Supplementary Information

Infrared neural stimulation with 7T fMRI: a rapid in vivo method for mapping cortical connections of primate amygdala

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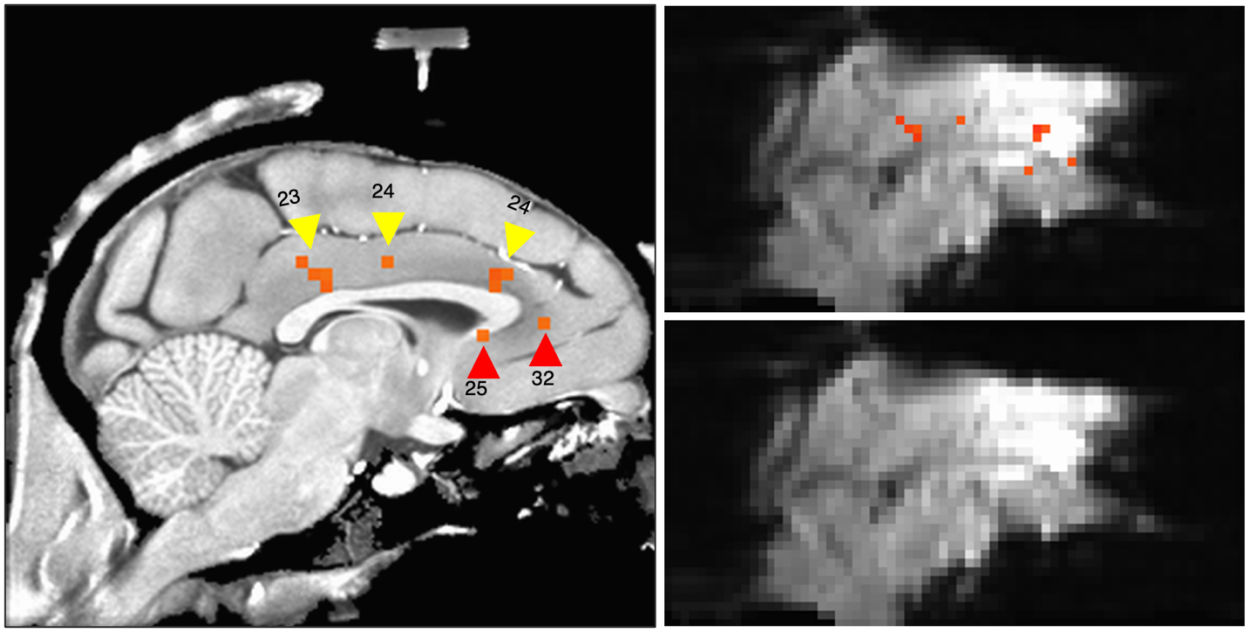
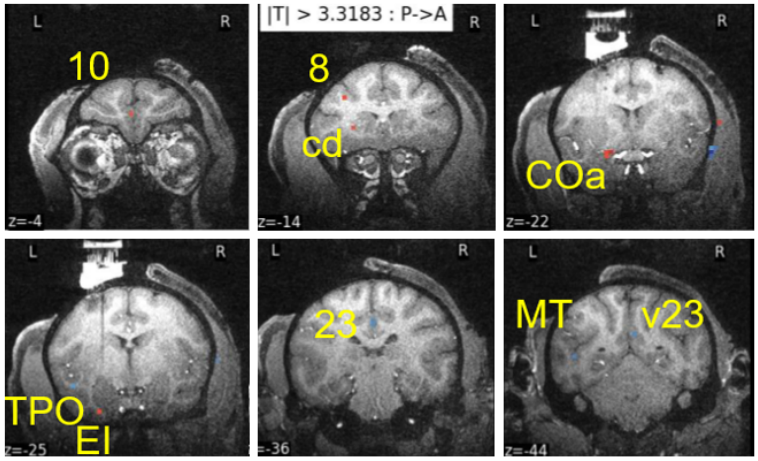
Supplementary Figure 1: No EPI ghosting



This figure addresses the concern that ghosting (e.g. N/2 N/4 ghosting...) may induce artificial repetitive patterns and thereby contribute to the patchy activations in cingulate. Here, we show that the functional EPI images do not display ghosting artifacts. In the figure above, significant voxels overlaid on structural image in panel A, and on functional EPI image in panel B. The same EPI slice is shown again on panel C without overlay of activation. One can see from panel C that the original EPI image does not display ghosting effect in cingulate cortex. Furthermore, N/2 N/4 ghosting exhibits artifacts with much lower spatial frequencies that are unlike the patchy profile patterns. Also, the signal intensities of ghosting voxels are usually much lower than normal ones, which make them hard to detect as significant BOLD activations.

