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Anatomic heterogeneity of the rat amygdaloid complex*

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The amygdala is a nuclear complex composed of 13 nuclei and cortical areas and their subdivisions. Tract-tracing studies performed over the past 20 years demonstrate that each nucleus is uniquely connected with other brain areas. Consistent with anatomic heterogeneity, the functions of the amygdala vary from attention to memory to formation of emotional responses to sensory stimuli. Here, we briefly review the principles of amygdaloid neuronal wiring that underlie the computations necessary to perform such complex behavioural functions.

key words: amygdala, emotion, epilepsy, temporal lobe

THE AMYGDALA IS A NUCLEAR GROUP

The rat amygdala can be partitioned into 13 nuclei and cortical areas and their subdivisions based on cytoarchitectonic and chemoarchitectonic criteria [4, 96, 102]. Therefore, the term „amygdaloid complex" rather than „amygdala" has been adopted. Connectional studies with anterograde and retrograde neuronal tracers further support the idea of the heterogeneity of the amygdaloid complex by demonstrating that each of the amygdaloid nuclei differs from the others connectionally [4,95,102].

Consistent with anatomic heterogeneity, the amygdala is involved in a large number of different behavioural functions. One of the most commonly investigated functions of the rat amygdala is the generation of appropriate motor and autonomic responses to emotionally relevant sensory stimuli in a fear-conditioning paradigm [56]. In rats, the amygdala is also a critical structure to the fear-potentiated startle response [32], modulation of memory formation in the hippocampus [20] and attention [34]. In humans, imaging studies performed over the past 5 years have initiated a renaissance in amygdala research and provided a new insight into the amygdaloid functions. A classic study by Adolphs and co-workers [1] reported that patient S.M. who had Urbach-Wiethe disease, causing bilateral amygdaloid damage, was impaired in recognising fear in facial expressions. Since then, the human amygdala has also been demonstrated to be critically involved in the recognition of emotion in auditory [117] and olfactory stimuli [153], acquisition of conditioned autonomic responses to visual or auditory stimuli [7, 55], recognition of approachability and trustworthiness in facial expressions [2], perception of body movements [14], acquisition [19] and retrieval [104] of memories for emotionally-arousing events, processing of affective aspects of dreams [63] and discrimination of stimuli based on their acquired behavioural significance [77].

These studies raise the question: How is the amygdala wired with other brain regions to allow it to perform complicated tasks that help rats to encounter and survive a predator, or humans to cope with ongoing social signalling in everyday-life situations? How are computations performed within the intra-amygdaloid circuitries? We will briefly review the major aspects of the connectivity of the amygdaloid nuclei in rats. On the basis of the anatomic findings, we speculate about the potential consequences of nucleus-specific damage to the functioning of the amygdala.

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EACH AMYGDALOID NUCLEUS HAS A UNIQUE SET OF AFFERENT, INTRINSIC AND OUTPUT CONNECTIONS

Nomenclature

The amygdaloid complex is partitioned into various nuclei and cortical areas based on the nomenclature described by Price et al. [102] with modifications [41,96] (Table 1). Briefly, the **deep nuclei** include the lateral nucleus, basal nucleus and accessory basal nucleus. The **superficial nuclei** include the anterior cortical nucleus, bed nucleus of the accessory olfactory tract, medial nucleus, nucleus of the lateral olfactory tract, periamygdaloid cortex and posterior cortical nucleus. The **remaining nuclei** include the anterior amygdaloid area, central nucleus, amygdalohippocampal area and the intercalated nuclei. The location of the different amygdaloid regions is shown in Figure 1. Cortical areas are partitioned according to McDonald [69] and the other brain areas according to the atlas of Paxinos and Watson [89] (Fig. 2). In the description of afferent, intrinsic and efferent connectivity, only those projections that are described in the original publications as „moderate" or „heavy" in density are summarised. The inter-amygdaloid connections that are relatively prominent in rats are also described. Based on current knowledge, however, it is difficult to judge the density of each inter-amygdaloid connection. Connectivity of the intercalated nuclei and the anterior amygdaloid area has not yet been systematically investigated and therefore these areas are excluded from the present description. For a detailed description of connections, see Pitkänen [95].

Lateral nucleus

Projections to the lateral nucleus. The connectivity of the lateral nucleus is summarised in Figure 3. The lateral nucleus receives substantial projections from the sensory-related cortical areas including the visual, auditory, somatosensory and gustatory/viscerosensory cortices. The heaviest projections from the frontal lobe originate in the infralimbic region and dorsal agranular insula. Projections from the medial temporal lobe memory system originate in the perirhinal and entorhinal cortices as well as from the temporal (*i.e.*, ventral) end of the subiculum. Other major projections originate in the midline and auditory thalamus, some hypothalamic nuclei and dorsal raphe.

Intra-amygdaloid connections. The lateral nucleus receives substantial inputs from the basal, accessory basal and medial nuclei and the periamygdaloid cortex. The intra-amygdaloid pathways originating in the lateral nucleus are more widespread than those originating in any other amygdaloid nucleus.

Table 1. Amygdaloid nuclei and nuclear divisions

Deep nuclei	dorsal part (Mcd)
Lateral nucleus (L)	ventral part (Mcv)
dorsolateral division (Ldl)	caudal division (Mc)
ventrolateral division (Lvl)	Periamygdaloid cortex
medial division (Lm)	periamygdaloid cortex (PAC)
Basal nucleus (B)	periamygdaloid cortex, medial subfield (PACm)
magnocellular division (Bmc)	periamygdaloid cortex, sulcal subfield (PACs)
intermediate division (Bi)	Posterior cortical nucleus (COp)
parvicellular division (Bpc)	**Other amygdaloid areas**
Accessory basal nucleus (AB)	Anterior amygdaloid area (AAA)
magnocellular division (ABmc)	Central nucleus (CE)
parvicellular division (ABpc)	capsular division (CEc)
Superficial nuclei	lateral division (CEl)
Nucleus of the lateral olfactory tract (NLOT)	intermediate division (CEi)
Bed nucleus of the accessory olfactory tract (BAOT)	medial division (CEm)
Anterior cortical nucleus (COa)	Amygdalohippocampal area (AHA)
Medial nucleus (M)	medial division (AHAm)
rostral division (Mr)	lateral division (AHAl)
central division	Intercalated nuclei (I)

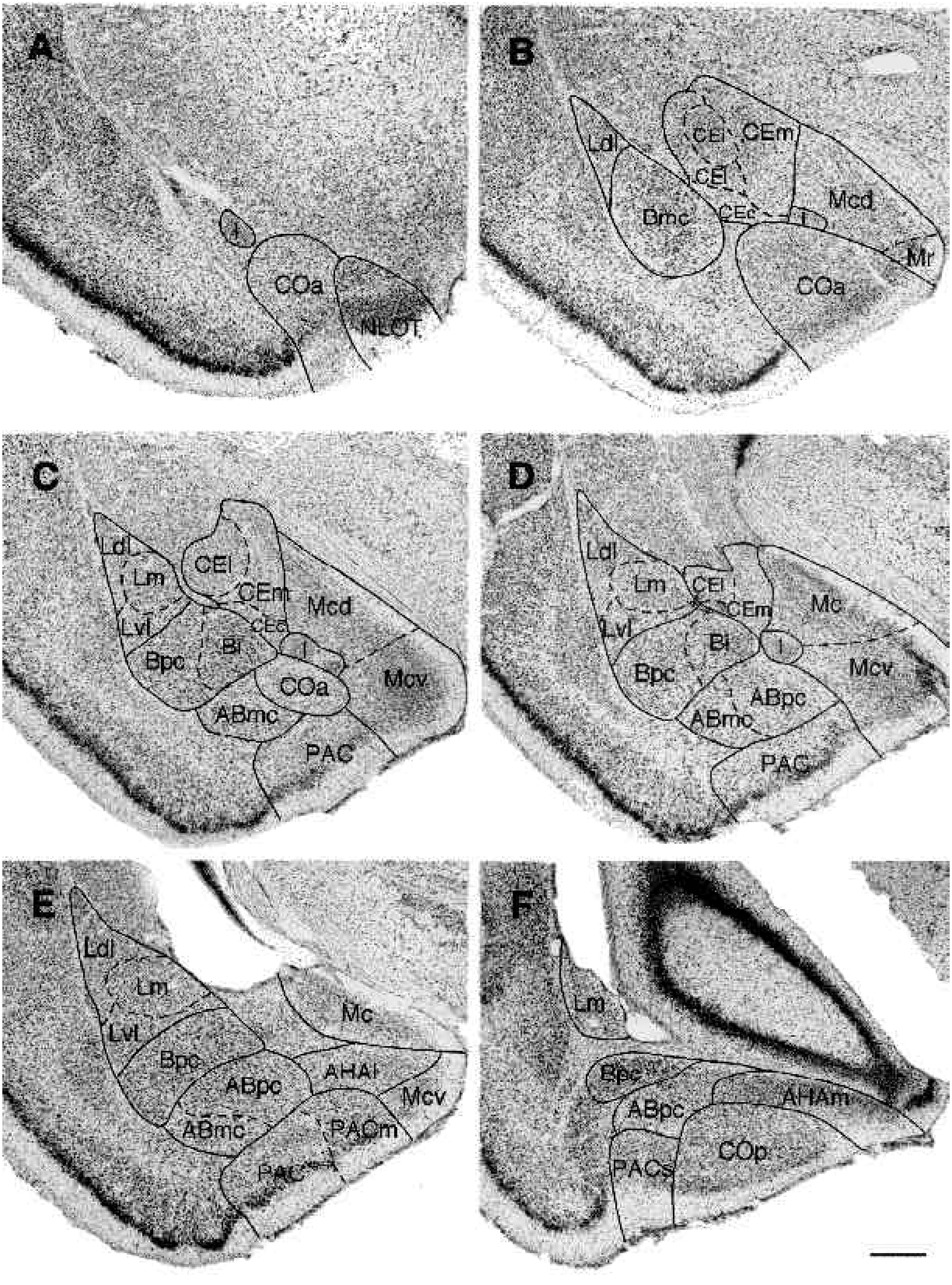


Figure 1. Brightfield photomicrographs from thionin-stained coronal sections of the rat amygdaloid complex showing the location of various amygdaloid nuclei and cortical areas and their subdivisions. Six rostrocaudal levels are presented (panel A is the most rostral and panel F the most caudal). Nuclear and divisional boundaries are indicated by continuous and dashed lines, respectively. For abbreviations, see Table 1. Scale bar equals 0.5 mm

