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Projections from cingulate cortex to the cat's thalamic reticular nucleus

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Abstract

The cingulate cortex (CG) and the adjacent region designated as the splenial visual area (SVA) project to areas of the extrageniculate thalamic system that are concerned with processing visual information. En route to the thalamus, they pass through the thalamic reticular nucleus (TRN), an important source of thalamic inhibition. We wished to determine whether SVA axon collaterals projected to the previously defined visual sector of the TRN or a separate projection zone and did this differ from the projection zone of CG. We iontophoretically injected different neuroanatomical tracers into several locations within CG/SVA and traced the labeled axons through the TRN. The CG and SVA have a projection zone that only partially overlaps the dorsorostral regions of the visuocortical projection zone; there was no evidence to suggest separate SVA and CG zones or tiers of label within the TRN. The projection formed only a weak topographic map in the TRN, which is largely defined in the rostrocaudal axis and is similar to that of the area 7 projection; both projections have a high degree of overlap in the dorsal TRN. We postulate that CG/SVA may be involved in the initiation of orientation behaviors *via* stimulation of thalamic nuclei and attentional mechanisms of the TRN.

Keywords: WGA-HRP, BDA, Neuroanatomical tracing, Thalamus, Corticoreticular maps

Introduction

Inhibition forms a major component of physiological processes within the brain and much of this inhibition is supplied by GABAergic neurons. The thin shell-like sheet of GABAergic cells comprising the thalamic reticular nucleus (TRN), derived from the ventral thalamus, forms an important part of this inhibitory system (for revises, see Steriade & Llinas, 1988; Steriade et al., 1997; Guillery et al., 1998; Pinault, 2004). Although thalamic nuclei are the primary target for TRN projections, the precise functional role that TRN inhibition plays in thalamic processing remains unresolved. It has been argued that the TRN functions to reduce the firing rate of thalamic cells and thus "gate" the flow of information from the thalamus to the cortex (for references, see Yingling & Skinner, 1975; Sherman & Koch, 1986; Steriade et al., 1997) and may be involved in attentional mechanisms (Crick & Koch, 1990; Montero, 1997; McAlonan et al., 2006, 2008; Zikopoulos & Barbas, 2006; for other possible roles in sleep–wakefulness and epilepsy, see Raeva & Lukashev, 1993; McCormick & Bal, 1997; Avanzini et al., 2000; Pinault, 2004).

The TRN is customarily subdivided into sectors according to the dominant modality of the projections within a particular region of the TRN (e.g., visual, somatosensory, or auditory sectors), and these may, in some cases, be subdivided further based on first- or higher-order (Guillery & Sherman, 2002) projections from thalamic nuclei or the cortex (Crabtree & Killackey, 1989; Conley & Diamond, 1990; Conley et al., 1991; Crabtree, 1992*a*,*b*, 1996, 1998; Coleman & Mitrofanis, 1996; Lozsádi et al., 1996; Kimura et al., 2005). It is also now clear that the arrangement is more complex than a simple model of lateral and medial tiers with segregated first- (topographic) and higher-order (loosely topographic) projections (Crabtree, 1996, 1998; Kolmac & Mitrofanis, 1998; Pinault & Deschênes, 1998; Crabtree & Isaac, 2002; Lam & Sherman, 2005, 2007). In addition, there is ample evidence demonstrating cross-modal thalamic inhibition *via* the TRN (Crabtree et al., 1998; Crabtree & Isaac, 2002; see also Sugitani, 1979; Shosaku & Sumitomo, 1983; Pinault & Deschênes, 1998; Kimura et al., 2007; Lam & Sherman, 2007).

The visual sector of the cat's TRN can be anatomically subdivided into a first-order region, the perigeniculate nucleus [PGN; retinotopically connected to the dorsal lateral geniculate nucleus (LGNd)], and a higher-order region consisting of the main body of the TRN [predominantly connected to higher-order thalamic nuclei such as the lateralis posterior–pulvinar complex (LP-Pul)]. Previously, we reported that axon collaterals from both striate cortex and visuotopically organized extrastriate cortices form a single, albeit, rough visuotopic map within the main body of the TRN (FitzGibbon et al., 1999). In addition, area 7, a cortical area that is visually active but has only a crude visuotopic map (Heath & Jones, 1971; Rosenquist, 1985; Ventre, 1985), also projects to similar regions of the TRN visual sector (FitzGibbon, 2000).

