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Spatial representations in rat orbitofrontal cortex

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34 **Abstract**

35 The orbitofrontal cortex (OFC) and hippocampus share striking cognitive and functional
36 similarities. As a result, both structures have been proposed to encode “cognitive maps” that
37 provide useful scaffolds for planning complex behaviors. However while this function has been
38 exemplified by spatial coding in neurons of hippocampal regions—particularly place and grid
39 cells—spatial representations in the OFC have been investigated far less. Here we sought to
40 address this by recording OFC neurons from male rats engaged in an open-field foraging task
41 like that originally developed to characterize place fields in rodent hippocampal neurons. Single
42 unit activity was recorded as rats searched for food pellets scattered randomly throughout a
43 large enclosure. In some sessions, particular flavors of food occurred more frequently in
44 particular parts of the enclosure; in others, only a single flavor was used. OFC neurons showed
45 spatially-localized firing fields in both conditions, and representations changed between flavored
46 and unflavored foraging periods in a manner reminiscent of remapping in the hippocampus.
47 Compared to hippocampal recordings taken under similar behavioral conditions, OFC spatial
48 representations were less temporally reliable, and there was no significant evidence of grid
49 tuning in OFC neurons. These data confirm that OFC neurons show spatial firing fields in a
50 large, two-dimensional environment in a manner similar to hippocampus. Consistent with the
51 focus of the OFC on biological meaning and goals, spatial coding was weaker than in
52 hippocampus and influenced by outcome identity.

53

54 **Significance statement**

55 The orbitofrontal cortex (OFC) and hippocampus have both been proposed to encode “cognitive
56 maps” that provide useful scaffolds for planning complex behaviors. This function is exemplified
57 by place and grid cells identified in hippocampus, the activity of which maps spatial
58 environments. The current study directly demonstrates very similar, though not identical, spatial
59 representatives in OFC neurons, confirming that OFC – like hippocampus – can represent a
60 spatial map under the appropriate experimental conditions.

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69 Introduction

70 Convergent work has found striking functional similarities between the orbitofrontal cortex (OFC)
 71 and hippocampus (Guitart-Mandila and Shapiro, 2017; Ramus et al., 2007; Wikenheiser and
 72 Schoenbaum, 2016). However, it is unclear to what extent spatial coding, a hallmark of
 73 hippocampal function (Knierim, 2015; O'Keefe and Nadel, 1978; Redish, 1999), occurs in the
 74 OFC. While place-cell-like representations have been reported in anterior cingulate, prelimbic,
 75 and infralimbic cortices (Hasz and Redish, 2020; Hok et al., 2005; Mashhoori et al., 2018;
 76 Powell and Redish, 2014; Remondes and Wilson, 2013; Tang et al., 2021; Zielinski et al., 2019),
 77 evidence for similar representations in OFC neurons is weaker (Feierstein et al., 2006; Grieves
 78 and Jeffery, 2017; Yang and Masmanidis, 2020).

79 For example, in operant decision making tasks, studies frequently identify strong neural
 80 correlates of response direction in OFC neurons (Feierstein et al., 2006; Roesch et al., 2006);
 81 while such activity may reflect differing spatial information, there is also a confound with past
 82 cues and impending reward. Indeed when response direction and these factors are dissociated
 83 in primate studies, directional correlates are reportedly rare (Padoa-Schioppa and Assad, 2006;
 84 but see Strait et al., 2016). Similarly, OFC recordings on maze-based decision making tasks
 85 find spatial regularities in OFC cell firing, however these correlates are interpreted as reflecting
 86 reward expectation/delivery or associative rather than spatial information (Riceberg and
 87 Shapiro, 2017; Steiner and Redish, 2012; Stott and Redish, 2014; Young and Shapiro, 2011).
 88 Perhaps the clearest demonstration of place as a modulator of OFC activity independent of
 89 reward comes from work showing that OFC cell firing discriminated odor ports located on
 90 different walls of an operant chamber. Yet such activity clearly clustered near preferred areas,
 91 and work was never done to identify whether such firing was mostly driven by the spatial
 92 location of the odor port versus the sensory and associative information (Lipton et al., 1999).
 93 Thus, outside the confines of operant boxes and relatively constrained maze-based tasks, tests
 94 of OFC representations in two-dimensional spaces are lacking.

95 The question of spatial representations in OFC has come to the fore recently for two reasons.
 96 First, it has been argued that both OFC and hippocampus encode “cognitive maps” that provide
 97 useful scaffolds for planning complex behaviors (Cohen and Eichenbaum, 1993; Farovik et al.,
 98 2015; Whittington et al., 2019; Wikenheiser and Schoenbaum, 2016; Wilson et al., 2014; Zhou
 99 et al., 2019b). This framework invites the obvious question of whether similarities between OFC
 100 and hippocampus extend to the level of spatial responses in individual OFC neurons. Second,
 101 recent neuroimaging and theoretical work has suggested that spatial coding schemes first
 102 identified in the rodent hippocampal system might in fact be general representational
 103 mechanisms for organizing information (Behrens et al., 2018). Specifically, signatures of grid-
 104 like representations, most often associated with the rodent entorhinal cortex (Hafting et al.,
 105 2005; Moser et al., 2008), have been identified in the OFC and associated regions in human
 106 participants trained to navigate abstract relational stimulus spaces (Bao et al., 2019;
 107 Constantinescu et al., 2016). However, while these representations show up in BOLD response,
 108 it is unclear whether the spiking activity of single neurons in the OFC show grid-like
 109 representations.

110 Here we sought to address these questions by recording OFC neurons from rats engaged in the
 111 classic open-field foraging task originally developed to characterize place fields in rodent
 112 hippocampal neurons (Muller and Kubie, 1987; Muller et al., 1987). Neural activity was

recorded as rats searched for food pellets scattered randomly throughout a large enclosure. Because OFC is known to care about features of appetitive outcomes like flavor, in some sessions, we arranged for particular flavors to occur more frequently in particular parts of the enclosure; in other sessions, only a single flavor was used. Data were analyzed for evidence of spatial firing fields, grid-like representations, and other correlates; comparisons were made to hippocampal recordings made in a similar open-field setting by the Buzsaki group (Mizuseki et al., 2009a, b).

Materials and Methods

Experimental Subjects. Subjects were four experimentally-naïve, male, Long-Evans rats purchased from Charles River. Rats were approximately 3 months of age and weighed 250-275 g at the beginning of the experiment. Rats were maintained on a 12-h light-dark cycle and housed singly in a facility accredited by the Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC). During behavioral testing and recording sessions rats were food restricted; rats were weighed daily and provided supplemental food in addition to what they earned on the behavioral task to maintain their weight at >85% of their free-feeding weight. Rats were handled for 5 days before behavioral training commenced.

