Specificity of An Amygdala-Prefrontal Projection for Integrating Emotional and Sensory Information in the Macaque

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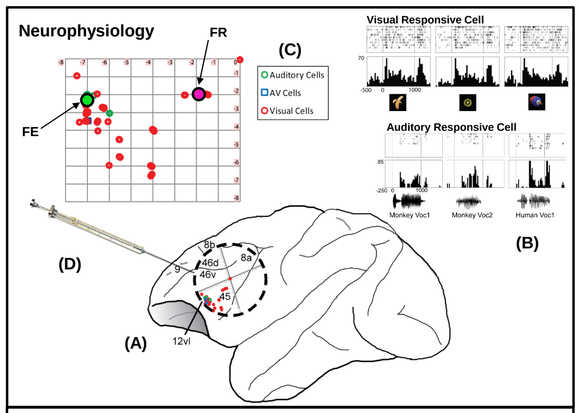
Introduction

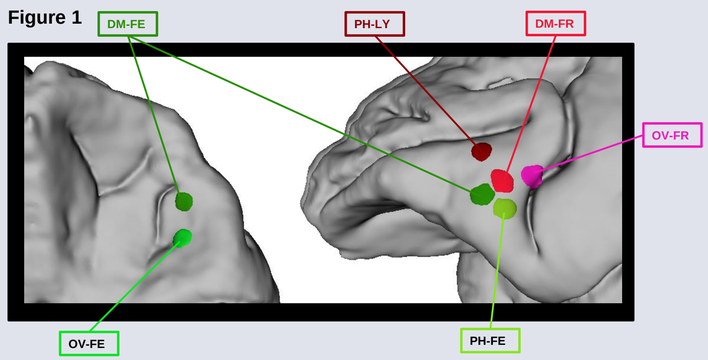
Neurons responsive to auditory, visual, and multisensory information are found in subregions of the ventrolateral prefrontal cortex (VLPFC). These neurons encode and integrate sensory information in complex, non-linear ways (1). The amygdala is also responsive to sensory stimuli, such as faces and voices, (2,3) and neurons in this region encode emotional and social variables during facial processing (4,5). Thus, both regions are poised to play a key role in processing salient, socially relevant, sensory information. In the current study we determined which specific subregions of the amygdala were connected with regions of VLPFC responsive to auditory and visual information including face and vocal stimuli. Our results demonstrate that sites within the VLPFC that are responsive to auditory or visual information receive input specifically from the intermediate division of the basal nucleus (Bi), of the amygdala. This pathway may support the integration of emotional and sensory information within the VLPFC.

Methods

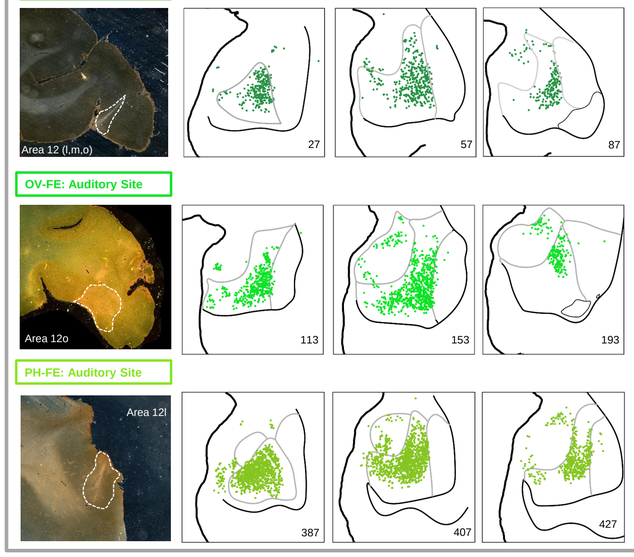


(A) Recording cylinders were implanted overlying VLPFC, in 3 Rhesus macaques. The cylinders were targeted to areas 12/47 and 45 in order to record auditory, visual, and multisensory responsive cells as previously published (1,6,7). The core task performed by all subjects in this study was a presentation task in which subjects fixated a central point and were presented with a 1 sec auditory, visual, or audiovisual stimulus. **(B)** Cells with selective responses for visual stimuli, auditory stimuli, or both (multisensory) were identified by their response profiles during presentation of lists of various visual or auditory stimuli. **(C)** Sites with responsive cells were plotted into a chamber grid and **(D)** fluorescent and dextran conjugated fluorescent (bi-directional) tracers were placed at these sites. **(E)** Maps of retrograde cell bodies in the ventrolateral prefrontal cortex were constructed by combining Neurolucida mapping of DAB stained sections with adjacent Nissl stained sections, to delineate amygdala nuclei. **(F)** Injection site surface maps were created by delineating injections sites in DAB stained prefrontal sections, marking comparable slices in the D99 single subject macaque atlas space (8), and rendering surface representations in 3D Slicer. **(G)** Using complimentary neuronal tracer microinjections placed in the amygdala, anterograde fibers in the VLPFC were identified or deemed absent by microscopic inspection under darkfield. **(H)** A "common zone" of labeling was constructed by manually delineating groups of cells within a middle section of the amygdala from all 6 injections and overlaying the sections (schematic and not quantitative).