Supplementary Figure 2: Control stimulation site, putamen



To support the specificity of the activation pattern following stimulation of basal nucleus of the amygdala, we present one example of a control stimulation outside the amygdala. In one of the penetrations, we stimulated putamen. Shown are all the slices containing activated voxels ($P<0.001$). Activated sites include: prefrontal 8, 10, possible COa (anterior cortical nucleus of amygdala or substantia innominata), caudate, temporal TPO, entorhinal EI, cingulate 23, and MT. No voxels were observed in the lateral sulcus and only one in the cingulate.

Supplementary Analysis 1: Significance of activation in insula & lateral sulcus

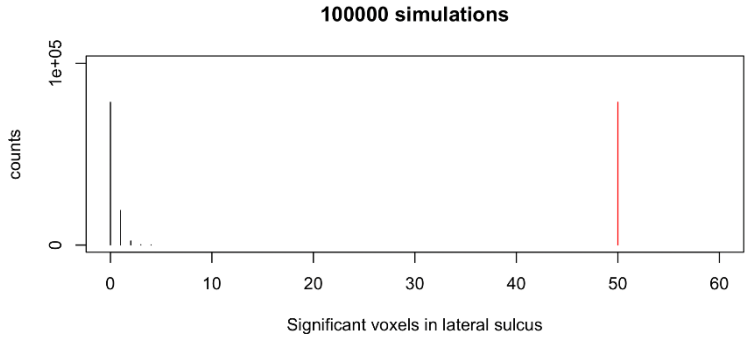
It is known that insula and amygdala are functionally similar, both involved in social and emotional behaviors. Anatomical tracer studies also showed that there are widespread reciprocal connections between them. Consistent with the literatures, our stimulation in basal nucleus of amygdala also resulted in activation in insula and lateral sulcus. Here, we evaluate the probability to observe this connection by chance. We found that these connections are highly unlikely to be random.

In a single scan, there are 36,030 voxels in a single EPI image, and 222,912 voxels in the entire monkey brain. When stimulating site 30, we got 70 significant voxels (p-value 0.001) responding to INS, with a majority of these voxels (50 voxels) located in the lateral sulcus (See figure below). This suggests a striking enrichment of significant voxels solely in lateral sulcus. Therefore, we performed both Fisher's exact test and a simulation test to estimate the probability for a such enrichment.

In the Fisher's exact test, we found that voxel significance and location in the lateral sulcus are independent events (p-value < 2.2e-16, odds ratio 764). In other words, there is an enrichment of significant voxels in the lateral sulcus (defined here as a combination of brain regions CM, RM, R, SII, Ig, Id, Ri, 7op, A1, AL), resulting in 771 voxels within the lateral sulcus.

	in lateral sulcus	not in lateral sulcus	total
significant voxels	50	20	70
non-significant voxels	721	222121	222842
total	771	222141	222912

In the simulation test, we randomly sampled 70 significant voxels over the whole brain, and then counted the number of significant voxels located in lateral sulcus. We repeated this for 100,000 simulations (See figure below). We found that in most of the simulations (79%), there were no significant voxels located in the lateral sulcus. In some simulations (19%), we found only 1 significant voxel in the lateral sulcus. None of the random samplings resulted in 50 voxels in lateral sulcus. We therefore conclude that the probability for our enrichment of 71% (50 out of 70) significant voxels in lateral sulcus is virtually 0 by chance.



Appendix A: References for figure 1

General Cortico-amygdala connections
(D. G. Amaral & Price, 1984)

(Turner, Mishkin, & Knapp, 1980)

(Van Hoesen, 1981)

(Stefanacci & Amaral, 2002)

Striate visual cortex
(D. G. Amaral, Behniea, & Kelly, 2003)

(Tigges et al., 1982)

(Mizuno et al., 1981)

(Iwai & Yukie, 1987)

Extrastriate visual cortex
(Webster, Ungerleider, & Bachevalier, 1991)

(Grimaldi, Saleem, & Tsao, 2016)

(Saleem, Miller, & Price, 2014)

(Saleem, Kondo, & Price, 2008)

(D. G. Amaral et al., 2003)

Perirhinal, entorhinal, temporal pole
(Insausti, Amaral, & Cowan, 1987)

(Morán, Mufson, & Mesulam, 1987)

(Stefanacci, Suzuki, & Amaral, 1996)

Insula
(Mufson, Mesulam, & Pandya, 1981)

(Jezzini et al., 2015)

(Evrard, 2019)

Cingulate and prefrontal cortex
(Vogt & Pandya, 1987)

(Morecraft et al., 2007)

(Morecraft & van Hoesen, 1992)

(Sharma, Kelly, Pfeifer, & Fudge, 2020)

(Porrino, Crane, & Goldman-Rakic, 1981)

(Ghashghaei & Barbas, 2002)

(D. Amaral, Price, Pitkanen, & Carmichael, 1992)

(Barbas & De Olmos, 1990)

(Carmichael & Price, 1995)

Auditory Association cortex

(Yukie, 2002)

(Kosmal & Kowalska, 1997)

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