Behavioral apparatus. Rats were trained to search a square, open-field arena for food pellets. The arena was 122 cm x 122 cm, and enclosed on all four sides by opaque, 50-cm walls. The arena was surrounded by black curtains, and a white cue card was affixed on one of the walls to provide a salient visual cue to orient the rats. Four food-pellet dispensers (Colbourn) were mounted above the arena, and connected via plastic tubing to custom, 3D-printed attachments positioned approximately 60 cm above the arena, at the center of each of the four walls. These attachments controlled the angle at which dispensed pellets dropped into the arena, and were designed to control the distribution of food pellets from each feeder and compose the flavor zones depicted in fig. 1a. Fig. 1a was constructed by firing 100 pellets from each feeder and manually counting where each pellet came to rest in a grid superimposed over the arena. One type of 20-mg food pellet was delivered from each feeder to define the standard flavor zones, which were identical for all rats. The four food pellet flavors used for the standard flavor zones were: fruit punch, raspberry, peanut butter, and banana.

Behavioral training and testing. Rats were habituated to the open-field arena by allowing them to explore it for 5-10 minutes on several consecutive days, after which behavioral training began. During training sessions, rats were placed in the center of the arena and food pellets were dispensed at random intervals. Inter-pellet intervals were drawn from a Gaussian distribution with a mean of 30 s and a variance to 10 s (rare negative values were removed). The identity of which feeder was activated was pseudorandomly determined such that for every 12 food pellet deliveries, each of the four feeders was activated three times, with the order of activation randomized. Pellet delivery was in no way contingent on rats' behavior. Daily training sessions lasted for 30 minutes and continued for 3 weeks to ensure that rats had sufficient opportunity to learn the flavor-location associations instantiated by the task.

Neural recordings. Rats were implanted with custom electrode arrays targeting OFC bilaterally, following procedures that have been detailed previously (Roesch et al., 2006; Stalnaker et al., 2014; Wikenheiser et al., 2017). For three rats, recording probes consisted of two drivable

156 bundles of sixteen formvar-insulated nichrome wires (25- μ m diameter; AM Systems). For one
 157 rat, recording probes consisted of two driveable bundles of eight stereotrodes, constructed by
 158 twisting together strands of 17.78- μ m diameter nichrome wire (AM Systems). All electrodes
 159 were electroplated to an impedance of approximately 200 kOhm measured at 1000 Hz using
 160 gold plating solution (Neuralynx). Electrode bundles were implanted 3.0 mm anterior to bregma
 161 and \pm 3.3 mm lateral to bregma. During surgery, electrode bundles were lowered 4 mm ventral
 162 to brain surface and secured via dental cement. Rats recovered for 5-7 days after surgery,
 163 during which time electrodes were advanced to reach dorsal OFC. After each recording session,
 164 electrodes were advanced 40-80 μ m to sample new neurons. Recording sites were
 165 reconstructed histologically and confirmed to lie with the lateral orbitofrontal and ventral anterior
 166 insular regions.

167 Neural recordings were collected using an OpenEphys acquisition system. Electrode signals
 168 were amplified and digitized by a 32-channel Intan headstage connected to the neural recording
 169 probe. Each channel was sampled continuously at 30 kHz, referenced to a common average
 170 signal that included all non-noisy channels, and filtered between 600-6000 Hz. Spike thresholds
 171 were set manually before each recording session. Threshold-crossing events were sorted into
 172 putative single units post-hoc using MClust
 173 (<http://redishlab.neuroscience.umn.edu/MClust/MClust.html>), following standard spike sorting
 174 procedures.

175 As a comparison to our OFC data, we also downloaded and analyzed an online data set of
 176 hippocampal recordings (Mizuseki et al., 2009a, b). These data have been described in detail
 177 elsewhere. Briefly, rats foraged for drops of water for ~50 minutes in a 120 cm square-shaped
 178 open field similar to the one used in our experiment. Recordings were made in right dorsal CA1
 179 hippocampus using 64-channel 8-shank silicon probes.

180 *Session sequence.* After recovery from surgery, rats first performed 30-minute sessions of the
 181 flavor gradient foraging task. These were identical to pre-surgery behavioral training sessions.
 182 When performance returned to pre-surgery levels for at least 4 consecutive sessions, rats were
 183 tested on a sequence of two-part recording sessions. In flavored-unflavored sessions, flavored
 184 pellets were delivered in their usual locations for one portion of the session, and a uniform
 185 distribution of unflavored, 20-mg sucrose pellets was delivered in a second portion of the
 186 session. The flavored and unflavored foraging periods each lasted 20 minutes, and were
 187 separated by approximately 10 minutes, during which the rat rested outside the enclosure. Each
 188 rat performed a total of 8 flavored-unflavored sessions, with the flavored period occurring in the
 189 first period for half of sessions and in the second period for the remainder. Intermixed with
 190 flavored-unflavored sessions, rats also performed 2 flavored-flavored sessions, which were
 191 structurally identical to flavored-unflavored sessions, except that flavored pellets were delivered
 192 in their previously-established locations for both portions of the session. The order of the 8
 193 flavored-unflavored sessions and 2 flavored-flavored sessions was randomized for each rat.
 194 Data from three flavored-unflavored sessions were lost due to a hardware synchronization
 195 issue. Finally, after the completion of neural recordings, rats underwent a series of four probe
 196 sessions. In probe sessions, rats foraged under the standard flavor gradient conditions for 20
 197 minutes, and under a modified version of the flavor gradients for a second 20-minute period; in
 198 this second period, flavor gradients were modified by replacing one of the usual pellet flavors
 199 with a novel type that rats had never encountered on the task arena previously, but which they
 200 had consumed previously in their home cage (substitute pellet flavors: grape, grain, chocolate,

201 and bacon). Rats underwent four probe sessions, such that each of the four familiar flavors
 202 were altered in the second half of one probe session. Table 1 summarizes the sessions each rat
 203 completed and the number of neurons recorded under each condition.

204 *Firing rate maps.* Firing rate maps were constructed by counting the number of spikes a cell
 205 fired while the rat was in each of 30 x 30 approximately 4 cm² bins, and dividing by the total
 206 amount of time rats spent in each bin. Periods of slow movement (running speed <5 cm/s) were
 207 excluded. Firing rate was not estimated for bins with a total visit duration of <0.2 s. For display
 208 only, firing rate maps were smoothed by convolution with a 2-D Gaussian kernel with sigma of 1
 209 bin; all analyses involving rate maps were performed on un-smoothed rate maps.