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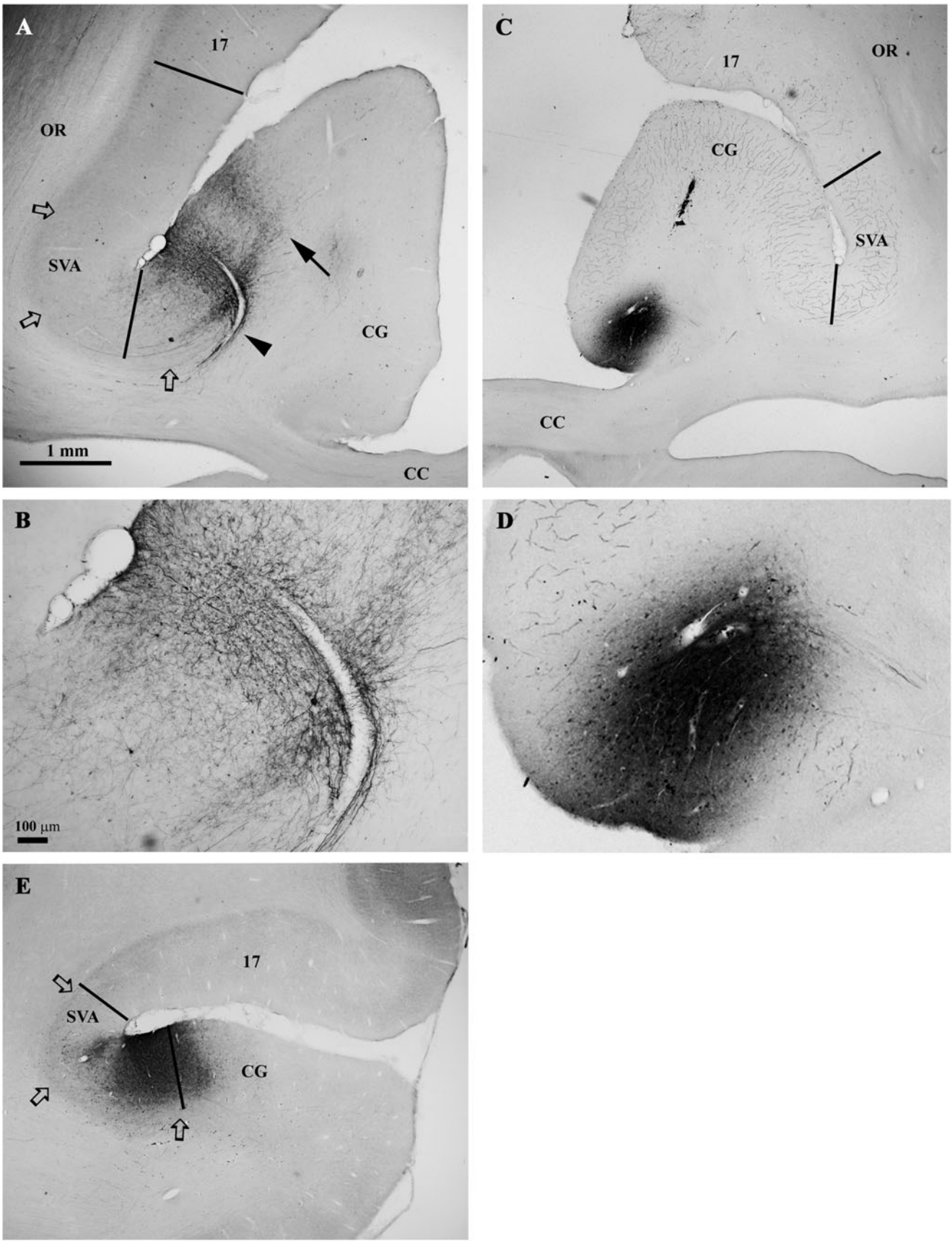


Fig. 1. Coronal sections through typical cortical injection sites. (**A**) A BDA injection site is shown within rostral cingulate cortex (CG) at an anterior-posterior level nine mm anterior to the interaural line (AP9) close to the area defined as the splenial visual area (SVA; Cat # TFG23). Note

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The splenial visual area (SVA), situated between the cingulate cortex (CG) and area 17, has also been described as a visually active area but with a poorly defined visuotopic map (Kalia & Whitteridge, 1973; Rosenquist, 1985). We used neuroanatomical tracers to ask the following questions. First, do axons from SVA make connections with the visual sector of the TRN? Second, do axons from the adjacent CG make connections to the same or different regions of the TRN?

