

3-dimensional reconstruction of the rat, monkey and human amygdala (rat: left; monkey: middle; human: right). Each amygdala nucleus has a different color (red: Lateral; orange: Basal; dark orange: paralaminar (in monkey only); blue: Accessory Basal; green: Central; pink: Medial). The medial nucleus in the human amygdala reconstruction is missing. The scale, represented by a gray cube, is different for the reconstruction in each species. Rat: 1 mm³; monkey: 2 mm³; human: 4 mm³.

3-dimensional reconstruction of the rat, monkey and human amygdala (rat: left; monkey: middle; human: right). Each amygdala nucleus has a different color (red: Lateral; orange: Basal; dark orange: paralaminar (in monkey only); blue: Accessory Basal; green: Central; pink: Medial). The medial nucleus in the human amygdala reconstruction is missing. The scale is the same for the three species, and is represented by the grey cube: 2 mm³.

RAT

Amygdala nucleus	Average number of sections	Distance between sections (μm)	Scan grid (random orientation) (μm)	Counting frame (μm)	Disector height (μm)	Guard zones (μm)	Average section thickness (μm)*	Average number of neurons counted	Average number of glia (astrocytes and oligodendrocytes) counted
Lateral	16	160	250 x 250	40 x 40	4	2	12.08 (range from 11.34 to 12.72)	250	171
Basal	16	160	250 x 250	40 x 40	4	2	13.32 (range from 12.50 to 14.30)	223	205
Accessory basal	9	160	200 x 200	40 x 40	4	2	10.99 (range from 10.62 to 11.23)	208	130
Central	11	160	230 x 230	40 x 40	4	2	11.14 (range from 9.84 to 11.89)	346	235
Medial	11	160	250 x 250	40 x 40	4	2	11.90 (range from 11.33 to 12.66)	407	224

MONKEY

Amygdala nucleus	Average number of sections	Distance between sections (μm)	Scan grid (random orientation) (μm)	Counting frame (μm)	Disector height (μm)	Guard zones (μm)	Average section thickness (μm)*	Average number of neurons counted	Average number of oligodendrocytes counted	Average number of astrocytes counted
Lateral	12	480	600 x 600	40 x 40	5	2	13.86 (range from 12.46 to 14.78)	321	226	211
Basal	11	480	600 x 600	40 x 40	5	2	14.00 (range from 12.62 to 14.83)	248	240	237
Paralaminar	13	480	250 x 250	20 x 20	5	2	12.86 (range from 11.98 to 13.61)	127	32	54
Accessory basal	11	480	475 x 475	40 x 40	5	2	13.67 (range from 12.29 to 14.90)	288	186	229
Central	9	480	300 x 300	40 x 40	5	2	12.80 (range from 12.03 to 13.20)	258	183	240
Medial	9	480	375 x 375	40 x 40	5	2	11.99 (range from 10.88 to 12.64)	169	62	140

*Section thickness was measured at every other counting site.

Neuron number

Species	Reference	Fixation	Subjects	L	B	AB	C	M	PL	Amygdala	Brain
Human	Schumann and Amaral (2005)	Imm - 10% FA	10	4'000'000	3'235'000	1'278'000	355'000			12'212'000	
	Kreczmanski et al. (2007)	Imm - 10 % FA / Celloidin	13	4'430'000							
	Berretta et al. (2007)	Imm - 4% PFA / Agar	12	2'068'000	1'239'000	596'000					
	Harding et al. (2002)	Imm - 15% FA / Paraffin	16	2'950'000	1'750'000						
	Vereecken et al. (1994)	Imm - FA 4% / Paraffin	6	2'982'000	2'285'000	1'079'500			1'051'500	10'225'500	
Monkey	Present study	Perf - 4% PFA	4	1'592'284	1'247'181	885'352	297'079	282'622	408'051		
	Carlo et al. (2009)	Perf - FA	4	1'500'000	1'460'000	728'000	406'000	342'000	396'000	6'460'000	
Rat	Present study	Perf - 4% PFA	4	117'486	115'774	57'017	127'174	188'742			
	Salm et al. (2004)	Perf - 4% PFA	8	22'000	20'000		32'000				
	Pêgo et al. (2008)	Perf - 4% PFA / GLY	6	85'000	88'000	96'000	100'000				
	Berdel et al. (1997)	Perf - 4% PFA	15	47'936	38'594						
	Tuunanen and Pitkänen (2000)	Perf - 4% PFA	5	60'193	47'522	29'871					
	Rubinow and Juraska (2008)	Perf - 4% PFA	16		128'000						
	Fan L (2008)	Perf - 4% PFA	9			124'000	177'000				
	Likhtik et al. (2008)	Perf - 4% PFA	11			37'949					