210 *Spatial information.* Using methods developed by others (Diehl et al., 2017; Markus et al., 1994;
 211 Skaggs et al., 1992), spatial information per spike was computed for each firing rate map using
 212 the following equation: $I = \sum_i P_i (R_i/R) \log(R_i/R)$, where I indexes the spatial bins in the rate map, P_i
 213 is the occupancy probability of each bin, R_i is the firing rate in each bin, and R is the average
 214 firing rate across bins. To test for significant spatial representations, each cell's spike train was
 215 shifted relative to video tracking data by a fixed random offset drawn from a uniform distribution
 216 ranging from 10-30s. Using the shifted spike train, a rate map and spatial information score
 217 were recomputed; this process was repeated 1000 times for each cell. Cells with a peak spatial
 218 firing rate >2 Hz and a spatial information score greater than 95% of shuffled rate maps were
 219 counted as having significant spatial representations.

220 *Firing field center locations.* To examine the distribution of firing fields across the arena (figs. 3
 221 and 4), firing fields were defined as contiguous pixels with a mean firing rate greater than or
 222 equal to 40% of the cell's maximum firing rate. In addition, individual fields whose area was less
 223 than 1% of the enclosure or greater than 25% of the enclosure were excluded from the field
 224 center analysis. Note that such cells might still encode spatial information; however, for cells
 225 whose firing is distributed widely over space, the concept of the field's center becomes less
 226 meaningful, so such neurons (66/487 cells, approximately 13.5%) were excluded from this
 227 analysis. More than one field could be detected per cell; in this case, the field with the highest
 228 average firing rate was used in constructing plots of field centers.

229 *Spatial cross-correlation.* For spatial cross-correlation analyses (fig. 5), rate maps for each cell
 230 were computed separately for the different conditions under investigation (i.e. flavor-zone
 231 foraging period vs. foraging for a uniform distribution of unflavored pellets). Cross-correlograms
 232 were computed by shifting one rate map relative to the other in the x and y directions, and
 233 taking the pixel-by-pixel correlation where the two rate maps overlapped. A shift of zero for both
 234 x and y corresponds to a perfect alignment of rate maps; therefore, two rate maps with similar
 235 spatial firing patterns should produce high correlation values for small shifts, more distinct
 236 representations across conditions result in low correlation values. To further visualize how
 237 cross-correlation changed with increasingly large shifts (fig. 5b), we averaged cross-
 238 correlograms over all cells in flavored-flavored and flavored-unflavored sessions (fig. 5a), and
 239 then plotted the value of each pixel in the average cross-correlogram as a function of that pixel's
 240 distance to the origin.

241 *Cross-temporal correlation.* We performed a further correlation analysis to measure
 242 representation stability over time, both with and across flavor contexts. For each cell recorded in
 243 flavored-flavored and flavored-unflavored sessions, rate maps were computed in six-minute
 244 sliding windows, which were stepped across each session half in 3.5 minute steps. Thus, the

245 first rate map spanned 0-6 minutes, the second spanned 3.5-9.5 minutes, the third 7-13
 246 minutes, and so on. For each cell, this procedure resulted in five rate maps for each session
 247 half, or ten rate maps for each session. Next, the correlation between every pair of a cell's rate
 248 maps was taken to produce the correlation matrices shown in fig. 6. As before, the spatial firing
 249 rate was not estimated for bins that the rat visited for less than 0.2 s, so these locations were
 250 not included in computing correlations. Correlation matrices were averaged across all neurons
 251 recorded in a particular session type to construct the average plots in fig. 6a.

252 *Gridness analysis.* To test for grid-like representations, we followed the approach outlined by
 253 Brandon and colleagues (2011) for computing the expanding gridness score with elliptical
 254 correction for each OFC neuron recorded in non-switch or flavored-unflavored task sessions.
 255 Briefly, spatial autocorrelograms were constructed for each cell following the same approach
 256 described for the spatial cross-correlation analysis, but shifting a copy of the rate map relative to
 257 itself, and computing the pixel-by-pixel correlation of overlapping portions. The correlation peak
 258 at the center was removed by defining an inner radius with a length of half the average distance
 259 to the four correlogram peaks nearest to the origin. Next, an annulus was extracted by choosing
 260 an outer radius with length greater than the inner radius. The annulus was then rotated relative
 261 to itself, the correlation was computed for every rotation, and plots of correlation as a function of
 262 rotation (fig. 7b) were examined for periodicity consistent with grid-like representations. The
 263 gridness score was defined as the difference between the minimum correlation value at 60 or
 264 120 degree rotations and the maximum correlation value at 30, 50, and 90 degree rotations. To
 265 mitigate potential difficulties in correctly choosing the length of the outer radius, we tested all
 266 possible lengths and report the greatest resulting gridness score. Because standard measures
 267 of gridness are sensitive to minor elliptical distortions in the arrangement of grid fields, we
 268 computed two possible corrections by defining the length of the long and short axes of the
 269 ellipse as the distance from the origin to the farthest and nearest autocorrelogram peaks,
 270 respectively. For each correction, the length of the missing elliptical axis was inferred as
 271 described previously (Brandon et al., 2011), and the autocorrelogram was warped to equalize
 272 the lengths of these axes. Gridness scores were computed for both corrections using the
 273 expanding outer radius approach outlined above, and the higher of the two scores is reported.

274 To test for significant grid tuning, we shifted spikes relative to video tracking data as described
 275 above and recomputed the gridness score for each shifted spike train. This process was
 276 repeated 500 times to generate a null distribution of gridness scores, and cells whose gridness
 277 score exceeded 95% of shuffled scores were considered to have significant grid tuning. This
 278 significance testing procedure has been shown to have a higher than expected false positive
 279 rate in simulated data with irregularly-distributed spatial firing fields (Barry and Burgess, 2017).
 280 Thus, though few OFC cells reached significance using the approach outlined above, it is
 281 possible that with a more stringent "field shuffling" test of significance even fewer cells would
 282 have been identified as having grid-like tuning.

283 *Analyses of hippocampal recordings.* The hc-2 neural recording data set was downloaded from
 284 CRCNS.org (Mizuseki et al., 2009a) and analyzed to provide a comparison between
 285 hippocampal and OFC neurons recorded under similar circumstances. We analyzed 148
 286 neurons from four sessions recorded under these conditions. All analyses of hippocampal units
 287 were performed following the same approaches as detailed above for OFC neurons.

288

289 Results

290 We recorded neurons in the lateral OFC as rats performed a foraging task inspired by the
 291 behavioral paradigms used in classic work investigating spatial representations (fig. 1a). Rats
 292 were placed in a large (122×122 cm), square-shaped enclosure, where flavored sucrose pellets
 293 were delivered from four dispensers mounted above the enclosure with an average frequency of
 294 two pellets per minute. The random scatter of pellets encouraged rats to fully explore the
 295 enclosure, allowing us to assess neurons' firing rates at each location in the enclosure. The task
 296 also ensured that behavioral patterns associated with seeking or consuming food pellets were
 297 distributed randomly over space, so that neural responses specific to such behaviors could not
 298 be mistaken for spatial correlates.