Materials and methods

Eight adult cats (2.5–4.5 kg) were used according to previously published methods (FitzGibbon et al., 1999). All experiments were conducted in accordance with the Declaration of Helsinki and according to the guidelines of the National Health and Medical Research Council of Australia and the Sydney University Animal Care and Ethics Committee. Every effort was made to minimize the number of animals. Animals were anaesthetized with sodium pentobarbitone (Nembutal, Boehringer; 30 mg/kg, i.p.) and injected with atropine sulfate (0.3 mg, i.m.; Apex Laboratories, Somersby, NSW, Australia) and dexamethasone sodium phosphate (2.5 mg, i.m., Dexapent; Troy Laboratories Pty, Glendenning, NSW, Australia) to minimize mucus secretion and brain edema, respectively. Body temperature was maintained automatically between 36° and 37°C with an electric heating blanket. The animal's head was fixed in a stereotaxic head holder and zero power air-permeable contact lenses fitted to the eyes to protect the corneas. Bilateral craniotomies were performed to allow two cortical injections per hemisphere. Two tracers were used, 4% wheat germ agglutinin–horseradish peroxidase (WGA-HRP; Sigma-Aldrich Pty., Castle Hill, NSW, Australia) and 4% dextran–biotin (BDA; Molecular Probes, Eugene, OR), but only one type of tracer was injected per hemisphere. Injections were placed between Horsley–Clarke anterior–posterior (AP) 0.0 and 10.5, lateral 0.5 and 4.5, and dorsal 8.5 and 12. SVA extends from approximately AP −0.5 to ~8.0, lateral 3.0 to 4.5, and dorsal 10 to 12 (Rosenquist, 1985). Injections were made using iontophoresis (positive current 1–10 μA; 2–4 s ON–OFF duty cycle for 5–30 min). After survival times of 2–6 days, the animals were killed with Nembutal (60–90 mg/kg, i.p.) and perfused through the heart with 400 ml of warm 0.9% saline followed by 1 l of 4% paraformaldehyde plus 0.5% glutaraldehyde in phosphate buffer (PB, 0.1 M, pH 7.4) and then 1 l of 10% sucrose in PB. The brains were removed and placed in 30% sucrose in PB overnight before being sectioned at 50 μm in the coronal plane. Sections containing WGA-HRP were reacted with 3,3',5,5'-tetramethylbenzidine (TMB; Sigma); sections containing BDA were incubated with ExtraAvidin (1:2000; Sigma) and reacted over ice with 3,3'-diaminobenzidine (Sigma). One series of sections was stained for acetylcholinesterase histochemistry to define nuclear boundaries within the thalamus (Graybiel & Berson, 1980).

Drawings showing the location of labeled fibers and presumptive synaptic contacts were made with the aid of a *camera lucida* attachment and a computer-aided morphology program. After mapping the injection site, the cortical location was determined by reference to previous reports (Tusa et al., 1978, 1981; Raczkowski & Rosenquist, 1983; Rosenquist, 1985). Regions containing labeled profiles were mapped in selected sections and the areas defined according to the nomenclature and AP coordinates in the stereotaxic atlas of Berman and Jones (1982).

Results

BDA or WGA-HRP injection sites (Fig. 1) were generally small and localized to the deeper layers of the cortex and did not involve the underlying white matter. BDA injections clearly gave better resolution for tracing axons within the brain, and for determining the location of axonal branches, swellings and boutons compared to TMB-reacted sections. Not all injections successfully produced usable data; therefore, the data represent a mixture of double- and single-labeled experiments. According to previous mapping studies, our injections were relatively restricted to CG or SVA and did not include area 17 (cf. Tusa et al., 1979, 1981; Raczkowski & Rosenquist, 1983; Rosenquist, 1985).

