

# A novel weight lifting task for investigating effort and persistence in rats

1 **Blake Porter<sup>1\*</sup>, Kristin L. Hillman<sup>1</sup>**

2 <sup>1</sup> Department of Psychology and Brain Health Research Centre, University of Otago, Dunedin, New  
3 Zealand

4 **\* Correspondence:**

5 Blake Porter

6 blakeporterneuro@gmail.com

7 **Keywords: motivation, persistence, effort, progressive ratio, rat behavior**

8 **Abstract**

9 Here we present a novel effort-based task for laboratory rats: the weight lifting task (WLT). Studies  
10 of effort expenditure in rodents have typically involved climbing barriers within T-mazes or operant  
11 lever pressing paradigms. These task designs have been successful for neuropharmacological and  
12 neurophysiological investigations, but both tasks involve simple action patterns prone to  
13 automatization. Furthermore, high climbing barriers present risk of injury to animals and/or tethered  
14 recording equipment. In the WLT, a rat is placed in a large rectangular arena and tasked with pulling  
15 a rope 30 cm to trigger food delivery at a nearby spout; weights can be added to the rope in 45 g  
16 increments to increase the intensity of effort. As compared to lever pressing and barrier jumping, 30  
17 cm of rope pulling is a multi-step action sequence requiring sustained effort. The actions are carried  
18 out on the single plane of the arena floor, making it safer for the animal and more suitable for  
19 tethered equipment and video tracking. A microcontroller and associated sensors enable precise  
20 timestamping of specific behaviors to synchronize with electrophysiological recordings. The rope  
21 and reward spout are spatially segregated to allow for spatial discrimination of the effort zone and the  
22 reward zone. We validated the task across five cohorts of rats (total n=35) and report consistent  
23 behavioral metrics. The WLT is well-suited for neuropharmacological and/or *in vivo*  
24 neurophysiological investigations surrounding effortful behaviors, particularly when wanting to  
25 probe different aspects of effort expenditure (intensity vs. duration).

26 **1 Introduction**

27 Physical effort is often required to perform activities and reach goals. Subjects vary naturally in their  
28 willingness and ability to expend effort, with significant alterations in effort-based decision-making  
29 being a clinical feature of certain neuropsychiatric conditions (e.g., depression (Treadway et al. 2012,  
30 Yang et al. 2014)). To decipher the underlying brain mechanisms governing effort exertion (and  
31 dysfunctions therein), researchers need laboratory tasks that require physical exertion but that are  
32 also amendable to simultaneous neuroimaging, neurophysiological, or optogenetic techniques.

33 In rodent research, effort has generally been assessed using climbing barriers or operant lever  
34 pressing paradigms. The barrier-climbing paradigm, originally devised by Salamone et al. (1994),  
35 involves placing a vertical climbing barrier within a T-maze arm such that an animal must climb or  
36 jump – i.e., they must exert an extra degree of physical effort – to reach a reward site. The intensity  
37 of the effort can be increased by increasing the height of the barrier with 25-30cm being the most

38 common. In rats, barrier paradigms have been used in lesion/inactivation studies (Walton et al. 2002,  
39 Rudebeck et al. 2006, Floresco and Ghods-Sharifi 2007, Holec et al. 2014, Karimi et al. 2017),  
40 pharmacological investigations (Schweimer and Hauber 2006, Bardgett et al. 2009), and  
41 electrophysiological recordings (Hillman and Bilkey 2010, Cowen et al. 2012) to assess the  
42 contribution of different brain areas and neurochemical systems to decisions which require physical  
43 effort. However, the protocol has limitations. Surmounting the barrier can become a simple, quickly  
44 executed motor action (i.e., a jump), especially when the barriers are small and/or the animal is  
45 frequently exposed to the apparatus. In theory effort difficulty can be increased, to an extent, by  
46 increasing the height of the barriers, however in practice this increases the risk of injury to the animal  
47 and/or tethered research equipment. Jumping into 3-dimensional space also complicates spatial  
48 tracking via an overhead camera and can generate noise in electrophysiological recordings.

49 In addition to barrier-climbing experiments, effort expenditure has also been investigated in rodents  
50 using operant lever pressing paradigms. Here, higher numbers of lever presses are equated with  
51 higher effort expenditure. Fixed ratio (FR) and progressive ratio (PROG) response schedules have  
52 been used effectively to probe the neurological mechanisms of effort-related cost-benefit decision-  
53 making (e.g., Floresco et al. 2008, Randall et al. 2014, Hart et al. 2017). The concurrent lever-  
54 press/reward choice paradigm in particular has been used to examine effort expenditure in relation to  
55 generalized behavioral activation (Salamone et al. 2002, Schweimer and Hauber 2005, Randall et al.  
56 2012), with subtle pharmacological shifts in behaviors being produced by various compounds (see  
57 Salamone et al. (2018) for recent review). While lever pressing is an action that can be carried out  
58 alongside tethered optogenetic or electrophysiological experimentation (e.g., Ma et al. 2014,  
59 Robinson et al. 2014, Proulx et al. 2018, Lindenbach et al. 2019), lever pressing – even more so than  
60 barrier jumping – is a simple, quickly executed motor action. Hence the intensity of effort in FR and  
61 PROG lever pressing tasks is largely related to the repetition of responses over time, which  
62 introduces a temporal cost confound to effort costs when interpreting resultant data.

63 Directly increasing the intensity/difficulty of physical effort associated with a single lever press  
64 would better isolate an effort cost component. Holec et al. (2014) tested this idea by engineering  
65 weight-adjustable seesaw levers within the choice arms of a Y-maze. Lever weight was modulated as  
66 a percentage of each animal's body weight, and the weight of a lever could be kept static during a  
67 single session or incrementally changed across trial blocks. While a novel paradigm, behavioral  
68 shortcomings were described in the report, including ceiling effects and failure to achieve pre-  
69 training criterion in a substantial number of subjects (Holec et al. 2014).

70 Due to the limitations of existing barrier and lever pressing paradigms, we aimed to design a task  
71 that: 1) was suitable for use with tethered cables and overhead tracking systems; 2) allowed the  
72 intensity of physical exertion to be directly modulated; and 3) involved an action that produced more  
73 noticeable/observable physical exertion – i.e., a more complex action sequence requiring sustained  
74 effort. Using Sprague-Dawley rats as subjects, we developed the Weight Lifting Task (WLT).

75 The WLT allows for behavioral characterizations of effort expenditure in laboratory rats, including  
76 those that are tethered for neurophysiological recording and/or optogenetic stimulation. In the WLT,  
77 the animal is placed in a large rectangular arena and tasked with pulling a rope 30 cm out of a rope  
78 conduit to trigger food delivery at a nearby reward spout; weights can be added to the rope in 45 g  
79 increments to increase the intensity of effort. As compared to lever pressing and barrier jumping,  
80 weighted rope pulling is a multi-step action sequence requiring sustained exertion. The actions are  
81 carried out on the single spatial plane of the arena floor, making it safer for the animal and more  
82 suitable for tethered equipment and video tracking. Automation of the WLT via an Arduino

83 microcontroller enables precise timestamping of task components, which can be synchronized  
84 alongside neurophysiological recordings or stimulation. Thus the WLT is well-suited for  
85 neuropharmacological, neurophysiological, or optogenetic investigations of effort, particularly when  
86 different domains of effort are of interest (e.g., high-intensity exertion versus sustained persistence).

## 87 **2 Materials and Equipment**

### 88 **2.1 WLT Arena**

89 The arena is a wooden rectangle measuring 120 x 90 x 60 cm with all surfaces painted matte black.  
90 At the center of one wall is the rope conduit – a polyvinyl chloride (PVC) tube that extends 7 cm into  
91 the arena, and is elevated 1 cm above the floor (Figure 1). This rope conduit is used to guide the rope  
92 attached to the weight system into the arena. Aligned with the conduit on the arena floor is a 7 x 30  
93 cm section of ribbed rubber to provide grip for the rat’s feet when pulling. Four cm left of the conduit  
94 a white light emitting diode (LED) is recessed into the arena wall to signal reward delivery. Seven  
95 cm left of the LED is the reward spout – a silicone tube (2.5 mm ID, 4.7 mm OD) that extends 20 cm  
96 into the arena at an approximate 45° angle to the wall and away from the rope conduit. This tube is  
97 used to deliver sucrose reward via a peristaltic pump; the pump is located outside the arena. The  
98 silicone tube is protected by an outer PVC tube (20 cm long, 3 cm in diameter) to prevent rats from  
99 chewing on the silicone tubing. At the end of the silicone tube spout is a plastic dish (3.5 cm  
100 diameter, 0.5 cm tall) to collect the sucrose. The rope PVC conduit and the silicone tube spout were,  
101 in later iterations of the task, separated by a wall which was 40 cm long, 20 cm high, and 4 cm thick  
102 (see *Discussion*). In the training phase (described below in *Methods*), a second, larger PVC tube  
103 measuring 25 cm long with a 3 cm diameter with horizontal slits down the sides is also inserted into  
104 the arena 12 cm to the right of the rope conduit.

