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1 **Changes in activity of fast-spiking interneurons of the**
2 **monkey striatum during reaching at a visual target**

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13 **Running Head:** Striatal FSIs and the control of movement
14

15 Abstract

16 Recent works highlight the importance of local inhibitory interneurons in regulating the
17 function of the striatum. In particular, fast-spiking interneurons (FSIs), which likely
18 correspond to a subgroup of GABAergic interneurons, have been involved in the control of
19 movement by exerting strong inhibition on striatal output pathways. However, little is known
20 about the exact contribution of these presumed interneurons in movement preparation,
21 initiation, and execution. We recorded the activity of FSIs in the striatum of monkeys as they
22 performed reaching movements to a visual target under two task conditions: one in which the
23 movement target was presented at unsignaled left or right locations, and another in which
24 advance information about target location was available, thus allowing monkeys to react
25 faster. Modulations of FSI activity around the initiation of movement (53% of 55 neurons)
26 consisted mostly of increases reaching maximal firing immediately before or, less frequently,
27 after movement onset. Another subset of FSIs showed decreases in activity during movement
28 execution. Rarely did movement-related changes in FSI firing depend on response direction
29 and movement speed. Modulations of FSI activity occurring relatively early in relation to
30 movement initiation were more influenced by the preparation for movement, compared with
31 those occurring later. Conversely, FSI activity remained unaffected as monkeys were
32 preparing a movement toward a specific location and instead moved to the opposite direction
33 when the trigger occurred. These results provide evidence that changes in activity of
34 presumed GABAergic interneurons of the primate striatum could make distinct contributions
35 to processes involved in movement generation.

36

37 **New & Noteworthy**

38 We explored the functional contributions of striatal fast-spiking interneurons (FSIs),
39 presumed GABAergic interneurons, to distinct steps of movement generation in monkeys
40 performing a reaching task. The activity of individual FSIs was modulated before and during
41 the movement, consisting mostly of increased in firing rates. Changes in activity also
42 occurred during movement preparation. We interpret this variety of modulation types at
43 different moments of task performance as reflecting differential FSI control over distinct
44 phases of movement.

45 **Keywords**

46 basal ganglia, movement initiation, motor preparation, non-human primate

47

48 **Introduction**

49 The striatum is composed of a vast majority of projection neurons and several types of
50 interneuron among which GABAergic interneurons constitute a diverse group of cells that can
51 be characterized by expression of different neurochemical markers and basic
52 electrophysiological properties (Tepper et al. 2010; Silberberg and Bolam 2015). These
53 interneurons have been implicated in regulating the information processing within the striatal
54 network. Among them, the fast-spiking inhibitory interneurons (FSIs), that correspond to the
55 parvalbumin-containing group of GABAergic interneurons (Kawaguchi 1993; Mallet et al.
56 2005; Sharott et al. 2012), have received the most interest. This electrophysiologically
57 identifiable cell type is regarded as the main source of inhibition onto neighboring output
58 neurons, thus shaping the output of the striatum to the downstream nuclei of the basal ganglia
59 (Koós and Tepper 1999; Mallet et al. 2005). Given that these presumed interneurons exert a
60 strong inhibitory effect on the activity of output neurons, it has been suggested that disruption
61 of FSI function can result in the inability to control or inhibit inappropriate motor responses.
62 Experimental studies in animals provide evidence for specific involvement of these
63 interneurons in striatal-based movement disorders, including dystonia (Gernert et al. 2000)
64 and dyskinesia (Gittis et al. 2011). In addition, neuropathological studies in humans have
65 demonstrated reduced density of striatal GABAergic interneurons containing parvalbumin in
66 Tourette syndrome (Kalanithi et al. 2005; Kataoka et al. 2010) and Huntington's disease
67 (Reiner et al. 2013). It is therefore crucial to understand how FSIs contribute to normal
68 behavioral states to gain an insight into their role in the pathophysiology of movement
69 disorders.

70 Single-neuron recording studies in behaving rats have investigated how striatal FSIs
71 modulate their firing rate during performance in a variety of tasks. The results have shown

72 different patterns of task-related changes in FSI activity occurring at specific times, such as
73 reaching a goal in the context of spatial navigation tasks (Berke et al. 2004; 2008; Schmitzer-
74 Torbert and Redish 2008) and selecting a particular action in the presence of a choice between
75 movement options (Gage et al. 2010). FSIs have also been shown to be sensitive to prediction
76 errors linked to changes in an action's expected value (Stalnaker et al. 2012) and to
77 expectation and receipt of rewards (Lansink et al. 2010). It therefore appears that FSIs might
78 make contributions to different aspects of task performance and information processing. In
79 addition, regional differences in the striatum are likely to be important for interpreting task-
80 related changes in FSI activity, with modulations related to actions resulting in rewarded
81 outcomes preferentially occurring in the dorsolateral striatum, assumed to subserve motor
82 functions (Berke 2008; Schmitzer-Torbert and Redish 2008; Gage et al. 2010), whereas
83 changes in FSI activity related to reward outcomes are assumed to be found in dorsomedial
84 (Stalnaker et al. 2012) and ventromedial portions of the striatum (Lansink et al. 2010) which
85 have been proposed to be more involved in cognitive and motivational functions, respectively.

86 In the primate striatum, electrophysiologically identifiable cell types generally fall into
87 two categories, called phasically active neurons (PANs), assumed to be projection neurons,
88 and tonically active neurons (TANs), thought to be cholinergic interneurons. Recently,
89 recording studies have pointed to the presence of a rarely encountered category displaying
90 spike waveforms and firing rates similar to those described for striatal FSIs in rodents (Adler
91 et al. 2013; Yamada et al. 2016). Knowledge about the functional contributions of FSIs in the
92 striatum of behaving monkeys is however still limited. In a Pavlovian conditioning procedure,
93 in which monkeys were passively exposed to pairings of visual stimuli with different
94 outcomes, striatal FSIs have been reported to display changes in activity consisting of
95 increases in firing rate after presentation of conditioned stimuli and occurrence of outcome
96 (Adler et al. 2013). More recently, a study has emphasized that FSIs are sensitive both to the

97 actions resulting in rewarded outcomes as well as to the outcomes themselves in monkeys
98 performing arm or eye movement to obtain rewards (Yamada et al. 2016). However, the exact
99 nature of their contribution to behavioral processes carried out in the striatum remains obscure
100 and we still lack an understanding of how this population of presumed GABAergic
101 interneurons participate in distinct steps of movement generation.

102 The purpose of this study was to further characterize the functional properties of
103 striatal FSIs by examining their capacity to carry signals related to the preparation, initiation,
104 and execution of target-directed arm movements. Our results indicate that individual FSIs that
105 were not restricted to the motor part of the striatum changed their firing rate around the time
106 of movement initiation, with distinct groups that either increase or decrease their activity,
107 suggesting that they may exert differential control over distinct phases of movement.

108 **Materials and Methods**

109 *Behavioral conditions.*

110 The experimental protocol was in compliance with the National Institutes of Health's Guide
111 for the Care and Use of Laboratory Animals and approved by the Comité d'éthique en
112 Neurosciences INT-Marseille (Protocol A2-10-12). Two adult male rhesus monkeys (*Macaca*
113 *mulatta*), F and T, were trained to make visually guided arm-reaching movements to obtain a
114 liquid reward. The behavioral apparatus was similar to that previously described (Deffains et
115 al. 2010). Each monkey was seated in a specially designed restraining box, facing a panel 30
116 cm from its head. The panel contained two metal knobs (10 x 10 mm) separated by 20 cm
117 horizontally, as well as two light-emitting diodes (two-color green/red LEDs), one above each
118 knob, at eye level of the animal. An unmovable metal bar was mounted at the center of the
119 panel at waist level. The temporal sequence of task events is schematically presented in
120 Figure 1A. The animals kept the hand on the bar until the illumination of a red LED either to

121 the left or to the right of the panel, the location of the stimulus varying pseudorandomly
122 across trials. In response to this stimulus, monkeys had to reach the target positioned just
123 below the illuminated LED and the movements were rewarded by a small amount of fruit
124 juice (0.3 ml) delivered immediately after touching the target. The monkey then brought the
125 hand back on the bar and waited for the total duration of the trial (6 s) to elapse before the
126 next trial started.

127 In the standard reaching task condition, called the *uncued condition*, the trigger stimulus
128 occurred at irregular time intervals and in the absence of any predictive cues, so that the
129 monkey could not predict the location of the target on each trial. In order to address the
130 question whether the state of preparation for movement influences neuronal activity, a *cued*
131 *condition* was also employed in which the monkeys received advance information about the
132 location of the trigger stimulus. In this case, the onset of a green light (duration: 500 ms)
133 presented either to the left or to the right served as a cue for the trigger stimulus which came
134 on 1.5 s later at the same location. In this condition, the cue allowed the animal to prepare arm
135 movement toward a specific location. In another version of the cued condition, called the
136 *unreliable cued condition*, advance information about target location was valid in 80% and
137 invalid in 20% of trials. On valid cued trials, the trigger stimulus was presented at the same
138 location as that indicated previously by the cue, whereas on invalid cued trials, the trigger
139 stimulus was presented on the side opposite to that indicated by the cue. In the latter case, a
140 motor reprogramming process is needed after trigger onset before the correct movement can
141 be executed. This condition was designed to test the monkeys' ability to inhibit the prepared
142 response and replace it with the other one. Task performance was assessed in terms of
143 reaction time (RT) and movement time (MT) which were the time taken to release the bar in
144 response to trigger onset and to move from the bar to a target, respectively. Both monkeys
145 performed the task with their right arm and the different conditions were presented to the

146 animals in successive blocks of 30-50 trials, except for the unreliable cued condition which
147 was run in blocks long enough (about 80 trials) to ensure at least 15 invalid cued trials.

148 *Neuronal recordings.*

149 Data were collected after monkeys were well trained on the three task conditions. After
150 completion of training, surgery was carried out under gas anesthesia (isoflurane 2.5%) and
151 sterile conditions to implant a head-holding device and a recording chamber aimed to the left
152 striatum. We recorded the extracellular activity of single neurons with movable glass-
153 insulated tungsten microelectrodes over a wide area of the anterior and posterior regions of
154 the striatum, mostly in the dorsal part of the putamen, some penetrations extending to the
155 ventral most part of this nucleus. The electrode was driven by a hydraulic microdrive (MO-
156 95; Narishige, Tokyo, Japan) through a stainless steel guide tube, which was used to penetrate
157 the dura. The electrode was manually advanced until the spikes generated by a single neuron
158 were isolated. Neuronal signals were amplified (x 5000), filtered with a band pass of 0.3 to
159 1.5 kHz, and monitored with oscilloscopes. Single neuron activity was detected on-line by
160 threshold crossing using a time-amplitude window discriminator (Neurolog; Digitimer), the
161 waveform of each discriminated spike being monitored continuously during recording. The
162 resulting standard digital pulses were stored on a computer, together with markers of task
163 events. Neuronal signals were also digitized and stored on computer (Spike2; Cambridge
164 Electronic Design, Cambridge, UK) for off-line analysis of spike duration. We classified each
165 unit as belonging to one of three major classes of neurons in the striatum identified by spike
166 waveform and firing rate criteria, as described previously (Adler et al. 2013). The relationship
167 between neuronal activity and behavioral performance was assessed on-line in the form of
168 rasters aligned on the task events using a custom-designed computer software (LabVIEW,
169 National Instruments, Dallas, TX). The same software was used to present visual stimuli, to
170 deliver liquid reward, to measure behavioral parameters, and to collect neuronal data for off-

171 line analyses. Once a neuron was isolated, we usually first examined its activity in the uncued
172 condition. If the isolation could be maintained satisfactorily, the neuron was then tested in
173 another condition, either the cued or unreliable cued condition, the order of the conditions
174 being counterbalanced across trial blocks.