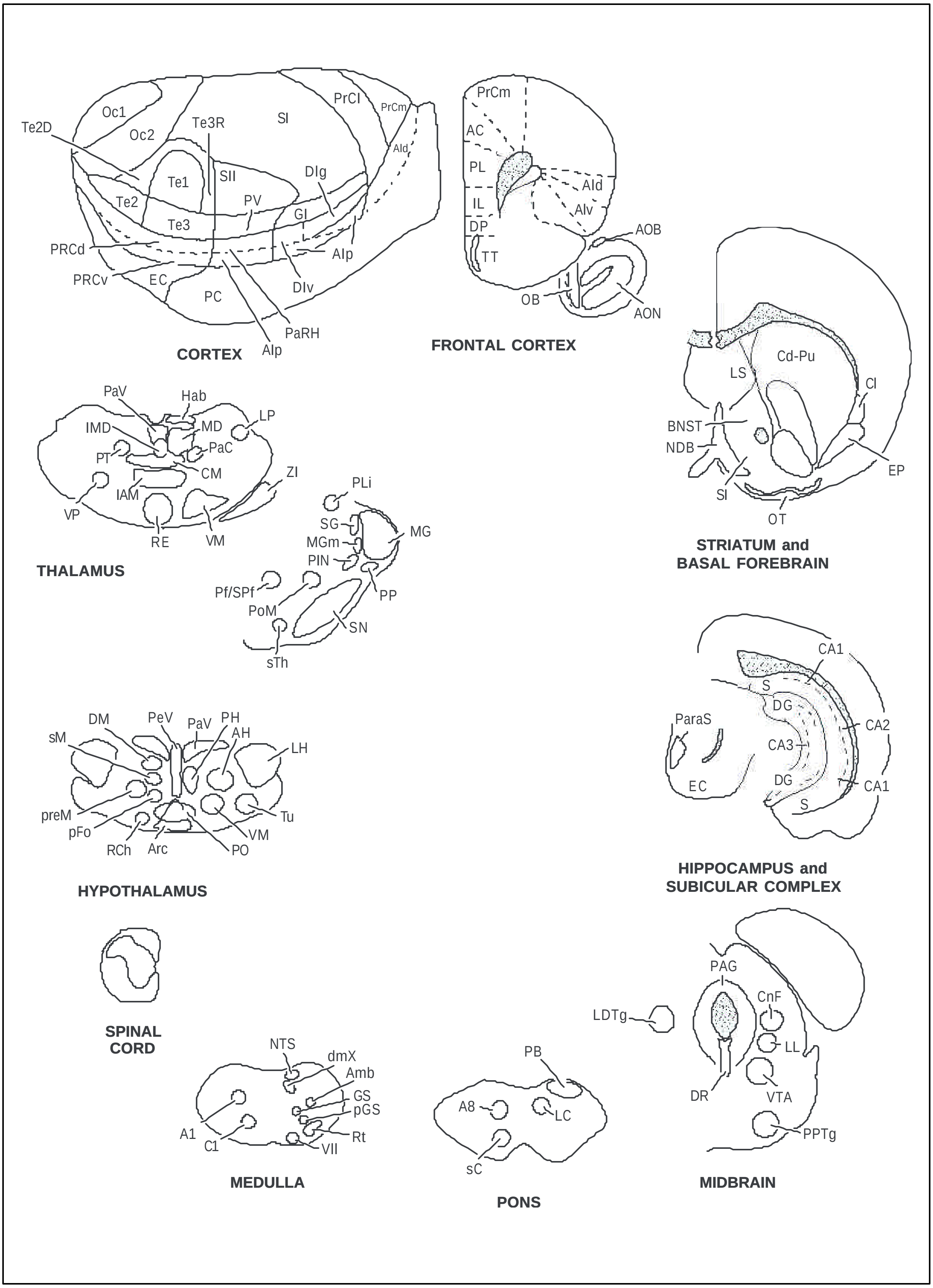


Figure 2. Schematic line-drawings describing the location of various brain areas used in the description of amygdaloid afferents and efferents in Figures 3 to 12. For the list of abbreviations, see Table 2 and for the list of references, see Table 3

CORTEX

Efferents: Te2D[12,18,20] Te2[6,12,18,19,21] Te3[12,16,17,18,19,21] PRCd[6,12,13,16,17,21] PRCv[6,12,16,21] EC[6,21,22,98] PaRH[12,33,114] DIv[12] AIp[6,12,13,84]

Afferents: PRCd[38,45] PRCv[45,89] EC[36,93,94] AIp[38]

FRONTAL CORTEX

Efferents: AId[12,13,35,84] IL[6,12,28,31,84]

Afferents: IL[37,42,46,66] AIv[46]

STRIATUM and BASAL FOREBRAIN

Efferents

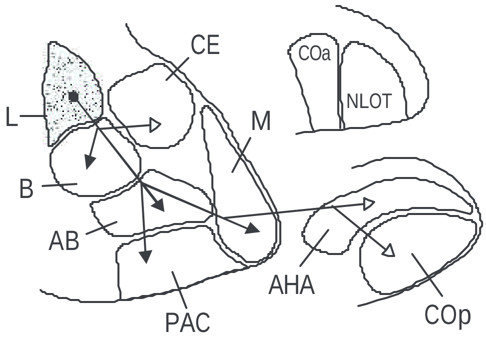
Afferents: Acc[30,40,83]

THALAMUS

Efferents: PaV[54,59,61] PIN[16,58,62,63] PP[53,58,63,120]

Afferents

LATERAL NUCLEUS



INTRINSIC CONNECTIONS

HIPPOCAMPUS and SUBICULUM

Efferents: S[6,12,24,25,27,119]

Afferents: ParaS[36]

HYPOTHALAMUS

Efferents: pFo[74] VM[67,73,] PH[113]

Afferents

MIDBRAIN

Efferents: DR[107,120]

Afferents

SPINAL CORD

MEDULLA

PONS

Figure 3. Afferent, intra-amygdaloid and efferent connections of the lateral nucleus. Only the moderate-to-heavy projections are indicated. In Figs. 3–12 closed arrow refers to a reciprocal connection and open arrow to an unidirectional projection

They terminate in the basal, accessory basal, medial, central and posterior cortical nuclei as well as in the periamygdaloid cortex and the amygdalohippocampal area. The lateral nucleus is not interconnected with the contralateral amygdala.

Projections from the lateral nucleus. Overall, the outputs originating in the lateral nucleus are not as widespread as the inputs. The heaviest projections to the sensory-related cortical areas terminate in the insular cortex. Within the frontal cortex, the infralimbic cortex and the ventral agranular insula receive a substantial input from the lateral nucleus. Amygdaloid outputs to the medial temporal lobe are directed to the perirhinal and entorhinal cortices as well as to the parasubiculum. Moderate-to-heavy projections to the nucleus accumbens have also been described.

Basal nucleus

Projections to the basal nucleus. The connectivity of the basal nucleus is summarised in Figure 4. Inputs to the basal nucleus from sensory related cortical areas are not as widespread as those to the lateral nucleus. There are moderate-to-heavy inputs from the dysgranular and agranular insula and the parietal rhinal cortex. In the frontal lobe, the prelimbic area and the dorsal agranular insula project substantially to the basal nucleus. Within the medial temporal lobe memory system, the basal nucleus receives inputs from the perirhinal cortex as well as from several levels of the hippocampal formation[1], including the entorhinal cortex, the temporal end of the CA1 and the subiculum. Other regions providing a moderate-to-heavy input to the basal nucleus include the paraventricular nucleus of the thalamus.

Intra-amygdaloid connections. The basal nucleus receives substantial intra-amygdaloid inputs from the lateral and anterior cortical nuclei. The basal nucleus projects to the lateral, central and anterior cortical nuclei as well as to the nucleus of the lateral olfactory tract and the amygdalohippocampal area. The basal nucleus projects to the contralateral basal nucleus as well as to the contralateral central nucleus, the nucleus of the lateral olfactory tract and the anterior amygdaloid area.

