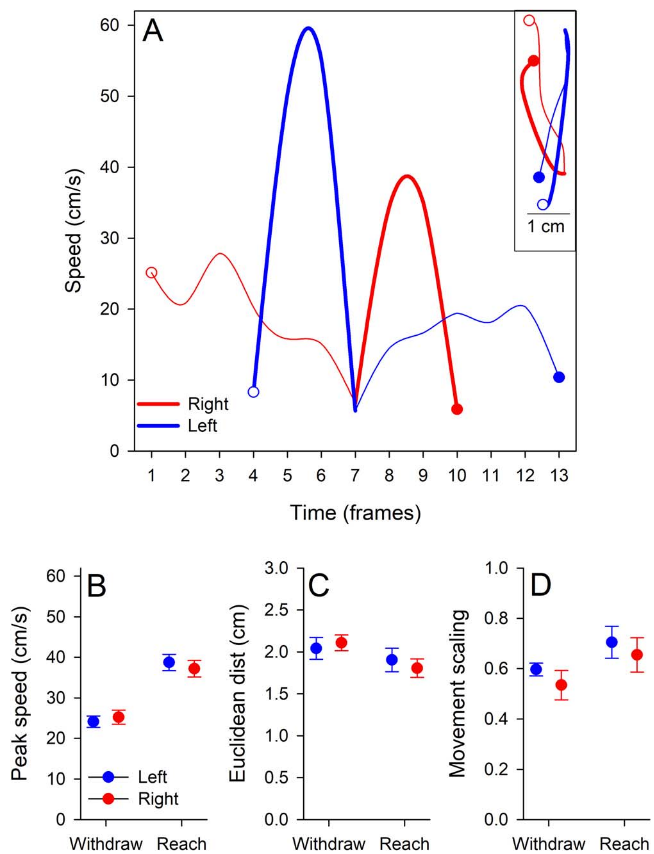


**Fig. 7.** Kinematic (inset: topography of movement) characteristics are plotted for a single cycle of string-pulling for right (red) and left (blue) hands of a Swiss mouse (panel A). Note, the staggered start (open circles) for each hand during the sequential progressions through the withdraw (light lines) and reach (heavy lines) phases followed by the staggered termination of the cycle (closed circles). The average peak speed is plotted for left and right hands across both phases of movement (B). The average Euclidean distance is plotted for each hand across withdraw and reach phases of movement (C). The average movement scaling is plotted for each hand across both phases of movement (D). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article).

conditions that affect hand function.

String-pulling by the mice occurred spontaneously and was maintained using food reinforcement with minimal training as has previously been reported for rats [6,7]. Although direct comparisons were not made, mice appeared to be much more likely to spontaneously engage in string-pulling than rats. Rats generally require more habituation than observed with mice; however, the organization of movement appears to be similar. A direct comparison would be an important next step in this line of studies. The ease of acquisition and performance with mice is probably due to a number of factors. First, the behavior may be akin to behaviors that form part of the mouse's natural behavioral repertoire. Mice manipulate bedding material with their hands to make nests and string has properties that make it ideal for bedding material [26,34,50]. When eating, mice also handle food items at the mouth and so grasping string at the mouth requires a somewhat similar action [44,41,38]. Mice are omnivores and are adept at acquiring many kinds of food that require handling before consumption, including pulling on the stems of grass to obtain seeds located at its head [5]. Aspects of string-pulling behavior are similar to walking and mice are adept at walking on narrow beams and so when pulling mice may be walking up the string [25]. Part of the ease of acquiring string-pulling behavior is that it is mediated by an online representation that does not depend on extensive shaping for success. A mouse is constantly monitoring the location of the string with its mouth/vibrissae, which facilitates making accurate grasping movements [9]. In short, string-pulling is a natural and easily performed behavior for mice as it has found to be for a number of other animal species (for review, see 19).