175 *Data analysis.*

176 The Student's *t*-test and one-way ANOVAs with Tukey's honestly significant difference
177 (HSD) post hoc tests were conducted to test for any significant differences in RT and MT
178 between task conditions (uncued, cued) and trial types (valid cued, invalid cued). As regards
179 neuronal activity changes, rasters and perievent time histograms of single-neuron activity
180 aligned to each of the three task events (trigger onset, movement onset, and target contact)
181 were first examined visually and then statistically analyzed. We determined whether neurons
182 showed significant changes in activity occurring at any particular moment during the
183 performance of the reaching task. The baseline firing rate was calculated during the 500 ms
184 preceding the presentation of the first visual stimulus (the trigger stimulus in the uncued
185 condition and the cue in the cued condition), defined as the control period. A test window of
186 100 ms duration was moved in steps of 10 ms, starting at the presentation of the trigger
187 stimulus, from 300 ms before movement onset, or from 300 ms before target contact. The
188 mean discharge rate in the 100-ms window was compared, at each step, with that in the
189 control period. The onset of a modulation was taken to be the beginning of the first of at least
190 5 consecutive steps showing a significant difference ($P < 0.05$, Dunn's test for multiple
191 nonparametric comparisons) as against the baseline activity. The offset of a modulation was
192 defined in the same manner by the first of at least 5 consecutive steps with activity back to
193 control. We then determined the onset and offset of the modulation in the firing of the neuron
194 centered on each task events with 10 ms resolution. In addition, task-related increases in
195 neuronal activity were evaluated in terms of the latency of the peak of activation. To do so,

196 we divided the trial into successive bins of 10 ms around each of the three task events and we
197 calculated the spike count in each bin. Peak latency was estimated, for each neuron, as the 10-
198 ms interval showing the highest level of activity in the perievent time histogram referenced to
199 each task event. Based on these measures, we classified FSIs into distinct categories
200 according to the timing of peak activations relative to movement onset.

201 For each neuron, we also used a 300 ms window immediately before or after
202 movement onset to test for dependence of neuronal activity on target location (left, right),
203 condition (uncued, cued), and trial type (valid cued, invalid cued), on the basis of mean firing
204 rate measured in these windows. The assessment of statistical differences between conditions
205 was performed with the use of multivariate analysis of variance (MANOVA). Further details
206 on data analysis are given at the appropriate place in the Results section. To examine the
207 temporal relation between changes in FSI activity and behavioral indices of task performance
208 (i.e., RT and MT), we made a correlation analysis on a trial-by-trial basis (Pearson's
209 correlation, $P < 0.05$).

210 In addition to the quantitative assessment of task-related activities of individual FSIs,
211 we pooled activities across samples of neurons modulated during particular task conditions
212 and trial types and made population activity curves. For each neuron, a normalized perievent
213 time histogram was obtained by dividing the content of each bin by the number of trials and
214 the population activity was obtained by averaging all normalized histograms referenced to a
215 particular task event. Data were analyzed using custom-written MATLAB (version R2015b,
216 Mathworks, Natick, MA) scripts and statistical analyses were performed using JMP software
217 (version 11, Chicago, IL).

218 *Reconstruction of recording sites.*

219 Histological confirmation of recording sites is available in monkey T, but not in monkey F
220 who is still participating in another study. Consequently, for this latter animal, approximated

221 recording sites were determined from the neuronal activity characteristic to the striatum and
222 electrophysiologic features of neighboring structures, including the external and internal
223 segments of the globus pallidus, the internal capsule, and the anterior commissure. In monkey
224 T, the block of tissue including striatal recording sites was cut into frontal sections of 40 μm
225 thickness on a freezing microtome and every section was stained with cresyl violet. Based on
226 the location of recording sites identified histologically in this animal, FSIs were recorded
227 between 4 mm anterior and 8 mm posterior to the anterior commissure, over the entire lateral
228 to medial extent of the nucleus, including some penetrations in the most ventral portion of the
229 precommissural putamen. Based on the known topographic organization of cortical
230 projections, the region of the striatum explored in the present study is divided into a “motor”
231 region, which predominantly includes the postcommissural part of the dorsal putamen, and an
232 “associative” region, which includes mainly the precommissural part of the dorsal caudate
233 nucleus and putamen. The ~~most~~ ventral region of the precommissural part of the caudate
234 nucleus and putamen is usually referred to the "limbic" striatum (Haber and McFarland 1999).

235 **Results**

236 *Behavior*

237 As shown in Figure 1B, both monkeys had significantly shorter RTs in the cued condition
238 than in the uncued condition (Student's t-test, $P < 0.01$), suggesting that the presence of prior
239 information on location of the trigger stimulus prepared the animals for directing their
240 movement at a specific target leading therefore to a shortening of RT. There was also a
241 significant effect of condition on MTs in monkey T ($P < 0.01$) and monkey F ($P < 0.05$) with
242 the MT in cued trials being shorter than the MT in uncued trials. Both monkeys continued to
243 perform well the task in the unreliable cued condition (above 90% correct) when unexpected
244 invalid cued trials occurred in the course of a block, namely they reached the target accurately

245 regardless of whether the cue was a valid predictor or not of target location. Figure 1C shows
246 the mean RTs and MTs for invalid cued trials and for trials immediately preceding and
247 immediately following them. In both monkeys, RTs for invalid cued trials were significantly
248 longer than for trials with a valid cue (one-way ANOVA, monkey F: $F(2, 594) = 143.59$, $P <$
249 0.01 ; monkey T: $F(2, 702) = 124.45$, $P < 0.01$), reflecting a slowness of movement initiation
250 when responding to the trigger stimulus which did not match the cued location. There was
251 also a significant effect of trial type on MT in monkey F ($F(2, 594) = 12.19$, $P < 0.01$) who
252 took longer to reach the target in invalid than in valid cued trials, whereas such a difference
253 was less evident in monkey T ($F(2, 702) = 3.33$, $P < 0.05$).

254 *Neuronal data*

255 We recorded from 701 neurons in two monkeys (413 and 288 neurons requiring 19 and 11
256 recording months in animals F and T, respectively). Of the 701 neurons, 83 (12%) were
257 judged to be FSIs and we report here on 64 of them (32 in each monkey) that were recorded
258 in at least one of the three task conditions employed in this study. Table 1 gives an overview
259 of the number of recorded FSIs in the different task conditions and the mean number of trials
260 per recording. Consistent with prior studies (Adler et al. 2013; Yamada et al. 2016), FSIs
261 were rarely encountered in awake monkeys compared to PANs and TANs. Despite their
262 relative scarcity, FSIs were clearly distinguishable from the other neuron types (i.e., PANs
263 and TANs) usually recorded in the monkey striatum. The patterns of neuronal discharge in the
264 striatum of our monkeys (Figure 1D) were similar to those described previously (Adler et al.
265 2013; Yamada et al. 2016). The FSIs had a mean baseline firing rate of 12.8 ± 8.9 spikes/s
266 ($n=64$), which is higher than that of the TANs (5.7 ± 2.2 , $n=85$) or PANs (1.4 ± 1.8 , $n=87$).
267 The duration of spikes of the FSIs, defined as the time interval between the first negative and
268 second positive peaks of the spike, was generally shorter (424 ± 57 μ s, $n=63$) than that of the
269 TANs (919 ± 198 μ s, $n=80$) and PANs (754 ± 80 μ s, $n=80$) (Wilcoxon's rank sum test, $P <$

270 0.01). These spike waveform and firing rate characteristics are very similar to those of FSIs
271 recorded in the rodent striatum which have been closely associated with PV-containing
272 GABAergic interneurons.

273 We first examined temporal profiles of activity changes for each neuron recorded in
274 the uncued condition (n=55) using the sliding time window procedure (see Materials and
275 methods), starting at the onset of the trigger stimulus and at 300 ms before the movement
276 onset and the target contact. Here we focused on FSI activity just before and during
277 movement for analysis, the modulations at a later stage of the task (i.e., reward period) being
278 addressed in another report. We found that 53% (29 of 55) of neurons (11 and 18 in monkeys
279 F and T, respectively) showed statistically significant changes in activity in relation to
280 movement initiation (Dunn's-test, $P < 0.05$). Among these, 17 neurons showed increases in
281 activity, 9 neurons showed decreases in activity, and 3 neurons had increases followed by
282 decreases. Figure 2 shows the activity profile for each of the 29 modulated FSIs, sorted
283 according to the latency of the peak of activation for neurons that showed increased activity
284 and to the earliest time of significant modulation for neurons that showed decreased activity
285 only. As it can be seen, increases in activity were more prominent before the onset of
286 movement, with neurons reaching their peak activation just after the presentation of the
287 trigger stimulus (3 neurons) or within a 300 ms window immediately preceding movement
288 onset (11 neurons). Other neurons reached their peak activation within a 300 ms window
289 immediately following movement onset (6 neurons). We classified the neurons that showed
290 increases in activity into two groups according to which of the two 300 ms windows was the
291 one in which the peak activation occurred. Neurons having peak activation time prior to or
292 following the initiation of arm movement were classified as early increase-type and late
293 increase-type, respectively. All neurons displaying decreased activity only were modulated
294 after movement onset and were included in a decrease-type category. Figure 3A shows

295 example neurons from each category. To give an overview of the modulations at the
296 population level, averaged activities of all FSIs of each of the three categories are illustrated
297 in Figure 3B. Neurons with no modulation in relation to movement initiation are also shown
298 for comparison.

299 We next examined whether FSIs were sensitive to the target location and/or the
300 direction of the arm movement. We performed this analysis by comparing the spike counts in
301 the 300 ms window before (early increase-type neurons) or after the movement onset (late
302 increase-type and decrease-type neurons) between leftward and rightward movements, for
303 each modulated neuron in our sample. Of the 29 modulated FSIs, 7 (24%) showed activity
304 that differed significantly between the two directions of movement (Wilcoxon's test, $P <$
305 0.05), of which one half showed stronger activity associated with movements directed to the
306 side ipsilateral to the moving arm and the other half with movements directed to the
307 contralateral side (Figure 4A). Although FSI modulations dependent on the direction of
308 movement were found in all three categories of neurons, they seem to be most frequent in
309 early increase-type neurons, but the sample sizes were too small to allow for adequate
310 statistical analysis. We also examined whether FSI activity was concerned with the
311 fluctuations of reaching performance. For each modulated neuron, we calculated the trial-by-
312 trial correlation (Pearson's r) between movement parameters (RT and MT) and FSI activity,
313 using the same time windows defined before. Across the sample of studied neurons, 17% (5
314 of 29) was sensitive to the RT and 17% (5 of 29) to the MT, and there was no trend toward a
315 more pronounced relationship between FSI modulation and motor variables in one category of
316 neuron than another (Figure 4B), significant correlations being either in the same or opposite
317 direction (i.e., the FSI activity increased or decreased as RT or MT increased). In sum, we
318 have provided evidence for FSIs increasing their firing rates around the initiation of
319 movements, most of them having their peak activations that preceded movement onset

320 whereas a comparatively lower number of FSIs had peak activations that followed movement
321 onset. We also found neurons that had opposite changes in activity (i.e., decreases in firing
322 rate) after movement onset. It therefore appears that striatal FSI can display a variety of
323 patterns of modulation as the monkeys initiated reaching movements in response to the trigger
324 stimulus.