299 Our version of the task was modified to provide a richer appetitive outcome structure aimed at
 300 better engaging the OFC. Four different flavors of nutritionally-equivalent and similarly-valued
 301 sucrose pellets were delivered within separate spatial zones across the arena (fig. 1b, top). We
 302 did not conduct preference tests for pellet types outside of the foraging task context, but
 303 behavioral data from probe test sessions (described below) suggests that the rats did not have
 304 strong preferences among the four flavors. The likelihood of finding a pellet (regardless of its
 305 flavor) was uniform across the arena (fig. 1b, bottom), but each of the four flavors was most
 306 likely to be encountered within its flavor zone. Thus, the expected pellet flavor varied over
 307 space, while the average density of pellets did not.

308 Rats responded to violations of flavor structure

309 To test whether rats attended to the similarly-valued flavors being delivered in the different
 310 zones, probe sessions were conducted after the collection of neural data was complete. Probe
 311 sessions were divided into two, 20-minute foraging periods. During the first portion of probe
 312 sessions, rats searched for pellets delivered in the four flavor zones as described above. During
 313 the second portion of the probe session, one flavor zone was altered by switching the usual
 314 pellet for that zone with a flavor that the rat had not encountered before on the task (but which
 315 had been experienced previously in the home cage to habituate neophobia). The order in which
 316 the flavor zones were altered during probe sessions was randomized, and across four probe
 317 sessions all four flavor zones were substituted for each rat.

318 We divided the enclosure into four flavor zones defined by the pellet flavor probability gradients
 319 (fig. 1c, top) and measured how much time rats spent searching in each location before and
 320 after the introduction of the different pellet type. In the first half of probe sessions, rats spent
 321 roughly equal amounts of time in the four flavor zones; however when a new flavor was
 322 introduced, the rats spent significantly more time in the zone containing that pellet type (fig. 1c-d
 323 "post-switch"). A two-way analysis of variance (ANOVA) on time spent in each zone showed a
 324 main effect of flavor zone ($F_{3,120} = 10.92$, $p = 2.14 \times 10^{-6}$) and a zone \times session half (familiar
 325 flavor vs. different flavor portion of the session) interaction ($F_{3,120} = 5.89$, $p = 8.69 \times 10^{-4}$). The
 326 main effect of session half was not significant ($F_{1,120} = 0.23$, $p = 0.63$). Bonferroni-corrected
 327 post-hoc paired t-tests showed that these significant effects reflected a significant increase in
 328 time spent in the different flavor zone during the second half of probe sessions relative to the
 329 first half of the session when the familiar pellet type was delivered ($t_{15} = -6.72$, $p = 2.73 \times 10^{-6}$).
 330 Familiar zones one and two showed concomitant decreases in search time during the second
 331 half of probe sessions (familiar zone one: $t_{15} = -3.93$, $P = 5.30 \times 10^{-3}$; familiar zone two: $t_{15} =$
 332 5.65 , $p = 1.85 \times 10^{-4}$), while there were no significant change for familiar zone three ($t_{15} = -1.51$,

333 $p = 0.59$). These data suggest that rats generally valued the familiar pellets similarly, however
 334 they were attending to the different flavors and recognized alterations to the flavor structure of
 335 the task, directing their search efforts towards regions where violations of expectations occurred
 336 (Costa and Averbeck, 2020).

337 **OFC neurons showed spatial representations**

338 We recorded lateral OFC neurons as rats performed the flavor zone task (fig. 1e-f). A complete
 339 summary of the number of cells recorded from each rat is given in table 1. To look for evidence
 340 of spatial representations, we divided the enclosure into a 30×30 grid of approximately 4 cm^2
 341 bins and computed each neuron's average firing rate for every location. Locations that rats did
 342 not visit for at least 0.2 s are represented by white pixels in firing rate maps. Many OFC neurons
 343 showed distinct spatial firing fields (fig. 2). We computed the spatial information score (Diehl et
 344 al., 2017; Markus et al., 1994; Skaggs et al., 1992) for each firing rate map. We also shifted
 345 each spike train relative to the rat's position tracking data by a random offset and re-computed
 346 firing rate maps and spatial information scores; this process was repeated 500 times and
 347 neurons were considered to have significant spatial representations if their spatial information
 348 score exceeded that of 95% of the shifted spike trains. By this metric, 64 of 185 OFC neurons
 349 recorded on the flavor zone task (34.5%) showed significant spatial tuning (fig. 3a). Spatially-
 350 tuned neurons typically showed firing fields that remained stable for the duration of the
 351 recording session (fig. 3b-e). The firing fields of spatially-tuned neurons were evenly distributed
 352 across the four flavor zones (fig. 3f; $\chi^2 = 2.16$; degrees of freedom = 3, $N = 50$, $p = 0.20$).

353 **Spatial tuning was not driven by flavor selectivity, but was sensitive to flavor context**

354 Previous work has established that OFC neurons often encode information about the properties
 355 of appetitive outcomes, such as flavor. Thus, OFC neurons that responded to consumption of a
 356 particular pellet flavor (or encoded memories or expectations of such experiences) could
 357 manifest a crude spatial representation, confined to the flavor zones over which each pellet type
 358 was delivered. The firing fields of OFC neurons were not constrained by the flavor zones we
 359 imposed in this way (fig. 2). However, the flavor structure of the environment may still have
 360 modulated firing patterns in OFC neurons. In hippocampal neurons, for instance, changing
 361 features of salient sensory cues in the environment can induce "remapping", causing neurons to
 362 gain or lose place fields, or form place fields in new locations.

363 To test for such effects directly, we recorded OFC neurons in a version of the task where
 364 location was correlated with or independent of flavor at different times in individual sessions. In
 365 these flavored-unflavored sessions, rats foraged for two, twenty-minute periods separated by
 366 ten minutes of rest outside the enclosure. For one foraging period, flavored pellets were
 367 delivered in their familiar flavor zones as before; for the other foraging period, unflavored but
 368 also familiar sucrose pellets were delivered uniformly over the enclosure. The order of flavored
 369 and unflavored foraging periods was randomized and counterbalanced across sessions.

370 Of 302 neurons recorded during flavored-unflavored sessions, 73 neurons showed significant
 371 spatial tuning during the flavored foraging period, while 100 neurons showed significant spatial
 372 tuning during the unflavored portion (fig. 4a). The mean spatial information score of significant
 373 neurons did not differ between flavored and unflavored periods of the session ($\mu_{\text{flavored}} = 0.96$
 374 bits/s; $\mu_{\text{unflavored}} = 0.82$ bit/s; $P = 0.30$; $t_{171} = 1.03$; two-sample t-test), and the firing fields of
 375 spatially-tuned neurons were evenly distributed across the four flavor zones, both during
 376 flavored and unflavored portions of sessions (fig. 4b; flavored portion: $\chi^2 = 1.87$; degrees of

freedom = 3, $N = 53$, $p = 0.21$; unflavored portion: $\chi^2 = 4.10$; degrees of freedom = 3, $N = 63$, $p = 0.10$). These data indicate that similar numbers of OFC neurons showed spatial tuning whether or not flavors were arranged in spatial patterns in the environment.