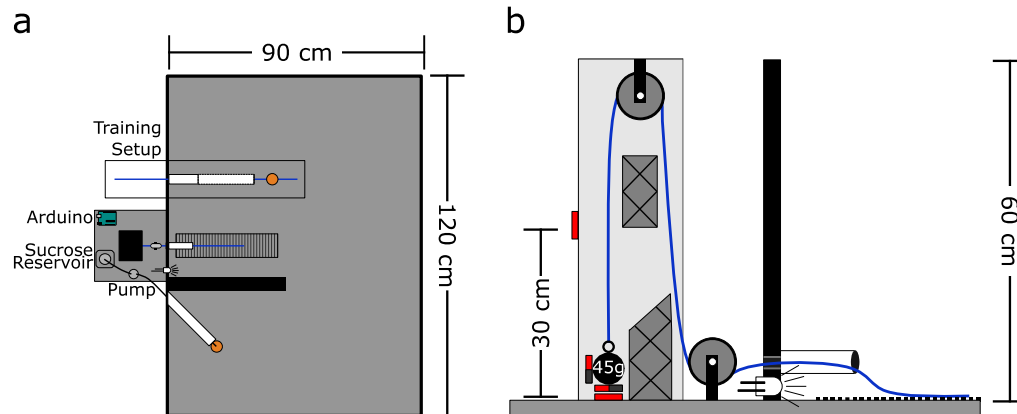
105

106

107

108

109



110

111 **Figure 1:** WLT schematic. a) Aerial view of task set-up. Outside the task area is the pulley system,  
112 Arduino microcontroller, and sucrose pump. Inside the task area, the training setup is outlined with  
113 the training tube (white) and training rope (blue) with sucrose dish attached (orange). Medial to the  
114 training setup is the working area containing the weight lifting rope conduit (white), weighted rope  
115 (blue), and rubber grip mat. The black wall divides the working area from the reward spout (white)  
116 and dish (orange). b) Profile view of the pulley system. Solid red boxes indicate magnetic reed switch  
117 placement. Styrofoam guide inserts are shown with cross hatches.

118

## 119 2.2 WLT Rope System

120 The rope system is comprised of a rope, two pulleys, and various weights (see Figure 1b). The rope is  
121 made of braided nylon and measures 4 mm in diameter with a length of 145 cm; one end of the rope  
122 extends into the arena for the rat to pull while the other end can be attached to a weight outside the  
123 arena. The rope runs through two nylon pulleys each with an outer diameter of 25 mm and track  
124 width of 8 mm (Zenith Inc.). The weight end of the rope uses a key chain clip to facilitate switching  
125 weights quickly. Lead fishing weights (bank sinkers; Maxistrike Inc.) are used to add weight as  
126 desired. Fishing weights were modified to range from 45 g to 225 g in 45 g increments. Each weight  
127 has 2-3 neodymium magnets (15 mm diameter x 4 mm thick) attached to it with two-part epoxy  
128 resin. The pulley set-up is enclosed in a wooden, open-faced box (7 x 9 x 60 cm tall) mounted so that  
129 the open face is oriented towards the arena. Two normally-open magnetic reed switches (Jaycar  
130 Electronics, Inc.) are embedded into the wooden housing, one switch is at the base where the weight  
131 statically sits and the second switch is 30 cm above the base. Two Styrofoam inserts within the  
132 wooden housing help to prevent the weight from swinging, and to keep the weight close to the reed  
133 switches to ensure they are triggered.

## 134 2.3 WLT Automation

135 An Arduino Uno microcontroller ([www.arduino.cc](http://www.arduino.cc)) is used to control the experiment. The two  
136 magnetic reed switches feed into the Arduino which controls the LED and peristaltic pump (12 Volt;  
137 Adafruit Industries, LLC) for sucrose delivery. Adafruit's "Motor Shield V2" for Arduino is used to  
138 power and control the peristaltic pump. The Arduino and pump are run off of a 12 Volt, 4.5 Amp

139 hour lead-acid battery (DiaMec Limited) to reduce electrical line noise during electrophysiology  
140 experiments. Rats have to pull the rope 30 cm in order to trigger the reed switch located 30 cm above  
141 the pulley system base. If this switch is triggered, the Arduino turns on the LED for 250 ms and 0.2  
142 mL of 20% sucrose solution is dispensed through the peristaltic pump. In the rare instance where a  
143 rat makes a successful pull and the reed switch fails to trigger, the Arduino has a button wired to it  
144 for manual dispensing of sucrose and LED illumination. This button also aids in autoshaping the rats  
145 during training (see Methods below). The Arduino is configured to send TTL signals to a Neuralynx  
146 acquisition system (Digital Lynx SX; Neuralynx Inc), such that all weight pulling events can be  
147 timestamped alongside neural recordings and video tracking. The Arduino signals: when the weight  
148 first leaves the base reed switch; when the weight reaches the 30 cm reed switch (or the experimenter  
149 uses the button); and when the weight returns to the base reed switch. This allows for capture of both  
150 successful pulls (rats pulling up the weight a full 30 cm for a reward) and unsuccessful pulls (lifting  
151 the weight but failing to lift it to 30 cm). A capacitive touch lick sensor can also be added to the  
152 reward dish. However, we found that this causes electrical noise when performing *in-vivo*  
153 electrophysiological recordings so we did not continue with this sensor feature. The Arduino code for  
154 the WLT is available on Github (<https://github.com/blakeporterneuro/weightLiftingTask>).

### 155 **3 Methods**

#### 156 **3.1 Subjects**

157 Thirty-five male Sprague-Dawley rats (450-650 g) were used in total to validate the WLT. These  
158 were run as five separate cohorts (7 + 6 + 8 + 4 + 10 rats) by two different experimenters over an 18  
159 month timespan. All rats were 2-6 months old at the start of the experiment and obtained from the  
160 University of Otago's Hercus-Taieri Resource Unit. Rats were housed in groups of two in plastic  
161 individually-ventilated cages (38 x 30 x 35 cm). The animal housing room was maintained on a 12  
162 hour reverse light-dark cycle and kept between 20 – 22°C. Rats were given two weeks from the time  
163 of arrival to acclimate to the new facility. During this time rats had *ad libitum* access to food (18%  
164 Protein Rodent Diet; Tekland Global) and water. After the acclimation period, each rat's free-feed  
165 weight was measured and rats were food deprived to no less than 85% of their free-feed weight  
166 throughout the experiment. Rats always had *ad libitum* access to water. All experiments were carried  
167 out during the dark phase. All experimental protocols were approved by the University of Otago  
168 Animal Ethics Committee and conducted in accordance with New Zealand animal welfare  
169 legislation.

#### 170 **3.2 Habituation and Autoshaping**

171 For three days rats were habituated to the experimental room and the experimenter by being handled  
172 on the experimenter's lap for 10 min/day. Starting on day four, rats spent one min in the  
173 experimenter's lap before being placed in the arena for 10 min/day. On days four through six, small  
174 drops of 20% sucrose solution were randomly scattered around the arena to promote interest in this  
175 food reward.

176 From day four to approximately day 22, rats were autoshaped to pull a rope for a sucrose reward.  
177 This was initially achieved by placing a "training rope" completely inside the arena. The training  
178 rope was 60 cm long and had a sucrose reward dish – identical to the dish located at the usual reward  
179 spout – epoxied at its midpoint. Sucrose could thus be obtained in the dish on the training rope  
180 ("training dish", ~0.2-0.5 mL) and/or at the usual reward spout ("reward dish"). Each time a rat  
181 consumed sucrose from the training dish, sucrose was also dispensed to the reward dish via a button  
182 press to the Arduino. Sucrose was replenished in the training dish by the experimenter using a

183 syringe when the rat was at the reward dish. Once rats were readily consuming sucrose from both the  
184 training and reward dishes, one end of the training rope and the training dish were inserted into the  
185 PVC “training tube” (see *Materials and Equipment* and Figure 1a). The other end of the training rope  
186 was extended out of the arena so that the experimenter could manipulate the position of the training  
187 dish.

188 Initially, the training dish was only partially inserted into the training tube, such that it would be  
189 easily accessible for the rat to reach in and retrieve the dish. Rats would generally pull the training  
190 dish out of the tube with their teeth or forelimbs. As rats became more familiar with this procedure,  
191 the training dish was put further and further into the tube – away from the arena opening – after each  
192 training sucrose consumption. The critical part of autoshaping occurred when the training dish was  
193 too far inside the training tube to grab directly and rats needed to pull the training rope to retrieve the  
194 dish. In our experience, some rats would lose interest in the training dish when it was no longer  
195 within reach of teeth or forelimbs. When this occurred, the training dish was placed closer to the  
196 arena opening so that the rat could once again retrieve the sucrose. Once consumption behavior was  
197 reinstated, the process of incrementally putting the training dish further and further into the tube –  
198 away from the arena opening – was repeated. The maximum distance that the training dish was  
199 placed inside of the training tube was 12 cm from the arena opening.