325 *Effect of motor preparation on FSI activity*

326 In order to determine whether the activity of FSIs was influenced by the presence of spatial
327 cues that allowed the monkeys to prepare themselves to react more quickly to the trigger
328 stimulus, the activity of 32 neurons was tested in the cued condition (14 and 18 in monkeys F
329 and T, respectively). In this condition, short-lasting increases in FSI activity in response to the
330 cue onset were seen in 4 neurons, whereas 2 other neurons exhibited increases in activity
331 which began at 200-410 ms before the trigger and terminated in close temporal relation to its
332 presentation, one neuron being activated both after cue onset and before trigger. Among FSIs
333 that were tested, none showed sustained changes in activity throughout the whole delay period
334 (i.e., the 1.5-s interval between cue and trigger presentations). Figure 5A (*left part*) shows an
335 example of early increase-type neuron displaying a phasic increase in activity in response to
336 the trigger stimulus in the uncued condition. When tested in the cued condition, the same
337 neuron responded to the cue, while the trigger stimulus became ineffective for eliciting a
338 response, as though the sensitivity was shifted from the trigger to the cue containing
339 information about the upcoming direction of movement. Figure 5A (*right part*) shows an
340 example of late increase-type neuron with a phasic increase in activity after the trigger
341 stimulus on both uncued and cued trials, the activation being well aligned to movement onset
342 in the two conditions.

343 To give an overview of changes in activity of the whole sample of neurons tested in
344 the two task conditions, we averaged separately the activity from early increase-type (n=11)

345 and late-increase type neurons ($n=5$). As can be observed in Figure 5B (*left part*), when early
346 increase-type neurons were grouped together, a brief activation in response to the cue was
347 visible at the population level. Also, the population level analysis for this category revealed
348 that the magnitude of activation in response to the trigger stimulus was affected by the task
349 condition, being higher in uncued trials than in cued trials (MANOVA during the 500 ms
350 period after the trigger onset, $P < 0.05$). On the other hand, the activity across the sample of
351 late increase-type neurons was not significantly modulated during the cue period and the
352 magnitude of activation after the trigger onset was not significantly different between the two
353 conditions (MANOVA during the 500 ms period after the trigger onset, $P > 0.05$) (Figure 5B,
354 *right part*).

355 To address the influence of motor preparation more quantitatively, we compared, for
356 each neuron, the magnitude of activity in the uncued and cued conditions. We performed this
357 analysis on averaged spike counts during the same 300 ms intervals defined before. If the
358 activity change was significantly larger (MANOVA during the 300 ms period after the trigger
359 onset, $P < 0.05$) in one condition than the other, the neuron was judged to be modulated by the
360 task condition. A total of 13 of the 20 movement-related neurons (65%) showed statistically
361 significant differences in their modulations between the two conditions. As shown in Figure
362 6A, it was found that neurons displaying a preferential sensitivity for either uncued or cued
363 condition occurred more frequently in the early increase-type category than other categories
364 (early increase-type: 73% (8 of 11) 3 and 5 in monkeys F and T, respectively; late increase-
365 type: 60% (3 of 5) all in monkey T; decrease-type 50% (2 of 4) both in monkey F). Figure 6B
366 shows the superimposed averaged activity for the FSIs tested in the two conditions, separately
367 for the three categories of neurons. For the early increase-type category, the two curves were
368 virtually identical during the period immediately preceding the onset of the trigger stimulus
369 with a rise in activity starting just after the trigger onset and reaching a peak before the

370 movement onset, the level of activation during the cued trials being significantly less than
371 during uncued trials, as mentioned before (MANOVA during the 300 ms period after the
372 trigger onset, $P < 0.05$). To estimate the timing of when FSI activity in uncued trials differed
373 from that in the cued trials, we performed time-series analysis for every 50-ms window
374 moved in 10-ms steps over the period from 300 ms before to 300 ms after the trigger and
375 movement onsets. Statistical analyses revealed that differences between uncued and cued
376 trials became significant (MANOVA, $P < 0.05$) 160 ms after the trigger presentation and were
377 maintained until 60 ms before movement onset (Fig. 6B). For the late increase-type category,
378 the population average showed a gradual increment for both cued and uncued trials which
379 reached a peak very close to movement onset. There was an extensive overlap between the
380 two curves, without significant differences in the level of activation between the two
381 conditions (MANOVA, $P > 0.05$). Although the small number of decrease-type neurons tested
382 in both conditions makes analysis of the data less reliable, the average activity was very
383 similar between uncued and cued trials for this category of neurons.

384 Finally, we further investigated the impact of motor preparation on FSI activity by
385 testing the monkeys on the unreliable cued condition, in which a prepared action was
386 unexpectedly replaced by the other movement option when the trigger occurred. As
387 mentioned in the behavioral results, both monkeys took longer to respond to the trigger
388 stimulus in invalid cued trials than in valid cued trials. This condition thus appeared well
389 suited for examining whether an increase in demands for response initiation would elicit
390 differences in FSI activity. A statistical analysis using the same two 300 ms windows as
391 previously defined was performed to examine, for each neuron in our sample, whether the
392 activity differed as a function of trial types. This comparison indicated that the activity of only
393 4 neurons of the 45 movement-modulated neurons (9%) varied significantly depending on the
394 trial type, these few neurons being assigned to all three categories. Among 58 neurons that

395 were tested in the unreliable cued condition, 45 (78%) showed significant changes in activity
396 surrounding the initiation of movement. Of these, 17, 12, and 16 were categorized as early
397 increase-type, late increase-type, and decrease-type, respectively, based on the temporal
398 profiles of their activity changes in the valid cued trials. The activity modulation occurred in
399 relation to any of the three classes of FSIs we have categorized (Figure 7A) (6% (1/17)
400 monkey T; 8% (1/12) monkey F; 13% (2/16) monkey T). We further examined FSI activity
401 across the population. Figure 7B shows that FSI activity averaged over all neurons of each
402 category overlapped almost completely in the two types of trials.

403 In sum, FSI activity did not vary markedly during the preparatory period preceding the
404 initiation of the movement. Specifically, the level of activity of early increase-type neurons
405 appeared to be influenced by motor preparation, thus indicating that cognitive demands, and
406 not just movement initiation, might be encoded by changes in FSI activity. The similarity of
407 the level of changes in FSI activity in the valid and invalid cued trials seen at the population
408 level indicates that increased latency of movement initiation was not associated with altered
409 FSI activity when an action should be re-specified at the time the trigger became available for
410 selection.

411 *Recording positions*

412 Finally, we took into account the functional specialization within the striatum and examined
413 whether the responses of FSIs could be related to their location in the ventral and dorsal
414 striatal regions. Recording sites were verified histologically in monkey T (Figure 8A), while
415 we confirmed that our recordings were in the striatum based on characteristic patterns of
416 neuronal activity in monkey F. The majority of the neurons were recorded in the putamen,
417 some of them being in the rostroventral putamen, which was identified as part of the ventral
418 striatum (see Material and Methods). Figure 8B illustrates the distribution of the neurons we
419 recorded. Among 64 neurons, 50 were considered to be located within the dorsal part (28 and

420 22 in monkeys F and T, respectively) and 14 within the ventral part (4 and 10 in monkeys F
421 and T, respectively). The three categories of FSIs were present in equal proportions and
422 showed a considerable overlap in their distributions throughout the anteroposterior extent of
423 the striatum explored. In particular, we found that FSIs with movement-related activity were
424 not only restricted to the posterior putamen, which subserves motor functions, but were also
425 found in the anterior putamen, including its ventral part. Early increase-type and late increase-
426 type neurons were found in the dorsal (14 of 64 neurons; 22%) and ventral striatum (8 of 64
427 neurons; 13%). The frequency of neurons with a sensitivity to movement failed to vary
428 significantly between the two regions ($\chi^2 = 0.411$, $df = 1$, $P > 0.05$).

429 **Discussion**

430 This study provides the first detailed analysis of the potential contribution of fast-spiking
431 interneurons (FSIs) in the monkey striatum to information processing during movement
432 preparation, initiation, and execution. Our analysis of changes in FSI activity highlighted the
433 following points. First, the variety of changes in FSI activity, in terms of timing relative to
434 movement initiation and the direction of these changes, suggests that these presumed
435 interneurons do not provide a homogeneous signal at a particular moment during reaching
436 task performance. Second, modulations of FSI activity occurring relatively early in relation to
437 movement initiation all consisted of increases in firing rate, whereas those that followed the
438 onset of movement consisted of either increases or decreases in firing rate. Third, increases in
439 FSI activity reaching a peak before movement onset appear to be more influenced by the state
440 of motor preparation, compared with those which peaked after movement onset. Fourth,
441 movement-related changes in FSI firing were not influenced by an unexpected change in
442 target location when monkeys were preparing a movement toward a specific location and
443 instead elicited a movement in the opposite direction. We interpret the variety of these

444 modulation types as reflecting a contribution of presumed GABAergic interneurons to
445 different aspects of motor performance through an inhibitory influence on striatal output
446 circuits.

447 *Characterization of FSIs in the monkey striatum*

448 In line with previous single-neuron recording studies in the striatum of behaving monkeys
449 (Adler et al. 2013; Yamada et al. 2016), we found that a particular class of neurons can be
450 identified as FSIs on the basis of spike waveform and firing rate criteria. In particular, they
451 are clearly distinguishable from the two other electrophysiologically determined types of
452 neurons in the primate striatum, i.e., PANs and TANs (Kimura et al. 1984; Aosaki et al. 1994;
453 Apicella 2002). It is noteworthy that studies of the functional properties of striatal FSIs,
454 particularly in behaving monkeys, have been limited due to the difficulty in targeting these
455 rarely encountered neurons for recordings. In the present study, the proportion of FSIs that we
456 detected (12%) is higher than reported in previous studies (~3-5%) (Adler et al. 2013;
457 Yamada et al. 2016) possibly because we paid special attention to the detection of these
458 neurons. Studies in freely moving rats have reported that the proportions of striatal FSIs may
459 vary from 11% (Gage et al. 2010) to 33% (Stalnaker et al. 2012), highlighting the fact that
460 extracellular recordings can be subjected to considerable sampling biases. Putative FSIs in the
461 monkey striatum have firing properties resembling those of FSIs described in the rodent
462 striatum, which are thought to correspond to the parvalbumin-containing group of
463 GABAergic interneurons and are the source of strong inhibitory influences on striatal output
464 pathways (Koós and Tepper 1999; Gittis et al. 2010). However, given the variety of striatal
465 GABAergic interneurons that have not been characterized *in vivo*, we cannot rule out that
466 neurons classified electrophysiologically into FSIs include, at least in part, one or more other
467 classes of interneurons.