Projections from the basal nucleus. The basal nucleus projects to the infralimbic cortex in the prefrontal cortex. In addition, it provides substantial inputs to the hippocampal formation, including the entorhinal cortex, the temporal end of CA3 and CA1 subfields, the temporal subiculum and the parasubiculum. Heavy topographically-organised projections also terminate in the bed nucleus of the stria terminalis, caudate-putamen, nucleus accumbens, claustrum, substantia innominata and the olfactory tubercle.

Accessory basal nucleus

Projections to the accessory basal nucleus. The connectivity of the accessory basal nucleus is summarised in Figure 5. Sensory-related cortical areas that provide major inputs to the accessory basal nucleus include the agranular insula, the parietal rhinal cortex and the caudal piriform cortex. Within the prefrontal cortex, projections originate in the infralimbic cortex. Other major inputs originate in the medial temporal lobe memory system, including projections from the perirhinal and entorhinal cortices and the temporal end of the subiculum. Other projections originate in the paraventricular nucleus of the thalamus and the perifornical region of the hypothalamus.

Intra-amygdaloid connections. The accessory basal nucleus receives substantial inputs from the lateral and medial nuclei of the amygdala. In general, its intra-amygdaloid outputs appear more widespread than its inputs. The outputs terminate in the lateral, central, medial and posterior cortical nuclei as well as in the periamygdaloid cortex and the amygdalohippocampal area. Contralaterally, the accessory basal nucleus projects to the accessory basal and medial nuclei.

Projections from the accessory basal nucleus. The accessory basal nucleus provides substantial projections to the prefrontal cortex, particularly to the infralimbic cortex. It also provides inputs to several levels of the medial temporal lobe memory system, including the perirhinal cortex, the entorhinal cortex, the temporal end of the CA1 and the subiculum and the parasubiculum. A substantial projection to the bed nucleus of the stria terminalis, the caudate-putamen, the nucleus accumbens, the substantia innominata and the ventromedial nucleus of the hypothalamus has also been described.

Central nucleus

Projections to the central nucleus. The connectivity of the central nucleus is summarised in Figure 6. The central nucleus receives a substantial amount of sensory information from a large variety of cortical areas. These include inputs from the visual, auditory, somatosensory and visceral/gustatory cortices. The central nucleus also receives substantial inputs from the medial and lateral prefrontal cortex, including the infralimbic cortex and dorsal agranular insula, respectively. Projections from the medial temporal lobe memory system originate in the perirhinal and entorhinal cortices and the ventral subiculum. The entorhinal and perirhinal inputs terminate largely in the capsular division of the central nucleus, according to McDonald and Mascagni [72] and McDonald [69]. Terminals located in this region were considered to belong to the projection terminating in the amygdalostriatal area by Shi and Cassell [123], who state that the perirhinal cortex does not project to the central nucleus. Otherwise, the rostral part of

[1]The hippocampal formation includes the entorhinal cortex, dentate gyrus, hippocampus, subiculum, presubiculum, and parasubiculum according to Amaral and Witter (1989).

Table 2. Abbreviations for figures 2–12

CORTEX	
AId	Dorsal agranular insular cortex
AIp	Posterior agranular insular cortex
DIg	Gustatory dysgranular insular cortex
DIv	Visceral dysgranular insular cortex
EC	Entorhinal cortex
GI	Granular insular cortex
Oc1	Primary occipital cortex
Oc2	Secondary occipital cortex
PaRh	Parietal rhinal cortex
PC	Piriform cortex
PRC	Perirhinal cortex
PRCd	Perirhinal cortex, dorsal portion
PrCl	Lateral precentral cortex
PrCm	Medial precentral cortex
PRCv	Perirhinal cortex, ventral portion
PV	Parietal ventral area
SI	Primary somatosensory area
SII	Secondary somatosensory area
Te1	Temporal cortex, area 1
Te2	Temporal cortex, area 2
Te2D	Temporal cortex, area 2, dorsal portion
Te3	Temporal cortex, area 3
Te3R	Temporal cortex, area 3, rostral portion
FRONTAL CORTEX	
AC	Dorsal anterior cingulate cortex
AId	Dorsal agranular insular cortex
AIv	Ventral agranular insular cortex
AOB	Accessory olfactory bulb
AON	Anterior olfactory nucleus
DP	Dorsal peduncular cortex
IL	Infralimbic cortex
LO	Lateral orbital cortex
MO	Medial orbital cortex
OB	Olfactory bulb
PL	Prelimbic cortex
PrCm	Medial precentral cortex
TT	Tenia tecta
HIPPOCAMPUS AND SUBICULAR COMPLEX	
CA1	CA1 field of the hippocampus
CA2	CA2 field of the hippocampus
CA3	CA3 field of the hippocampus
DG	Dentate gyrus
EC	Entorhinal cortex
ParaS	Parasubiculum
S	Subiculum
STRIATUM AND BASAL FOREBRAIN	
Acc	Nucleus accumbens
BNST	Bed nucleus of stria terminalis
Cd-Pu	Caudate-Putamen
Cl	Claustrum
EP	Endopiriform nucleus
GP	Globus pallidus
ICa	Islands of Calleja
LS	Lateral septum
MS	Medial septum
NDB	Nucleus of the horizontal limb of the diagonal band
SI	Substantia innominata
OT	Olfactory tubercle
MIDBRAIN	
bPN	Basilar pontine nucleus
CnF	Cuneiform nucleus
CS	Nucleus centralis superior
DR	Dorsal raphe nucleus
LDTg	Laterodorsal tegmental nucleus
LiC	Nucleus linearis caudalis
LL	Lateral lemniscus
PAG	Periaqueductal grey
PPTg	Pedunculopontine tegmental nucleus
R	Raphe nucleus
VTA	Ventral tegmental area
PONS	
A8	A8 dopamine cells
LC	Locus coeruleus
PB	Parabrachial nucleus
RPC	Nucleus reticularis pontis caudalis
sC	Nucleus subcoeruleus
V	Mesencephalic nucleus of trigeminal nerve
MEDULLA	
A1	A1 noradrenaline cells
Amb	Nucleus ambiguus
C1	C1 adrenaline cells
dmX	Dorsal motor nucleus of vagus
GS	Nucleus gigantocellularis
NTS	Nucleus of the solitary tract
pGS	Nucleus paragigantocellularis
Rt	Reticular formation
VII	Facial nucleus
THALAMUS	
CM	Central medial nucleus
Hab	Habenula
IAM	Interanteromedial nucleus
IMD	Intermediodorsal nucleus
LP	Lateral posterior nucleus
LT	Lateral terminal nucleus of the accessory optic tract
MD	Mediodorsal nucleus
MG	Medial geniculate nucleus
MGm	Medial geniculate nucleus, medial part
PaC	Paracentral nucleus
PaV	Paraventricular nucleus
Pf	Parafascicular nucleus
PIN	Posterior intralaminar nucleus
PLi	Posterior limitans nucleus
PM	Posteromedian nucleus
PoM	Posterior thalamic complex, medial group
PP	Peripeduncular nucleus
PT	Paratenial nucleus
RE	Reuniens nucleus
SG	Suprageniculate nucleus
SN	Substantia nigra
SPf	Subparafascicular nucleus
sTh	Nucleus subthalamicus
VM	Ventromedial nucleus
VP	Ventral posterior nucleus
ZI	Zona inserta
HYPOTHALAMUS	
Arc	Nucleus arcuatus
AH	Anterior hypothalamic area/nucleus
DM	Dorsomedial nucleus
LH	Lateral hypothalamus
PaV	Paraventricular nucleus
PeV	Periventricular nucleus
PH	Posterior hypothalamic area/nucleus
preM	Premamillary nucleus
pFo	Perifornical area
PO	Preoptic area/nucleus
RCh	Retrochiasmatic area
SCh	Suprachiasmatic nucleus
sM	Supramamillary nucleus
SO	Supraoptic nucleus
TC	Tuber cinereum
tM	Tuberomamillary nucleus
Tu	Tuberal nucleus
VM	Ventromedial nucleus