Glia number

Species	Reference	Fixation	Subjects	L	B	AB	C	M	PL	Amygdala	Brain
Monkey	Present study	Perf - 4% PFA	4	2'156'678	2'513'417	1'273'935	486'762	338'080	288'184		
Rat	Present study	Perf - 4% PFA	4	80'744	106'521	35'780	86'691	103'936			
	Salm et al. (2004)	Perf - 4% PFA	8	12'000	13'000		24'000				
	Rubinow and Juraska (2008)	Perf - 4% PFA	16		200'000						

Neuron density (cells/mm³)

Species	Reference	Fixation	Subjects	L	B	AB	C	M	PL	Amygdala	Brain
Human	Schumann and Amaral (2005)	Imm - 10% FA	10	8'852	9'440	8'419	10'472			8'851	
	Kreczmanski et al. (2007)	Imm - 10 % FA / Celloidin	13	10'800							
	Berretta et al. (2007)	Imm - 4% PFA	12	8'599	8'174	8'520					
	Harding et al. (2002)	Imm - 15% FA / Paraffin	16	3'471						14'158	
	Bowley et al. (2002)	-	10								
Monkey	Present study	Perf - 4% PFA	4	42'000	26'000	36'000	37'000	52'000	46'000	36'000	
	Carlo et al. (2009)	Perf - FA	4	43'783	34'762	36'455	46'936	65'267	63'360	40'060	
Rat	Present study	Perf - 4% PFA	4	99'000	96'000	92'000	130'000	152'000		115'000	
	Salm et al. (2004)	Perf - 4% PFA	8	54'000	31'000		72'000				
	Berdel et al. (1997)	Perf - 4% PFA	15	64'778	51'458						
	Rubinow and Juraska (2008)	Perf - 4% PFA	16		193'939						
	Fan L (2008)	Perf - 4% PFA	9			140'909	210'464				

Glia density (cells/mm³)

Species	Reference	Fixation	Subjects	L	B	AB	C	M	PL	Amygdala	Brain
Human	Hamidi et al. (2004)	-	10							59'569	
	Bowley et al. (2002)	-	10							73'150	
Monkey	Present study	Perf - 4% PFA	4	57'000	53'000	53'000	61'000	63'000	33'000	53'000	
Rat	Present study	Perf - 4% PFA	4	68'000	89'000	57'000	89'000	84'000		78'000	
	Salm et al. (2004)	Perf - 4% PFA	8	27'000	20'000		52'000				
	Rubinow and Juraska (2008)	Perf - 4% PFA	16	303'030							

Glia/neuron ratio

Species	Reference	Fixation	Subjects	L	B	AB	C	M	PL	Amygdala	Brain
Human	Bowley et al. (2002)	-	10							5.19	
	Bezchlibnyk et al. (2007)	Imm - 4% FA	15	2.50	3.04	2.83					
Monkey	Present study	Perf - 4% PFA	4	1.35	2.02	1.44	1.64	1.20	0.71	1.47	
Rat	Present study	Perf - 4% PFA	4	0.69	0.92	0.63	0.68	0.55		0.68	
	Salm et al. (2004)	Perf - 4% PFA	9	0.55	0.65		0.75				
	Rubinow and Juraska (2008)	Perf - 4% PFA	16		1.56						
	Morris et al. (2008)	Perf - 10% FA	10					0.71			

Volume (mm³)

