Supplementary Information: The effect of face patch microstimulation on perception of faces and objects

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Supplementary Text, Experiment 6: Bilateral stimulation

We performed an experiment in M1 during which we not only stimulated during both cues in the face patch AM, but did so in both hemispheres simultaneously (Suppl. Fig. 9a, top row, shows an MR image of both electrode trajectories into the two AM patches). We reasoned that this would make the representation of the face during cues 1 and 2 maximally uniform across the entire brain (by negating any possibilities for comparison of face representation in the stimulated with that in the non-stimulated hemisphere), and thereby potentially lead to a reversal in the direction of the effect (i.e., rendering different faces more similar). The two sessions presented in Suppl. Fig. 9a & b show that dual AM stimulation indeed resulted in an increased report of “sameness” (see the middle row: microstimulation increased the performance in same identity trials and decreased the performance in different identity trials, opposite to what we observed in Experiments 1 to 5). This further shows that microstimulation can have a metrically reproducible effect on the percept of a face, instead of distorting it in an arbitrary unpredictable way.

Supplementary Methods, Estimation of the spatial extent of microstimulation

In the experiments reported in this study we electrically stimulated macaque cortex with stimulation currents from 50 to 300 µA. While it seems relatively straightforward to expect that the amount of recruited neurons will increase with the stimulation current, it is much harder to actually estimate the extent of cortical microstimulation at each current level.

At the low end Murphey and Maunsell showed that macaques are able to detect electrical microstimulation trains (similar in parameters to the ones used in the present study) in IT cortex with stimulation currents as little as 5µA, with median detection thresholds around 10 µA and almost perfect performance at 25 µA [1]. They employed a two alternative forced choice task in which the animals had to report which of two sequential epochs (temporally defined by two separate tones) was paired with a microstimulation event. This indicates that the current level we used fall into the well perceived range.

Histed et al. (2009) used two-photon *in-vivo* calcium imaging in rat and cat cortex to elucidate how electrical microstimulation recruits neurons during low current stimulation events [2]. They show that electrical microstimulation with threshold currents (<= 10 µA) typically recruited more than one neuron at once; given that this study only measured calcium signal in one plane instead of the volume this in all likelihood underestimated the number of excited neurons. Interestingly the stimulation does not recruit those cell bodies closest to the electrode first, but rather diffusely cells with up to several 100 µm distance to the electrode tip. This seems to be caused by supra-threshold activation mainly of axons close to the electrode tip, while extracellular electrodes mainly record activity from the cell soma [3]. The corollary of this seems to be that at least low current microstimulation through extracellular electrodes will not recruit those neurons that where recorded through the same electrode even at the identical site. Short of juxtacellular or nano-stimulation it seems extracellular electrodes will not allow stimulation of individual characterized neurons at all [4]. One consequence of this seems to be that stimulation results as those of Murphey and Maunsell are most likely not mediated by exciting single neurons, but small ensembles.

At higher currents Histed et al. report a gradual filling-in of the stimulated volume with more and more neurons being recruited, but since they only tested current up to 30 µA their data does not overlap the larger current range used in the current study.

At higher stimulation currents what cortical volume is recruited by different stimulation currents? Stoney et al. showed that, assuming spherical current spread around the stimulation electrode, the radius of the excited sphere follows approximately the following formula:[5]

$$Distance\ [mm] = \sqrt[2]{\frac{Current\ [\mu A]}{Current - Distance - Constant\ k\ [\mu A/mm^2]}}$$

The current-distance-constant *k* determines the inverse "excitability" of the neurons in that sphere, neurons with a lower k will be stimulated from a larger distance; for cat cortex k ranges from 272 to 3460 with a mean of 1292 µA/mm^2. This approximation seems partly at odds with Histed et al.'s modern view of filling-in a volume[2] defined by the lateral connections of the specific area of cortex stimulated. If one interprets Stoney et al.'s *k* as a property of all neuronal processes and not simply of the initial axon segments at the neuron's somata, this discrepancy disappears. Since the *k's* of the stimulated sites in this study are not known we will use the minimum, mean, and maximum numbers reported by Stonet et al. to generate a range estimate of the volume of excited cortex for the different current amplitudes used in the current study. Supplementary Methods Table 1 shows the estimated activated cortical spread for the three different *k's*.

Current [µA]	low-k [µA/mm^2]	mean-k [µA/mm^2]	high-k [µA/mm^2]	radius low-k [mm]	radius mean-k [mm]	radius high-k [mm]
50	272	1292	3460	0.428746463	0.196722369	0.120211759
100	272	1292	3460	0.606339063	0.278207442	0.1700051
200	272	1292	3460	0.857492926	0.393444738	0.240423518

300	272	1292	3460	1.050210063	0.481869425	0.294457471

Supplementary Methods Table 1: Estimated radial spread of excitation inside the cortex for different distance-current constants *k*.

Collins et al. showed in PFA-perfused primates that different cortical areas have a different density of neurons per mass of cortical matter[6] while Beckmann et al. measured the density of PFA-perfused cortex to have a mean of 0.992 g/cm^3 [7]. Roughly selecting the face patch positions from Fig 1a) and extracting the neuron density by weight from Collins et al. Fig 2 and using Beckmann's conversion factor yields the neuronal density estimates in Supplementary Methods Table 2

Patch	Neuron density [millions/gram]	Neuron density [neurons/mm^3]
ML	91	90272
MF	85	84320
outFP	63	62496
AL	58	57536
AF	63	62496
AM	46	45632

Supplementary Methods Table 2: Neuronal densities of the six different stimulation sites.

The best estimate of how many neurons were excited per stimulation site now can be determined by calculating the volumes of the excited spheres for the three different k-values at the 4 current amplitudes from Supplementary Methods Table 1, and multiplying them with the neuronal densities at the 6 different stimulation sites from Supplementary Methods Table 2; the results of these operations are shown in Supplementary Methods Table 3.

Current		**Stimulation site**					
[µA]	**k**	**ML**	**MF**	**outFP**	**AL**	**AF**	**AM**
50	**low**	29801.9	27836.9	20632.1	18994.6	20632.1	15064.7
	mean	2878.7	2688.9	1993.0	1834.8	1993.0	1455.2
	high	656.9	613.6	454.8	418.7	454.8	332.0
100	**low**	84292.4	78734.6	58356.3	53724.8	58356.3	42609.3
	mean	8142.3	7605.5	5637.0	5189.6	5637.0	4115.9
	high	1857.9	1735.4	1286.3	1184.2	1286.3	939.2
200	**low**	238414.9	222695.2	165056.4	151956.7	165056.4	120517.4
	mean	23029.9	21511.5	15943.8	14678.4	15943.8	11641.5
	high	5255.0	4908.5	3638.1	3349.3	3638.1	2656.4
300	**low**	437996.1	409117.2	303228.0	279162.3	303228.0	221404.6
	mean	42308.7	39519.1	29290.6	26966.0	29290.6	21386.8
	high	9654.0	9017.5	6683.6	6153.1	6683.6	4880.1

Supplementary Methods Table 3: Estimated number of neurons stimulated per stimulation site, stimulation current, and different values of excitability.

Even at the stimulation site with the lowest neuron density and with the lowest stimulation current used, we estimate that we drove at least a few of hundred neurons (high k); with a less conservative excitability assumption (mean k) we estimate that we drove roughly 1500- 2900 neurons. At the more commonly used currents of 200 and 300 µA we conservatively estimate that we drove at least a few thousand and up to several tens of thousands of neurons.

References

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