The arm and hand movements used for string-pulling were highly consistent across reach-withdraw cycles and were performed in a similar way by both hands. From an aiming position with a hand held at the level of the chest in a collect posture with the fingers lightly closed and flexed, a mouse advanced its hand by an upward movement of the upper arm and opening of the elbow with the fingers extending and opening fully in an overgrasp, a configuration larger than a grasp. From this position the hand is adducted in a downward direction to grasp the string, using a whole hand grasp or by catching the string between the fingers. With a firm grip, the mouse makes a pull by lowering the upper arm and closing the elbow to bring the hand to the level of the chest. From this position, the string is further lowered by opening at the elbow to push the hand to the level of the contralateral mid-body. At this point a release is achieved by extending the fingers and a lift raises the hand accompanied by finger flexion to the starting position. This organization depends on movements that have been observed on other test of fine motor control.

As a test of skilled hand use, string-pulling involves movements that have similarities and differences with arm/hand movements made by the mouse in other tests. For example, in the single-pellet reaching test and the staircase test, mice display the hand movements of collect, overgrasp, grasp and release in a way that is similar to that used for string-pulling [47]. Similarly, in the single-pellet reaching test the lift and the advance are similar to those of string-pulling. In the single-pellet reaching task, however, a mouse withdraws its hand containing the food juxtaposed to the mouth for eventual transfer to the mouth and there is no equivalent withdraw movement associated with string-pulling, because the pull and the push carry the hand away from the location of the mouth. The single-pellet and the staircase tasks also require hand pronation in order to place the hand on the food that is located on a horizontal surface and require hand supination to present the food to the mouth. All of the hand movements of string-pulling occur with the palm of the hand aligned in a vertical position parallel to the orientation of the trunk. The similarities and differences between the string-pulling task and other reaching tasks may well produce performance differences that give test specific results. For example, hand pronation has been found to be sensitive to rubrospinal tract injury [27]; whereas, hand supination has been found to be sensitive to corticospinal tract injury, [43]. Further studies are needed to confirm the extent that localized damage spares the movement organization during string-pulling behavior. The organization of mouse string-pulling described in the current study adds to a growing literature supporting a role for polar coordinate system guiding spontaneously occurring behaviors. Directional estimates derived from online representation of current position may guide spontaneously occurring behaviors. Movement segments observed during spontaneous occurring behaviors can be characterized as highly focused trajectories. In the current study, mice spontaneously cycled through reach and withdraw phases, each phase with consistent directional heading. These observations parallel work examining string-pulling behavior in rats [6]. It is possible that rodents are using an online representation of current position to guide direction of each phase. Interestingly, networks of neurons have been discovered with firing of action potentials tuned to the direction of movements at ambulatory [37] and manipulatory [17] scales. Damage to brain structures that mediate these directional signals have been show to disrupt focused directional movements. For example, damage to structures with the head direction network have been shown to impair ambulatory scale direction estimation in homing tasks [16,33,51]. In addition, unilateral sensorimotor cortex lesions in rats have been shown to significantly influence reach and withdraw heading variability during string-pulling behavior [7]. These observations demonstrate the potential of mouse string-pulling behavior to investigate genetic models of neurological disorders that may impact multiple scales of direction estimation.