468 *The role of FSIs in the initiation and execution of movement*

469 Although there is considerable interest in the role of FSIs in regulating the excitability of
470 striatal output pathways, the exact nature of their contribution to movement generation
471 remains unclear. Accordingly, the present study was designed to determine how FSIs
472 modulate their firing in monkeys performing a reaching task that allows to distinguish
473 between initiation and execution of movements. We found that the modulation of FSI firing
474 rate were heterogeneous, with some neurons modulated at the presentation of the trigger
475 stimulus and others being modulated later during the execution of movement. Most
476 modulations of FSI firing around the time of movement initiation consisted of increases,
477 whereas other FSIs changed their firing in the opposite direction. The variety of these
478 modulation types may indicate the presence of distinct FSI subgroups involved in the
479 processing of different movement-related information.

480 There are only a few studies in behaving monkeys that have reported changes in FSI
481 activity consisting in phasic increases in activity after cue presentation and outcome delivery
482 in a Pavlovian conditioning protocol (Adler et al. 2013) or more complex changes related to
483 actions and outcomes in instrumental conditioning paradigms (Yamada et al. 2016). A
484 comparatively large number of studies in rats trained in a variety of behavioral procedures
485 have shown that FSIs can display changes in activity at certain phases of task performance,
486 such as stimulus presentation, initiation of movement, position in space, and outcome delivery
487 (Berke 2008; Schmitzer-Torbert and Redish 2008; Gage et al. 2010; Lansink et al. 2010;
488 Stalnaker et al. 2012). It therefore appears that FSIs do not modify their activity in a
489 homogeneous manner during task performance in behaving animals, suggesting that they are
490 involved in different processes depending on the task demands. As discussed further below,
491 variations in the location of the recording sites could also account for differences in task-
492 related activities of FSIs in the striatum.

493 Although the sample of FSIs recorded in the present study was heterogeneous in terms
494 of the timing of activity changes and the direction of these changes (i.e., increased or
495 decreased in firing rates), the limited diversity of FSI modulations around the time of
496 movement contrasted with the wide variety of task-related activations observed in output
497 neurons of the striatum (i.e., PANs). Numerous studies in behaving monkeys have reported
498 that PANs display transient or sustained increases in firing rate occurring in several
499 distinctive forms during the initiation and execution of actions (Kimura 1990; Crutcher and
500 Alexander 1990). PAN activations may also reflect representational processes, such as
501 preparation of movement, expectation of a trigger stimulus for movement (Alexander and
502 Crutcher 1990; Apicella et al. 1992), or the motivational value of reward obtained at trial end
503 (Hollerman et al. 1998; Hassani et al. 2001; Cromwell and Schultz 2003).

504 In rats performing a nose-poke task with a choice between two movement options, a
505 relatively uniform increase in FSI activity has been reported at the time of the initiation of
506 movement, with most activations reaching their peak just after choice execution (Gage et al.
507 2010). These findings have led to the hypothesis that changes in FSI activity constitute signals
508 for selecting between competing actions, by suppressing unwanted action commands to
509 facilitate the selection of the appropriate response. Our task design did not allow us to
510 examine whether FSI activity can be preferentially modulated in the presence of a choice
511 requirement, an issue which remains to be investigated with a task designed specifically to
512 add demands for decision making.

513 We found that the target location and/or the direction of movement associated with
514 reaching influenced the firing rate changes of about one-third of the FSIs (24%), with no
515 systematic preference for one against the other movement direction. This modest selectivity
516 for target location is somewhat different from the study of Gage et al. (2010) showing that a
517 large majority of FSIs (78%) displayed directional selectivity with either ipsilateral or

518 contralateral movements. It is possible that we recorded from fewer direction selective FSIs
519 because our task design did not require sufficient demands on response selection. In addition,
520 we found only few FSIs whose magnitude of changes in activity was correlated with latency
521 or duration of the reaching movement, indicating that the firing level of FSIs may not be
522 particularly predictive of variability in the monkey's performance speed.

523 *The role of FSIs in the preparation for movement*

524 Until now, studies of the role of striatal FSIs have not examined in detail their possible
525 involvement in the preparation of movements and the expectation of task events. In the
526 present study, we tested if FSI activity was sensitive to the preparation component of the task
527 when the monkeys could improve the speed of their movements by using advance information
528 about target location. We found that 65 % of the recorded FSIs exhibited transient changes in
529 firing during the cue-trigger interval. Furthermore, these changes were mostly observed in the
530 subset of FSIs that we classified as early increase-type, whereas late increase-type neurons did
531 not change the magnitude of their movement-related activity, with or without motor
532 preparation. Although the functional implications of these distinct groups of FSIs remain to be
533 determined, our findings suggest that perhaps the FSIs are functionally more heterogeneous
534 than currently appreciated, with the activity of early increase-type neurons time-locked to the
535 trigger onset being more influenced by the state of preparation for movement, compared to
536 late increase-type neurons. Specifically, modulation by predictive cues indicates that
537 cognitive processes, and not just the process of movement initiation, might influence FSI
538 activity.

539 Some FSIs showed a transient activation (less than 500 ms in duration) toward the end
540 of the delay period of the task, just before trigger presentation, but none of them displayed
541 activity changes that were maintained for a longer duration through the cue-trigger interval.
542 This suggests that even if the preparatory period may introduce additional demands for

543 behavioral inhibition (i.e., active withholding of movement until trigger onset), sustained
544 changes in FSI activity did not appear to be necessary for the behavioral expression of that
545 preparation. On the other hand, short-lasting activations immediately preceding the trigger
546 onset might represent a FSI signal in adjusting the movement preparation to the initiation of
547 the subsequent movement. In the monkey putamen, it is relatively common to find striatal
548 PANs displaying sustained activations that are thought to reflect movement preparation
549 and/or stimulus expectation during delayed-response tasks (Alexander and Crutcher 1990;
550 Apicella et al. 1992), while other PANs are phasically activated during movement initiation
551 and execution (Kimura 1990; Crutcher and Alexander 1990). Different populations of PANs
552 are therefore activated in sequence during the delay period and during the motor components
553 of the task. It is possible that the observed changes in FSI activity may be required to facilitate
554 the transition between subsets of PANs representing distinct steps of movement generation.

555 To further examine the influence of motor preparation on FSI activity, we also tested
556 monkeys on a condition in which they were preparing a movement toward a specific location
557 and instead must move in the opposite direction when the trigger occurred. Both monkeys
558 slowed down in the trials where the cue was invalid, indicating that the recalibration of the
559 movement direction places increased demands on the timing of movement initiation. We then
560 examined whether this movement recalibration was accompanied by a change in FSI activity.
561 We found that very few FSIs were differentially modulated on invalid and valid cued trials,
562 despite the fact that the stimulus–response remapping had a strong impact on task
563 performance. This finding indicates that the firing level of FSIs around movement initiation
564 was not correlated with how quickly the monkey responds to the trigger stimulus, further
565 confirming that FSI activity was not directly correlated with changes in the monkey’s
566 performance. However, in our task design, the switch in movement direction occurred when
567 the prepared movement was not yet initiated and it is possible that FSIs are critical for the

568 behavioral adjustment when the decision on the movement direction has to be replaced by
569 another after the movement onset.

570 *Functional properties of FSIs and regional specializations of the striatum*

571 Based on evidence of regional specializations of information processing within the striatum,
572 we examined the possibility that the functional properties of FSIs could be related to their
573 location in different parts of the striatum. Neuronal recording in behaving rats have outlined
574 differences in the way striatal FSIs are modulated during task performance according to their
575 anatomical location, namely FSIs in the dorsolateral striatum may be important for controlling
576 motor functions (Gage et al. 2010), whereas those in the dorsomedial and ventromedial
577 striatum may contribute to outcome processing (Stalnaker et al. 2012; Lansink et al. 2010). In
578 our study, no difference was found in the distribution of movement-related FSIs over the
579 extent of the putamen sampled, encompassing motor putamen caudal to the anterior
580 commissure and associative putamen rostral to it. This appears to confirm findings from
581 previous recording studies in behaving monkeys (Adler et al. 2013; Yamada et al. 2016) in
582 which FSI modulations related to task events were evenly distributed throughout the explored
583 striatum. Interestingly, we found that a subset of FSIs located in the most ventral part of the
584 anterior putamen, which is to say in limbic striatum, also exhibited movement-related activity.
585 This differs from PANs recorded in the ventral striatum which have been reported to be
586 specialized in processing motivational information (Apicella et al. 1991). However, given the
587 low neuron number obtained in the present study, it is premature to draw any firm conclusions
588 concerning a variation of functional properties of FSIs that may be related to the regional
589 specializations of the striatum. In addition, it remains to be determined, in our study, whether
590 the impact of reward on FSI activity may be particularly strong in the ventral striatum, as has
591 been observed in behaving rats (Lansink et al. 2010).

592

593 *How FSI signals are used by the striatal output pathways that control action?*

594 It is thought that FSIs form a local inhibitory circuit that targets selectively the output of the
595 striatum to downstream targets (Szydlowski et al. 2013). Increases in FSI activity are
596 supposed to lead to inhibition of striatal output pathways and therefore suppression of
597 movements by decreasing inhibition of basal ganglia output structures. One can assume that
598 the reverse may occur in the case of decreases in FSI activity, resulting in facilitation of
599 movements. This suggests that the two types of FSI modulations described in the present
600 study might be differently involved in movement generation, one suppressing and the other
601 facilitating movements. Our findings have shown that increases in FSI activity can occur
602 sufficiently early to be involved in preparation and initiation of movements. It is possible that
603 this type of FSI modulation may reflect an enhanced inhibitory level necessary for the
604 expression of the correct response by preventing inappropriate motor commands from being
605 selected. On the other hand, we observed a prevalence of decreases in FSI activity after the
606 onset of movement, suggesting that these modulations may play a role in ongoing motor
607 performance. This may be associated with a release of output neurons from inhibition and
608 therefore facilitation of motor commands. This late FSI signal may be related to the inhibition
609 of competing responses when the action has already been initiated. It is still an open question
610 whether increased and decreased in FSI firing rates might reflect differential influences on
611 functionally distinct output pathways thought to exert opposing effects on motor behavior
612 (Gittis et al. 2010; Planert et al. 2008).

613 In conclusion, evidence in favour of prominent involvement of striatal FSIs in motor
614 control has come from inactivation studies in animals (Gernert et al. 2000; Gittis et al. 2011;
615 Burguière et al. 2013; Xu et al. 2016), as well as from clinical studies in humans (Kalanithi et
616 al. 2005; Kataoka et al. 2010; Reiner et al. 2013). Our results are the first demonstration of
617 modulations of activity from individual FSIs during the successive stages of movement

618 generation, reflecting contributions to different aspects of motor performance, rather than an
619 exclusive involvement in movement initiation. Although it is still unclear what features are
620 precisely encoded by these changes, it is conceivable that disturbed FSI signaling might
621 interfere with action selection, resulting in an impaired ability to inhibit inappropriate
622 behaviors.