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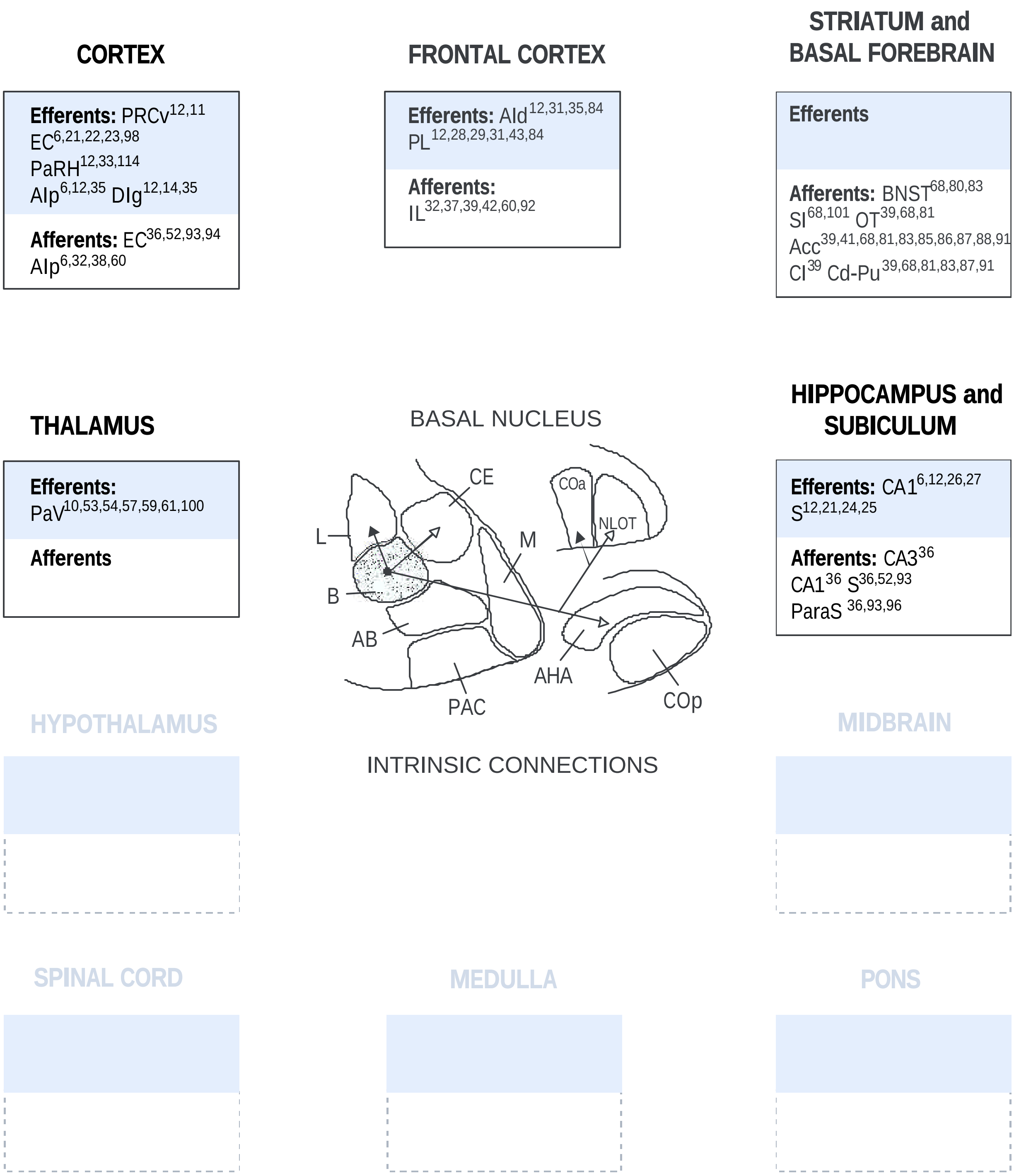

Figure 4. Afferent, intra-amygdaloid and efferent connections of the basal nucleus. Only the moderate-to-heavy projections are indicated

the entorhinal cortex, which is partly included in the AE subfield of the entorhinal cortex by Insausti et al. [40], is often considered to be the amydalopiriform transition area [89, 129]. This area provides a robust projection to the lateral division of the central nucleus [42, 72]. According to our recent observations [Jolkkonen and Pitkänen, unpublished], this area does not project to the dentate gyrus, which is considered a hallmark for the connectivity of the entorhinal cortex and this therefore suggests that the heavy input to the lateral division of the central nucleus does not originate in the entorhinal cortex. Other projections terminating in the central nucleus include inputs from the bed nucleus of the stria terminalis,

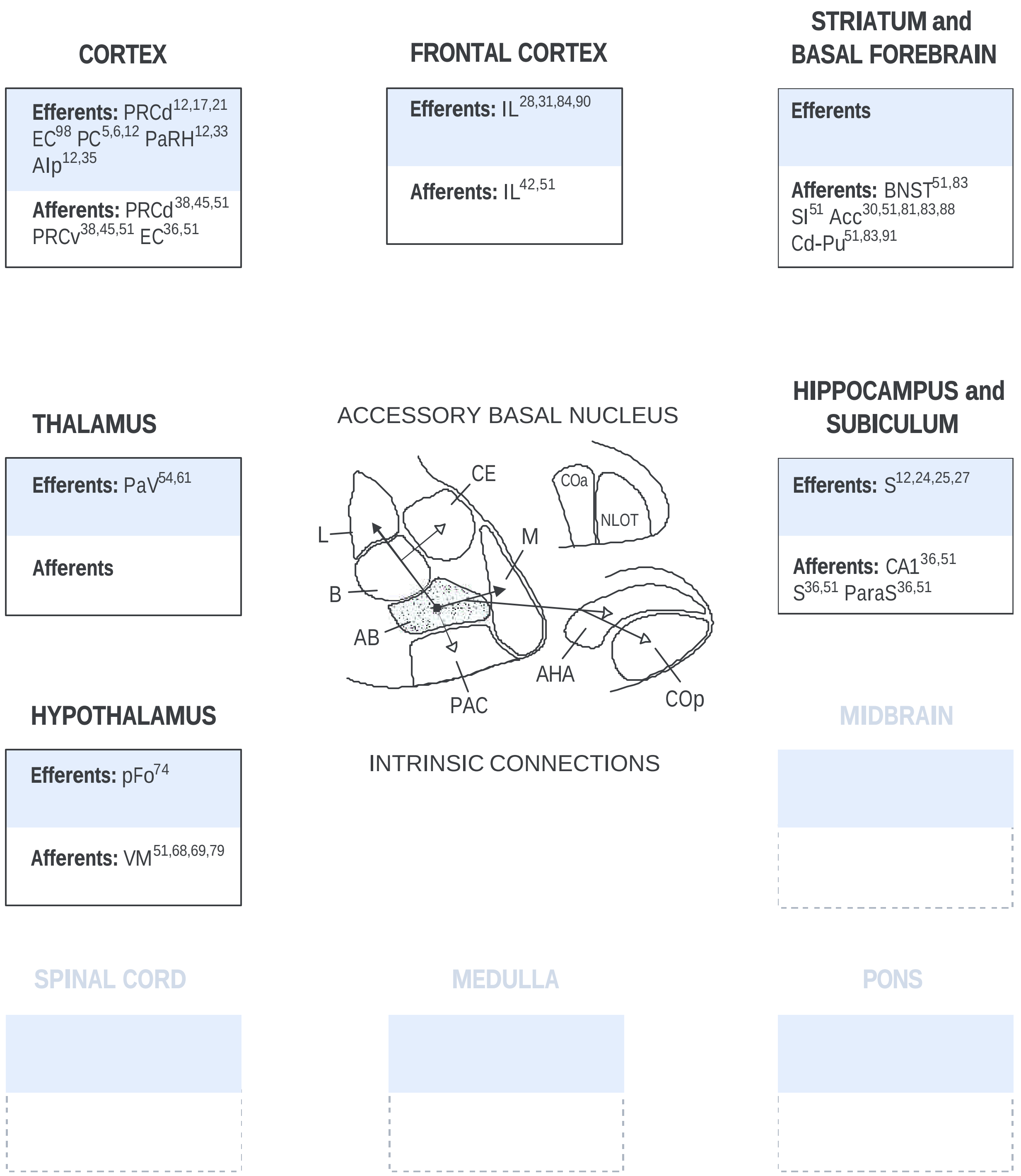

Figure 5. Afferent, intra-amygdaloid and efferent connections of the accessory basal nucleus. Only the moderate-to-heavy projections are indicated

the substantia innominata, the thalamus (paraventricular nucleus), the hypothalamus (premamillary nucleus and lateral hypothalamic area) and the pons (nucleus parabrachialis and nucleus subceruleus).

Intra-amygdaloid connections. The central nucleus converges inputs from almost all other amygdaloid nuclei. These include the lateral, basal, accessory basal, medial and anterior cortical nuclei, as well as the amygdalohippocampal area. It does not, however, provide any substantial inputs back to other amygdaloid regions. The central nucleus receives projections from the contralateral amygdala, including the basal and anterior cortical nuclei as well as the nucleus of the lateral olfactory tract.