Labeled BDA profiles in the TRN and thalamus

In the BDA material, axons passing through the TRN were characterized by the presence of numerous ~0.5–1.0 μm diameter axonal swellings (presumptive "*en passant*-" type contacts), although small boutons at the end of a short side branch or club-like endings (~0.5–2.0 μm) were also present (Fig. 2: see also Robson, 1984; Paré & Smith, 1996; FitzGibbon et al., 1999). In some cases, both axonal swellings and boutons were present on the same fiber (Fig. 2A); labeled fibers ranged from ~0.3 to 4.5 μm, and these profiles were not observed on fibers greater than ~2.0 μm (see also Guillery et al., 2001; Reichova & Sherman, 2004). Although electron microscopic analysis is required to unequivocally determine a synaptic status for these profiles, previous reports indicate that a large proportion of them are likely to be synaptic sites (Asanuma, 1992; Lozsádi, 1994; Paré & Smith, 1996). TRN somata are not evenly distributed in the dorsoventral axis of the TRN due to the bundles of corticothalamic and thalamocortical fibers passing through the nucleus (hence, the reticulated appearance of the TRN). Boutons and axonal swellings were not specifically concentrated in areas containing patches of somata but were scattered across cell-rich and cell-spares regions (Figs. 2 and 3). Boutons were also observed in close proximity to TRN somata (Fig. 2B) suggesting the presence of somatic contacts. Corticothalamic fibers tended to cross either at right angles to the dorsoventral/anterioposterior axes of the TRN or with a slight ventrodorsal trajectory before entering the thalamus (Fig. 3B). There were no qualitative differences between CG and SVA projections.

Previous reports have indicated that many species have mediolateral subdivisions or tiers in the TRN that are related to first- or higher-order connections (Conley & Diamond, 1990; Conley et al., 1991; Crabtree, 1992*a*,*b*, 1996; Lozsádi, 1994). However, the projections from CG and SVA were distributed across the full

that there is a prominent connection within the CG itself from this injection site (indicated by the arrow). The open arrows indicate the edge of layer 6 and the corpus callosum (CC) is marked. The scale bar in (A) also refers to (A), (C), and (E). The approximate borders between visual striate cortex (area 17), CG, and SVA are indicated by the bars (see also Tusa et al., 1981; Rosenquist, 1985; Scannell et al., 1999). (**B**) The area of the injection site is shown at higher magnification. The arrowhead shows the path of fibers beneath the injection site within the white matter. Scale bar refers to both (B) and (D). (**C**) A WGA-HRP injection site within the ventromedial portion of CG (AP 5) is shown (cat # NK3). The TMB methodology causes considerably more shrinkage than the DAB process, hence, the size difference between the sections. (**D**) The WGA-HRP injection site is shown at higher magnification. (**E**) Coronal section through a caudal (AP 0) BDA injection site in SVA (cat # JY3).