Yet, while spatial tuning was present in both portions of the task, relatively few neurons retained significant spatial tuning for both flavored and unflavored portions of the task, suggesting that flavor context may modulate OFC spatial representations. Indeed, of the 149 OFC neurons that showed spatial tuning for at least one foraging period of flavored-unflavored sessions, only 16.1% (24 neurons) had significant spatial tuning for both the flavored and unflavored portions (fig. 4c, left). To explore the tendency of neurons to gain or lose tuning between the flavored and unflavored portion of these sessions, we also recorded neurons on flavored-flavored sessions. These sessions were structurally identical to flavored-unflavored sessions except that both 20-minute foraging periods were in the flavor zone context. Of 105 OFC neurons recorded in flavored-flavored sessions, 37 neurons showed significant spatial representations in the first flavored period, while 38 neurons showed significant spatial tuning the second flavored period. Of the neurons with significant spatial tuning in at least one period of the session, 36.3% were significant for both periods (fig. 4c, right). Notably, the proportion of neurons that maintained spatial tuning in both session periods was significantly greater for flavored-flavored sessions ($z_{42} = -3.12$; $p = 1.79 \times 10^{-3}$; z-test for population proportions), suggesting that spatial tuning in OFC neurons was sensitive to the current flavor context under which animals were foraging.

Spatial representations were more similar within flavor context than across flavor context

Identifying neurons as spatially tuned does not speak to their actual firing patterns. A neuron may have significant spatial representations in both foraging portions of the task without firing in the same location for both contexts. Hippocampal place cells, for instance, show statistically-independent spatial representations across different contexts (Bostock et al., 1991; Colgin et al., 2008; Kubie et al., 2020; Muller and Kubie, 1987).

To investigate this question, we calculated the spatial cross-correlation between firing rate maps computed separately for each period of flavored-unflavored and flavored-flavored sessions. In this analysis, the pixel-by-pixel correlation is measured between the two firing rate maps as one map is shifted relative to the other. If representations are similar between two firing rate maps, the correlation will be strongest near shifts of zero, corresponding to the origin of 2-D spatial cross-correlograms, and progressively weaken with increasingly large shifts. Importantly, this method measures the similarity of firing rate maps without making assumptions about the shape or complexity of firing fields.

Both exemplar (fig. 5a, left column) and average (fig. 5b, left) spatial cross-correlograms of OFC neurons recorded during flavored-flavored sessions ($N = 105$) showed a high correlation centered around shifts of zero, indicating that representations were—on average—similar between the first and second flavor zone foraging periods of these sessions. By contrast, exemplar (fig. 5a, right column) and average (fig. 5b, right) spatial cross-correlograms for OFC neurons recorded during flavored-unflavored sessions ($N = 305$) showed a substantially lower correlation around shifts of zero, indicating less similar representations between contexts in these sessions. A statistical analysis showed that the average cross-correlation strength for spatial shifts less than 20 cm was significantly greater for cells recorded in flavored-flavored sessions than it was for cells recorded in flavored-unflavored conditions (fig. 5c; $t_{405} = -5.57$; $p =$

421 4.60×10^{-8} ; two-sample t-test). As described previously, the spatial information of neurons that
 422 had firing fields in flavored foraging periods was not significantly different from neurons with
 423 firing fields in unflavored sessions, and neither was the proportion of neurons with significant
 424 spatial tuning different between flavored and unflavored foraging periods. Thus, at the
 425 population level, the quality of OFC spatial representations did not differ between flavored and
 426 unflavored contexts. However, the pattern of spatial firing for any individual OFC unit was more
 427 likely to change between flavored and unflavored foraging periods than when flavor context was
 428 held constant.

429 We performed an additional correlation analysis to assess how similar representations were
 430 across time, both within and across the two session periods. Firing rate maps were computed in
 431 sliding windows (window length = 6 minutes; step size = 3.5 minutes), and the correlation
 432 between firing rate maps for each pair of windows was calculated for individual exemplars (fig.
 433 6a) and averaged across all cells (fig. 6b). As expected, pixels near the diagonal of the
 434 correlation matrix showed strong correlations, indicating that firing rate maps from nearby time
 435 bins were more similar than rate maps separated by long durations. However, consistent with
 436 our previous analyses, the tuning of neurons recorded in flavored-unflavored sessions showed
 437 weaker correlations across the two periods compared with neurons recorded in flavored-
 438 flavored sessions. We computed the mean across-context correlation for each neuron by
 439 averaging pixels in the lower-left and upper-right quadrants of the correlation matrix of each cell.
 440 The mean within-context correlation was computed analogously, by averaging correlation
 441 values in the upper-left and lower-right quadrants (excluding pixels along the diagonal where
 442 entries always take the maximal value of one). While the strength of the within-context
 443 correlation did not significantly differ for neurons recorded in different types of sessions (fig. 6c;
 444 $t_{405} = 0.47$; $p = 0.64$; two-sample t-test), the average between-context correlation was
 445 significantly lower for neurons recorded in flavored-unflavored sessions (fig. 6c; $t_{405} = 4.95$; $p =$
 446 1.07×10^{-6} ; two-sample t-test). These analyses indicate that, independent of temporal effects, the
 447 spatial tuning in OFC was significantly more stable when flavor remained the same across two
 448 contexts than when flavor changed.

449 **Lack of grid-like representations in OFC neurons**

450 Recent neuroimaging experiments have suggested that grid-like tuning, a spatial firing motif first
 451 identified in the entorhinal cortex of rats, may be a general coding mechanism for structuring
 452 representations of abstract, non-spatial concepts into a mental map (Hafting et al., 2005; Moser
 453 et al., 2008). Organization of representations in this manner could facilitate planning and
 454 decision making, and signatures of such grid-like representations have been identified in
 455 portions of frontal cortex, including the OFC (Bao et al., 2019; Constantinescu et al., 2016). It is
 456 unknown, however, whether single cells in OFC show grid cell tuning. This is an important
 457 question, since BOLD signal is significantly influenced by afferent input and local processing
 458 (Logothetis and Wandell, 2004), whereas fine-wire recording electrodes like those used here
 459 are biased to pick up activity from large “regular spiking” putative pyramidal neurons (Connors
 460 and Gutnick, 1990; McCormick et al., 1985).

