SUPPLEMENTAL METHODS FOR:

Multiple routes of communication within the amygdala-mPFC network: a comparative approach in humans and macaques

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The objective of the review was to identify potential homologies and differences in the network formed by the Amygdala (AMG) and medial prefrontal cortex (mPFC) between humans and macaques using anatomical and functional (i.e., resting-state fMRI) data. This analysis is based on a search in the Pubmed database using a combination of keywords in the advanced search builder.

Amygdala and nuclei volumes in humans, chimpanzees and macaques.

Selected studies.

We selected studies including the whole AMG volume and the volume of the main nuclei (namely, lateral, basal, accessory basal and central) in the three species. Importantly, given our aim to compare volumes between humans and non-human primate species (macaque, chimpanzee), we focused on 'ex-vivo' histological studies to ensure a similar quantification method between the 3 species. We excluded MRI volumetry studies from the present review given their scarcity in NHP and their inherently limited spatial resolution to access the details of the AMG nuclei in the 3 species compared to 'ex-vivo' histological studies.

We used a combination of keywords with Title/Abstract query box containing one or multiple of the following search terms: "Amygdala", "Amygdaloid complex", "Amygdala nuclei", "Volume", Volumetric", "Stereological", "Post-mortem", "Ex-vivo" without any criterion regarding the dates of the studies. We also included "Primate", "Macaque" or "Chimpanzee". For macaques, we only included studies with rhesus macaque to avoid any interspecies differences and because this model is the most commonly used in cognitive neurosciences and notably in functional neuroimaging studies.

For the 3 species, we therefore selected ex-vivo stereological studies that specifically reported the volumes of the entire AMG and AMG main nuclei, as well as parameters such as the mean volume, standard deviation and sample size.

Computation of the confidence interval at 95%. Using the R software, we calculated the 95% confidence intervals around the mean of each study and specie:

$$CI = \underline{x} \pm t_{n-1,1-\alpha/2} \times \frac{s_x}{\sqrt{n}}$$

$\underline{x}$ = mean volume;

t= calculated t.scores for a T distribution with n-1 = degree of freedom and with a risk of 0.05 : $1 - \alpha/2$ = 0.975 ;

$\frac{s}{\sqrt{n}}$ = the standard error of the mean calculated by dividing the sd by the square root of the sample size.

Relative volume of amygdala nuclei. The relative volume of AMG nuclei refers to the volume occupied by each nucleus within the whole AMG. In that goal, among the selected studies, we further selected the ones that contain both whole AMG and nuclei volume. For each species, we calculated the relative volume by dividing the volume of each nucleus with the whole AMG volume that we expressed as a percentage.

Amygdala and amygdala subregions resting-state functional connectivity in humans. Selected studies. Similarly, to what we have done for the volumes, we proceeded with a combination of keywords in the Pubmed database with Title/Abstract query box including “amygdala” AND “medial prefrontal cortex” AND “resting-state”. We then carried out a second search replacing the item “amygdala” by “amygdala nuclei” OR “amygdala subregions/subdivisions” AND with “resting-state”. Finally, we also carried out a search using the following items “basolateral” or “laterobasal” as well as “centromedial” and “central” AND “resting-state”. In the context of this review, we only considered studies reporting amygdala subregions presenting a significant peak of correlation with mPFC in adult healthy humans excluding study with children, adolescent and older adults.

Studies processing. To assess the functional connectivity of AMG subdivisions (laterobasal and centromedial) with mPFC regions, we positioned each correlation with significant peaks extracted from our selected studies on a midsagittal section diagram of the brain. Correlation peaks coordinates were expressed in MNI coordinates and positioned accordingly. Peak localizations were identified in the different mPFC subdivisions: vmPFC, ACC, MCCa and MCCp (gyrus or sulcus) nomenclature, based on sulci landmarks defined by C.A. We also removed significant peaks that were out of range (e.g., located in the corpus callosum for example). Note that for a few studies we converted Talairach coordinates into MNI coordinates.