623

624 **Author contributions**

625 P.A. designed research, K.M. and P.A. performed research, analyzed data, and wrote the
626 paper.

627

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633

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- 728

729 **Figure Legends**

730 Figure 1. Behavioral task conditions, reaching performance, and classification of striatal
731 neurons. **A.** The monkey kept the hand on a bar while waiting for the presentation of a visual
732 stimulus (red light) on either the right or the left side of a panel in front of it. In response to
733 this signal, the animal was required to release the bar and reach for the target located below
734 the light, which it had to touch to receive a liquid reward. There were three task conditions
735 with the same basic structure: (1) an uncued condition, in which the trigger stimulus occurred
736 at irregular time intervals and in the absence of any predictive cues; (2) a cued condition, in
737 which a visual stimulus (green light) gave advance information regarding the location of the
738 forthcoming trigger presented 1.5 s later; (3) an unreliable cued condition in which the
739 specification of trigger location was invalid on a small percentage of trials (invalid cued
740 trials). In the example shown, a rightward movement is cued and the trigger stimulus is
741 presented on the opposite side thereby eliciting a leftward movement. The three conditions
742 were tested in separate blocks of trials. **B.** Reaction times and movement times for the uncued
743 and cued conditions. Values are means \pm SEM (numbers of trials: 283-317 for monkey F,
744 238-403 for monkey T). **P<0.01, *P<0.05. **C.** Reaction times and movement times from the
745 invalid cued trials and the valid cued trials immediately before and after the invalid ones.
746 Each value was obtained by calculating the mean \pm SEM (199 and 235 trials of each type for
747 monkey F and monkey T, respectively). **P<0.01, *P<0.05. **D.** Comparison of the
748 electrophysiological characteristics of the three main types of neurons found in the striatum of
749 the awake macaque monkey. *Left part* Sample spike trains from each category of neuron.
750 *Middle part* Mean waveforms for one representative striatal neuron of each category. ptp,
751 peak-to-peak, i.e., time elapsed between the first negative peak and the following positive
752 peak. *Right part* Scatter plots of mean spike waveform durations (x-axis, firing rate

753 (logarithmic scale); y-axis, peak-to-peak time). Each dot represents a single neuron colored
754 according to its category.

755 Figure 2. Time courses of change in FSI activity around the initiation of reaching movement.
756 The scheme shows the temporal profile of activity changes for all FSIs tested in the uncued
757 condition ($n = 29$), separately referenced to trigger onset (left), movement onset (middle) and
758 target contact (right). Each horizontal line represents the duration of statistically significant
759 changes in activity for a single neuron. Red and blue indicate neuronal activity above and
760 below the baseline firing rate, respectively. The small losanges on red lines indicate the onset
761 time of the peak activation. Lines are ordered according to the timing of the peak for neurons
762 with increased activity and to the timing of the onset of modulation for neurons with
763 decreased activity only.

764 Figure 3. FSI activity during the initiation and execution of reaching movements. **A.** Activity
765 of three example neurons with significant changes in activity around the initiation of
766 movements. Data are shown as corresponding raster displays and perivent histograms aligned
767 on the onsets of the trigger stimulus (left) and the movement (right). Each dot in the raster
768 displays represents a single spike, and each line of dots corresponds to the activity during one
769 trial. Trials were ordered off-line according to the latency of movement. Trigger and
770 movement onsets are indicated by red and gray markers in raster displays, respectively.
771 Binwidth for histograms, 20 ms. **B.** Population activities for each of the 3 categories of
772 movement-related FSIs. Colored curves depict mean activity (\pm SEM) for the three categories
773 of FSIs: early increase-type ($n=14$), late increase-type ($n=6$), and late decrease-type ($n=9$).
774 FSIs that were not activated during movement initiation are indicated for comparison ($n=26$).
775 Shading indicates SEM. Activity is aligned to the onset of the trigger (*left*) and movement
776 (*right*), which are marked by vertical dashed lines.

777 Figure 4. FSI activity in relation to the location of the target stimulus and motor variables. **A.**
778 Changes in FSI activity as a function of target location (left or right). Significant differences
779 ($P < 0.05$) are indicated by black lines. **B.** Correlation of movement latency and duration with
780 changes in FSI activity. Black dots indicate the data with a significant r value ($P < 0.05$). RT,
781 reaction time; MT, movement time.

782 Figure 5. Effect of movement preparation on FSI activity. **A.** Comparison of the activity of
783 two individual neurons during uncued and cued trials. Conventions are the same as in Fig. 3A,
784 except that the superimposed average firing rate for the two types of trial is plotted as colored
785 curves smoothed by a three-point median filter. **B.** Time courses of the population activity
786 preceding the trigger onset under the uncued and cued conditions for early increase-type
787 neurons ($n=11$) and late increase-type neurons ($n=5$) recorded in both conditions.

788 Figure 6. Comparison of FSI activity in the presence or absence of movement preparation. **A.**
789 Relative proportions of neurons with statistically significant differences in movement-related
790 activity between the uncued and cued conditions. The percentages are calculated from the
791 total number of recorded neurons of each category. n , number of neurons. **B.** Population
792 average activity included all FSIs recorded in the two task conditions. Each panel shows the
793 averaged activity for uncued and cued trials for a category of FSIs aligned on trigger
794 presentation and movement onset. The *orange horizontal lines* below the curves indicate the
795 periods when neuronal activity during uncued trials differed significantly from that during
796 cued trials.

797 Figure 7. Comparison of FSI activity during invalid and valid trials. **A.** Relative proportions
798 of neurons with statistically significant differences in movement-related activity between the
799 invalid and valid trials. The percentages are calculated from the total number of recorded
800 neurons of each category. n , number of neurons. **B.** Same conventions as in Fig. 3B.

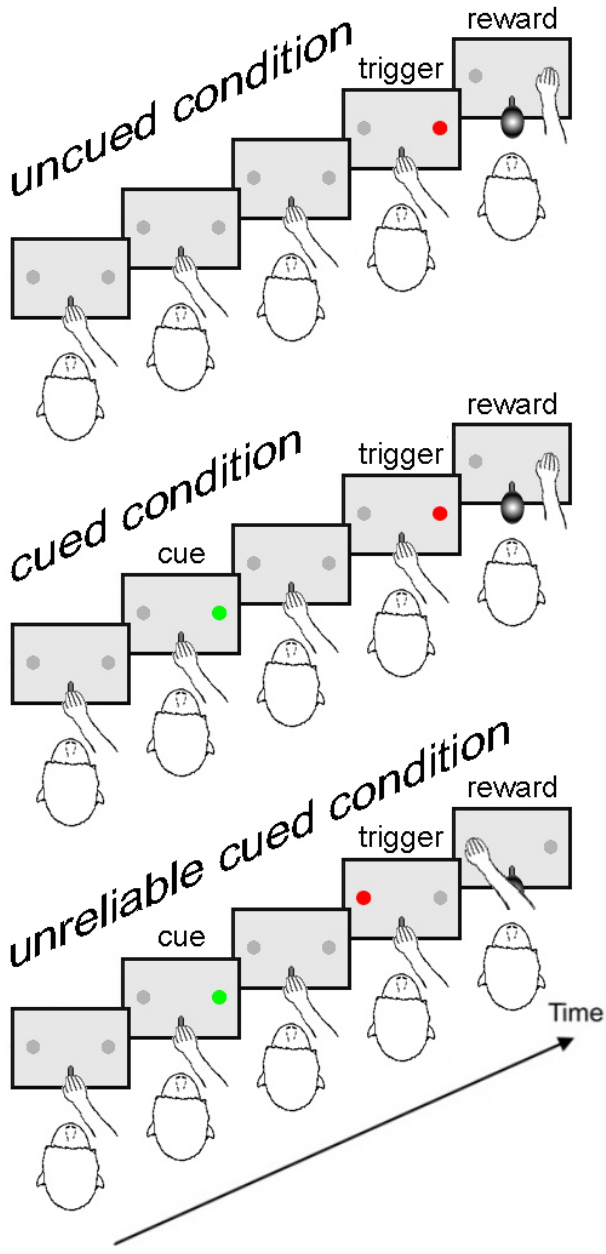
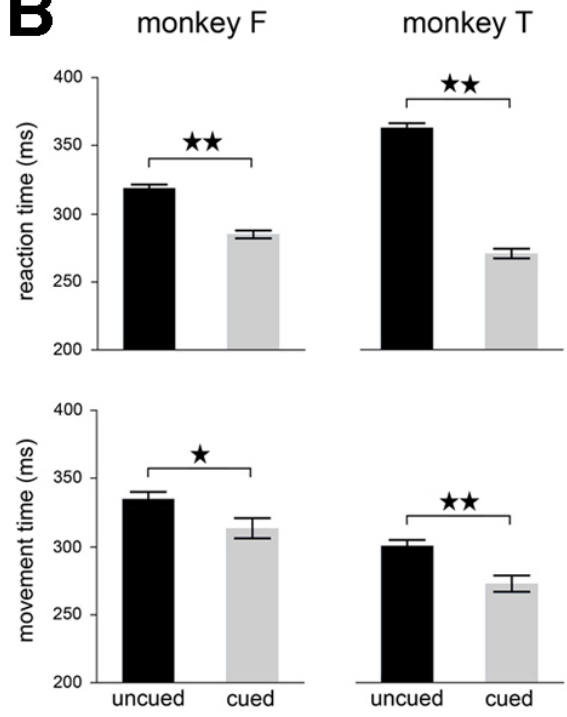
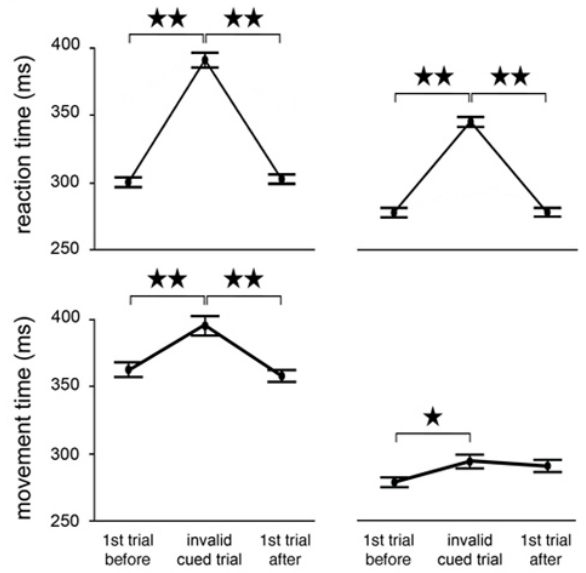
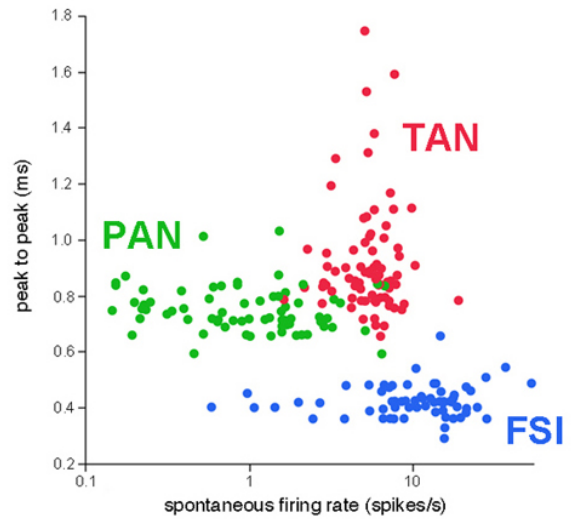
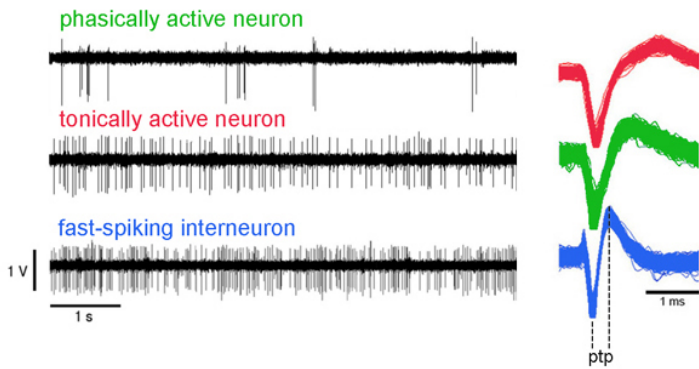
801 Figure 8. Recording positions of FSIs. **A.** Coronal section stained with cresyl violet at the
802 level of the striatum, showing traces of electrode paths above the putamen. **B.** Sagittal view of
803 positions of recorded neurons plotted along the reconstructed electrode penetrations. Each dot
804 corresponds to the position of a single FSI. For each neuron, the anteroposterior location (zero
805 indicates the approximate level of the anterior commissure) is plotted against the depth of the
806 electrode at which it was recorded. The recording depth was measured from a zero reference
807 point as determined by using microdrive depth readings. Color and gray dots indicate neurons
808 that were or were not modulated during movement, respectively. The dashed line indicates the
809 approximate boundary between dorsal and ventral striatum. Cd, caudate nucleus; Put,
810 putamen; GPe, globus pallidus external segment; GPi, globus pallidus internal segment.