### 200 **3.3 WLT Training**

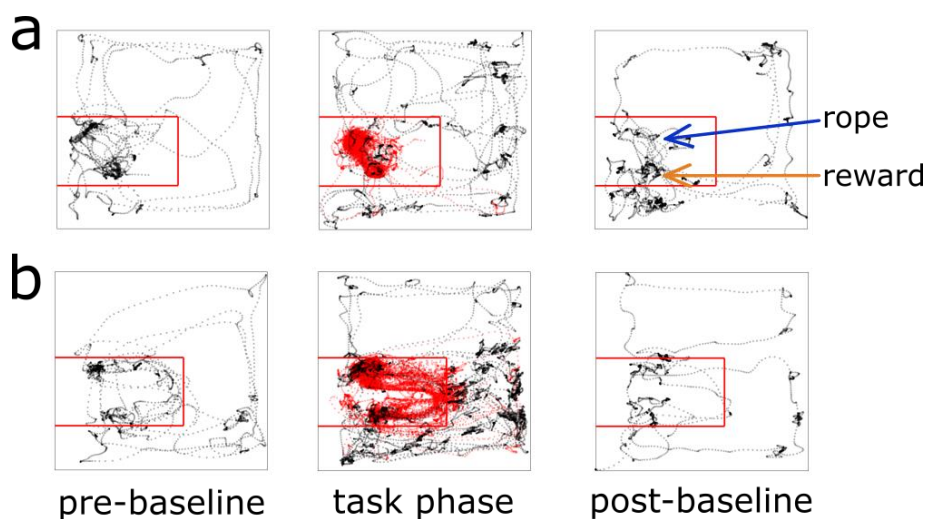
201 Once the rats learned to consistently pull the training rope to get the training dish out of the training  
202 tube, WLT training commenced. Now, sucrose was no longer provided in the training dish and was  
203 only provided via the usual reward spout. Rats were first placed in the arena and allowed to perform  
204 5 trials using the training rope extending from the training tube. The training rope and tube were then  
205 removed, leaving only the regular WLT rope conduit and reward spout (see Figure 1a). Rats would  
206 then learn to pull the regular, non-training rope for sucrose reward; the rope was not weighted with  
207 lead weights at this stage (“0 g”) but did carry the weight of the magnets (~5 g). Initially, rats would  
208 be manually rewarded (via the Arduino button) for very small pulls on the regular rope. As training  
209 progressed, rats would need to pull the rope further and further to get rewarded. Rats were trained on  
210 this “0 g” level (no lead weight, only magnets) until they were making successful 30 cm pulls to  
211 trigger automated reward delivery on greater than 80% of their attempted pulls. After this, training  
212 sessions consisted of 10 successful 0 g pulls followed by addition of a 45 g lead weight (“45 g”).  
213 WLT training was deemed complete when rats were able to successfully pull the 45 g weight on  
214 more than 80% of attempts and completed 10 successful attempts each of 0 g and 45 g in less than  
215 five min.

### 216 **3.4 Surgical Window**

217 After reaching the WLT training criterion, rats underwent surgical implantation of electrode arrays.  
218 This was a one day surgery, involving stereotaxic craniotomies under isoflurane anesthesia, as  
219 previously described (Porter et al. 2019). Rats were given 10 days of post-operative recovery and  
220 then re-tested on the WLT using the last training parameter, i.e., 10 successful attempts each of 0 g  
221 and 45 g in less than five min. Rats were now performing the WLT with a headplug connected to a  
222 headstage (Neuralynx HS-36-LED or HS-32-mux-LED), tethered to a commutator (3 meter tether,  
223 Neuralynx Saturn-1). All rats achieved the WLT training criterion within one to eight days of re-  
224 testing. Electrophysiological data are not analyzed in this manuscript, however we mention this  
225 surgical window here to demonstrate that the WLT is conducive for use in surgically implanted,  
226 tethered animals. Example LFP traces from the anterior cingulate cortex of a rat making 10  
227 successful pulls on 135 g can be seen in Supplemental Figure 1.

### 228 3.5 Behavioral Experiments – General Design

229 Each experiment described below was performed in this general sequence: two min pre-baseline,  
230 experimental task, two min post-task baseline, satiation check. In the two min pre-baseline, the  
231 animal was placed in the arena but the rope was not available. The purpose of this pre-baseline was to  
232 collect two min of neural and locomotor behavior when not performing the task. At the two min mark  
233 the rope was inserted through the rope conduit and the experimental task was immediately started. At  
234 the end of the task, the rope was again made unavailable and the rat remained in the arena for two  
235 min to enable collection of end-of-task neural and locomotor behavior. Two sucrose rewards were  
236 then manually delivered via the reward spout. The purpose of this was to determine if the rat was still  
237 motivated to consume sucrose, or satiated. Ready consumption of two rewards was scored as “non-  
238 satiated”, one of two rewards as “partially satiated”, and none of the rewards as “satiated.” The two  
239 min pre- and post-recordings successfully provided non-task, ‘open field’ behavior as compared to  
240 the experimental task period (Figure 2). For the experimental task period, we defined two spatial  
241 regions of interest (ROIs) for subsequent analysis purposes: the on-task ROI and the off-task ROI.  
242 The on-task ROI was defined as the 45 x 50 cm area encompassing the rope conduit and reward  
243 spout. Rats also had to be making attempts while in the on-task ROI in order to be considered on-  
244 task. The off-task ROI was designated as the remaining area of the arena outside the on-task ROI as  
245 well as when the rats were in the on-task ROI but making no attempts at pulling the rope.



246

247 **Figure 2:** Animal tracking and ROI examples. Tracking data from two different recording sessions is  
248 shown; panel (a) is a session from an early iteration of the task where there is no wall between the  
249 rope and reward, panel (b) illustrates a session where the wall is present. The on-task ROI is outlined  
250 with the red square. Rat tracking data is shown as black dots if off-task and red dots if on-task.

251

#### 252 3.5.1 Progressive Weight Paradigm

253 The progressive weight paradigm used progressively heavier weights to increase effort intensity  
254 across time. After the two min pre-baseline, the weight rope with 0 g was inserted into the arena.  
255 After 10 successful trials, 45 g was added to the end of the rope. This was repeated every 10  
256 successful trials until either 225 g was reached or the rats quit the task. Quitting was defined as the  
257 rats making no attempts to pull the rope for one min (cohorts 1-2) or two min (cohorts 3-5;  
258 empirically we had determined from the initial cohorts that one min was too short of a duration to

259 define quitting). Although rare, if a rat managed 10 successful trials on 225 g, the task would be  
260 made “impossible” by wrapping the rope around a solid bar outside the arena to prevent it from being  
261 pulled high enough to trigger a reward. We refer to the amount of weight at this stage as “infinity”.  
262 Rats would never receive a reward during this impossible phase despite their persistent, frustrated  
263 efforts. However, rats often quit before completing 10 successful 225 g trials.

### 264 **3.5.2 Fixed Weight Paradigm**

265 The fixed weight paradigm used a fixed weight of 180g to investigate persistence and quitting in a  
266 fixed difficulty context. The fixed weight was determined for each rat based on their performance on  
267 the progressive weight paradigm – their highest achievement weight was used, that is, the highest  
268 weight on which the rat completed 10 successful trials. For most rats the fixed weight was 180 g.  
269 After the two min pre-baseline, the weight rope with 0 g was inserted into the arena. After 10  
270 successful trials, the fixed weight was immediately added to the end of the rope. Rats could complete  
271 as many trials as desired until they quit or until one hour elapsed, whichever came first. Quitting was  
272 defined as the rats making no attempts to pull the rope for two minutes.

### 273 **3.6 Data Analysis**

274 All data analyses were carried out using custom Matlab scripts. First, Neuralynx TTL events and  
275 tracking data were imported into Matlab along with an info txt file that contained the times the  
276 weights were changed (e.g., when 45 g replaced 0 g) and when the rat quit. Time spent on each  
277 weight was calculated by the duration it took the rat to complete 10 trials of a weight or, for the quit  
278 weight, the duration from when the weight was attached until the rat quit. The duration of a trial was  
279 calculated by the time between reward TTL signals. The number of attempts the rats made for each  
280 weight was determined by the number of times the weight was lifted high enough to trigger the reed  
281 switch at the base of the weight lifting apparatus. Attempts were further broken down into successful  
282 and failed attempts. Successful attempts were attempts where the rat pulled the weight high enough  
283 to trigger a reward. Failed attempts were attempts where the rat lifted the weight but not high enough  
284 to trigger a reward. The quit weight was the weight in which the rat did not complete 10 trials and  
285 stopped making attempts for two minutes. The achievement weight was the highest weight the rat  
286 completed 10 successful trials on. Time on-task was determined by calculating the time that the rat  
287 was located in the on-task ROI of the arena and was making attempts while within this ROI. If the rat  
288 left the on-task ROI but returned within three seconds he was still considered on task. If the rat was  
289 not present in the on-task ROI or in the on-task ROI but not making any attempts while in the ROI,  
290 they were considered to be off-task. In order to analyze the fixed weight paradigm over time, we took  
291 the first, middle, and last 30 trials on 180g when analyzing the percentage of failed attempts. For  
292 analyzing the duration of successful trials we took the first, middle, and last 10 successful trials on  
293 180g. All data were first tested for normality using D'Agostino & Pearson normality test before the  
294 appropriate statistical test was conducted.