Tables

Table S1. **Summary of volumetric studies selected.**

Study	Species	Sample (n)	AMG & nuclei	Mean volume ± sd (mm^3)
(Schumann and Amaral 2005; Schumann and Amaral 2006; Avino et al. 2018)	Human	10	AMG	1380±114
			LA	452±43
			BL	342±30
			BM	152±16
			CE	34±6
(Berretta et al. 2007)		11	LA	243.01±67.25
			BL	151.37±51.04
			BM	69.58±41.7
(Amunts et al. 2005; Kedo et al. 2018)		7	AMG	1521±279
			LA	446±62
			BL	267±43.5
			BM	131±20
			CE	52±9.5
(García-Amado and Prensa 2012)		7	AMG	956±149
			LA	376±68
			BL	259±40
			BM	123±21
			CE	60±8
(Wegiel et al. 2014)		14	LA	367±13
			BL	211±8
			BM	138±6
			CE	20±1
(Rubinow et al. 2016)		10	LA	288±16.9
			BL	224±10.9
			BM	98±3.5
(Lew et al. 2018)		7	LA	362±102.9
			BL	266.3±90.08
			BM	109.5±30.96
			CE	25.12±7.37

(Barger et al. 2007)	Chimpanzee	3	AMG	657.5±77.20
		2	LA	126.25±14.50
			BL	212.25±38.54
			BM	72.18±9.02
(Stimpson et al. 2016)		7	AMG	851.3±150
			LA	177±42.7
			BL	245.9±59.7
			BM	103±11.6
			CE	48.6±17.7
(Emery et al. 2001)	Macaque *rhesus*	4	AMG	277.98±21.89
			LA	57.14±4.51
			BL	64.53±8.05
			BM	37.89±3.89
			CE	15.3±1.47
(Carlo et al. 2010)		4	AMG	161.26±18.74
			LA	34.23±5.08
			BL	42±6.12
			BM	19.97±1.73
			CE	9.59±2.02
(Chareyron et al. 2011; Chareyron et al. 2012)		5	AMG	192±6.26
			LA	38.4±3.57
			BL	47.15±2.67
			BM	24.38±2.14
			CE	8.15±1.44
(Villard et al. 2021)		10	AMG	178.85±17.81
			LA	33.32±4.95
			BL	39.49±5.83
			BM	23.10±1.30
			CE	4.70±0.70

***Table S2*. Functional connectivity peaks between AMG subdivisions and mPFC in each study.**

Studies	Protocol	Sample (n)	AMG Seeds	Parcellation Methodology	Hemisphere	mPFC regions coordinate (MNI) X	Y	Z	mPFC Region	Correlation sign
(Roy et al. 2009)	3T Eyes open 197 vol (1)(2)(3)	65	LB	SPM Anatomy Toolbox Probabilistic map	Right	4	40	-18	vmPFC	Positive
						6	24	28	aMCC gyrus	Negative
						-2	40	8	ACC	Negative
					Left	4	-28	26	PCC	Negative
						0	20	40	aMCC sulcus	Negative
						6	30	20	aMCC gyrus	Negative
						4	44	0	ACC	Negative
			CM		Right	8	8	34	aMCC gyrus	Positive
						-10	-12	40	pMCC sulcus	Positive
						0	52	-8	vmPFC	Negative
						0	34	-18	vmPFC	Negative
					Left	-4	22	26	aMCC gyrus	Positive
						-6	4	38	aMCC	Positive
(Tahmasian et al. 2013)	3T Eyes closed 300 vol (1)(2)	20	LB	SPM Anatomy Toolbox Probabilistic map	Right/Left	3	24	36	aMCC	Negative
(Coombs et al. 2014)	3T Eyes open 124 vol (1)(2)(3)	38	LB	SPM Anatomy Toolbox Probabilistic map	Right	5	31	38	aMCC	Negative
					Left	-6	23	-22	vmPFC	Negative
(Shao et al. 2014)	3T Eyes closed 189 vol (1)(2)	14	LB	SPM Anatomy Toolbox Probabilistic map	Right	5	49	16	ACC	Negative
			CM		Right	1	0	45	pMCC sulcus	Positive
(Nicholson et al. 2015)	3T Eyes closed 120 vol (1)(2)	40	LB	SPM Anatomy Toolbox Probabilistic map	Left	-4	-10	44	pMCC sulcus	Positive
						-6	12	40	aMCC sulcus	Positive
			CM		Left	-8	8	44	aMCC sulcus	Positive
						6	8	34	aMCC gyrus	Positive
						-4	6	38	aMCC gyrus	Positive
					Right	-4	12	36	aMCC sulcus	Positive
						6	8	46	aMCC sulcus	Positive
						-2	16	48	aMCC	Positive
						-4	18	44	aMCC	Positive
(Engman et al. 2016)	3T Eyes open	96	LB		Left	4	16	-22	vmPFC	Positive
						2	-4	40	pMCC gyrus	Positive