811

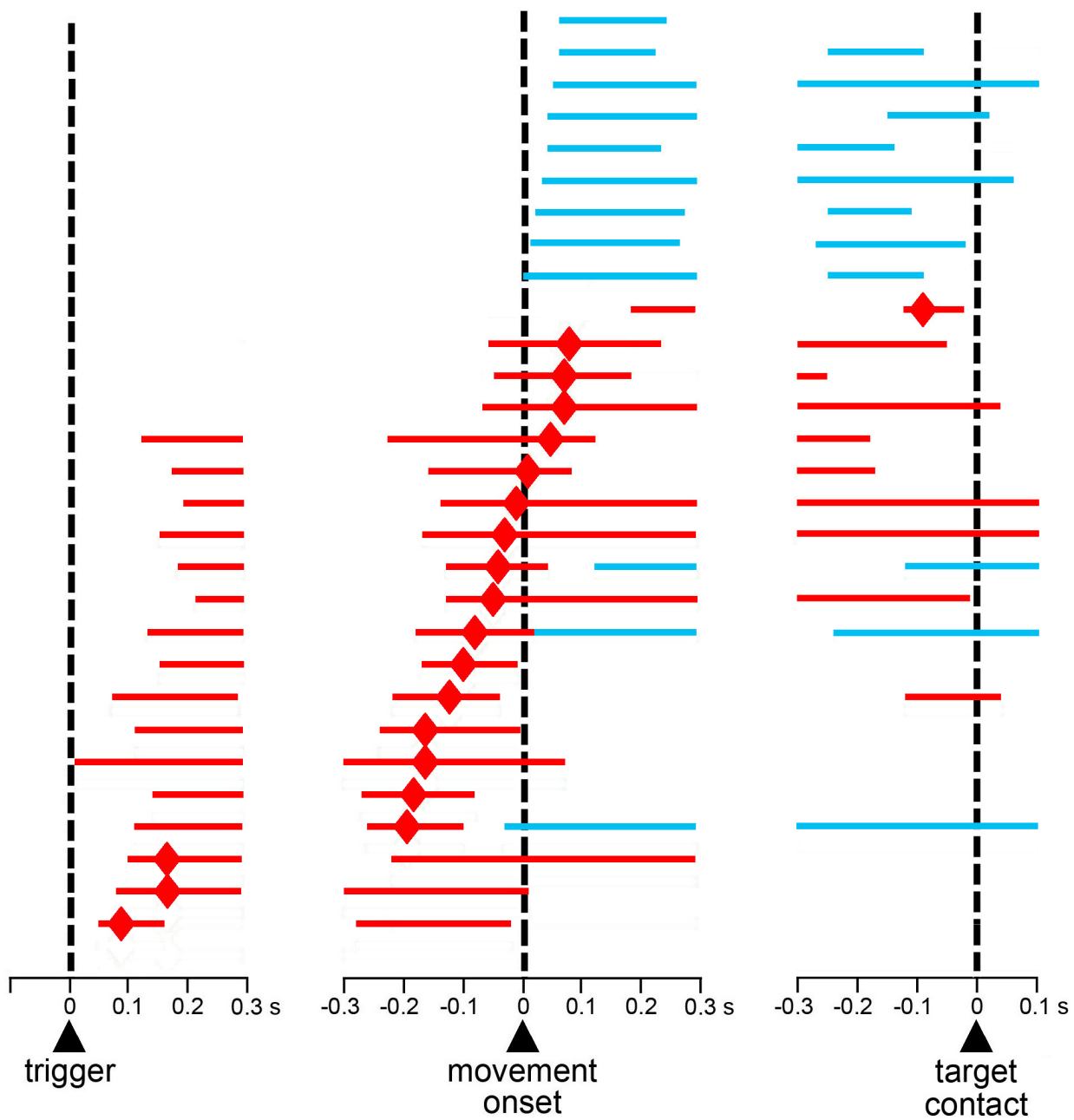
Table 1. Numbers of recorded neurons and recorded trials in the different task conditions

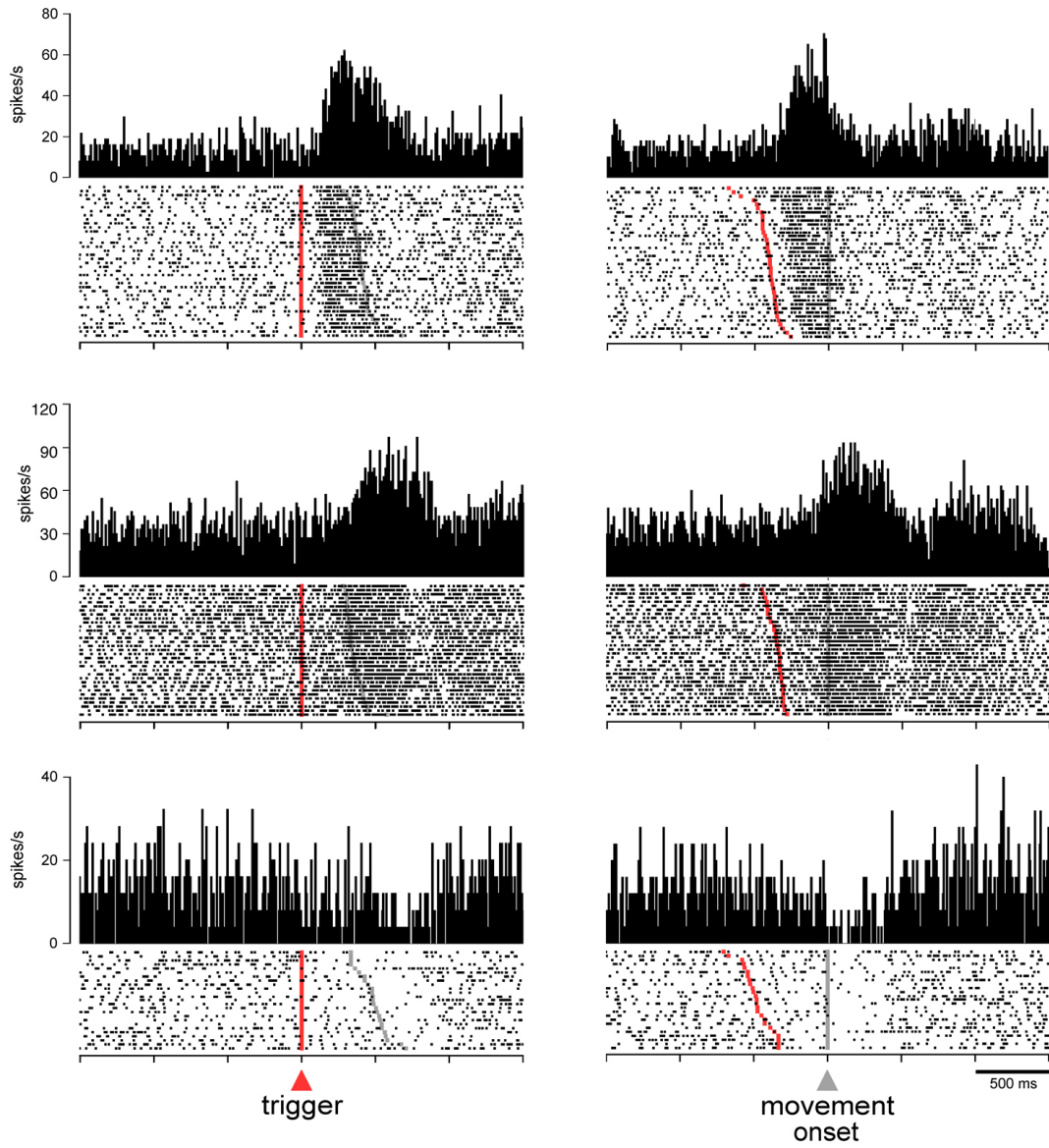
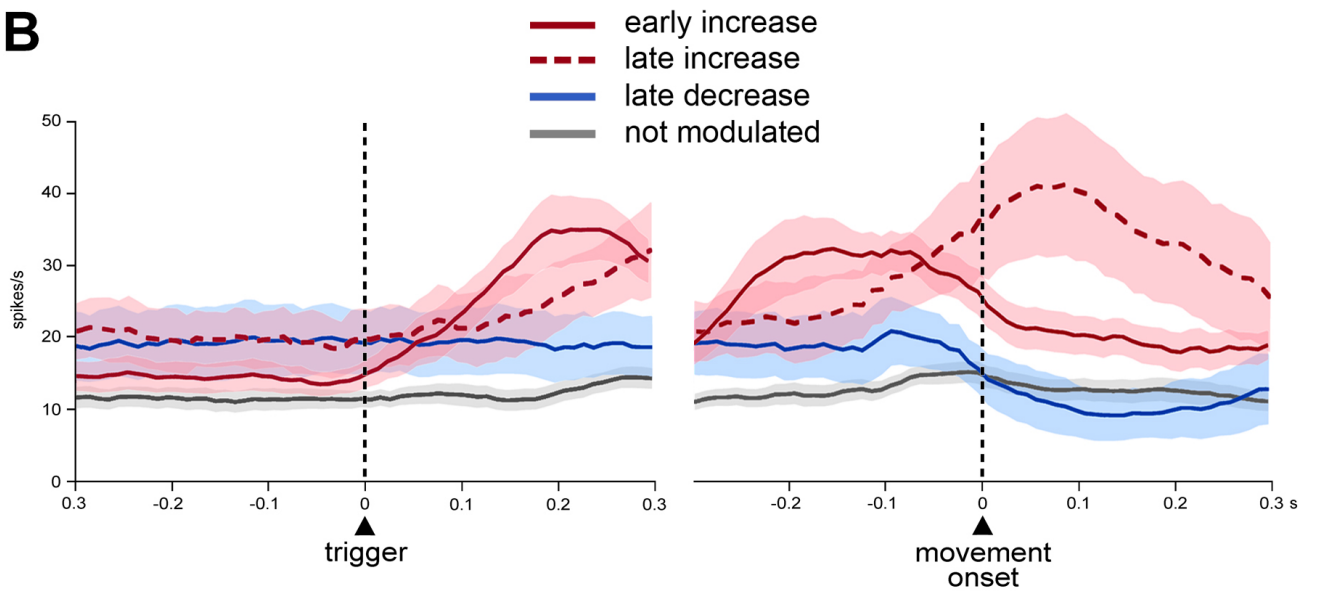
task conditions	N	increase early	late	decrease	number of recorded trials	range of recorded trials
uncued	55	14	6	9	33 ± 6	21-49
cued	32	11	5	4	34 ± 8	15-54
unreliable cued	58	17	12	16	43 ± 11	22-70