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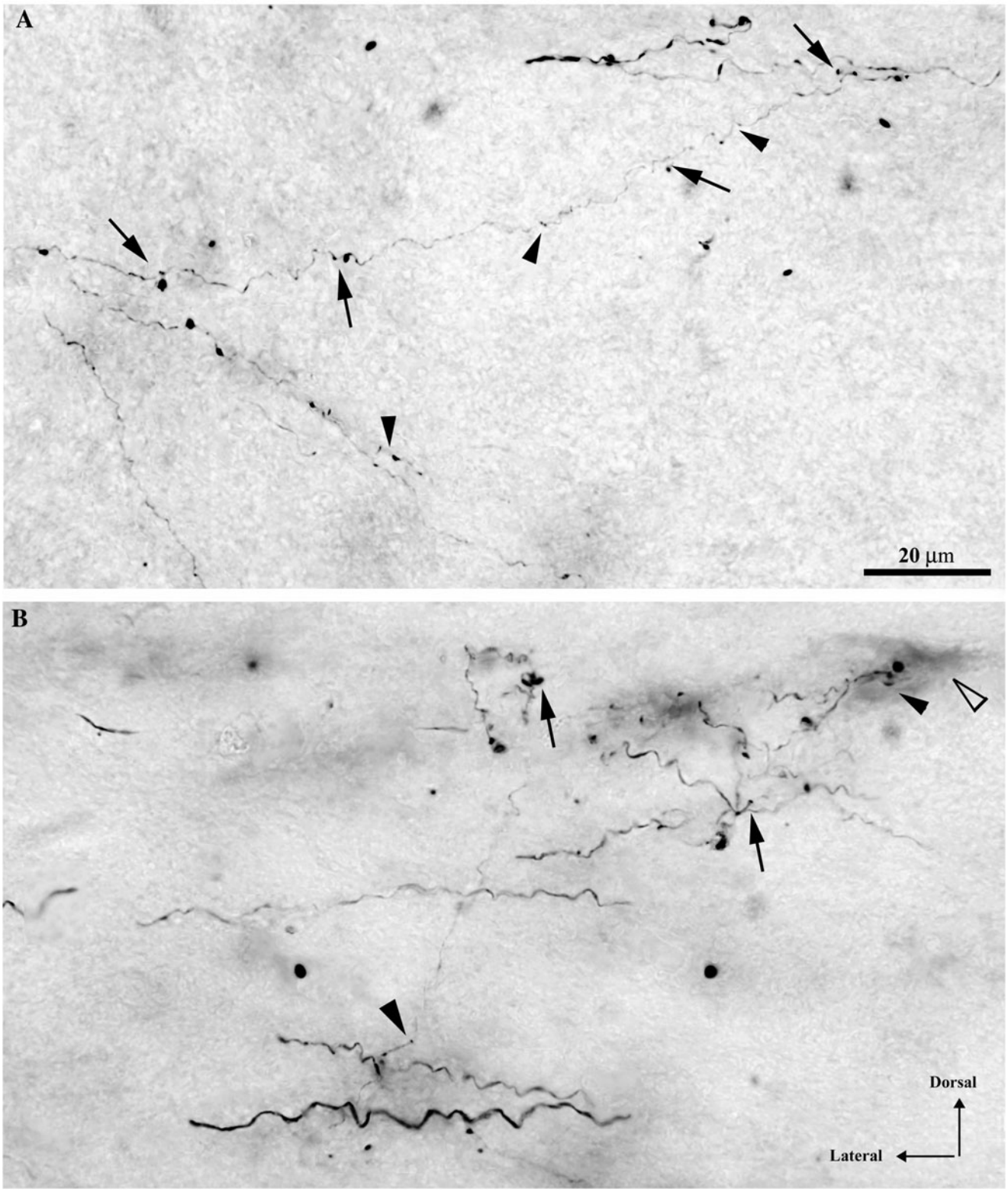


Fig. 2. Terminal labeling within the TRN. (**A**) Presumptive contacts after a BDA injection into CG were characterized as axonal swellings (possible *en passant*-type contacts; arrows), small bouton-like swellings or club-like endings on short side branches (arrowheads). Although not quantified, the majority of these profiles appeared as axonal swellings. Fibers take an oblique or mediolateral path across the TRN. (**B**) Presumptive contacts after a BDA injection into caudal SVA. There appeared to be no qualitative difference in the contacts seen after injections within SVA compared to CG. Note the range of corticothalamic axon sizes within the TRN. The open arrow indicates the position of a TRN soma lightly stained by background labeling. The proximity of the cortical axon close to this cell is suggestive of somatic contacts *via* small boutons. Scale bar applies to (A) and (B).