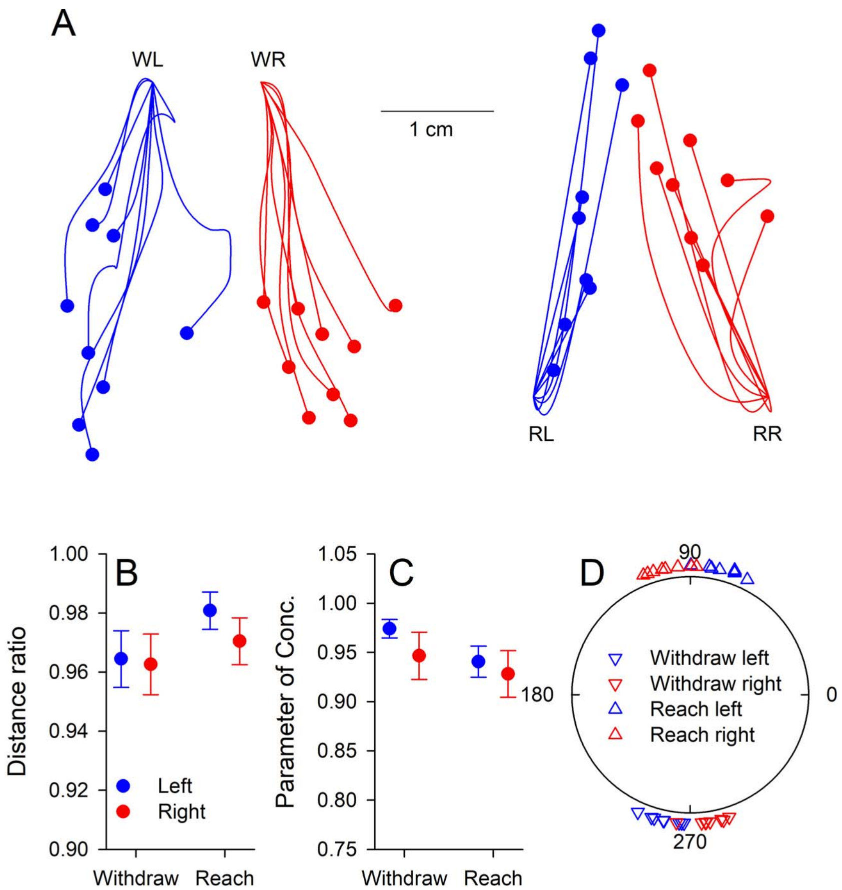


**Fig. 8.** Topographic characteristics are plotted for left (blue) and right (red) hands during a bout of string-pulling (panel A). Note, the start of the withdraw (left) and reach (right) phases have been normalized to a common point, with the termination of the path indicated by a filled circle. The average distance ratio is plotted for left and right hands across both phases of movement (B). The average parameter of concentration is plotted for each hand across withdraw and reach phases of movement (C). The average heading direction is plotted for each Swiss mouse's left and right hand across both phases of movement (D). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article).

Distance estimates derived from an online representation of current position also appear to contribute to the organization of spontaneously occurring behaviors. In the current study, mice scaled peak speeds during both movement phases to the Euclidean distance of the movement. Similar movement scaling has been observed in rats engaged in string-pulling behavior [6]. It is possible that the online representation of current position could also be used to guide the distance of each movement segment. This view is supported by work demonstrating that scaling of movement recruits distinct networks of neurons, each tuned to a parameter related to distance of movement. The septohippocampal system function has been implicated in guiding the magnitude of movement in rats at the ambulatory scale. For example, hippocampal theta frequency has been observed to vary with the distance of a vertical jump [48] or lateral food protection behavior [30,31]. In contrast, non-human primate motor cortex neurons have been shown to be tuned to movement force at the manipulatory scale [11,2]. Recent work has suggested this brain and behavior relationship may be conserved in rats. Specifically, unilateral damage to the rat sensorimotor cortex was observed to disrupt withdraw phase movement scaling in the contralateral hand during string-pulling behavior [7]. Further work is needed to confirm if similar relationships are observed in mice; however, these observations demonstrate the potential of string-pulling behavior to investigate genetic models of neurological disorders that may impact manipulatory scale distance estimation.

The current study demonstrates that Swiss and C57 mice spontaneously engage in string-pulling behavior. No differences in movement organization were observed between the left and right hands; however, evidence of paw preference may have been lost when collapsing for the left vs. right analyses. Future work should examine whether aspects of movement organization observed during string-pulling behavior are related to performance on tests of paw preference. String-pulling behavior is bimanually coordinated and appears to be guided by haptic cues of the string contacting the nose. Hand shape and movement consistently changes across reach and withdraw phases of string-pulling behavior. This movement organization presents a novel tool to investigate the neurobiology of fine motor control in mice.

## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.bbr.2018.02.025.

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