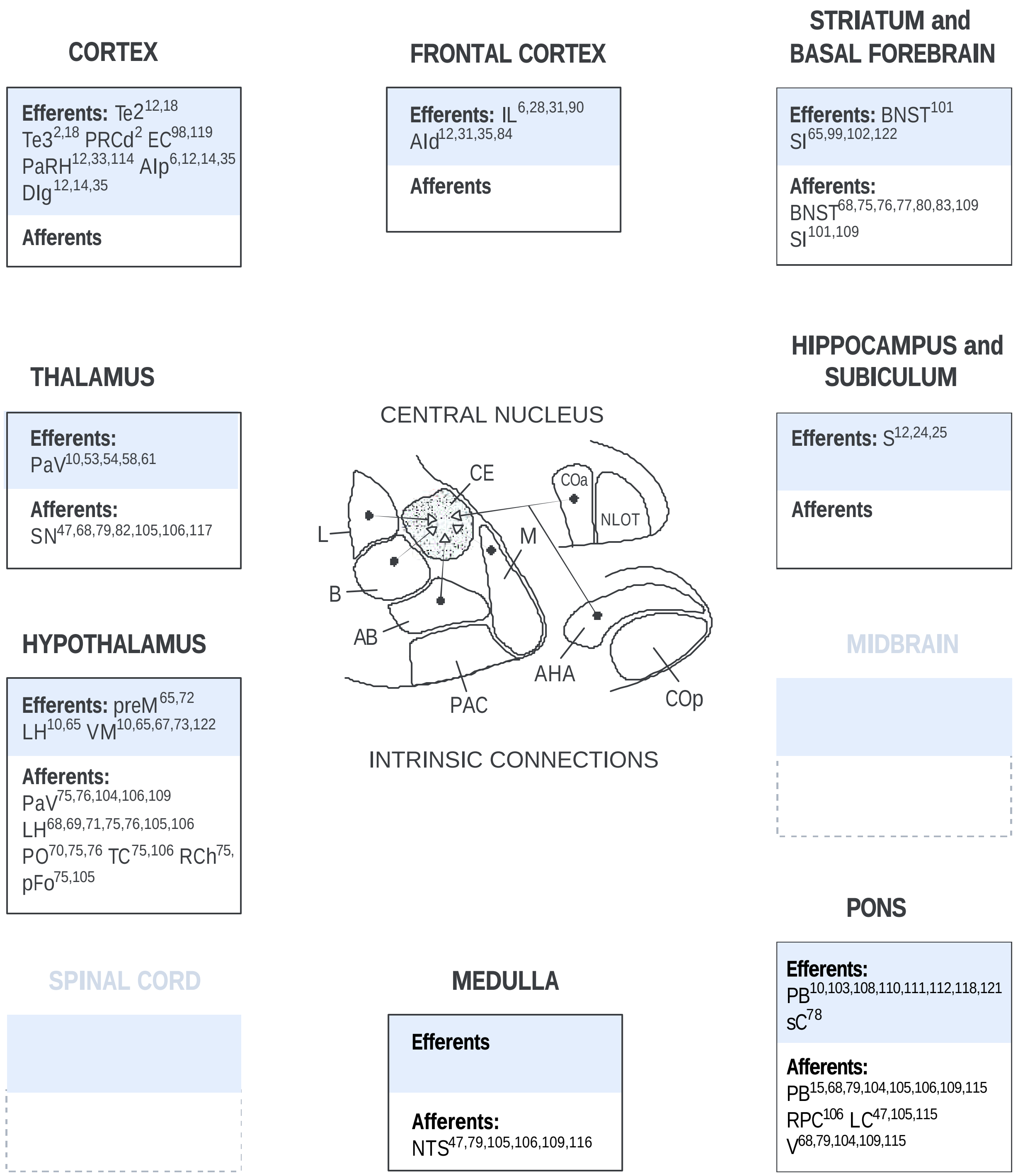

Figure 6. Afferent, intra-amygdaloid and efferent connections of the central nucleus. Only the moderate-to-heavy projections are indicated

Projections from the central nucleus. Conspicuously, the central nucleus does not project to cortical areas. It does provide substantial inputs to the bed nucleus of the stria terminalis, the substantia innominata and the substantia nigra. It provides the most prominent and widespread amygdaloid projections to the brain stem, which terminate in the parabrachial nucleus, the locus ceruleus, mesencephalic nucleus of the trigeminal nerve, the nucleus reticularis pontis caudalis and the nucleus tractus solitarius. Also, projections to many of the hypothalamic nuclei are substantial, including those to the paraventricular nucleus, the lateral hypothalamic area, the preoptic area, the perifornical region, tuber cinereum and the retrochiasmatic area.

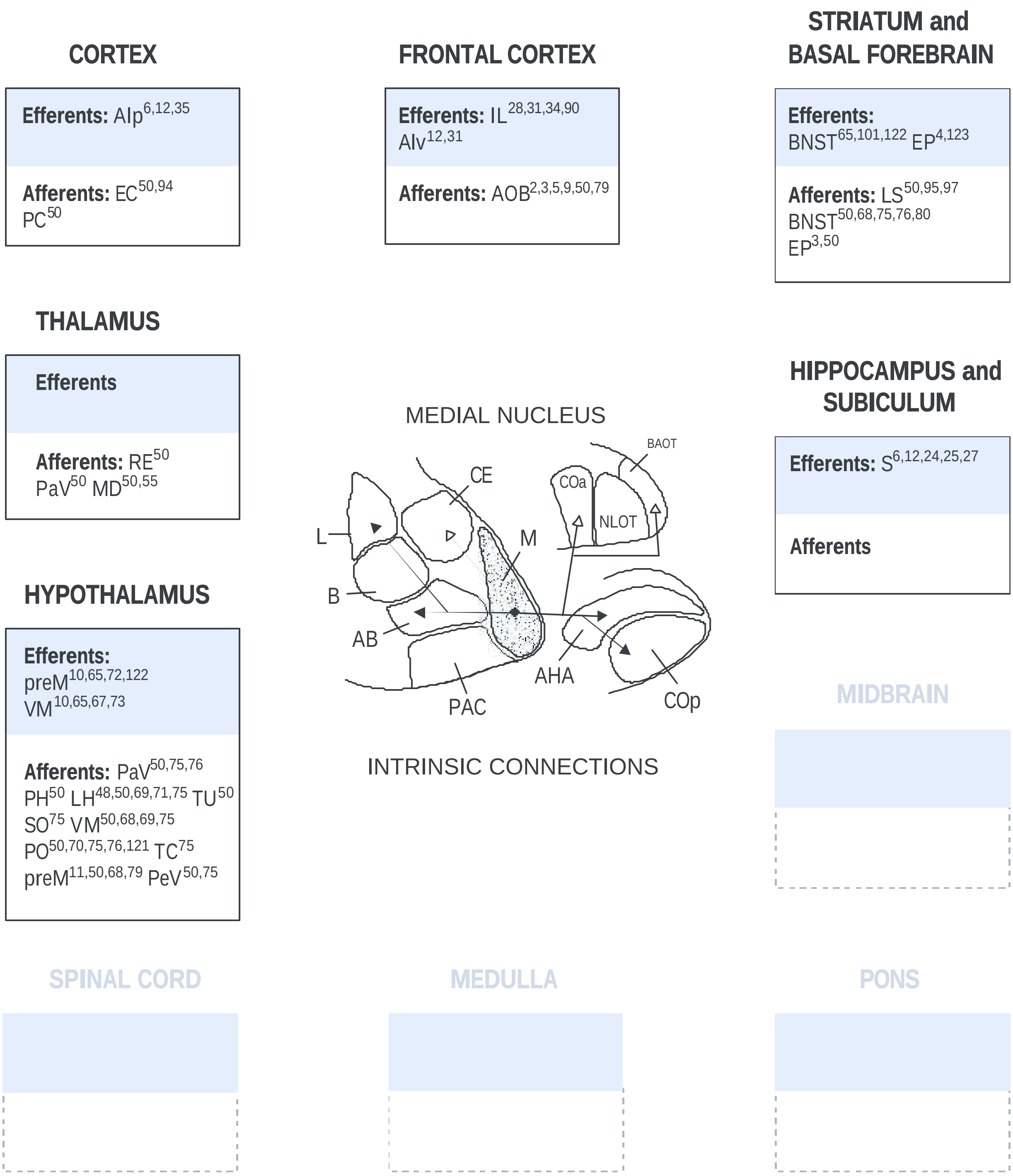

Figure 7. Afferent, intra-amygdaloid and efferent connections of the medial nucleus. Only the moderate-to-heavy projections are indicated

Medial nucleus

Projections to the medical nucleus. The connectivity of the medial nucleus is summarised in Figure 7. The heaviest cortical projections to the medial nucleus originate in the agranular insula and the infralimbic cortex. Projections from the medial temporal lobe memory system are meagre, including only a projection from the temporal subiculum. The bed nucleus of the stria terminalis and the endopiriform nucleus project to the medial nucleus. Other major inputs originate in the premamillary and ventromedial nuclei of the hypothalamus.

Intra-amygdaloid connections. The medial nucleus receives inputs from the lateral and accessory basal nuclei as well as from the amygdalohippocampal area and the posterior cortical nucleus. The intra-amygdaloid outputs are widespread and terminate in the lateral, accessory basal, central, anterior cortical and posterior cortical nuclei, as well as in the amygdalohippocampal area and the bed nucleus of the accessory olfactory tract. The medial nucleus receives inputs from several contralateral amygdaloid areas, including the nucleus of the lateral olfactory tract, the accessory basal nucleus, the periamygdaloid cortex and the posterior cortical nucleus.

Projections from the medial nucleus. The medial nucleus projects to several levels of the olfactory system including the caudal aspects of the piriform cortex, the accessory olfactory bulb and the endopiriform nucleus. The medial nucleus also projects heavily to the bed nucleus of stria terminalis and the lateral septum. The entorhinal cortex also receives a projection. Substantial projections are directed to the paraventricular, reuniens and mediodorsal nuclei of the thalamus. Finally, several hypothalamic areas are heavily innervated by the medial nucleus. These include the paraventricular nucleus, periventricular nucleus, posterior and lateral hypothalamic areas, tuberal nucleus, supraoptic nucleus, preoptic area, ventromedial nucleus, premamillary nucleus and tuber cinereum.

