FINAL SCRIPT: APPROVED FOR FILMING

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Title: A Fine Motor Task to Study Joint Kinematics in a Preclinical Model of Neurodegenerative Disease

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Author Questionnaire

1. **Microscopy**: Does your protocol require the use of a dissecting or stereomicroscope for performing a complex dissection, microinjection technique, or something similar? **No**

2. **Software:** Does the part of your protocol being filmed include step-by-step descriptions of software usage? **No**

3. **Filming location:** Will the filming need to take place in multiple locations? **No**

Current Protocol Length
Number of Steps: 13
Number of Shots: 30

Introduction

Videographer: Obtain headshots for all authors available at the filming location.

1.1. **Jessica Verpeut.:** Our research focuses on fine motor skills in models of neurodegeneration. Specifically, we aim to use our new task as a novel biomarker for motor dysfunction.

1.1.1. INTERVIEW: Named Talent says the statement above in an interview-style shot, looking slightly off-camera. *Suggested B.roll:3.5*

What are the most recent developments in your field of research?

1.2. **Jessica Verpeut:** Machine learning algorithms have advanced systems neuroscience to provide an unbiased and automatic way of analyzing clustered animal movement into behavior that typically cannot be deciphered by the human eye.

1.2.1. INTERVIEW: Named Talent says the statement above in an interview-style shot, looking slightly off-camera.

What technologies are currently used to advance research in your field?

1.3. **Jessica Verpeut:** By combining body part tracking and computer clustering methods, we are able to reliably detect, classify, and predict transitions between animal movements in our novel fine motor task.

1.3.1. INTERVIEW: Named Talent says the statement above in an interview-style shot, looking slightly off-camera. *Suggested B.roll:3.3*

What are the current experimental challenges?

1.4. **Alexandria Melick:** Behavior can create a lot of noise, in particular with our task where pellets can be knocked off the platform. We solve this problem with keypoint-moseq.

1.4.1. INTERVIEW: Named Talent says the statement above in an interview-style shot, looking slightly off-camera.

1.5. **Alexandria Melick:** Our protocol improves upon past research behavior paradigms that do not allow for self-perturbing features of movement.

1.5.1. INTERVIEW: Named Talent says the statement above in an interview-style shot, looking slightly off-camera. *Suggested B.roll:2.12*

Videographer: Obtain headshots for all authors available at the filming location.

Testimonial Questions (OPTIONAL):

Videographer: Please capture all testimonial shots in a wide-angle format with sufficient headspace, as the final videos will be rendered in a 1:1 aspect ratio. Testimonial statements will be presented live by the authors, sharing their spontaneous perspectives.

How do you think publishing with JoVE will enhance the visibility and impact of your research?

1.6. **Jessica Verpeut, PhD, Assistant Professor**: (authors will present their testimonial statements live)

Can you share a specific success story or benefit you've experienced—or expect to experience—after using or publishing with JoVE? (This could include increased collaborations, citations, funding opportunities, streamlined lab procedures, reduced training time, cost savings in the lab, or improved lab productivity.)

1.7. **Jessica Verpeut, PhD, Assistant Professor**: (authors will present their testimonial statements live)

Ethics Title Card

This research has been approved by the Institutional Animal Care and Use Committee (IACUC) at Arizona State University.

Protocol

2. Shaping and Testing Procedures for Reach Task in Rodents

Demonstrator: Alexandria Melick and Jessica Verpeut

2.1. To begin the 10-day shaping phase, first turn on the infrared light, the camera, and the computer **[1]**. Transfer the cages containing the rats into the testing room and allow them to acclimate for 5 minutes **[2]**.

2.1.1. WIDE: Talent powering on the infrared light, then the camera and computer sequentially.

2.1.2. Talent will have rats in cages on a cart which has been used for transport from the colony room to the testing room.

2.2. Using the training bowl, provide 1 to 5 pellets along the extension with the extension placed fully inside the apparatus on the first day **[1]**. Conduct 10-minute training sessions with each animal **[2]**.

2.2.1. Talent placing pellets along the extension of the training bowl.

2.2.2. Talent setting a timer and observing the rat during the 10-minute session.
AND
LAB MEDIA: 2.2-Bowl-Placement-Impacts-Rodent-Engagement.mov 00:00-00:10
Video Editor: Please play both shots side by side

2.3. On subsequent days, place the pellets at the end of the bowl closest to the rodent **[1]** and gradually move them farther away to encourage reaching behavior **[2]**.

2.3.1. LAB MEDIA: 2.3.1-Place-Pellet-Close-to-Rat-to-Encourage-Eating-.mov. 00:00-00:08 **AND** 2.3.1-Placing-Pellets-Close-to-Rat-on-Extension.mov 00:00-00:04

2.3.2. LAB MEDIA: 2.3.2-Placing-Pellets-Farther-to-Encourage-Reaching.mov 00:00-00:08
AND
2.3.2-Placing-Pellets-Outside-of-Apparatus-.mov 00:00-00:06

2.4. Once rodents take pellets from the edge of the extension, even if only with their mouths**[1]**, introduce pellet presentation with tweezers to promote reaching behavior

[2].