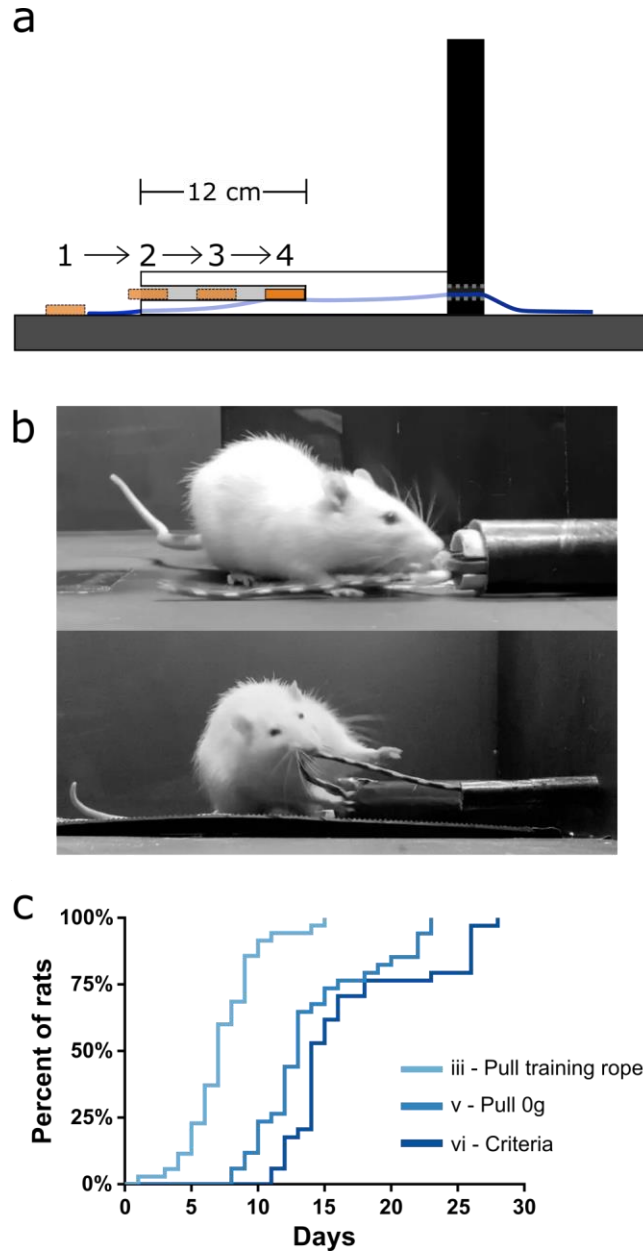
## 295 **4 Results**

### 296 **4.1 Shaping and Training of Weight Pulling**

297 After three days of habituation to the apparatus, rats began the shaping procedure using a training  
298 rope outfitted with a sucrose training dish (see *Materials and Equipment, Methods*). Shaping stages  
299 were defined as: i) consuming sucrose readily from both the training sucrose dish and reward spout;  
300 ii) retrieving the sucrose dish readily with forelimbs/teeth when the training dish is placed  
301 progressively further inside of the training tube (Figure 3a); iii) retrieving the training dish readily by



302 pulling the attached training rope when the dish could no longer be reached inside the training tube  
303 (Figure 3b, top); iv) pulling the training rope with no sucrose in the training dish and receiving  
304 sucrose only from reward spout; v) transitioning from the training rope to the 0 g weighted rope  
305 (Figure 3b, bottom); and vi) reaching WLT training criteria of 10 trials each of 0 g and 45 g within  
306 five min. Shaping stages i to iv can be seen in Supplemental Video 1.



307

308 **Figure 3:** WLT training. a) Schematic showing profile of training tube and the progressive placement  
309 of the sucrose dish further and further inside the training tube. b) Picture of a rat learning to pull the  
310 training dish (stage ii; top) and pulling the 0 g weighted rope (stage v; bottom) c) Training data for 35  
311 rats indicating mastery of stages iii, v, and vi.

312

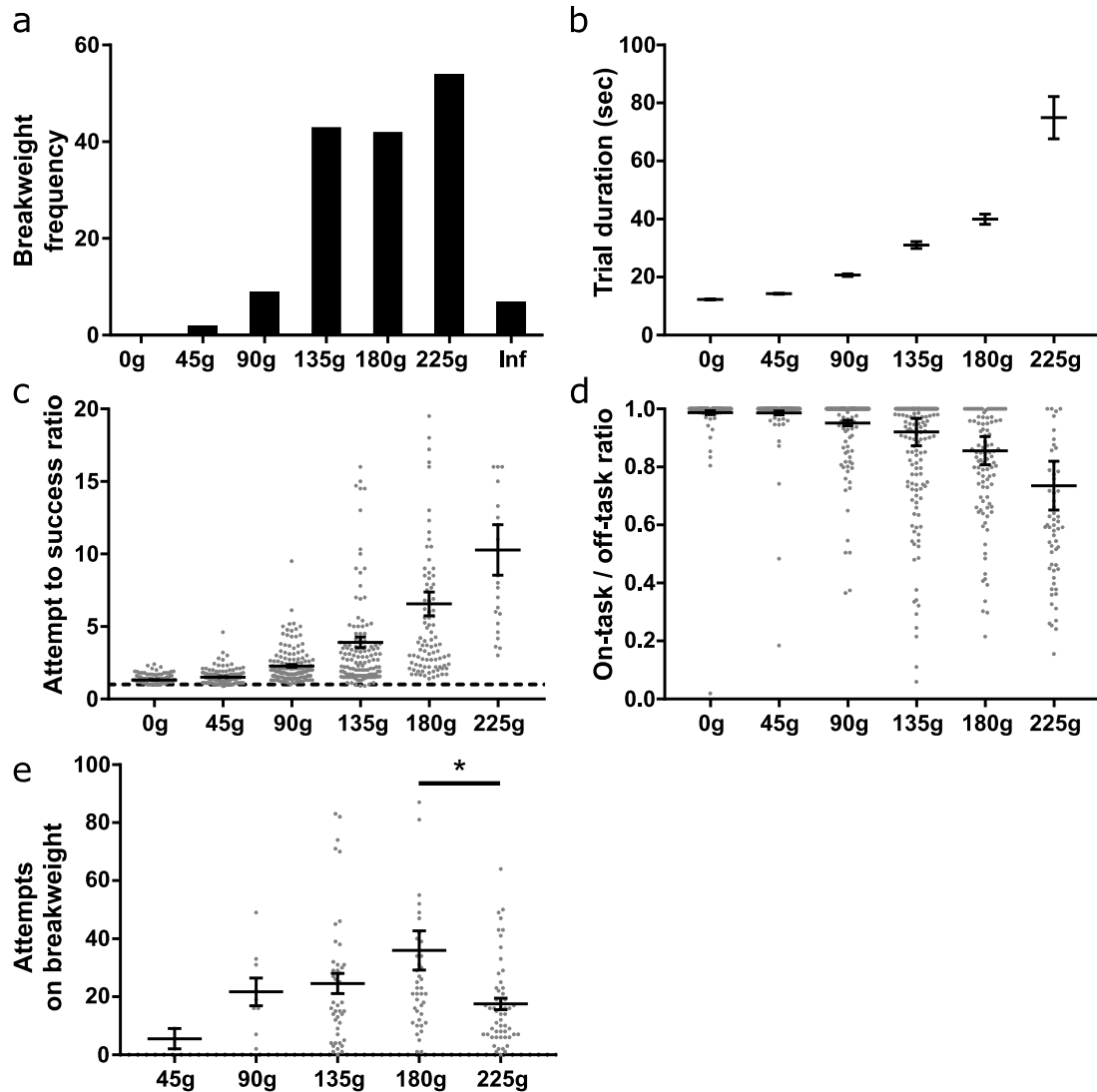
313 After the initial three days of habituation, it took  $7.3 \pm 2.8$  days (mean  $\pm$  SD) for rats to reach stage iii  
314 and become proficient in pulling the training rope (Figure 3c). Transitioning from the training rope to  
315 the WLT rope with 0 g (stage v) took an average of  $14.0 \pm 4.5$  days while reaching stage vi  
316 proficiency required an average of  $16.9 \pm 5.4$  training days. We found that training frequency was an  
317 important consideration. Anecdotally, conducting shaping and training seven days/week tended to be  
318 more successful than taking weekend breaks, where rats would regress a stage or two after each two  
319 day break.