Results

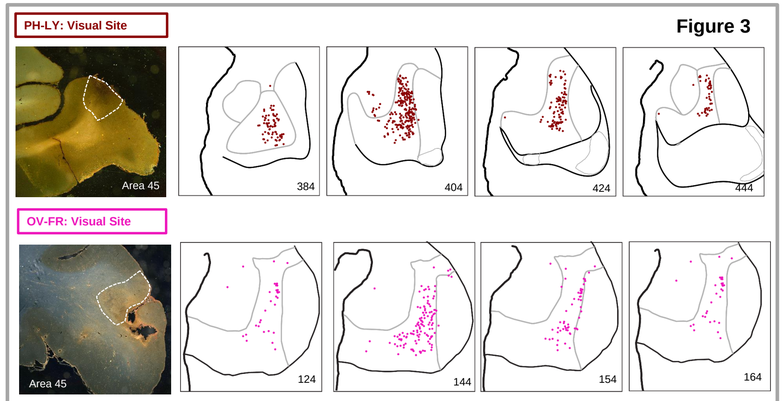


Injections sites in the VLPFC from tracers placed at sites with selective responses to auditory and/or visual stimuli. Injection sites were placed into areas 12 lateral, 12 orbital and 45 of the VLPFC in the inferior convexity of the frontal lobe (ie. OV-FE = Subject OV; Tracer used = Fluoro-Emerald). FE = Fluoro-Emerald; FR = Fluoro-Ruby; LY = Lucifer Yellow. Injection sites were placed in the D99 Macaque Atlas space and represent the center of the injection extrapolated to the surface of the brain (when necessary).

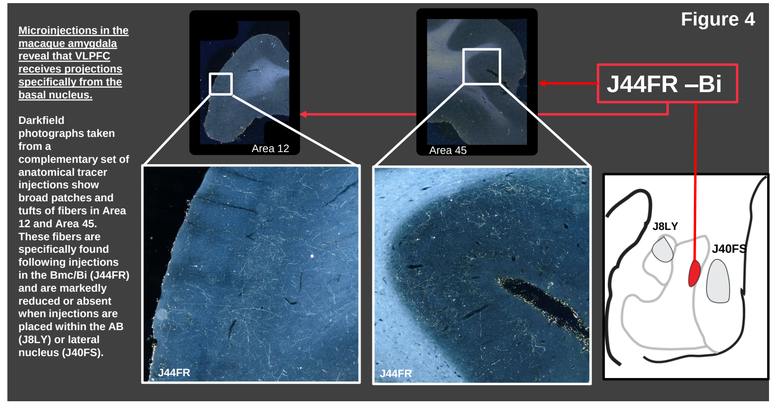


Injections in inferior and orbital VLPFC have robust input from the basal nucleus of the amygdala.

Injections of FE were placed at sites in the VLPFC where neurophysiology recordings identified cells specifically responsive to auditory stimuli with selectivity for vocalizations. Retrograde labeling was found mainly within the basal nucleus of the amygdala and portions of the accessory basal nucleus.



Injections in dorsocaudal VLPFC receive inputs from the basal nucleus. Injections of FR and LY in sites in the VLPFC where neurophysiology recordings identified cells with responses to visual stimuli. One injection (DM-FR) was placed at a site where cells responded to auditory and visual stimuli (multisensory site). Retrograde labeling was highly restricted to the basal nucleus in a similar region to the labeling in the anterolateral region.

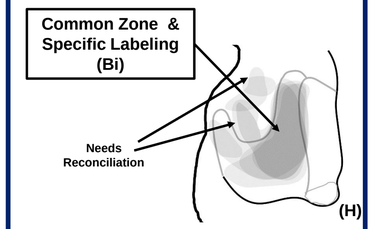


Microinjections in the macaque amygdala reveal that VLPFC receives projections specifically from the basal nucleus.

Darkfield photographs taken from a complementary set of anatomical tracer injections show broad patches and tufts of fibers in Area 12 and Area 45. These fibers are specifically found following injections in the Bmc/Bi (J44FR) and are markedly reduced or absent when injections are placed within the AB (J8LY) or lateral nucleus (J40FS).

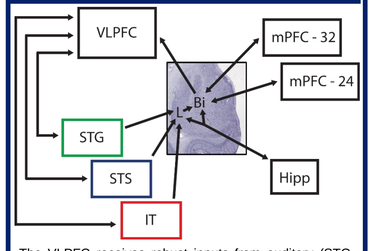
Conclusions

The Intermediate Division of the Basal Nucleus (Bi) is a common source of input to sensory VLPFC



An overlay of the cell groups found across all 6 cases identifies a Common Zone of retrograde labeling within the basal nucleus. This region closely approximates the boarders of the intermediate division of the basal nucleus (Bi) (9). This specificity to the Bi is corroborated by anterograde fiber labeling in the VLPFC after microinjections in across amygdala nuclei.

A Microcircuit for Sensory-Emotional Integration



The VLPFC receives robust inputs from auditory (STG, superior temporal gyrus), visual (IT, inferotemporal cortex) and multisensory (STS, superior temporal sulcus) processing regions in the temporal lobe (10). The amygdala, specifically the Bi, is interconnected with medal prefrontal area (25 & 32) implicated in social monitoring and salience detection (11) as well as the hippocampus (9). Therefore, the Bi may convey socio-emotional and contextual information to the VLPFC, where it can be integrated with incoming sensory information to identify and interpret social cues.

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Acknowledgments

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