461 To test for the presence of grid tuning in OFC neurons, we calculated rate maps (fig. 7b, left
 462 column), rate map autocorrelograms (fig. 7b, middle column) and gridness scores for each OFC
 463 neuron we recorded in the flavored-flavored and flavored-unflavored sessions described above.
 464 The gridness score quantifies the 6-fold rotational symmetry that is characteristic of grid cells
 465 (Barry and Burgess, 2017; Brandon et al., 2011; Sargolini et al., 2006). The correlation is

466 computed between each cell's rate map, and a rotated version of the rate map, with grid tuning
 467 resulting in higher correlations at rotations of 60 and 120 degrees (fig. 7b, right column). Cells
 468 with gridness scores exceeding 95% of scores generated from randomly shuffled data were
 469 considered to have significant grid tuning. Because we found that representations depended on
 470 flavor context in our task, we computed grid scores separately for flavored and unflavored
 471 portions of flavored-unflavored sessions.

472 This analysis revealed that grid-like representations were rare in OFC neurons. In non-switch
 473 sessions, only 2% of cells (4/185) showed significant grid tuning, which was not significantly
 474 different than the 5% of neurons expected to pass the statistical threshold for grid-like tuning (p
 475 = 0.09, two-tailed binomial test). Similarly in flavored-unflavored sessions 4% of cells (12/302 p
 476 = 0.51, two-tailed binomial test) passed the statistical threshold for grid tuning during the
 477 flavored portion, while 6% of cells (18/302, p = 0.43, two-tailed binomial test) were significant in
 478 the unflavored session periods (fig. 7a). None of these proportions differed significantly from
 479 what would be expected by chance, suggesting that although some examples could be
 480 identified in this task (fig. 7b), grid-like representations were an uncommon motif in the
 481 representations of the OFC neurons sampled by our recording electrodes.

482 **Comparison to hippocampal spatial coding**

483 Lastly, it is interesting to consider how spatial coding in OFC compares with the canonical
 484 spatial representations found in hippocampal neurons. To facilitate this comparison, we
 485 performed the same analyses described above on a freely-available dataset of 148 dorsal CA1
 486 hippocampal neurons (Mizuseki et al., 2009a, b). These neurons were recorded in rats
 487 performing a foraging task for water in an enclosure with the same shape and similar
 488 dimensions as ours and therefore provided a reasonable comparison. These hippocampal
 489 recording experiments did not include flavor manipulations, so it was not possible to compare
 490 representations across flavor contexts; however we did divide hippocampal recording sessions
 491 into two 20-minute periods, creating a situation analogous to flavored-flavored sessions in our
 492 experiment, where context is held constant over time. It should be noted that subtle differences
 493 in experimental procedures and behavioral task demands can have a strong effect on neural
 494 activity, so these comparisons, while informative, should be interpreted with care.

495 Analyzing these data using the same methods applied to the OFC data revealed that
 496 hippocampal neurons generally showed stronger and more temporally-reliable spatial
 497 representations than OFC neurons. Spatial information scores (fig. 8a-b) were significantly
 498 higher in the sample of hippocampal neurons than in OFC neurons recorded in flavored-flavored
 499 sessions ($t_{251} = 6.63$; $p = 2.10 \times 10^{-10}$; two-sample t-test). The average spatial cross-correlation
 500 (fig. 8c) at shifts less 20 cm was significantly greater for hippocampal than for OFC neurons (t_{251}
 501 = 5.71; $p = 3.02 \times 10^{-8}$; two-sample t-test, fig. 8d), as was the average temporal correlation (fig.
 502 8e), both within ($t_{251} = 5.80$; $p = 1.99 \times 10^{-8}$; two-sample t-test) and between ($t_{251} = 7.20$; $p =$
 503 6.81×10^{-12} ; two-sample t-test) session periods (fig. 8f).

504

505 **Discussion**

506 Striking cognitive and functional similarities between the OFC and hippocampus have led to
 507 recent proposals that the two regions interact to encode "cognitive maps" that provide useful

scaffolds for planning complex behaviors (Boorman et al., 2021; Cohen and Eichenbaum, 1993; Wikenheiser and Schoenbaum, 2016; Wilson et al., 2014). Cognitive maps have long been exemplified in hippocampal regions by the encoding of spatial and navigation-related information; place cells, grid cells, and other members of the “hippocampal zoo” are concrete evidence of this general mapping function. To date, no such demonstration has been provided in the OFC. Here we directly addressed this gap in the literature by recording OFC neurons from rats engaged in a classic open-field foraging task (Muller et al., 1987). We found that, as in hippocampus, neurons in the OFC exhibit correlates of place in this task, their activity varying with the location of the rat in the arena. Like classic place fields in other foraging tasks, these neurons have place fields that are temporally-stable and uniformly distributed across the enclosure. Direct comparisons to similar recordings from hippocampus indicated that the spatial acuity of the OFC representations, while significant, was weaker than that of the very precise representations in CA1 neurons, and there was little evidence of grid cells in the OFC recordings. Additionally, the spatial encoding in OFC was sensitive to changes in the sensory features of food available in the arena; while a direct comparison to hippocampus for this was not possible, the influence of outcome on OFC representations was substantial. Overall these data provide straightforward evidence of place-like representations in OFC neurons in a task that makes the data easily comparable to data from hippocampal studies. The results are consistent with ideas that OFC formats information so that it can be read out as a cognitive map, while at the same time providing interesting contrasts with the cognitive map in hippocampus.

Although directional correlates or correlates of reward locations have been described in previous OFC recording experiments, typically these firing patterns have been confounded by associative information or other features of behavioral tasks occurring at those unique locations (Feierstein et al., 2006; Lipton et al., 1999; Roesch et al., 2006; Steiner and Redish, 2012; Stott and Redish, 2014). Results presented here do not suffer from this shortcoming, since recordings were made in a classic open-field foraging task and stable and distributed spatial encoding was observed. Thus these data show that OFC neurons can map a feature space in a manner similar to what has been observed in hippocampus. These data establish a modicum of continuity across lateral and medial parts of frontal cortex in terms of neural representations. Location-specific firing patterns—along with other processes associated with the hippocampus, such as theta phase precession (Jones and Wilson, 2005), theta sequences (Tang et al., 2021), and replay of both spatial (Euston et al., 2007; Kaefer et al., 2020; Shin et al., 2019) and non-spatial (Peyrache et al., 2009) factors—are well established in anterior cingulate and medial prefrontal regions of the rat brain. Our results raise the possibility that spatial tuning may be a common organizing principle for activity in frontal cortex generally. Beyond frontal cortex, this work contributes to growing evidence of spatial representations outside of the hippocampal formation proper (Esteves et al., 2021; Flossmann and Rochefort, 2021; Long et al., 2021; Long and Zhang, 2021; Peyrache and Duzskiewicz, 2021; Saleem et al., 2018).