320 The most critical and arduous step in shaping was the transition from stage ii to stage iii, where the  
321 training dish was out of forelimb/teeth reach in the training conduit. At this stage rats had to learn to  
322 pull the rope rather than the dish. Initially, rats become quickly uninterested in the dish when it was  
323 out of reach. This was remedied by moving the dish back within reach to reinstate interest in the  
324 sucrose reward (see *Methods*). An additional strategy to aid in the stage ii to iii transition was to  
325 initially place the training dish within a rat's reach within the training tube but then as the rat  
326 approached, the experimenter would pull the dish (via the end of rope outside the arena) such that the  
327 dish was no longer within reach of the rat. This encouraged the rats to scramble with their paws for  
328 the dish and happen upon pulling the rope (see Supplemental Video 1 at 0:54 seconds). Out of 35 rats  
329 trained on the WLT, one rat never overcame this within-reach/out-of-reach obstacle despite lengthy  
330 shaping sessions (more than 30 days) and was removed from further study. Thus in our experience,  
331 the WLT shaping period is relatively short and has a high success rate, with 97% of our subjects  
332 reaching training criteria in under four weeks (Figure 3c).

333 In our experience, all rats developed the strategy of grabbing the rope in their teeth, pulling with their  
334 bodies, then holding the rope in their forepaws before pulling again with their teeth (see  
335 Supplemental Video 2). Some rats would, on low weights (0 and 45 g), simply hold the rope in their  
336 teeth and run away from the conduit until the reward triggered. However, this running strategy was  
337 not feasible for heavier weights and generally extinguished over time. To facilitate uniform pulling  
338 behavior and consistent effort loads during the shaping and training phase, if rats tried to pull the  
339 rope out of the conduit at  $90^\circ$  angles to the conduit, the experimenter held the rope before it reached  
340 the reward trigger height to discourage this behavior.

## 341 **4.2 Progressive Weight Paradigm**

342 In this experiment rats were tasked with progressively heavier weights after every 10 successful  
343 trials. The experimental session started with 0 g and the weight was increased in 45 g increments  
344 until either the rat quit the task or a pulling weight of 225 g was reached. The weight of the rope at  
345 time of quitting was deemed the "breakweight" in line with PROG-lever pressing "breakpoint"  
346 terminology. Of the 35 rats trained on the task, 22 of them have completed the progressive weight  
347 paradigm across 157 sessions (average of  $7 \pm 1$  SD sessions per rat); behavioral data are shown in  
348 Figure 4. The most frequent breakweight observed was 225 g, occurring on 54 out of the 157  
349 sessions (34%; Figure 4a). Of the 157 sessions there were only seven sessions where a rat achieved  
350 10 successful trials on the 225 g weight and progressed to the "infinity" stage described in the  
351 *Methods*. Thus "infinity" data is provided in Figure 4a but is absent from other panels as there were  
352 so few occurrences and rewards (successes) never occurred on this condition.



353

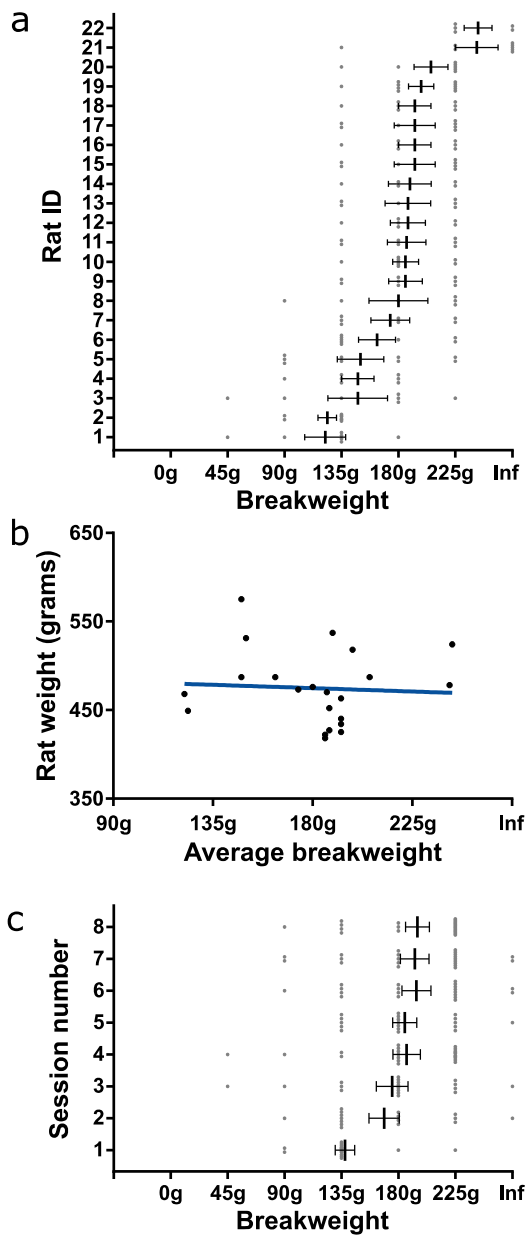
354 **Figure 4:** Progressive weight behavioral analyses. a) Breakweight distribution across all sessions. b)  
 355 Average trial durations for each weight as measured by the time between successful trials. c) The  
 356 ratio of attempts to successful trials for each weight. Dashed line indicates a 1-to-1 ratio. d) Ratio of  
 357 time spent on-task / off-task for each weight. e) The number of attempts rats made on a session's  
 358 breakweight before quitting. Throughout the figure, grey dots indicate individual sessions, bars  
 359 indicate mean ± 1 SEM.

360

361 The progressive weight paradigm exhibited predictable relationships between behavioral metrics  
 362 associated with increasing effort and increasing weight. As the weight got heavier, trial duration  
 363 significantly increased (KW (6) = 2277,  $p < 0.0001$ ; Figure 4b) likely due to the rats failing more  
 364 often in their attempts to pull the rope the full 30 cm (KW (6) = 371.5,  $p < 0.0001$ ; Figure 4c).  
 365 Furthermore, as the weights got heavier rats spent more time off-task (KW (6) = 271,  $p < 0.0001$ ;  
 366 Figure 4d). Specific examination of the breakweight trial blocks revealed a significant main effect for

367 the number of attempts made on the breakweight before quitting (KW (6) = 12.22,  $p = 0.032$ ; Figure  
368 4e). However, a great deal of variation can be seen for each breakweight where some rats make many  
369 attempts before quitting while others quit after just a few attempts. Satiation checks carried out after  
370 the quit point (see *Methods*) were always 100% successful, suggesting that animals had not quit the  
371 WLT due to sucrose satiation.

372 In order to get a better understanding of the rats' quitting behavior we broke down breakweights by  
373 individual rats and by session day. There was a main effect for rat on average breakweight (KW (22)  
374 = 56.42,  $p < 0.0001$ ) indicating that individual rats had different breakpoints (Figure 5a). This  
375 variance was unrelated to body size differences between individual rats, as animal weight and  
376 average breakweight was not correlated ( $R^2 = 0.004$ ,  $p = 0.79$ ; Figure 5b). Breakweight was  
377 significantly influenced by session day (KW (8) = 21.4,  $p = 0.003$ ; Figure 5c), largely driven by day  
378 1 which had a significantly lower average breakweight compared to days 4, 6, 7, and 8 (all  $p$ 's <  
379 0.05; Dunn's test for multiple comparisons). No other pairwise comparisons were significantly  
380 different. Taken together, the progressive weight paradigm is suited for investigating the effects of  
381 incremental changes in effort on persistence behaviors and quitting behaviors.



382

383 **Figure 5:** Detailed quitting behavior on progressive weight paradigm. a) Individual rat's  
384 breakweight. b) Rat's average breakweight by body weight. Blue line indicates line of best fit. c)  
385 Average breakweights across consecutive sessions. Throughout the figure, grey dots indicate  
386 individual sessions, bars indicate mean  $\pm$  1 SEM.