Species	Reference	Fixation	Subjects	L	B	AB	C	M	PL	Amygdala	Brain
Human	Schumann and Amaral (2005)	Imm - 10% FA	10	452	343	152	34			1'380	
	Kreczmanski et al. (2007)	Imm - 10 % FA / Celloidin	13	414	227	60					
	Berretta et al. (2007)	Imm - 4% PFA / Agar	12	243	151	70					
	Harding et al. (2002)	Imm - 15% FA / Paraffin	16	850						1'820	1'307'000
	Barger et al. (2007) ¹	Imm - 4% FA / Paraffin	1	573	441	198				1'903	1'151'000
	Bielau et al. (2005)	Imm - 4% PFA / Paraplast	22							1'539	
	Brabec et al. (2010)	Imm - 2% FA	20							1'240	
	Chance et al. (2002)	Imm - FA / paraffin	18							630	1'063'000
	Present study	Perf - 4% PFA	4	38.40	47.15	24.38	8.15	5.42	8.84	192.60	52'360.00
Monkey	Carlo et al. (2009)	Perf - FA	4	34.26	42.00	19.97	8.65	5.24	6.25	161.26	
Rat	Present study	Perf - 4% PFA	4	1.19	1.20	0.63	1.00	1.28		10.62	994.00
	Salm et al. (2004)	Perf - 4% PFA	8	0.42	0.64		0.47				
	Pêgo et al. (2008)	Perf - 4% PFA / GLY	6	0.79	0.93	0.75	0.78				
	Berdel et al. (1997)	Perf - 4% PFA	15	0.74	0.75						
	Rubinow and Juraska (2008)	Perf - 4% PFA	16		0.66						
	Fan L (2008)	Perf - 4% PFA	9				0.88	0.84			
	Cooke et al. (2000)	Perf - 10% FA	12					1.67			

Neuron soma volume (μm^3)

Species	Reference	Fixation	Subjects	L	B	AB	C	M	PL	Amygdala	Brain
Human	Schumann and Amaral (2006)	Imm - 10% FA	10	3'099	3'245	3'393	1'893			2'762	
	Berretta et al. (2007)	Imm - 4% PFA	12	2'234	3'262	3'027					
	Aliashkevich et al. (2003)	Imm - 4% FA / paraffin	8	3'071	3'071						
	Bezchlibnyk et al. (2007)	Imm - 4% FA	15	5'000	6'000	5'250					
Monkey	Present study	Perf - 4% PFA	4	1'433	2'154	1'804	1'374	1'176	1'470		
Rat	Present study	Perf - 4% PFA	4	963	1'187	932	726	651			
	Berdel et al. (1997)	Perf - 4% PFA	15	1'120	1'753						
	Rubinow and Juraska (2008)	Perf - 4% PFA	4		1'817						
	Morris et al. (2008)	Perf - 10% FA	10				1'014				
	Ichikawa et al. (1993)	Perf - 2% GLA - 2% PFA	18					1'180			
	Cooke et al. (2000)	Perf - 10% FA	12					669			

¹ values calculated with correction factor

Imm: immersion fixation; Perf: perfusion fixation

FA: formalin; PFA: paraformaldehyde; GLA: Glutaraldehyde; GLY: Glycolmethacrylate