Our results also show that spatial mapping can emerge in brain regions with vastly different organizational and input/output structure, identifying one more functional similarity between OFC and hippocampus. However, comparisons with hippocampal spatial encoding also revealed intriguing differences. Specifically, the weaker spatial representations and likely higher impact of biologically-relevant local sensory information about reward in OFC neurons accord well with the general consensus that processing in the OFC is biased to emphasize information – spatial or otherwise – relevant to the goals of the subject, even at the expense of other

554 information in the environment. It is also important to note that while rats' behavior on the task
 555 suggests that rats did not have strong preferences for any of the flavors used to define flavor
 556 zones, we cannot rule out the possibility that rats had weaker preferences amongst the flavors
 557 that our behavioral measures were not sensitive enough to detect. As such, the influence of
 558 pellet value on OFC spatial representations is an important question for future work to address.

559 Interestingly, removing outcome flavor as a variable did not result in reduced spatial encoding,
 560 but there was a significant turnover in the neurons encoding that information. This shift in the
 561 population representing location in the arena lines up well with proposals that OFC provides a
 562 "map layer" that incorporates context and even hidden or latent information, allowing the same
 563 location – in real or abstract task space – to be discriminated (Schuck et al., 2016; Wilson et al.,
 564 2012; Zhou et al., 2019a). Here, the same location is represented very differently by OFC when
 565 various flavored pellets are present versus when only a single pellet flavor is present. It is
 566 unclear whether hippocampal place cells would similarly discriminate flavor contexts in this way,
 567 though it is interesting to note that taste coding and spatial responses partially overlap in the
 568 hippocampus (Herzog et al., 2020; Herzog et al., 2019). It is well established, however, that
 569 other sorts of contextual changes—defined by changes to both external sensory cues (Colgin et
 570 al., 2008), or internal, cognitive (Markus et al., 1995) or motivational (Kennedy and Shapiro,
 571 2009) factors—drive similar alterations in the spatial representations of hippocampal place cells,
 572 a phenomenon termed remapping. In fact, recent work has cast hippocampal remapping as a
 573 state inference process (Kubie et al., 2020; Sanders et al., 2020), suggesting another functional
 574 similarity hippocampus shares with OFC, which has been characterized as a cognitive map of
 575 task state that is especially important for inferring hidden states not fully defined by external
 576 sensory inputs (Wilson et al., 2014).

577 The absence of significant numbers of grid cells in our dataset is also of interest, given that
 578 there are now several reports of gridness in OFC in another measure of neural activity, the
 579 BOLD response (Bao et al., 2019; Constantinescu et al., 2016). Although this could reflect
 580 species or regional differences between our study and this other work, it might also reflect
 581 differences in the basis of the neural measures. One of the useful things about extracellular
 582 recording in cortical regions is that fine wire microelectrodes are biased to pick up activity from
 583 large "regular spiking" neurons likely to be pyramidal output neurons (Connors and Gutnick,
 584 1990; McCormick et al., 1985). BOLD does not appear to suffer from this bias (Logothetis and
 585 Wandell, 2004). As a result, one interpretation of the low number of grid cells in our dataset is
 586 that the gridness reported in BOLD response reflects the influence of input from hippocampal
 587 areas, functioning to help support and properly organize or coordinate the map in OFC with that
 588 in other areas (Raithel and Gottfried, 2021). Another possibility is that the foraging task used in
 589 the present work was not sufficiently challenging to require or evoke grid-like representations in
 590 OFC neurons. In hippocampus, for instance, there is evidence that behavioral demands alter
 591 spatial representations, with place cells showing increased temporal reliability on tasks that
 592 require solving more challenging navigation problems (Fenton et al., 2010; Jackson and Redish,
 593 2007; Olypher et al., 2002; Wikenheiser and Redish, 2011). Grid-like representations might
 594 similarly emerge on behavioral tasks that require decision making, inference, or generalization
 595 (Behrens et al., 2018; Lee et al., 2021).

596 There is increasing evidence that OFC plays a role in spatial decision making tasks, and that
 597 the hippocampus or hippocampal formation is critical to normal processing in the OFC. Lesions
 598 or inactivation of OFC result in behavioral deficits on tasks that include a spatial component

(Corwin et al., 1994; Kolb et al., 1983; Young and Shapiro, 2011; Young, 2009). Consolidation of information about task state in human OFC correlates with offline replay of that information in hippocampus (Schuck and Niv, 2019), and OFC-hippocampal interaction is increased during OFC-dependent inference (Wang et al., 2020). Further, when that interaction is disrupted in real-time by optogenetic inactivation of hippocampal outflow in subiculum, neurons recorded in rat OFC show a selective reduction in the integration of information about the value, location and sensory features of expected outcomes was lost (Wikenheiser et al., 2017). The apparent interdependence of OFC and hippocampus for proper representation of task state and the real-time collapse of the normal multidimensional representations in OFC upon disruption of that interaction might reflect the loss of the support function provided by the hippocampal formation. The lack of such support leads to behavioral deficits; disconnection of OFC and ventral hippocampal regions cause deficits in reversal learning in rats (Thonnard et al., 2021), and manipulations of OFC targeted to selectively disrupt hippocampal-mediated theta oscillations impair value-based decision making in monkeys (Knudsen and Wallis, 2020).

Clearly, more work will be necessary to understand the functional importance of spatial representations in OFC. Foremost, more challenging behavioral tasks could provide insight into the cognitive functions these representations support, and causal manipulations of hippocampus and adjacent structures could reveal whether spatial representations in OFC are inherited from spatially-tuned neurons in other brain regions or computed locally. Other processes associated with hippocampal spatial representations, such as remapping, reactivation, coupling of spikes to local field potential oscillations, and more could profitably be investigated in OFC. The extensive literature on hippocampal representations and interactions between hippocampus and other parts of the brain provides a roadmap for such future work and a natural basis for comparison. Answering these and similar questions will define how cognitive maps in hippocampus coordinate with similar, though distinct, representations in OFC to form a convergent, global cognitive map that supports adaptive behavior (Boorman et al., 2021; Patai and Spiers, 2021; Wikenheiser and Schoenbaum, 2016).