387

### 388 **4.3 Fixed Weight Paradigm.**

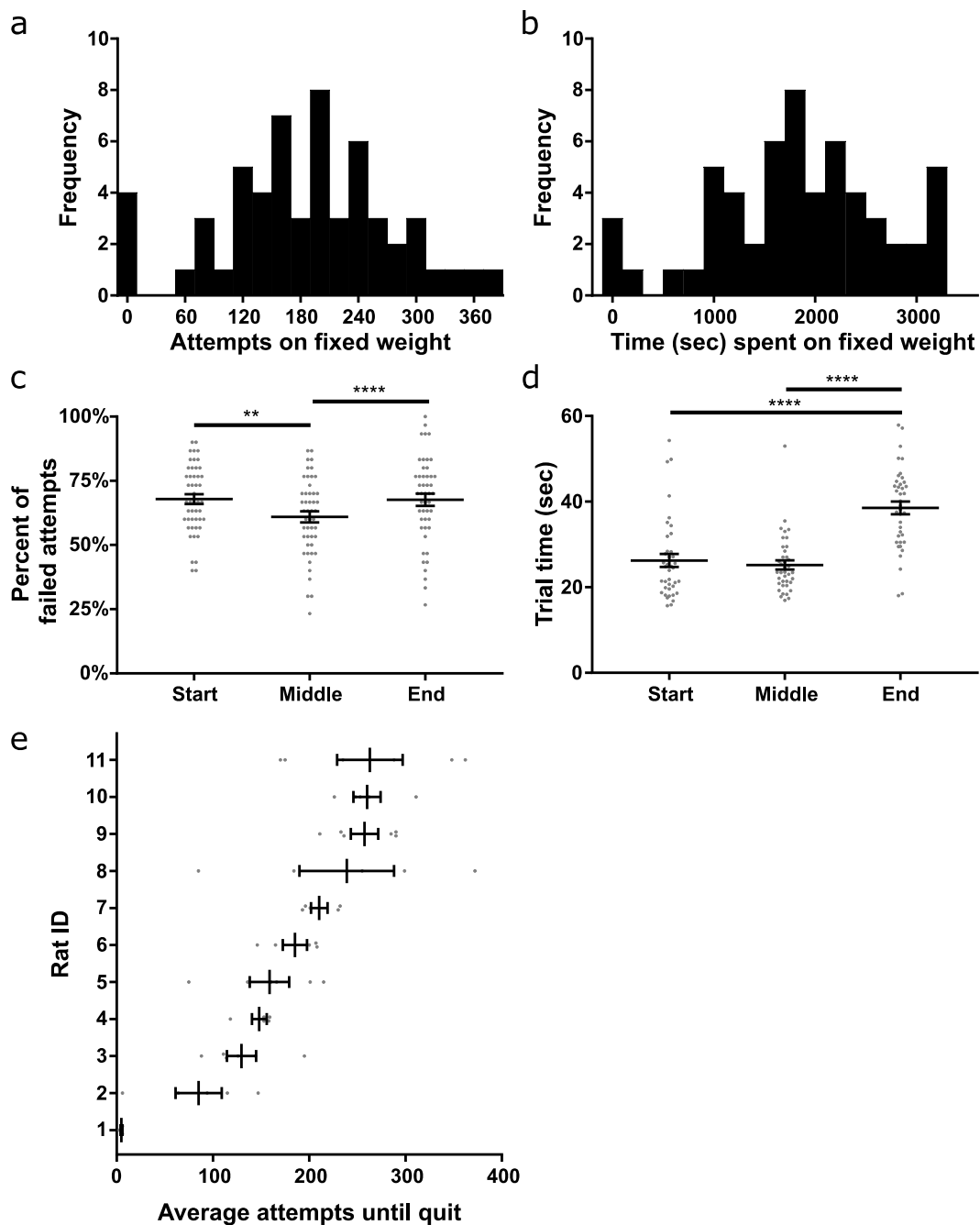
389 In this experiment, rats were tasked with pulling a fixed weight (180 or 225 g) for as long as desired  
390 within a 60 min window; there were no progressive increases in weight. Ten trials on 0 g was used  
391 to start the session, after which the higher weight (180 or 225 g) was immediately attached. Eleven rats

392 that carried out the progressive weight paradigm were subsequently tested on this fixed weight  
393 paradigm. Ten of these rats were tested with a 180 g fixed weight while one rat had 225 g. Across the  
394 10 rats, 57 fixed weight sessions were completed in total, with each rat contributing three to six  
395 sessions. Performance on the fixed weight paradigm was variable across sessions and rats.  
396 Nonetheless, the number of attempts on the fixed weight before quitting, and the total time spent on  
397 the fixed weight task, both fit normal distributions ( $p = 0.93$  and  $p = 0.67$  respectively, D'Agostino &  
398 Pearson normality test; Figure 6a, 6b).

399

400

401



402

403 **Figure 6:** Fixed weight behavioral analyses. a) Histogram of the number of attempts made on the  
404 fixed weight (180 or 225 g) before quitting. b) Histogram of the time spent on the fixed weight  
405 before quitting. c) Percent of failed attempts and d) time for each successful trial at the start,  
406 middle, and end of the session. e) Individual rat's average attempts on the fixed weight before quitting.  
407 Throughout the figure, grey dots indicate individual sessions, bars indicate mean  $\pm$  1 SEM.

408

409 We tested whether or not performance on the fixed weight changed over time, presumably due to  
410 fatigue developing across the session. Sucrose satiation checks (see *Methods*) were always 100%  
411 successful at the end of the task, suggesting that performance changes were likely unrelated to

412 satiation. Time had a significant effect on the percent of failed attempts to all attempts ( $F(2) = 4.48$ ,  
413  $p < 0.0001$ , RM ANOVA; Figure 6c). Multiple comparisons testing revealed a significant difference  
414 between the failure ratio of pulls when comparing the start of the session to the middle of the session  
415 ( $p < 0.008$ ), as well as when comparing the middle of the session to the end of the session ( $p <$   
416  $0.0001$ ; Holm-Sidak's test). Anecdotally, rats tended to fail when the weight was immediately  
417 changed from 0 g to the heavier fixed weighted, after 10 successful pulls on 0 g. The rats would then  
418 acclimate to the heavier weight and the percent of failed pulls would reduce in the middle of the  
419 session, before increasing again towards the end of the session prior to quitting. Furthermore, time  
420 had a significant effect on the speed at which rats completed successful trials ( $F(3) = 34.67$ ,  $p <$   
421  $0.0001$ , Friedman's test; Figure 6d). Rats slowed down significantly towards the end of the session –  
422 prior to quitting – as compared to the start of the session ( $p < 0.0001$ ) and the middle of the session ( $p$   
423  $< 0.0001$ , Dunn's test).

424 We further broke down fixed-weight task behavior by individual rat, and found a significant  
425 difference in the number of attempts before quitting across rats ( $KW(11) = 39.66$ ,  $p < 0.0001$ ; Figure  
426 6e). Rat #1 in particular hardly performed the task over three days, generally making three successful  
427 attempts on the fixed weight and then quitting, despite doing 10 pulls of the same weight (180 g)  
428 only days prior on the progressive weight paradigm. The number of attempts made before quitting  
429 was not significantly correlated to rat body weight (all rats:  $R^2 = 0.28$ ,  $p = 0.10$ ; excluding Rat #1:  $R^2$   
430  $= 0.25$ ,  $p = 0.14$ ). Overall, the majority of rats we tested were willing to perform the fixed weight  
431 paradigm for extended durations, making the task suitable for investigations of fatigue and  
432 persistence.

433

## 434 **5 Discussion**

435 Here we report a novel weight lifting task that can be used to investigate effort-based behaviors in  
436 rats. Rats can be trained on the WLT within a reasonable timeframe and are willing to carry out the  
437 positively-reinforced task. Once rats are trained on weighted rope pulling, the WLT can be used in a  
438 variety of ways to test different aspects of effortful behavior. We systematically tested two versions  
439 of the task – the progressive weight paradigm and the fixed weight paradigm – each modeled after  
440 traditional operant box PROG and FR response schedules. The progressive weight paradigm allows  
441 for investigating the role of increasing effort intensity on behavior. In contrast, the fixed weight  
442 paradigm is better suited for long term effort expenditure, endurance, and persistence. Many other  
443 experimental paradigms are possible – such as a choice-based decision-making WLT – due to the  
444 flexibility of the WLT. The WLT is constructed from inexpensive, easy to obtain components. Task  
445 automation and event detection via an Arduino allows for user-friendly, low cost implementation for  
446 labs looking to enhance their effort behavior investigations.

447 Holec and colleagues (2014) were the first, to our knowledge, to develop a rodent weight lifting-type  
448 task to investigate effort-based behaviors. They utilized weighted levers, one at the end of the two  
449 choice arms of a Y-maze, as a means of weight lifting. The weight required to depress the lever was  
450 chosen based on the animal's body weight, with a maximum value of 40% of the rat's body weight.  
451 Their weighted lever task was part of a task battery used to investigate the role of the anterior  
452 cingulate cortex (ACC) in effort behaviors and decision-making. In previous studies that have  
453 utilized climbing barrier tasks, lesioning or neurochemically manipulating the ACC has been shown  
454 to bias rats away from choosing effortful high-cost, high-reward (HCHR) choices and towards low-  
455 cost, low reward (LCLR) choices (Walton et al. 2002, Rudebeck et al. 2006, Schweimer and Hauber



456 2006). In contrast, Holec et al. found that ACC lesions did not have a large impact on rodent's effort  
457 preference in the weighted lever task when using 20% of body weight. However, when Holec et al.  
458 repeated the experiment with a higher effort cost (40% of body weight), many behavioral issues were  
459 reported. For example, 8/20 rats could not complete the training phase of the task. Furthermore,  
460 behavioral results were difficult to interpret as four ACC lesioned rats showed no difference in  
461 HCHR preference as compared to controls, while the other two ACC lesioned rats essentially never  
462 chose the HCHR option. Their findings that ACC lesions may affect some effort behaviors (barrier  
463 jumping) but not others (20% value weight lifting), makes an important distinction in effort behavior  
464 research. We think our WLT – which requires more complex motor movements as compared to lever  
465 pressing, and fewer training and behavioral difficulties as compared to weighted lever pressing –  
466 could help investigators better elucidate subtle differences in effort exertion, such as those reported  
467 by Holec et al. (2014).