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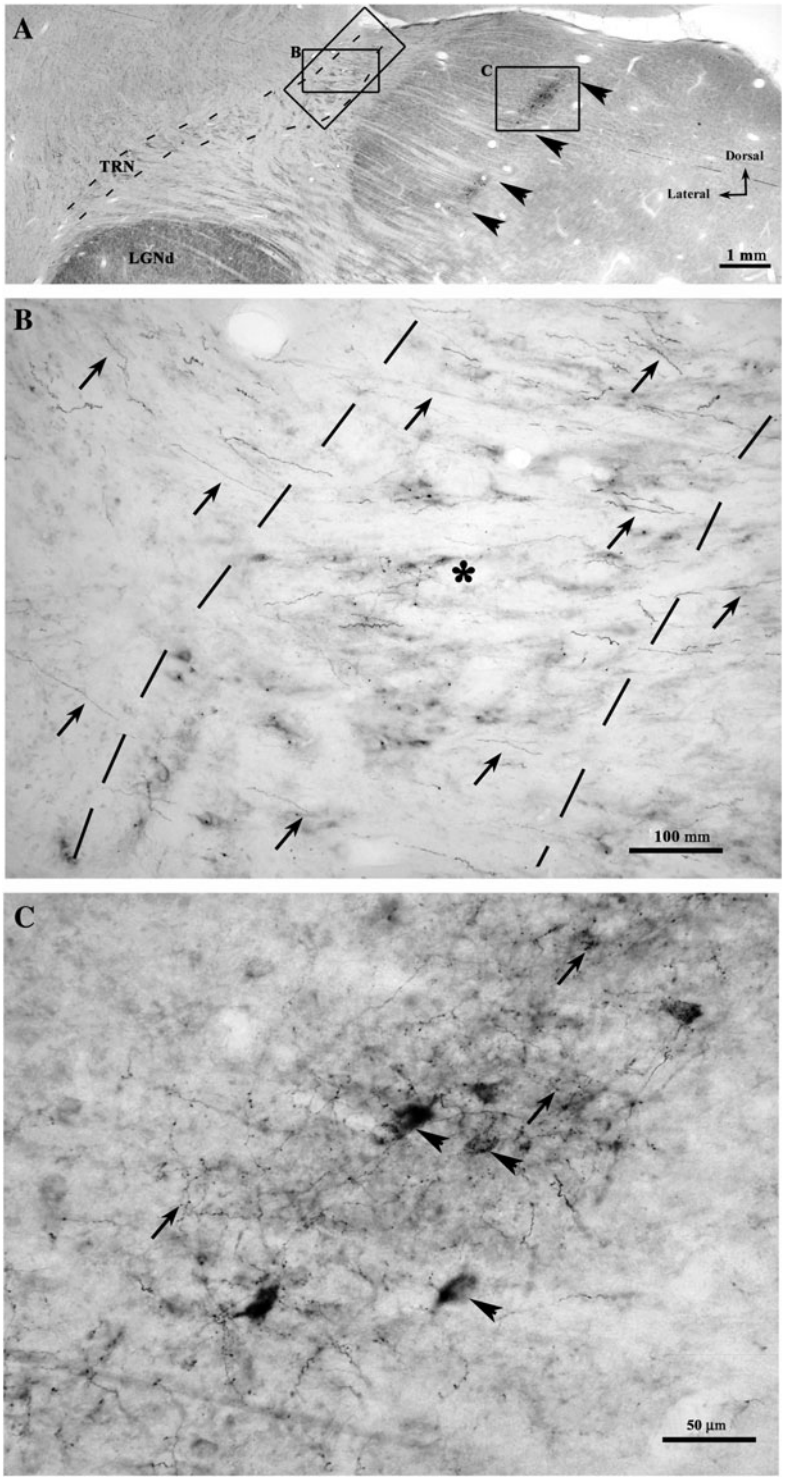


Fig. 3. (**A**) Low-power micrograph showing the location at ~AP 7.5 of labeled terminals and fibers following a caudal BDA injection within the SVA (cat # JY3). The boxed region indicates the extent of dorsoventral labeling within the TRN. The arrowheads indicate a region of labeling between the pulvinar and lateral posterior complex. Note the more intense staining in the dorsal thalamus compared to the TRN. (**B**) The smaller boxed region in (A) is shown at higher magnification to illustrate the trajectory of labeled fibers (arrows) through the TRN. Cells of the TRN are not evenly distributed within the nucleus due to the bundles of corticothalamic and thalamocortical fibers passing through the nucleus and giving it a reticulated appearance. Note that labeling is not confined to cell-rich areas (*) within the borders of the TRN, although there are obvious areas of lower staining in areas of high fiber density. (**C**) Labeled regions within the dorsal thalamus, particularly subdivisions of the lateralis posterior complex, were characterized by areas containing heavily and lightly labeled somata (arrowheads) surrounded by corticothalamic terminal labeling. Labeled profiles were of various sizes, although the projections were predominantly of the small *en passant* and small bouton type (arrows). Labeling was similar to that observed after injections within area 7 (FitzGibbon, 2000).