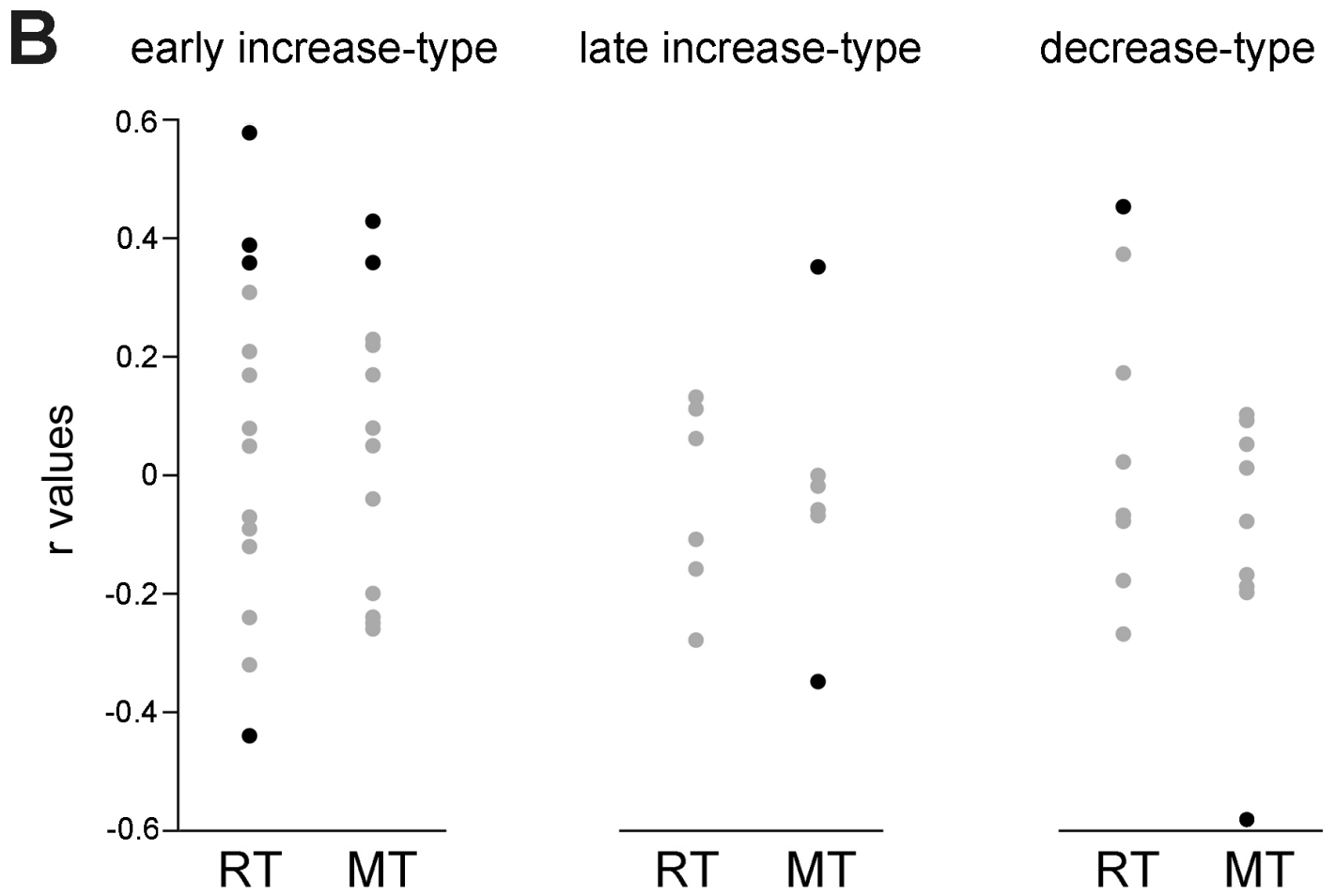
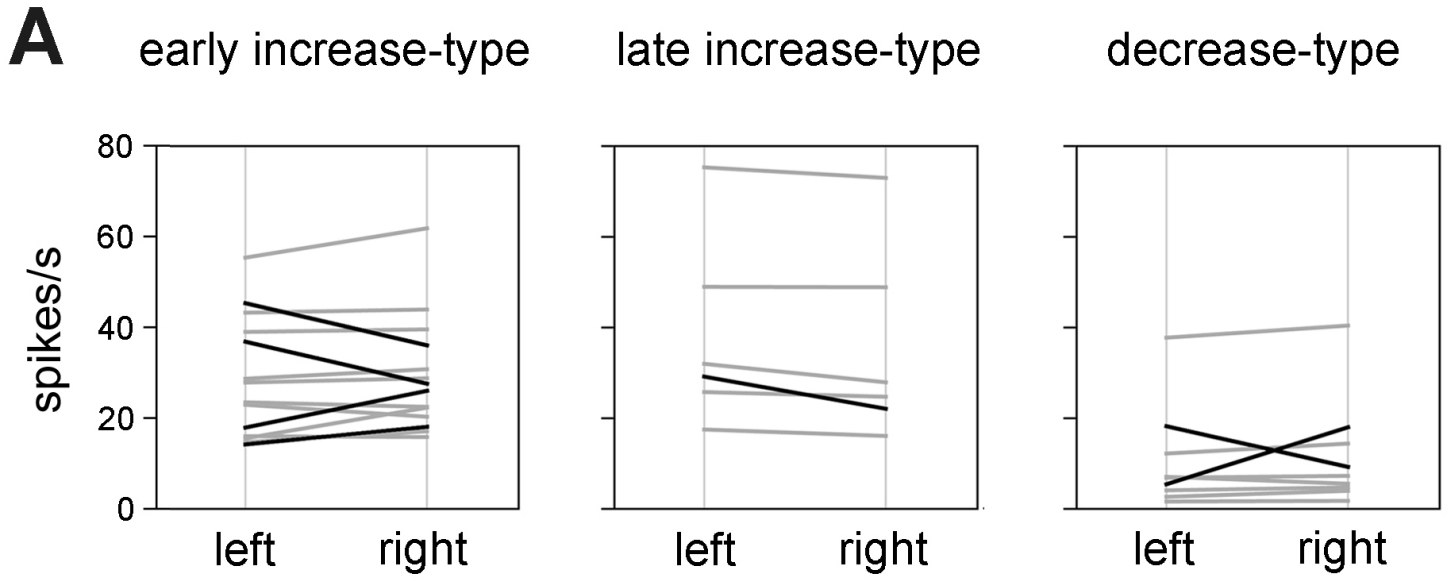
N: total number of neurons recorded in each task condition; "increase" and "decrease" denote neurons that are activated and depressed around the time of movement, respectively; "early" and "late" denote neurons whose activations peaked before and after movement onset, respectively; number of recorded trials per condition is mean \pm SD.

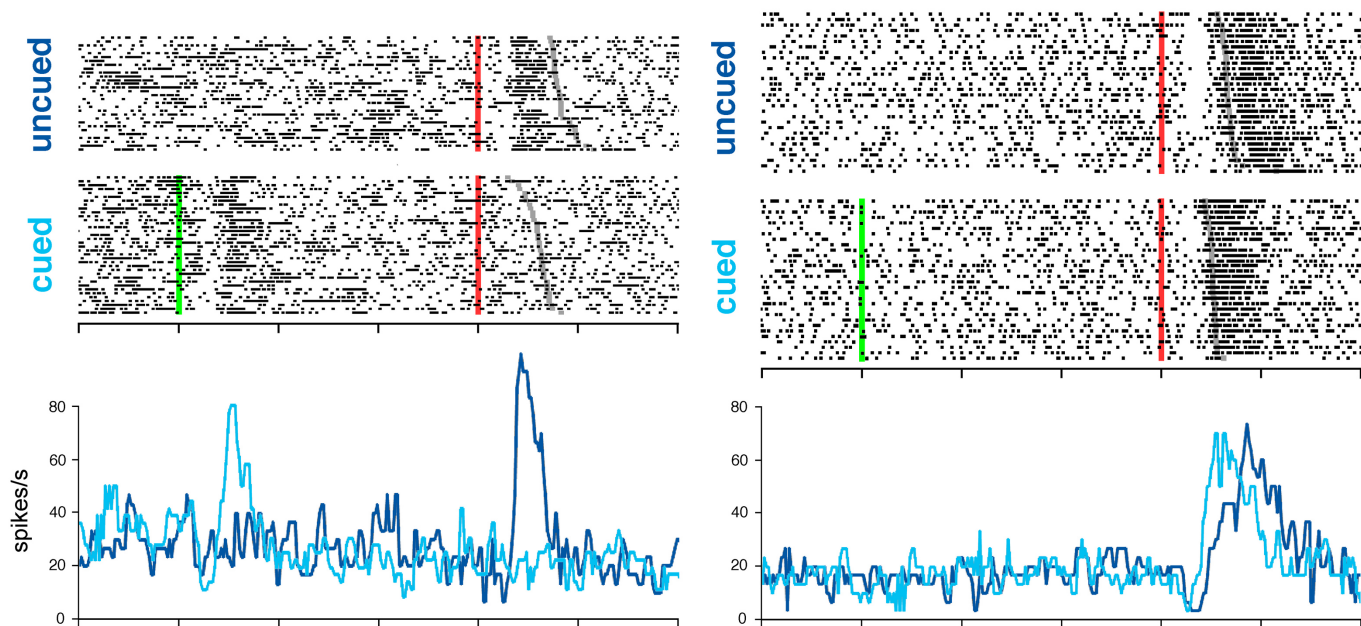
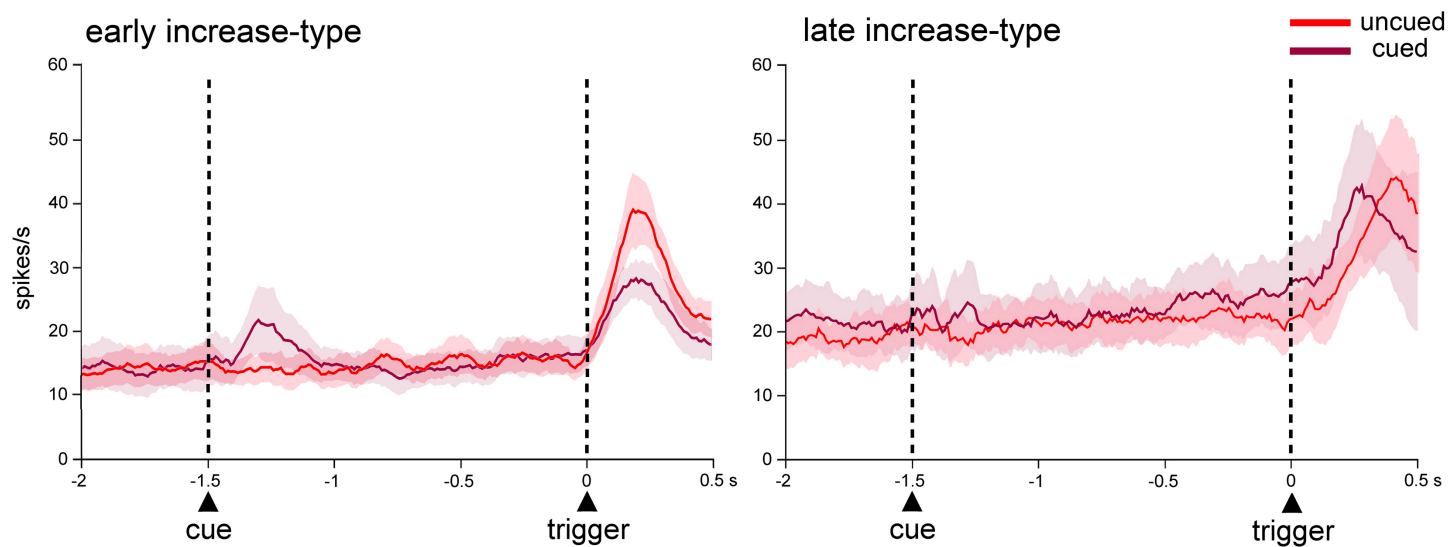
A**B****C****D**