468 Our weight lifting task overcomes some of the common problems encountered in traditional effort-  
469 based tasks that use climbing barriers (Salamone et al., 1994) or operant box lever pressing (e.g.,  
470 Floresco et al., 2008). While climbable barriers have been used successfully to investigate effort  
471 behaviors to date, climbable barriers have inherent experimental constraints. Experimenters can only  
472 make barriers so tall – and thus effortful – before rats either refuse to make attempts or do make an  
473 attempt but fail, resulting in the possibility of animal injury and/or damage to hardware devices. Our  
474 WLT allows for fine control over the amount of effort (weight amount) necessary to carry out the  
475 task. Furthermore, if a rat fails on lifting a weight there is no possibility of injury to the rat or damage  
476 to equipment, and any neurophysiological signals being recorded remain in-tact. While we have not  
477 carried it out, the WLT could be designed as a choice-based, decision-making task by putting a  
478 pulley system at the end of each arm of a Y-maze, similar to Holec et al.'s (2014) weighted lever  
479 task. Different weights or reward amounts could then be used to create traditional HCHR vs LCLR  
480 choice paradigms.

481 Additional paradigms could also be easily implemented using the WLT arena we have detailed here,  
482 that is, one with a single pulley system and an Arduino. For example, a progressive ratio schedule  
483 could be programmed into the Arduino requiring an increasing number of successful pulls to obtain a  
484 reward. Other weight and reward manipulations are also possible. For example, we have piloted a  
485 paradigm where, after a number of successful pulls on a low weight (e.g., 45 g), the task becomes  
486 impossible (“infinity weight,” see *Methods*) and no reward can be obtained. This paradigm lends  
487 itself well to effort-based reinforcement learning and investigations into frustration as rats become  
488 very annoyed when faced with the infinity weight situation.

489 Our WLT also confers benefits over operant box lever pressing effort tasks. Lever pressing tasks use  
490 the number of lever presses as the metric for effort. Effort-based lever pressing tasks generally use a  
491 fixed number of presses or a progressive ratio of increasing press numbers required to obtain a  
492 reward (e.g., Floresco et al. 2008, Randall et al. 2014, Hart et al. 2017). Number of lever presses has  
493 also been used as an effort metric in non-human primate effort studies (Kennerley et al. 2009). While  
494 operant box lever pressing tasks work well with tethered animals, the simple act of lever pressing  
495 does not lend itself well to study sustained, effortful action execution. Furthermore, using the number  
496 of lever presses to manipulate effort has a correlated confound of time making it difficult to parse  
497 behavioral changes due to the effort of many lever presses or due to the temporal discounting of  
498 rewards. Our WLT avoids this issue as the rats must always perform the same action (pulling the  
499 rope 30 cm) while the intensity of effort associated with that action can be manipulated via the  
500 attached weights. Furthermore, rope pulling is a more prolonged sequence of motor actions that may  
501 be better suited for studying the brain mechanisms behind effortful action planning and execution.

502 In addition to improving upon existing rodent-based effort tasks, we suggest that our rodent-based  
503 WLT offers a better behavioral comparison to the effort tasks used in non-human primate and  
504 human-based research. The primary motor-based effort task used with non-human primates and  
505 humans is grip-force (e.g., Pessiglione et al. 2007, Kurniawan et al. 2010, Varazzani et al. 2015).  
506 Generally, participants need to grip and squeeze a force meter with their dominant hand for a  
507 sustained time period or/and for a certain level of force. The grip force task is widely used as it can  
508 be done in a variety of experimental settings such as during EEG recording (Harris and Lim 2016)  
509 and fMRI scanning (Klein-Flugge et al. 2016). Our WLT is similar in nature as rats must pull the  
510 rope for a sustained period of time and with an appropriate level of force to obtain a reward. In  
511 contrast, barrier jumping or lever pressing is a single, quick exertion of effort. We hope that the WLT  
512 can be used with a variety of manipulations to help bridge the gap between human effort behavioral  
513 studies and rodent effort behavioral studies.

514 One limitation in early iterations of developing the WLT was the proximity of the rope to the reward  
515 spout. Rats figured out that they could pull the rope to the reward spout and get rewarded there with  
516 minimal movement between the rope area and reward area. To better spatially and temporally  
517 segregate the working area from the rewarded area, we placed a wall between the rope conduit and  
518 reward spout (see Figures 1 & 2, *Materials and Equipment*). This wall had the additional benefit of  
519 keeping the rats on the rubber mat. Without the wall, rats would sometimes try to pull the rope while  
520 standing on the wooden arena floor and this would result in the animals slipping, especially on  
521 weights above 90 g.

522 We specifically designed the rope conduit and reward spout to extend from the apparatus wall in  
523 order to prevent tethered rats from hitting their implants on the arena walls, which can produce  
524 electrophysiological artefacts. It would be feasible to outfit a bespoke operant box with the WLT for  
525 high throughput behavioral studies. However, in our experience, rats will need at least 35 cm of space  
526 in front of the rope in order to pull the rope successfully. In addition, we purposefully used a large  
527 arena because it allowed us to spatially segregate different behaviors. Anecdotally, when rats would  
528 grow frustrated with the task or when they would quit, they would sprint around the large arena then  
529 groom in a corner (see tracking data in Figure 2). Such nuanced behaviors may not be captured when  
530 using a more confined operant box.

531 We think it is important to discuss the behavioral variability produced by our WLT and the value of  
532 this variability. Performance across rats can be quite variable, and variability was also observed  
533 within a rat's day-to-day performance. Figure 5 and Figure 6e depict this variability showing that  
534 some rats are willing to exert much more effort as compared to others. Furthermore, individual rats  
535 may, on some sessions, work very hard while on other sessions give up quickly. Overall, however, all  
536 but one rat we have tested was able to successfully pull 180 g (roughly 38% of average body weight,  
537 min: 31%, max: 43%). Thus, while there is rat-to-rat and day-to-day variability, all rats are able to  
538 carry out the task to a high degree of proficiency; comparisons across weights and across rats is  
539 feasible. Importantly, this variability in performance is not simply correlated with the rat's body  
540 weight. We think this variability could lead to exciting investigations into the neural mechanisms  
541 underlying motivation, persistence, and quitting behaviors, including individualized intrinsic levels  
542 of motivation. In addition, the WLT is well-suited for the recent advances in animal behavioral  
543 tracking analyses such as DeepLabCut (Mathis et al. 2018) or DeepBehavior (Arac et al. 2019) which  
544 provide highly detailed, three dimensional kinematic data. For example, the motor action sequence of  
545 pulling the rope is quite complex compared to a lever press or jump, and likely requires extensive  
546 motor planning and sensory feedback for successful performance. The wide repertoire of behaviors  
547 elicited by the WLT, such as complex motor movements, reward consumption, task approach and

548 avoidance, and quitting – when coupled with neurophysiological techniques – can provide a better  
549 understanding of the neural circuits involved in effort-based behaviors (Krakauer et al. 2017).

## 550 **6 Conflict of Interest**

551 *The authors declare that the research was conducted in the absence of any commercial or financial*  
552 *relationships that could be construed as a potential conflict of interest.*

## 553 **7 Author Contributions**

554 B.P. and K.H. designed the experiments. B.P. built the WLT, programmed the Arduino, trained the  
555 rats, and ran the experiments. B.P. analyzed the data and B.P. and K.H. interpreted the results. B.P.  
556 and K.H. wrote the manuscript.

## 557 **8 Funding**

558 This study was supported by Marsden Fund grant U001617 (K.H.) from the Royal Society of New  
559 Zealand Te Apārangi.

## 560 **9 Acknowledgments**

561 We would like to thank Kunling Li for his help in collecting behavioral data.

## 562 **10 Data Availability**

563 Datasets are available on request. The raw data supporting the conclusions of this manuscript will be  
564 made available by the authors, without undue reservation, to any qualified researcher.

## 565 **11 References**

566 Arac, A., P. Zhao, B. H. Dobkin, S. T. Carmichael and P. Golshani (2019). DeepBehavior: A Deep  
567 Learning Toolbox for Automated Analysis of Animal and Human Behavior Imaging Data. *Front Syst*  
568 *Neurosci*, 13, 20.