Anterior cortical nucleus

Projections to the anterior cortical nucleus. The connectivity of the anterior cortical nucleus is summarised in Figure 8. Inputs from the sensory-related cortex originate in the agranular and dysgranular insula. The prefrontal input originates in the infralimbic cortex and ventral agranular insula. Olfactory information comes from the piriform cortex and the endopiriform nucleus. The ventral subiculum is the only region in the hippocampal formation known to project to the anterior cortical nucleus. Other moderate-to-heavy inputs originate in the paraventricular nucleus of the thalamus and the parabrachial nucleus in the pons.

Intra-amygdaloid connections. The heaviest intra-amygdaloid inputs to the anterior cortical nucleus originate in the basal and medial nuclei. The anterior cortical nucleus projects to the central and basal nuclei. It also projects to the contralateral central nucleus.

Projections from the anterior cortical nucleus. The only cortical area that receives a substantial input from the anterior cortical nucleus is the piriform cortex. Other projections terminate in the bed nucleus of stria terminalis, substantia innominata and the lateral hypothalamus.

Periamygdaloid cortex

Projections to the periamygdaloid cortex. The connectivity of the periamygdaloid cortex is summarised in Figure 9. The agranular insula, the perirhinal cortex and the piriform cortex provide moderate inputs to the periamygdaloid cortex. Also, there are substantial projections from the infralimbic cortex. Another projection originates in the nucleus of the diagonal band and the endopiriform nucleus.

Intra-amygdaloid connections. The lateral and accessory basal nuclei provide substantial projections to the periamygdaloid cortex. The periamygdaloid cortex provides a heavy reciprocal connection back to the lateral nucleus. It also projects to the contralateral periamygdaloid cortex, the medial nucleus and the posterior cortical nucleus.

Projections from the periamygdaloid cortex. The periamygdaloid cortex provides substantial projections to several regions of the frontal cortex, including the infralimbic cortex, the dorsal peduncular cortex, the tenia tecta and the ventral agranular insula. It also provides an input to the entorhinal cortex as well as to the olfactory system, including the piriform cortex, the olfactory tubercle and the endopiriform nucleus.

Posterior cortical nucleus

Projections to the posterior cortical nucleus. The connectivity of the posterior cortical nucleus is summarised in Figure 10. The posterior cortical nucleus receives inputs from the entorhinal cortex. Substantial projections also originate in several olfactory-related areas including the piriform cortex, the accessory olfactory bulb and the endopiriform nucleus.

Intra-amygdaloid connections. The most substantial intra-amygdaloid projections come from the lateral, accessory basal and medial nuclei. The posterior cortical nucleus projects to the medial nucleus, periamygdaloid cortex and the bed nucleus of the accessory olfactory tract. It projects contralaterally to the posterior cortical nucleus, medial nucleus and the amygdalohippocampal area. The posterior cortical nucleus also receives an input from the contralateral periamygdaloid cortex.

Projections from the posterior cortical nucleus. The posterior cortical nucleus projects back to several levels of the olfactory system. These include the piriform cortex, the accessory olfactory bulb, the olfactory tubercle and the endopiriform nucleus. Other substantial projections are directed to the entorhinal cortex, the infralimbic cortex and the agranular insula. Also, the bed nucleus of the stria terminalis receives an input from the posterior cortical

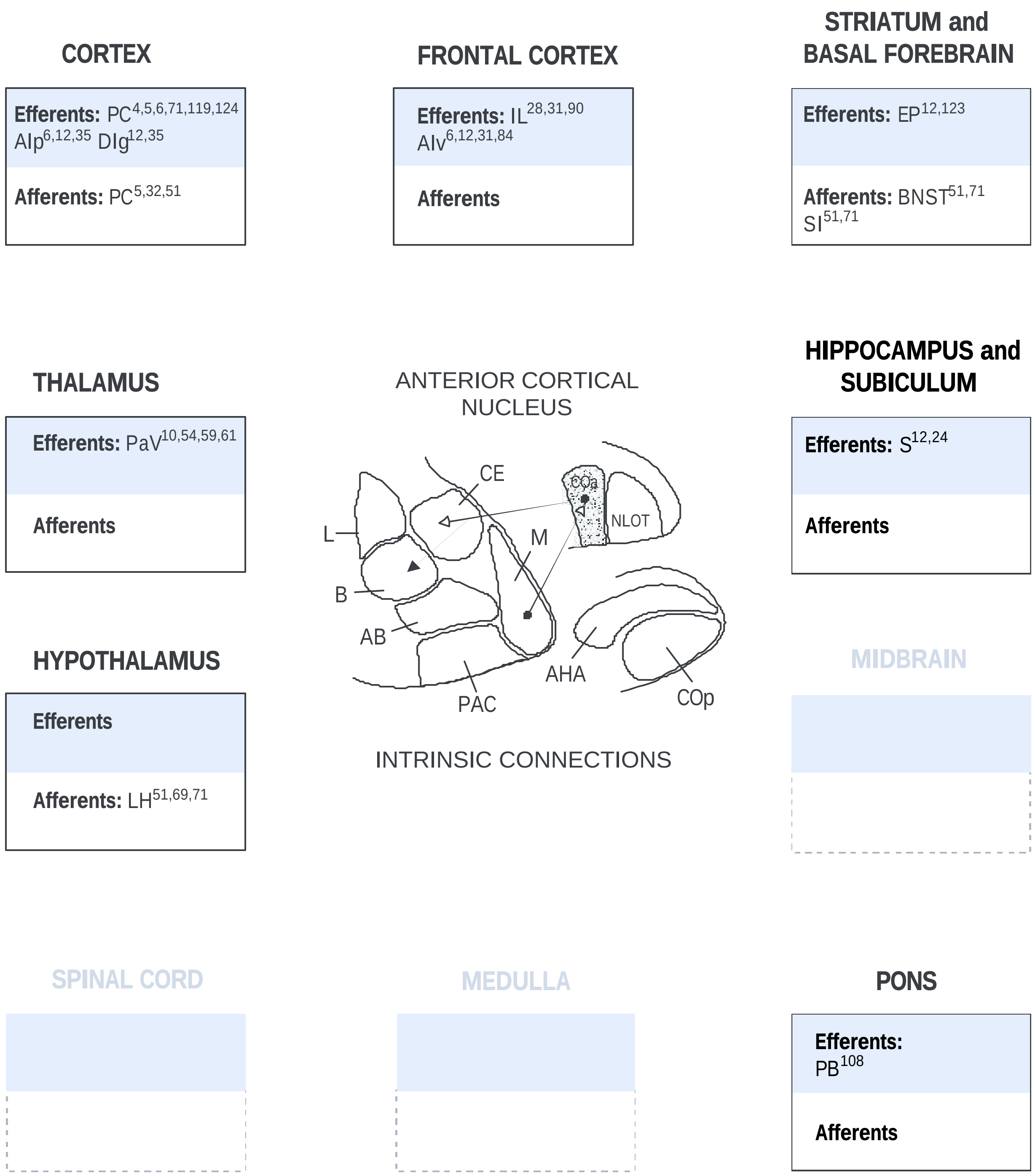

Figure 8. Afferent, intra-amygdaloid and efferent connections of the anterior cortical nucleus. Only the moderate-to-heavy projections are indicated

nucleus, as does the temporal end of the CA1 subfield of the hippocampus.

Amygdalohippocampal area

Projections to the amygdalohippocampal area. The connectivity of the amygdalohippocampal area is summarised in Figure 11. Substantial inputs originate in the medial temporal lobe memory system, including those from the temporal end of the CA1 subfield and the subiculum. Other projections originate in the hypothalamus, including the premamillary nucleus and the lateral hypothalamic area.

Intra-amygdaloid connections. The lateral, basal, accessory basal and medial nuclei as well as the bed nucleus of the accessory olfactory tract project