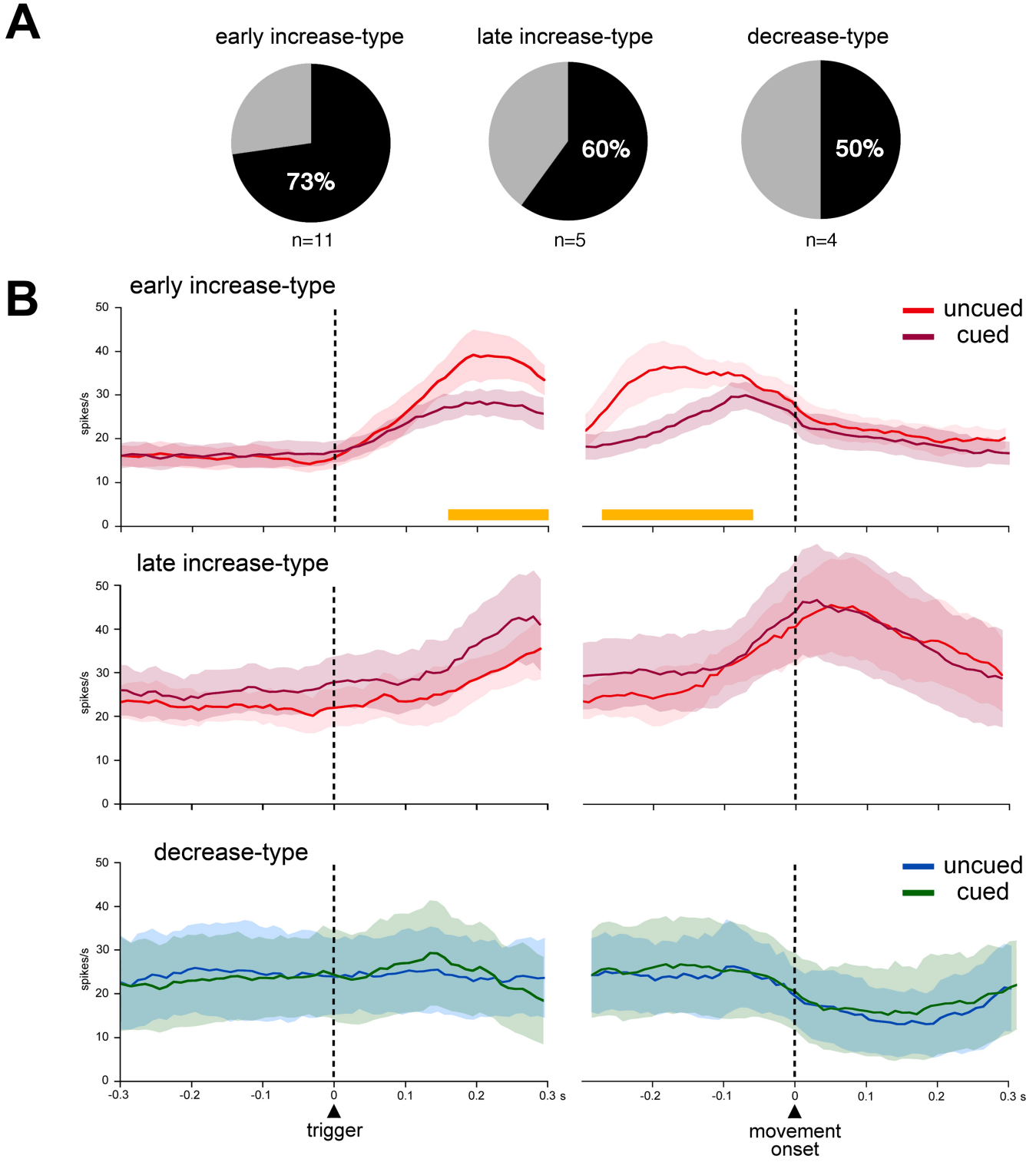
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A**B**



A**B**



A

early increase-type

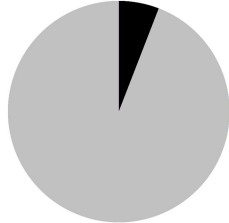
late increase-type

decrease-type

6%

8%

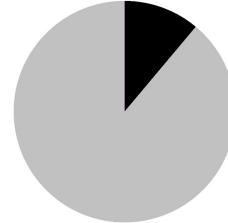
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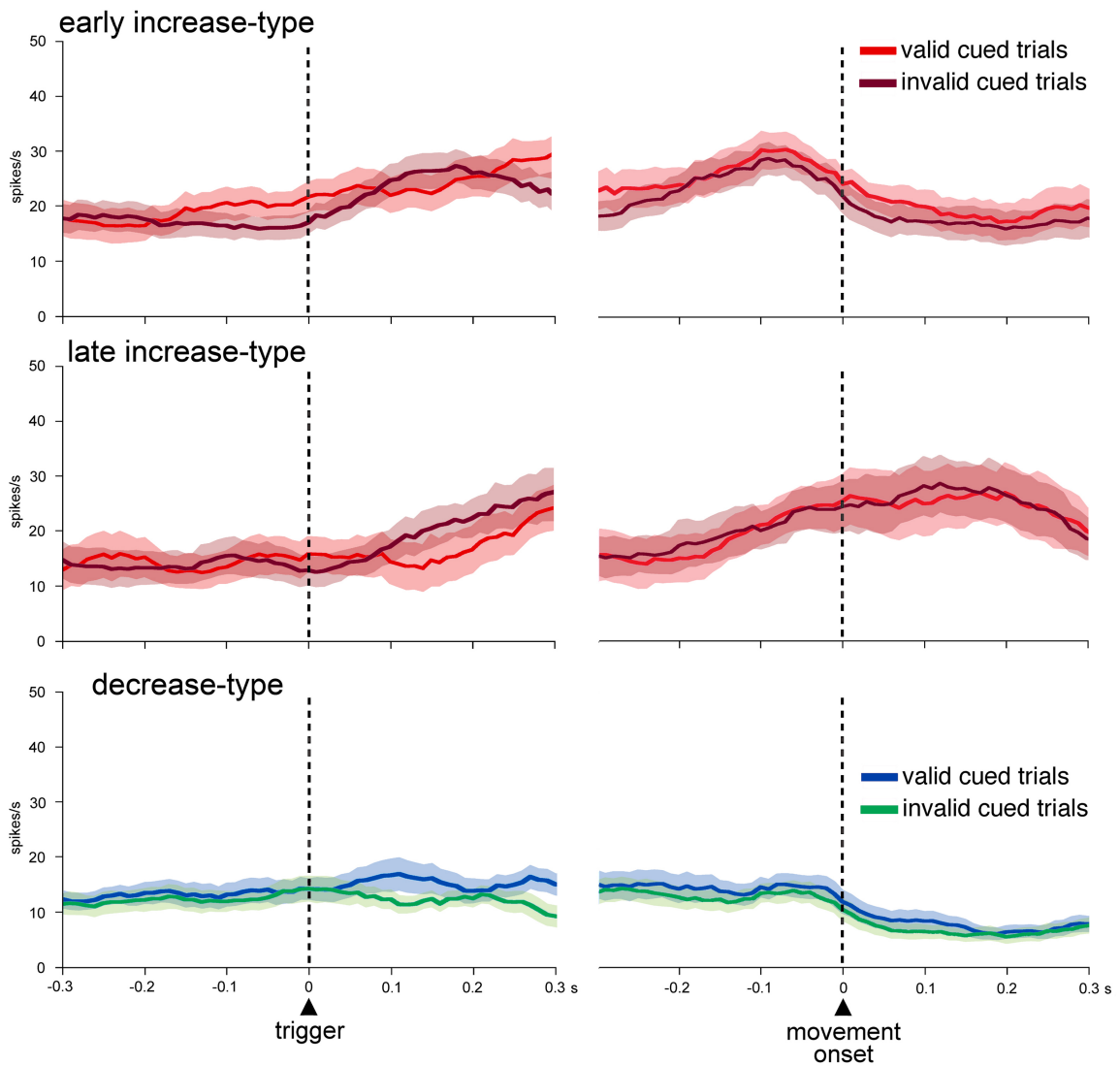
n=17

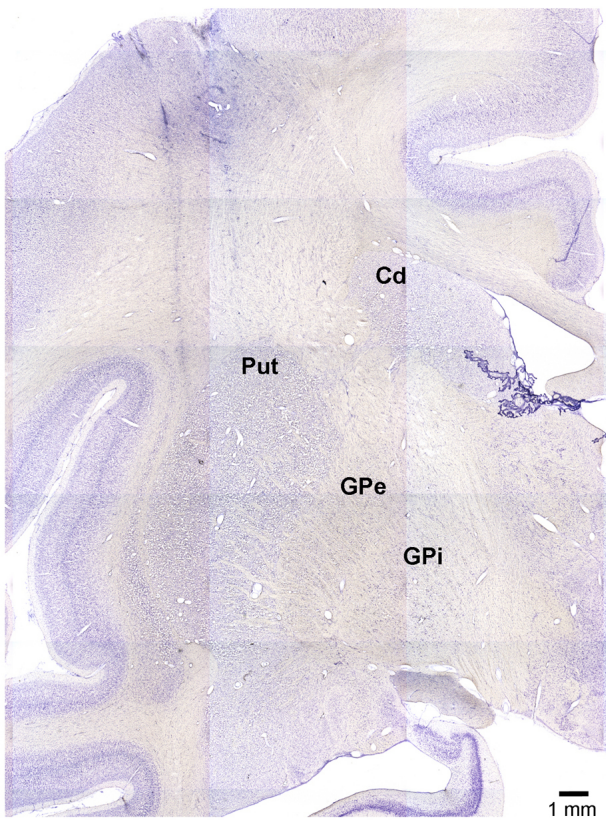


n=12



n=16

B

A**B**