569 Bardgett, M. E., M. Depenbrock, N. Downs, M. Points and L. Green (2009). Dopamine modulates  
570 effort-based decision making in rats. *Behav Neurosci*, 123(2), 242-251.

571 Cowen, S. L., G. A. Davis and D. A. Nitz (2012). Anterior cingulate neurons in the rat map  
572 anticipated effort and reward to their associated action sequences. *J Neurophysiol*, 107(9), 2393-  
573 2407.

574 Floresco, S. B. and S. Ghods-Sharifi (2007). Amygdala-prefrontal cortical circuitry regulates effort-  
575 based decision making. *Cereb Cortex*, 17(2), 251-260.

576 Floresco, S. B., M. T. Tse and S. Ghods-Sharifi (2008). Dopaminergic and glutamatergic regulation  
577 of effort- and delay-based decision making. *Neuropsychopharmacology*, 33(8), 1966-1979.

578 Harris, A. and S. L. Lim (2016). Temporal Dynamics of Sensorimotor Networks in Effort-Based  
579 Cost-Benefit Valuation: Early Emergence and Late Net Value Integration. *J Neurosci*, 36(27), 7167-  
580 7183.

581 Hart, E. E., J. O. Gerson, Y. Zoken, M. Garcia and A. Izquierdo (2017). Anterior cingulate cortex  
582 supports effort allocation towards a qualitatively preferred option. *Eur J Neurosci*, 46(1), 1682-1688.

- 583 Hillman, K. L. and D. K. Bilkey (2010). Neurons in the rat anterior cingulate cortex dynamically  
584 encode cost-benefit in a spatial decision-making task. *J Neurosci*, 30(22), 7705-7713.
- 585 Holec, V., H. L. Pirot and D. R. Euston (2014). Not all effort is equal: the role of the anterior  
586 cingulate cortex in different forms of effort-reward decisions. *Front Behav Neurosci*, 8, 12.
- 587 Karimi, S., A. Mesdaghinia, Z. Farzinpour, G. Hamidi and A. Haghparast (2017). Reversible  
588 inactivation of the lateral hypothalamus reversed high reward choices in cost-benefit decision-making  
589 in rats. *Neurobiol Learn Mem*, 145, 135-142.
- 590 Kennerley, S. W., A. F. Dahmubed, A. H. Lara and J. D. Wallis (2009). Neurons in the frontal lobe  
591 encode the value of multiple decision variables. *J Cogn Neurosci*, 21(6), 1162-1178.
- 592 Klein-Flugge, M. C., S. W. Kennerley, K. Friston and S. Bestmann (2016). Neural Signatures of  
593 Value Comparison in Human Cingulate Cortex during Decisions Requiring an Effort-Reward Trade-  
594 off. *J Neurosci*, 36(39), 10002-10015.
- 595 Krakauer, J. W., A. A. Ghazanfar, A. Gomez-Marin, M. A. MacIver and D. Poeppel (2017).  
596 Neuroscience Needs Behavior: Correcting a Reductionist Bias. *Neuron*, 93(3), 480-490.
- 597 Kurniawan, I. T., B. Seymour, D. Talmi, W. Yoshida, N. Chater and R. J. Dolan (2010). Choosing to  
598 make an effort: the role of striatum in signaling physical effort of a chosen action. *J Neurophysiol*,  
599 104(1), 313-321.
- 600 Lindenbach, D., J. K. Seamans and A. G. Phillips (2019). Activation of the ventral subiculum  
601 reinvigorates behavior after failure to achieve a goal: Implications for dopaminergic modulation of  
602 motivational processes. *Behav Brain Res*, 356, 266-270.
- 603 Ma, L., J. M. Hyman, A. G. Phillips and J. K. Seamans (2014). Tracking progress toward a goal in  
604 corticostriatal ensembles. *J Neurosci*, 34(6), 2244-2253.
- 605 Mathis, A., P. Mamidanna, K. M. Cury, T. Abe, V. N. Murthy, M. W. Mathis and M. Bethge (2018).  
606 DeepLabCut: markerless pose estimation of user-defined body parts with deep learning. *Nat*  
607 *Neurosci*, 21(9), 1281-1289.
- 608 Pessiglione, M., L. Schmidt, B. Draganski, R. Kalisch, H. Lau, R. J. Dolan and C. D. Frith (2007).  
609 How the brain translates money into force: a neuroimaging study of subliminal motivation. *Science*,  
610 316(5826), 904-906.
- 611 Porter, B. S., K. L. Hillman and D. K. Bilkey (2019). Anterior cingulate cortex encoding of effortful  
612 behavior. *J Neurophysiol*, 121(2), 701-714.
- 613 Proulx, C. D., S. Aronson, D. Milivojevic, C. Molina, A. Loi, B. Monk, S. J. Shabel and R. Malinow  
614 (2018). A neural pathway controlling motivation to exert effort. *Proc Natl Acad Sci U S A*, 115(22),  
615 5792-5797.
- 616 Randall, P. A., C. A. Lee, S. J. Podurziel, E. Hart, S. E. Yohn, M. Jones, M. Rowland, L. Lopez-  
617 Cruz, M. Correa and J. D. Salamone (2014). Bupropion increases selection of high effort activity in  
618 rats tested on a progressive ratio/chow feeding choice procedure: implications for treatment of effort-  
619 related motivational symptoms. *Int J Neuropsychopharmacol*, 18(2).
- 620 Randall, P. A., M. Pardo, E. J. Nunes, L. Lopez Cruz, V. K. Vemuri, A. Makriyannis, Y. Baqi, C. E.  
621 Muller, M. Correa and J. D. Salamone (2012). Dopaminergic modulation of effort-related choice  
622 behavior as assessed by a progressive ratio chow feeding choice task: pharmacological studies and  
623 the role of individual differences. *PLoS One*, 7(10), e47934.

- 624 Robinson, M. J., S. M. Warlow and K. C. Berridge (2014). Optogenetic excitation of central  
625 amygdala amplifies and narrows incentive motivation to pursue one reward above another. *J*  
626 *Neurosci*, 34(50), 16567-16580.
- 627 Rudebeck, P. H., M. E. Walton, A. N. Smyth, D. M. Bannerman and M. F. Rushworth (2006).  
628 Separate neural pathways process different decision costs. *Nat Neurosci*, 9(9), 1161-1168.
- 629 Salamone, J. D., M. N. Arizzi, M. D. Sandoval, K. M. Cervone and J. E. Aberman (2002). Dopamine  
630 antagonists alter response allocation but do not suppress appetite for food in rats: contrast between  
631 the effects of SKF 83566, raclopride, and fenfluramine on a concurrent choice task.  
632 *Psychopharmacology (Berl)*, 160(4), 371-380.
- 633 Salamone, J. D., M. Correa, S. Ferrigno, J. H. Yang, R. A. Rotolo and R. E. Presby (2018). The  
634 Psychopharmacology of Effort-Related Decision Making: Dopamine, Adenosine, and Insights into  
635 the Neurochemistry of Motivation. *Pharmacol Rev*, 70(4), 747-762.
- 636 Salamone, J. D., M. S. Cousins and S. Bucher (1994). Anhedonia or anergia? Effects of haloperidol  
637 and nucleus accumbens dopamine depletion on instrumental response selection in a T-maze  
638 cost/benefit procedure. *Behav Brain Res*, 65(2), 221-229.
- 639 Schweimer, J. and W. Hauber (2005). Involvement of the rat anterior cingulate cortex in control of  
640 instrumental responses guided by reward expectancy. *Learn Mem*, 12(3), 334-342.
- 641 Schweimer, J. and W. Hauber (2006). Dopamine D1 receptors in the anterior cingulate cortex  
642 regulate effort-based decision making. *Learn Mem*, 13(6), 777-782.
- 643 Treadway, M. T., N. A. Bossaller, R. C. Shelton and D. H. Zald (2012). Effort-based decision-  
644 making in major depressive disorder: a translational model of motivational anhedonia. *J Abnorm*  
645 *Psychol*, 121(3), 553-558.
- 646 Varazzani, C., A. San-Galli, S. Gilardeau and S. Bouret (2015). Noradrenaline and dopamine neurons  
647 in the reward/effort trade-off: a direct electrophysiological comparison in behaving monkeys. *J*  
648 *Neurosci*, 35(20), 7866-7877.
- 649 Walton, M. E., D. M. Bannerman and M. F. Rushworth (2002). The role of rat medial frontal cortex  
650 in effort-based decision making. *J Neurosci*, 22(24), 10996-11003.
- 651 Yang, X. H., J. Huang, C. Y. Zhu, Y. F. Wang, E. F. Cheung, R. C. Chan and G. R. Xie (2014).  
652 Motivational deficits in effort-based decision making in individuals with subsyndromal depression,  
653 first-episode and remitted depression patients. *Psychiatry Res*, 220(3), 874-882.

654