626

627 References

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Table 1

Number of sessions by session type				
Rat	Non-switch	Switch	Switch	Probe
		(Flav→Unflav)	(Flav→Flav)	

1	4	7	2	4
2	4	7	2	4
3	4	7	2	4
4	4	8	2	4
total:	16	29	8	16

Cells recorded by session type			
Rat	Non-switch	Switch (Flav→Unflav)	Switch (Flav→Flav)
1	41	65	23
2	39	80	40
3	33	64	23
4	72	93	19
total:	185	302	105

Figure captions

Figure 1. Behavioral task and probe test behavior. (a) Four flavors of sucrose pellets were delivered in four spatial flavor zones, such that each of the four flavors was most likely to be found in a particular location (top), but the probability of finding any pellet was even across the enclosure. Color indicates the probability of finding pellets of individual pellets (top) and any pellet (bottom). Data were generated by delivering 20 pellets of each flavor and counting the number that landed at each location within the arena. (b) In probe session, rats spent similar amounts of time in each flavor zone for the first foraging period, when flavors were delivered in their familiar locations. However, when one familiar flavor was switched to a novel pellet type, rats distributed more time to searching the pellet zone corresponding to the novel flavor. Color indicates grand average of time spent at each location, across four probe sessions for each of four rats. (c) Quantification of data in (b). Mean time in each flavor zone was obtained by averaging pixels defining each zone as shown in far left panel of (b). (d) We recorded neurons bilaterally in OFC using single wire electrodes (left; $n = 3$ rats; 16 electrodes per hemisphere) or stereotrodes (right; $n = 1$; 8 stereotrodes per hemisphere). (e) Histological reconstruction of recording sites confirmed that electrode placements were localized to the lateral orbitofrontal and ventral anterior insular regions.

Figure 2. Example cells. Examples of spatial representations in twelve OFC neurons are shown. Heat maps show firing rate maps constructed by dividing the enclosure into a 30×30 grid of bins, and computing the session average firing rate for each location. Each cell's maximum firing rate is plotted near the upper left corner of firing rate maps. Regions of the enclosure that rats did not spend at least 0.2 s in over the course of the 30-minute session are represented with a white pixel. Below each firing rate map, a corresponding plot of the rat's location (blue) and the location of each action potential (black dots) is shown.

Figure 3. Spatial information in OFC cells. (a) The spatial information score for each OFC neuron is plotted against the mean spatial information score averaged over 500 random misalignments of each cell's activity and the rat's location. Neurons plotted with black dots met the statistical criterion for significant spatial information. (b) Same as (a), except the logarithm of spatial information is plotted for better visibility. (c–e) Firing rate maps for the neurons labelled in

(a) are computed over three different periods of the recording session. Generally similar patterns of firing are evident for these neurons throughout the three portions of the recording session. (f) To examine the distribution of firing fields, we extracted contiguous regions of elevated firing rate, and found the center of such fields. For cells with more than one region of elevated firing, we extracted the field with the greatest average firing rate. Firing fields were distributed relatively uniformly over the enclosure for non-switch sessions.

Figure 4. Spatial tuning across contexts. (a) Many OFC neurons showed significant spatial tuning for both foraging periods of flavored-unflavored sessions. (b) Firing fields were detected and the locations of their centers were plotted for flavored and unflavored foraging periods. Fields were evenly distributed over the enclosure for both flavored and unflavored foraging periods. (c) The proportion of neurons with significant spatial tuning during both periods of the session was greater in flavored-flavored sessions than in flavored-unflavored sessions.

Figure 5. Firing rate map cross-correlations. (a) Firing rate maps and cross-correlograms are plotted for four neurons recorded in flavored-flavored sessions (left) and four neurons recorded during flavored-unflavored sessions (right). The maximum firing rate across both session periods is plotted near the upper left corner of the firing rate map. Neurons recorded during flavored-flavored sessions tend to show more similar representations across foraging periods, resulting in high correlation coefficients near the origin of spatial cross-correlograms. (b) The mean spatial cross-correlation between firing rate maps from the foraging periods of flavored-flavored sessions (left) indicated less similar representations than between the foraging periods of flavored-unflavored sessions (right). (c) Cross-correlation values of the average correlograms are plotted as a function of the total shift distance. At small shifts, the correlation coefficient is greater for flavored-flavored sessions than for flavored-unflavored sessions, suggesting that representations were more similar between the two foraging periods of the former session type.

Figure 6. Temporal correlations. (a) Firing rate maps and correlograms are plotted for four OFC neurons recorded during flavored-flavored sessions (left column), and four neurons recorded during flavored-unflavored sessions (right column). The maximum firing rate across both session periods is plotted near the upper left corner of the firing rate map. Correlograms were constructed by computing firing rate maps in sliding windows (window size = 6 minutes, step size = 3.5 minutes), and taking the correlation between all pairs of rate maps. (b) Mean correlograms were constructed by averaging over all OFC neurons recorded during flavored-flavored sessions and flavored-unflavored sessions. (c) Within context correlations were similarly strong for cells recorded in flavored-flavored and flavored-unflavored sessions. The between-context correlation was significantly stronger for neurons recorded during flavored-flavored sessions. Error bars indicated standard error of the mean.

Figure 7. Lack of grid-like representations in OFC neurons. (a) We computed gridness scores for OFC neurons recorded in non-switch sessions (left), and separately for flavored (middle) and unflavored (right) portions of flavored-unflavored sessions. Cells were considered to have significant grid tuning if their gridness score exceeded the score computed for 95% of their randomly-shuffled spike trains. Cells that passed this statistical test are plotted with blue dots. Generally, grid tuning was sparse under all behavioral conditions. (b) Examples of OFC neurons with significant grid tuning are plotted. For each neuron, the firing rate map (left column), and the firing rate map autocorrelation (middle column) were computed. The gridness score was computed based on the strength of correlation between the actual rate map and the rotated rate map (right column). Grid cells are expected to show high correlation values at

915 rotations of 60 and 120 degrees and low values at 30, 90, and 150 degrees. Cells' maximum
916 firing rate is plotted below each rate map. The color scale on autocorrelograms ranges from -0.5
917 to 0.75.

918 **Figure 8. Comparison of hippocampal spatial tuning.** (a) The log spatial information score
919 for each hippocampal neuron is plotted against the mean spatial information score averaged
920 over 500 random shuffles. Neurons plotted with black dots met the statistical criterion for
921 significant spatial information. Compare with OFC data in figure 3a. (b) Firing rate maps for two
922 hippocampal neurons show stable spatial tuning over a 30-minute interval. Compare with OFC
923 examples in figure 3b-e. (c) The mean cross-correlogram of hippocampal neuron rate maps
924 computed from the first and second portions of recording sessions. (d) Cross-correlation
925 strength was greatest for small shifts, indicating stable representations across the first and
926 second portions of recording sessions. Compare with OFC data in figure 5a-b. (e) Firing rate
927 maps were computed in sliding time bins for hippocampal neurons (as for OFC data in figure 6)
928 and the correlation was computed for all pairs of rate maps. Note the high correlation values
929 both along and off the diagonal, indicating stable representations over time. (f) Average
930 correlation strength was high both for rate maps from the same half of the recording session
931 ('within context') and for rate maps from different halves of the recording session ('between
932 context').

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