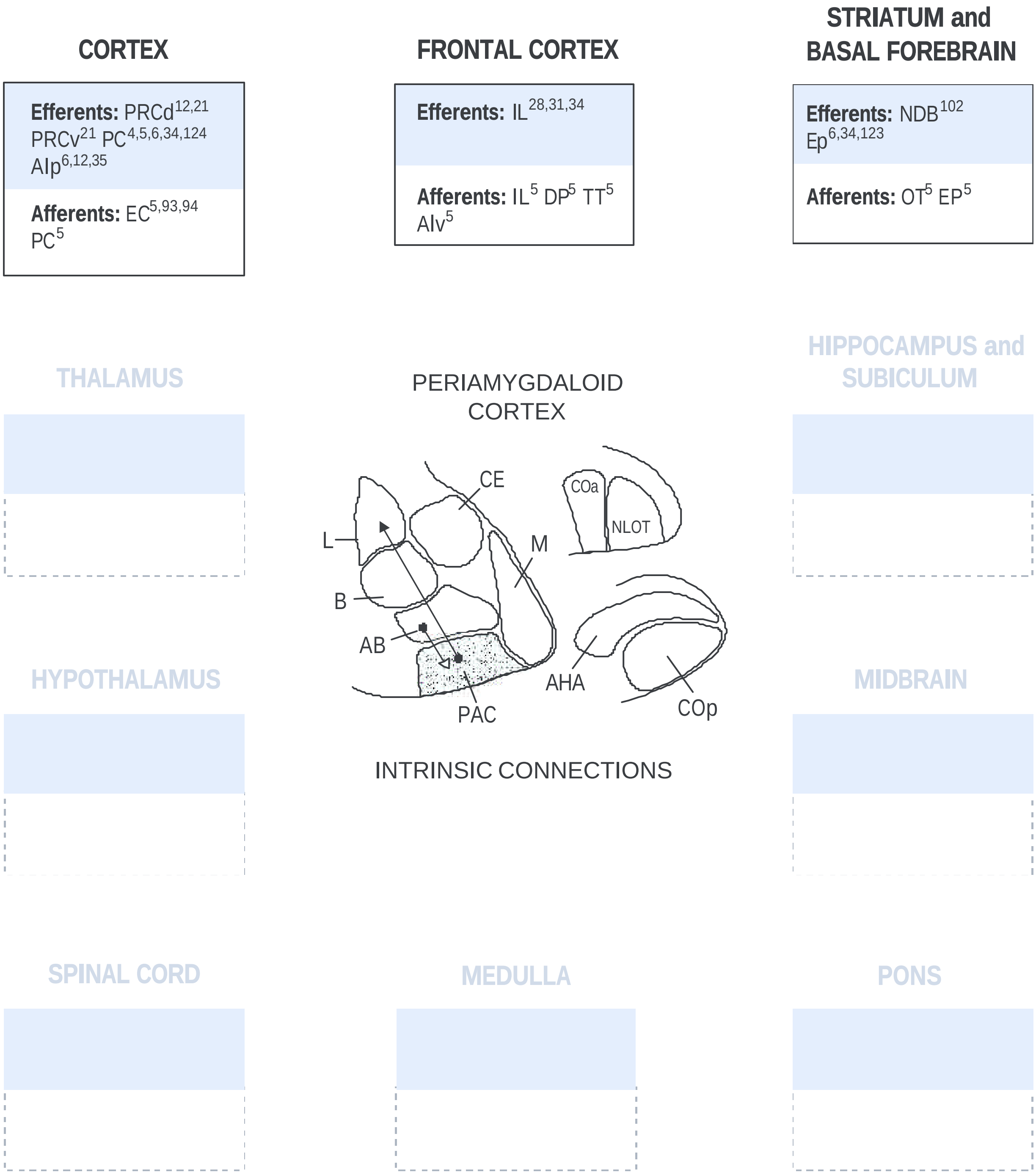

Figure 9. Afferent, intra-amygdaloid and efferent connections of the periamygdaloid cortex. Only the moderate-to-heavy projections are indicated

to the amygdalohippocampal area. It projects to the medial and central nuclei. The amygdalohippocampal area receives a contralateral input from the posterior cortical nucleus.

Projections from the amygdalohippocampal area. The amygdalohippocampal area provides substantial projections to the bed nucleus of the stria terminalis and several hypothalamic nuclei, including the premamillary nucleus, the preoptic area and the ventromedial nucleus.

Nucleus of the lateral olfactory tract

Projections to the nucleus of the lateral olfactory tract. The connectivity of the nucleus of the lateral olfactory tract is summarised in Figure 12. Overall, data about the inputs to the nucleus of the lateral olfactory tract are meagre. It receives projec-

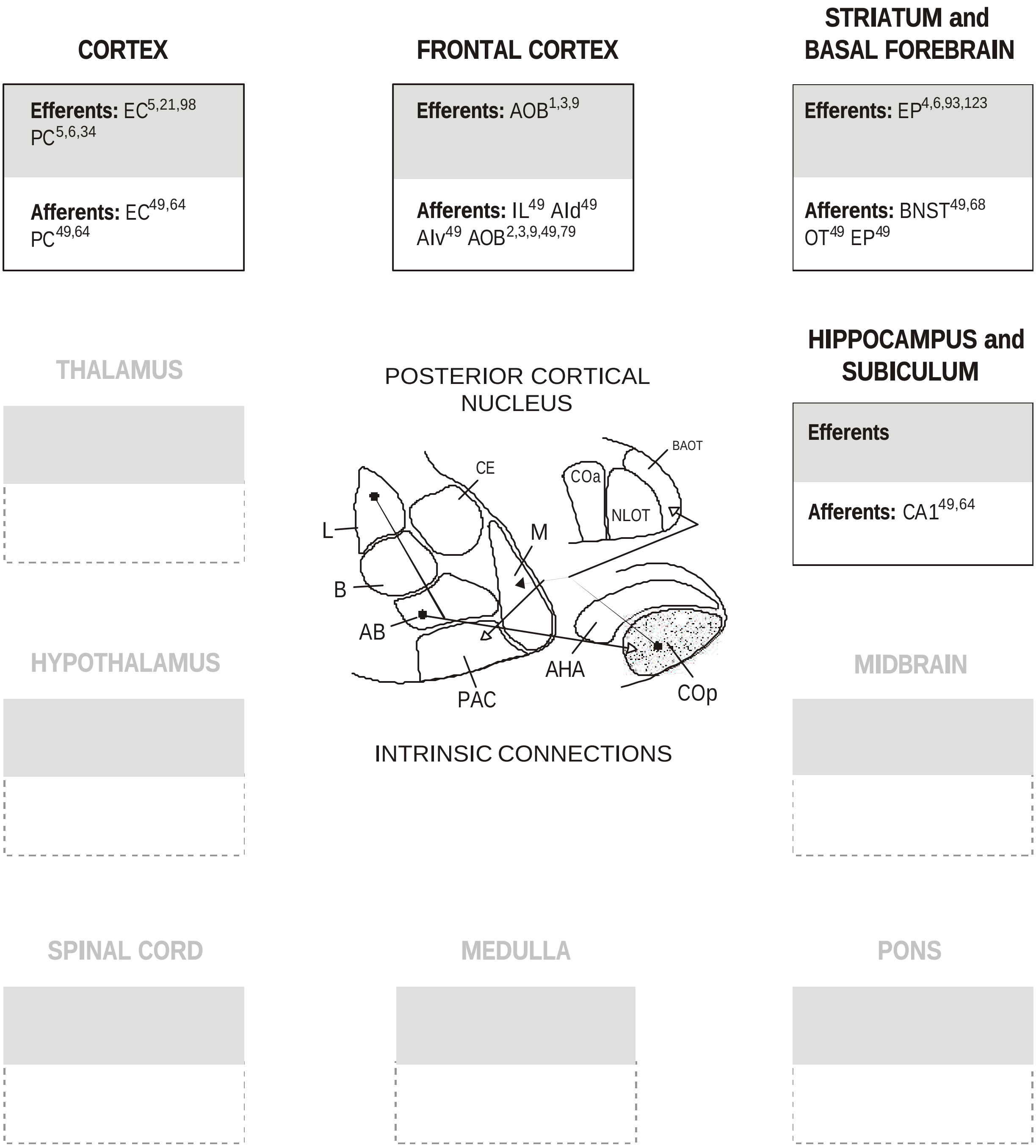

Figure 10. Afferent, intra-amygdaloid and efferent connections of the posterior cortical nucleus. Only the moderate-to-heavy projections are indicated

tions from the agranular insula, the nucleus of the diagonal band of Broca , the olfactory tubercle, the endopiriform nucleus and the temporal subiculum.

Intra-amygdaloid connections. The basal nucleus projects to the nucleus of the lateral olfactory tract. Intra-amygdaloid projections originating in the nucleus of the lateral olfactory tract are poorly described. It does, however, project contralaterally to the nucleus of the lateral olfactory tract, the medial nucleus and the central nucleus. It also receives a projection from the contralateral basal nucleus.

Projections from the nucleus of the lateral olfactory tract. The nucleus of the lateral olfactory tract provides moderate-to-heavy projections to several levels of the olfactory system, including the ol-