2.4.1. LAB MEDIA: 2.4.1-Rat-Takes-Pellets-From-End-of-Extension-by-Mouth.mov. 00:00-00:09

2.4.2. LAB MEDIA: 2.4.2-Feeding-with-Tweezers.mov 00:00-00:05

AND

2.4.2-Offer-with-Tweezers-at-End-of-Bowl.mov 00:00-00:06

2.5. Reward the rodent immediately upon touching the tweezers **[1]**. Then, hold the tweezers slightly farther to prompt the rodent to reach further **[2]**.

2.5.1. LAB MEDIA: 2.5-Immediately-Rewarding-When-Touching-Bowl-with-Tweezers.mov 00:00-00:04

2.5.2. LAB MEDIA: 2.5.2-Using-Tweezers-Farther-Away-to-Encourage-Reaching.mov 00:00-00:10

2.6. For the 9-day testing phase, place the rats in the room to habituate for 1 hour **[1]**.

2.6.1. Talent bringing the rats inside the room.

2.7. Apply dental wax to the platform to fix it in place, then position the first bowl ~~on the bowl platform **[1].** Secure it with dental wax,~~ ensuring the front is flush and centered with the apparatus opening **[1]**.

2.7.1. Talent applying dental wax to the platform to fix it in place, placing the bowl, and aligning the bowl. ~~Shot of the first bowl being placed on the bowl platform.~~

2.7.2. ~~Talent aligning the bowl and applying dental wax to fix it in place.~~

2.8. Name the video file in Spinview *(Spin-View)* with the rat identification number, date of recording, and time of recording **[1]**.

2.8.1. SCREEN: 2.8.1-NamingFile.mp4 00:24-00:41

2.9. Transfer the rat into the apparatus **[1].** Close the lid and position a white cardstock on top to deflect light **[2]**. Double-check the camera angle to ensure the appropriate scene is captured and adjust the bowl if it is not centered **[3]**.

2.9.1. Talent transferring the rat into the apparatus.

2.9.2. Talent closing the lid and placing the cardstock.

2.9.3. Talent reviewing the camera feed and repositioning the bowl for correct alignment.

2.10. Pour the specified number of pellets into the bowl **[1]** and press **Start Recording [2]**.

2.10.1. Talent adding pellets to the bowl.

And

TEXT ON PLAIN BACKGROUND:
Day 1–3: Plain bowl: ~100 pellets

Day 4–6: Less bowl: ~50 pellets

Day 7–9: Plinko bowl: ~50 pellets
Video Editor: Please play both shots side by side

2.10.2. Talent pressing **Start Recording.**

2.11. Stay in the room to monitor the rat, take behavioral notes, and replenish pellets as needed **[1]**.

2.11.1. Talent observing and jotting down notes while maintaining pellet quantity.

2.12. For the Plain bowl, ensure pellets are visible and accessible over the bowl edge **[1]**. For the Less bowl, verify that pellets are not stacked and remain loosely scattered **[2]**. For the Plinko bowl, check that pellets are adequately distributed between obstructions **[3]**.

2.12.1. LAB MEDIA: 2.12.1-Adjusting-Pellets-for-Plain-.mov 00:00-00:04

2.12.2. LAB MEDIA: 2.12.2-Adjusting-Less-Bowl.mov 00:00-00:14

2.12.3. LAB MEDIA: 2.12.3-Adding-and-Distributing-Pellets-in-Plinko.mov 00:00-00:09

2.13. Return the rat to its home cage **[1]** and provide the allotted food **[2]**. Wipe the chamber with a disinfectant between animals **[3]**. At the end of the day, spray the entire chamber with ethanol for disinfection **[4]**.

2.13.1. Talent placing the rat back in the cage.

2.13.2. Talent dispensing food into the cage.

2.13.3. Talent using disinfectant wipes to clean the chamber.

2.13.4. Talent spraying the inside of the chamber thoroughly with ethanol and wiping it down. .

AUTHOR'S NOTE: Shots 2.13.3 and 2.13.4 are combined

Results

3. Results

3.1. During Baseline testing, rats showed increased total reaches as the bowl design became more complex **[1].** Under Harmaline treatment, total reaches decreased across all bowl types compared to Baseline, indicating impaired motor function **[2].**

3.1.1. LAB MEDIA: Figure 3A. *Video editor: Highlight the three boxplots from Plain to Plinko.*

3.1.2. LAB MEDIA: Figure 3B. *Video editor: Highlight the three boxplots from Plain to Plinko*.

3.2. During Baseline, total reaches increased with bowl difficulty, showing behavioral persistence despite task complexity **[1].** Failures increased with the Plinko bowl **[2].** Harmaline disrupted typical reach performance **[3].**