References

- Aliashkevich AF, Yilmazer-Hanke D, Van Roost D, Mundhenk B, Schramm J, Blumcke I. 2003. Cellular pathology of amygdala neurons in human temporal lobe epilepsy. *Acta Neuropathol* 106(2):99-106.
- Barger N, Stefanacci L, Semendeferi K. 2007. A comparative volumetric analysis of the amygdaloid complex and basolateral division in the human and ape brain. *Am J Phys Anthropol* 134(3):392-403.
- Berdel B, Morys J, Maciejewska B. 1997. Neuronal changes in the basolateral complex during development of the amygdala of the rat. *Int J Dev Neurosci* 15(6):755-765.
- Berretta S, Pantazopoulos H, Lange N. 2007. Neuron numbers and volume of the amygdala in subjects diagnosed with bipolar disorder or schizophrenia. *Biol Psychiatry* 62(8):884-893.
- Bezchlibnyk YB, Sun X, Wang JF, MacQueen GM, McEwen BS, Young LT. 2007. Neuron somal size is decreased in the lateral amygdalar nucleus of subjects with bipolar disorder. *J Psychiatry Neurosci* 32(3):203-210.
- Bielau H, Trubner K, Krell D, Agelink MW, Bernstein HG, Stauch R, Mawrin C, Danos P, Gerhard L, Bogerts B, Baumann B. 2005. Volume deficits of subcortical nuclei in mood disorders A postmortem study. *Eur Arch Psychiatry Clin Neurosci* 255(6):401-412.
- Bowley MP, Drevets WC, Ongur D, Price JL. 2002. Low glial numbers in the amygdala in major depressive disorder. *Biol Psychiatry* 52(5):404-412.
- Brabec J, Rulseh A, Hoyt B, Vizek M, Horinek D, Hort J, Petrovicky P. 2010. Volumetry of the human amygdala - an anatomical study. *Psychiatry Res* 182(1):67-72.
- Carlo CN, Stefanacci L, Semendeferi K, Stevens CF. 2009. Comparative analyses of the neuron numbers and volumes of the amygdaloid complex in old and new world primates. *J Comp Neurol* 518(8):1176-1198.
- Chance SA, Esiri MM, Crow TJ. 2002. Amygdala volume in schizophrenia: post-mortem study and review of magnetic resonance imaging findings. *Br J Psychiatry* 180:331-338.
- Cooke BM, Chowanadisai W, Breedlove SM. 2000. Post-weaning social isolation of male rats reduces the volume of the medial amygdala and leads to deficits in adult sexual behavior. *Behav Brain Res* 117(1-2):107-113.
- Fan L, Hanbury R, Pandey SC, Cohen RS. 2008. Dose and time effects of estrogen on expression of neuron-specific protein and cyclic AMP response element-binding protein and brain region volume in the medial amygdala of ovariectomized rats. *Neuroendocrinology* 88(2):111-126.
- Hamidi M, Drevets WC, Price JL. 2004. Glial reduction in amygdala in major depressive disorder is due to oligodendrocytes. *Biol Psychiatry* 55(6):563-569.
- Harding AJ, Stimson E, Henderson JM, Halliday GM. 2002. Clinical correlates of selective pathology in the amygdala of patients with Parkinson's disease. *Brain* 125(Pt 11):2431-2445.
- Ichikawa M, Matsuoka M, Mori Y. 1993. Effect of differential rearing on synapses and soma size in rat medial amygdaloid nucleus.

- Synapse 13(1):50-56.
- Kreczmanski P, Heinsen H, Mantua V, Woltersdorf F, Masson T, Ulfig N, Schmidt-Kastner R, Korr H, Steinbusch HW, Hof PR, Schmitz C. 2007. Volume, neuron density and total neuron number in five subcortical regions in schizophrenia. *Brain* 130(Pt 3):678-692.
- Likhtik E, Popa D, Apergis-Schoute J, Fidacaro GA, Pare D. 2008. Amygdala intercalated neurons are required for expression of fear extinction. *Nature* 454(7204):642-645.
- Morris JA, Jordan CL, Breedlove SM. 2008. Sexual dimorphism in neuronal number of the posterodorsal medial amygdala is independent of circulating androgens and regional volume in adult rats. *J Comp Neurol* 506(5):851-859.
- Pêgo JM, Morgado P, Pinto LG, Cerqueira JJ, Almeida OF, Sousa N. 2008. Dissociation of the morphological correlates of stress-induced anxiety and fear. *Eur J Neurosci* 27(6):1503-1516.
- Rubinow MJ, Juraska JM. 2008. Neuron and glia numbers in the basolateral nucleus of the amygdala from preweaning through old age in male and female rats: A stereological study. *J Comp Neurol* 512(6):717-725.
- Salm AK, Pavelko M, Krouse EM, Webster W, Kraszpulski M, Birkle DL. 2004. Lateral amygdaloid nucleus expansion in adult rats is associated with exposure to prenatal stress. *Brain Res Dev Brain Res* 148(2):159-167.
- Schumann CM, Amaral DG. 2005. Stereological estimation of the number of neurons in the human amygdaloid complex. *J Comp Neurol* 491(4):320-329.
- Schumann CM, Amaral DG. 2006. Stereological analysis of amygdala neuron number in autism. *J Neurosci* 26(29):7674-7679.
- Tuunanen J, Pitkänen A. 2000. Do seizures cause neuronal damage in rat amygdala kindling? *Epilepsy Res* 39(2):171-176.
- Vereecken TH, Vogels OJ, Nieuwenhuys R. 1994. Neuron loss and shrinkage in the amygdala in Alzheimer's disease. *Neurobiol Aging* 15(1):45-54.