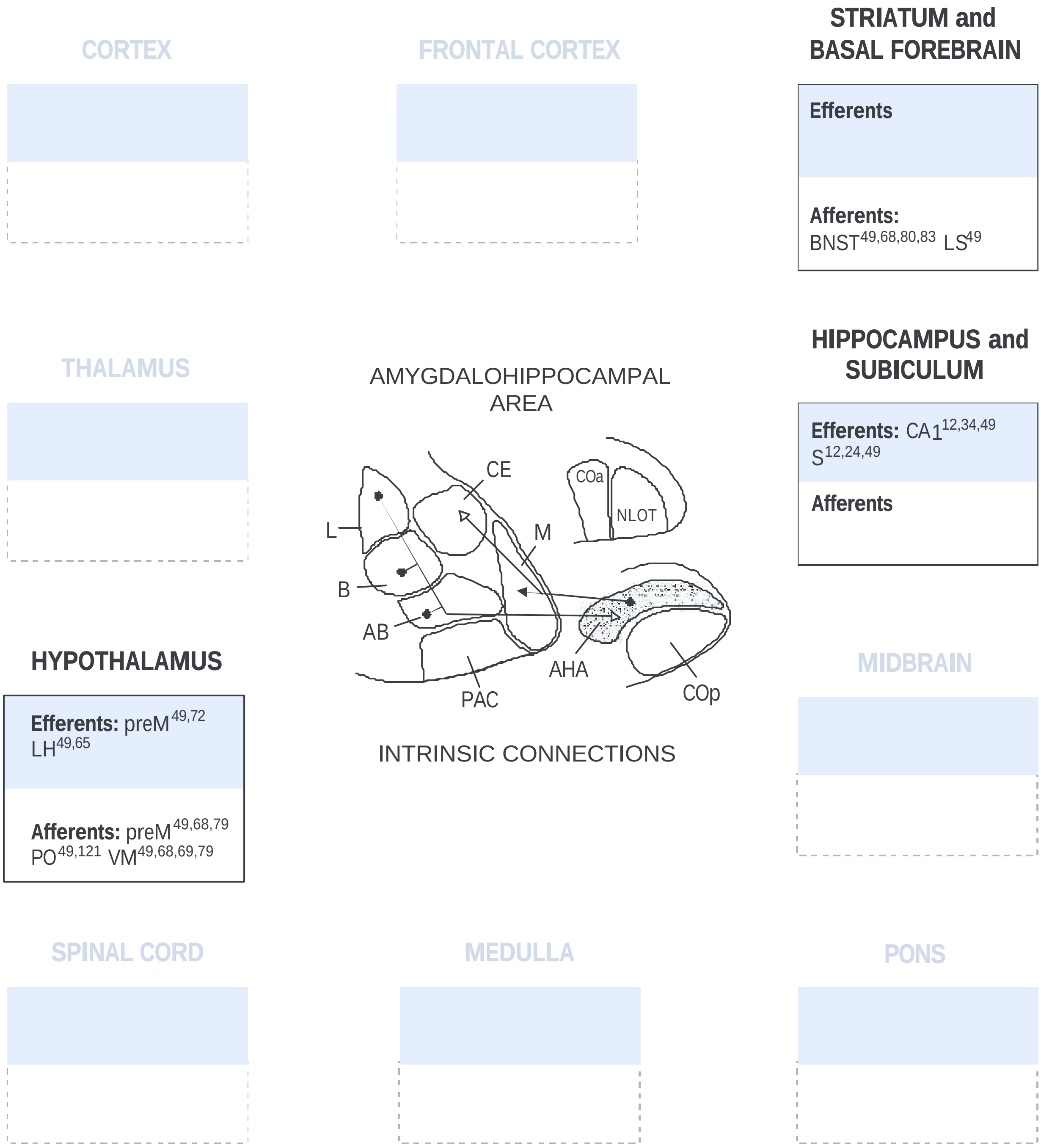

Figure 11. Afferent, intra-amygdaloid and efferent connections of the amygdalohippocampal area. Only the moderate-to-heavy projections are indicated

factory bulb, the olfactory tubercle, the endopiriform nucleus, as well as the Islands of Calleja.

PRINCIPLES OF ORGANISATION OF AMYGDALOID CONNECTIONS

Investigation of the pattern of connectivity of the amygdala with other brain areas suggests several principles in the organisation of information flow to and from the amygdala. As is evident from Figures 3 to12, each of the amygdaloid nuclei has a unique set of interconnections with other brain areas. Second, one brain area might project to several amygdaloid nuclei in parallel. Third, one amygdaloid nucleus might receive information from (a) several functional systems or (b) several levels of the same functional system. Fourth, some functional systems,

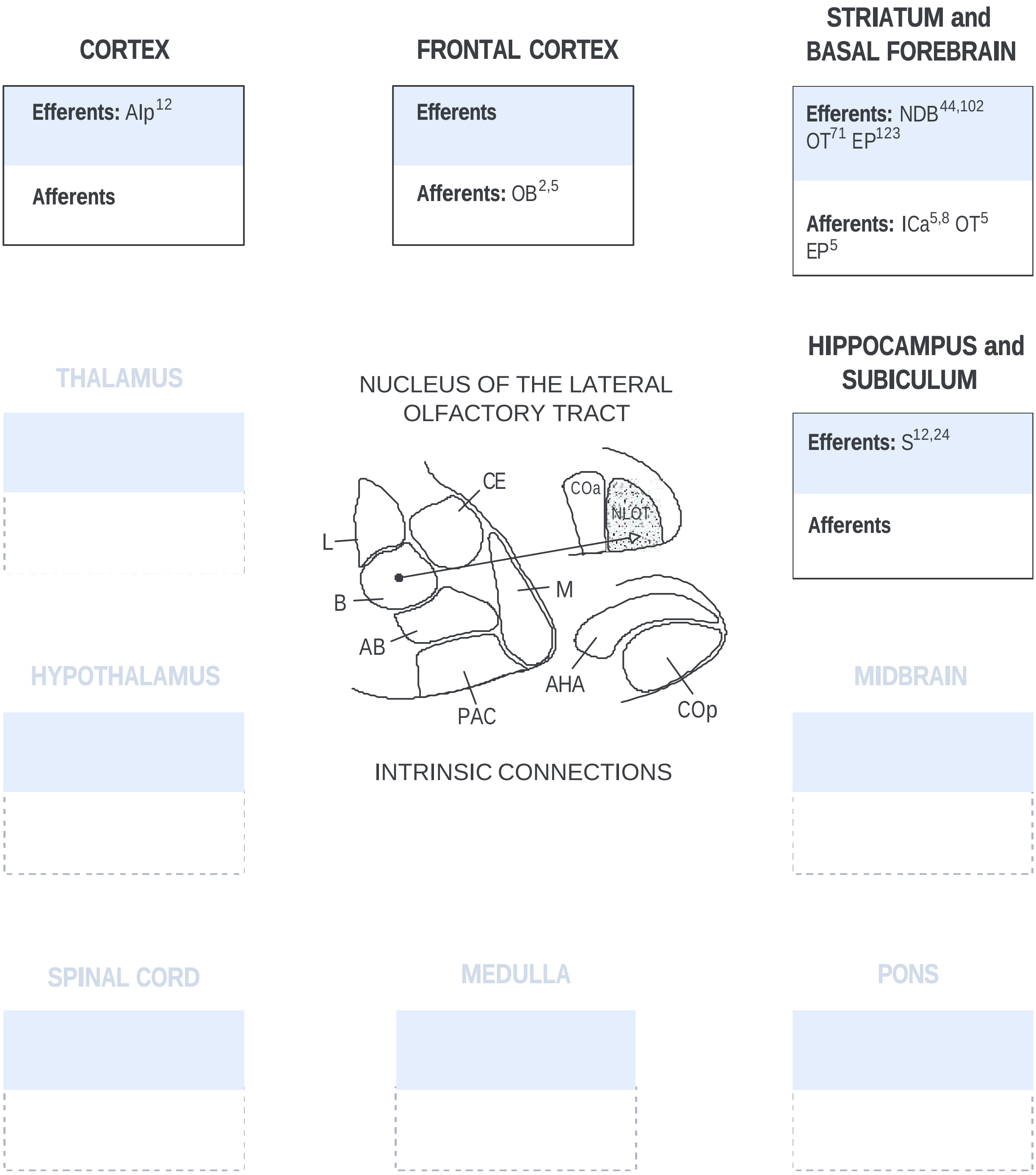

Figure 12. Afferent, intra-amygdaloid and efferent connections of the nucleus of the lateral olfactory tract. Only the moderate-to-heavy projections are indicated

however, terminate in a selective amygdaloid region. The parallel intra-amygdaloid circuitries probably multiply the number of iterations that each of the stimulus representations will have within the amygdaloid complex. The amygdaloid projections appear to obey the following principles: First, one amygdaloid nucleus might project to several functional systems or several levels of the same functional system in parallel. Second, several amygdaloid nuclei might send converging inputs to the same functional system. Third, some amygdaloid nuclei project more selectively to a few functional systems.

FUNCTIONAL IMPLICATIONS

Studies using magnetic resonance imaging volumetry, positron emission tomography, or histologic analysis of autopsy tissue demonstrate amygdaloid damage in several human brain diseases, including temporal lobe epilepsy [97], Alzheimer's disease [142], Parkinson's disease [15], schizophrenia [106], depression [119] and autism [6], to mention a few. A more detailed histologic analysis of autopsy tissue or the volumetric analysis of different amygdaloid nuclear groups using magnetic resonance imaging reveal some disease specificity in the „knock-out" of amygdaloid regions. For example, the medial division of the lateral nucleus and the parvicellular division of the basal nucleus are the most vulnerable amygdaloid regions in temporal lobe epilepsy [97]. The central nucleus and the periamygdaloid cortex contain the highest densities of Lewy bodies in Parkinson's disease [15]. The lateral, basal and accessory basal nuclei have the most prominent volume reduction in depression [119]. Finally, the basal and accessory basal nuclei have the most pronounced neuronal loss in Alzheimer's disease [142]. Considering the connectional differences of various amygdaloid nuclei with other functional systems, it is tempting to speculate that the impairments of amygdaloid functioning vary in different diseases because of the variable location of the amygdaloid lesion. One area yet to be explored is how much damage is needed and where in the amygdala to induce functional impairments; for example, the recognition of emotion in facial expressions. Further, would the same damage also impair other amygdaloid functions, such as the modulation of memory formation by emotional experiences?

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