3.2.1. LAB MEDIA: Figure 4A. *Video editor: Highlight the increasingly taller green bars from Plain to Plinko*

3.2.2. LAB MEDIA: Figure 4C. *Video editor: Highlight the pink (Failure) bars and green bars in Plain and Less then highlight the red bar in Plinko*

3.2.3. LAB MEDIA: Figure 4D. *Video editor: Highlight the pink and red bars across all three bowl types under Harmaline.*

3.3. Prior to Harmaline treatment, failures increased with task difficulty under Baseline but remained consistent under Harmaline **[1].** Harmaline significantly reduced the learning rate of the task **[2]** and reaching rate across all bowl types **[3].**

3.3.1. LAB MEDIA: Figure 5B. *Video editor: Highlight the increasing bar height from Plain to Plinko in Baseline columns (the one with black dots)*

3.3.2. LAB MEDIA: Figure 6A. *Video editor: Highlight the blue boxplot corresponding to Harmaline*

3.3.3. LAB MEDIA: Figure 6B. *Video editor: Highlight the blue dots and corresponding columns for Harmaline*

3.4. Analysis of reaches using machine learning revealed unique poses and task strategy between Baseline and Harmaline conditions and within each bowl type **[1].** Distinct reaching syllables were used by rats within each bowl type **[2]** and during different bowl conditions **[3].**

3.4.1. LAB MEDIA: Figure 7 A and B

3.4.2. LAB MEDIA: Figure 7 C

3.4.3. LAB MEDIA: Figure 7 D

3.5. TgF344-AD *(T-G-F-Three-Forty-Four-A-D)* transgenic rats had reduced total reaches compared to matched Wild-type rats **[1].** Wild-type rats showed increased total reaches with bowl complexity **[2].**

3.5.1. LAB MEDIA: Figure 8A *Video Editor: Please highlight the Tg grey curve*

3.5.2. LAB MEDIA: Figure 8B. *Video editor: Highlight the WT boxplots from Plain to Plinko.*

3.6. While performance type was variable within each group **[1]**, the TgF344-AD rats had significantly reduced success performance **[2].** As bowls became more challenging, the number of failures increased in both strains **[3].**

3.6.1. LAB MEDIA: Figure 8D and E *Video Editor: please highlight success, dropped, failure columns in both graphs, sequentially*

3.6.2. LAB MEDIA: Figure 8F *Video Editor: highlight the grey dots and columns for all 3 conditions (Plain, Less, Plinko)*

3.6.3. LAB MEDIA: Figure 8G

Pronunciation Guide:

kinematics
Pronunciation link: https://toipa.org/AmE/kinematics toIPA
IPA: /ˌkɪnəˈmætɪks/
Phonetic Spelling: kin-uh-MAT-iks

perturbing
Pronunciation link: https://www.merriam-webster.com/dictionary/perturbing
IPA: /pərˈtɝbɪŋ/
Phonetic Spelling: per-TURB-ing

acclimate
Pronunciation link: https://www.merriam-webster.com/dictionary/acclimate
IPA: /əˈklaɪmɪt/
Phonetic Spelling: uh-KLY-mit

syllables
Pronunciation link: https://www.merriam-webster.com/dictionary/syllable
IPA: /ˈsɪləbəlz/
Phonetic Spelling: SIL-uh-buhlz

TgF344-AD
(This is a construct/name rather than a dictionary word; pronunciation is letter-by-letter for clarity.)
IPA: /ˌtiˌdʒiˌɛfˌθriˌfɔːr-ˌeɪ-diː/
Phonetic Spelling: T-G-F-three-four-four A-D

harmaline
Pronunciation link: https://www.merriam-webster.com/medical/harmalines Merriam-Webster
IPA: /ˈhɑrməˌlin/
Phonetic Spelling: HAR-muh-leen

amyloidosis
Pronunciation link: https://www.merriam-webster.com/dictionary/amyloidosis
IPA: /ˌæmɪlɔɪˈoʊsɪs/
Phonetic Spelling: am-ih-loy-OH-sis

gliosis
Pronunciation link: https://www.merriam-webster.com/dictionary/gliosis
IPA: /glaɪˈoʊsɪs/
Phonetic Spelling: gly-OH-sis

neurodegenerative
Pronunciation link: https://www.merriam-webster.com/dictionary/neurodegenerative
IPA: /ˌnʊroʊdɪˈdʒɛnərətɪv/
Phonetic Spelling: noo-roh-dih-JEN-uh-ruh-tiv

 preclinical
Pronunciation link: https://www.merriam-webster.com/dictionary/preclinical
IPA: /ˌpriːˈklɪnɪkəl/
Phonetic Spelling: pree-KLIN-ih-kul

 shaping
Pronunciation link: https://www.merriam-webster.com/dictionary/shaping
IPA: /ˈʃeɪpɪŋ/
Phonetic Spelling: SHAY-ping

 acclimate (already listed #3) — I'll add **clustering** instead:
clustering
Pronunciation link: https://www.merriam-webster.com/dictionary/clustering
IPA: /ˈklʌstərɪŋ/
Phonetic Spelling: CLUS-ter-ing