	124 vol (1)(2)(3)			SPM Anatomy Toolbox Probabilistic map	Right	8	30	36	aMCC	Negative
			CM		Left	4	6	40	aMCC gyrus	Positive
					Right	-12	4	44	aMCC sulcus	Positive
						6	-14	36	pMCC	Positive
(Kerestes et al. 2017)	3T Eyes close 260 vol (1)(2)	200	LB	SPM Anatomy Toolbox Probabilistic map	Left	2	48	-16	vmPFC	Positive
					Right	0	44	-18	vmPFC	Positive
(Caparelli et al. 2017)	HCP subject 3T Eyes open 1200 vol (1)(2)	100	LB	SPM Anatomy Toolbox Probabilistic map	Left	4	34	38	aMCC	Negative
						2	52	-16	vmPFC	Positive
						2	-22	30	PCC	Negative
						0	-26	28	PCC	Negative
			CM		Right	0	-4	48	pMCC	Positive
(Eckstein et al. 2017)	1.5T Eyes closed 110 vol (2)	52	LB	SPM Anatomy Toolbox Probabilistic map	Left	-2	26	44	aMCC	Negative
(Zhang et al. 2018)	7T Eyes closed 200 vol (1)(2)(3)	20	LB	SPM Anatomy Toolbox Probabilistic map & data-based clustering	Left	9	1.5	49.5	pMCC	Positive
						-9	-24	45	PCC	Positive
					Right	3	-13.5	42	pMCC gyrus	Positive
						3	-22.5	25.5	RSC	Negative
						-9	39	21	aMCC	Negative
						4.5	28.5	36	aMCC sulcus	Negative
			CM		Left	0	3	37.5	pMCC gyrus	Positive
						-1.5	24	16.5	aMCC gyrus	Positive
(Sylvester et al. 2020)	3T Eyes open 818 vol (1)(3)	10	LB	SPM Anatomy Toolbox Probabilistic map & data-based clustering	/	12.7	31.93	24.62	aMCC sulcus	Negative
						-10.4	31.64	22.57	aMCC sulcus	Negative
			CM		/	6.1	30.9	-11.1	vmPFC	Positive
						-7	40.4	-14.3	vmPFC	Positive
						12.6	25.3	31	aMCC – sulcus	Negative
						-11.6	29.3	25.4	aMCC sulcus	Negative
(Cao et al. 2022)	3T Eyes closed 200 vol (1)(2)	93	CM	SPM Anatomy Toolbox Probabilistic map & data-based clustering		9	-6	48	pMCC	Positive
			LB			9	-6	48	pMCC	Positive

(1) Motion parameters regression
(2) Cerebral Spinal Fluid (CSF) and White Matter (WM) regression
(3) Global signal regression

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