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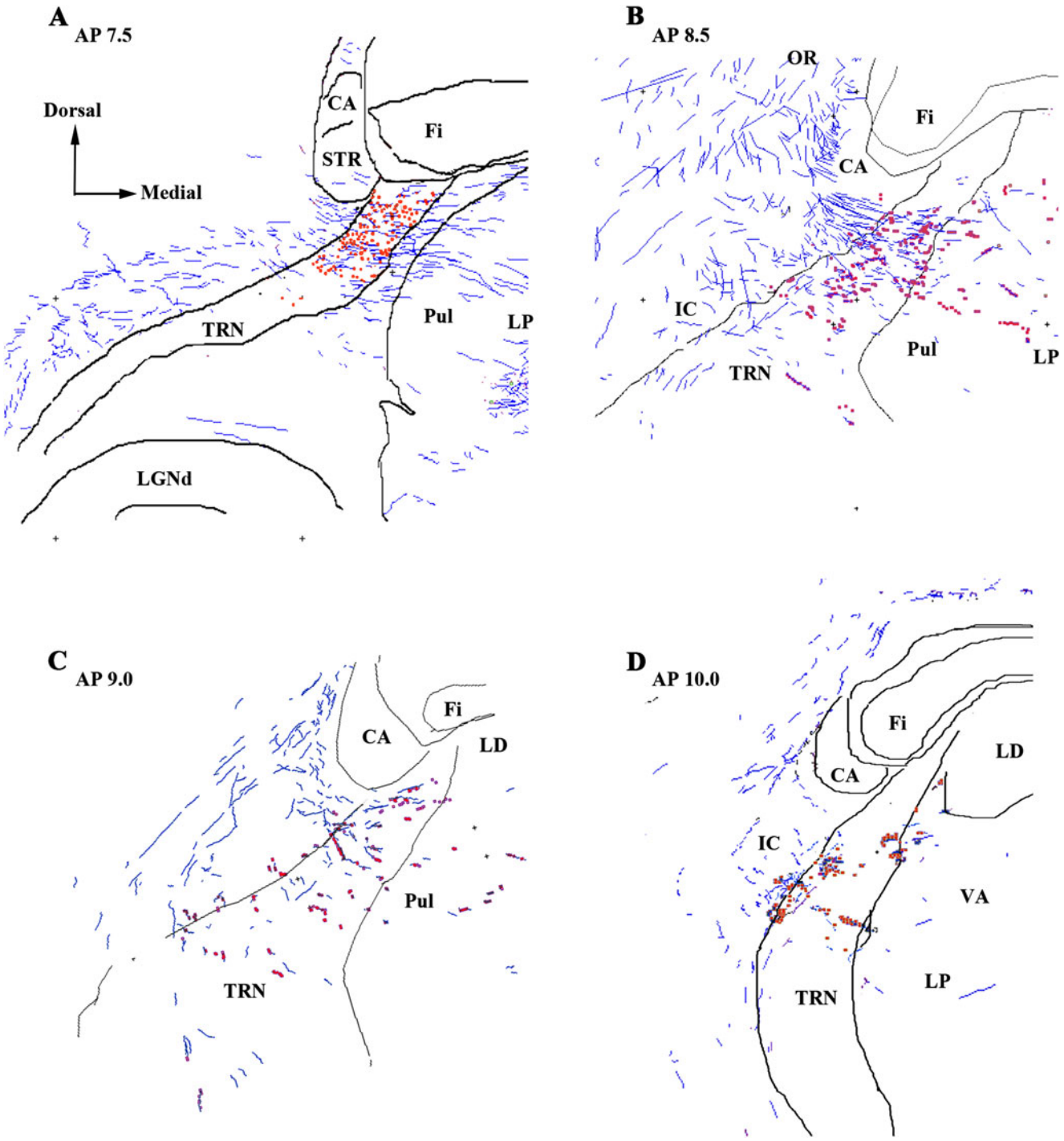


Fig. 4. Drawings show the location of fibers (blue) and axon swellings and boutons (red) within the TRN following cortical injections of BDA. Sections were drawn using a computer-aided morphometry program and are representative of regions showing the highest density of label. (**A**) Labeling in TRN at AP 7.5 following an injection within SVA at AP 0.0. (**B**) Labeling in TRN at AP 8.5 following an injection within SVA at AP 6.0. (**C**) Labeling in TRN at AP 9.0 following a relatively small injection within SVA at AP 8.5. (**D**) Labeling in TRN at AP 10.0 following a small injection within CG at AP 9.0. Abbreviations: CA, caudate nucleus; Fi, fimbria; IC, internal capsule; LGNd, dorsal lateral geniculate nucleus; LD, lateral dorsal nucleus; LP, nucleus lateralis posterior; OR, optic radiation; Pul, pulvinar nucleus; STR, stria terminalis; VA, ventroanterior nucleus.

mediolateral width of the TRN and did not indicate any mediolateral organization (Fig. 4). Following small cortical injections, the numbers of boutons were also proportionately low. When dealing with low bouton numbers, this could lead to an apparent positioning bias within the TRN. Nevertheless, any bias seen in one section was not maintained in adjacent sections producing a wider overall scatter of the boutons and suggests a lack tiers within the SVA/CG projection to the TRN.

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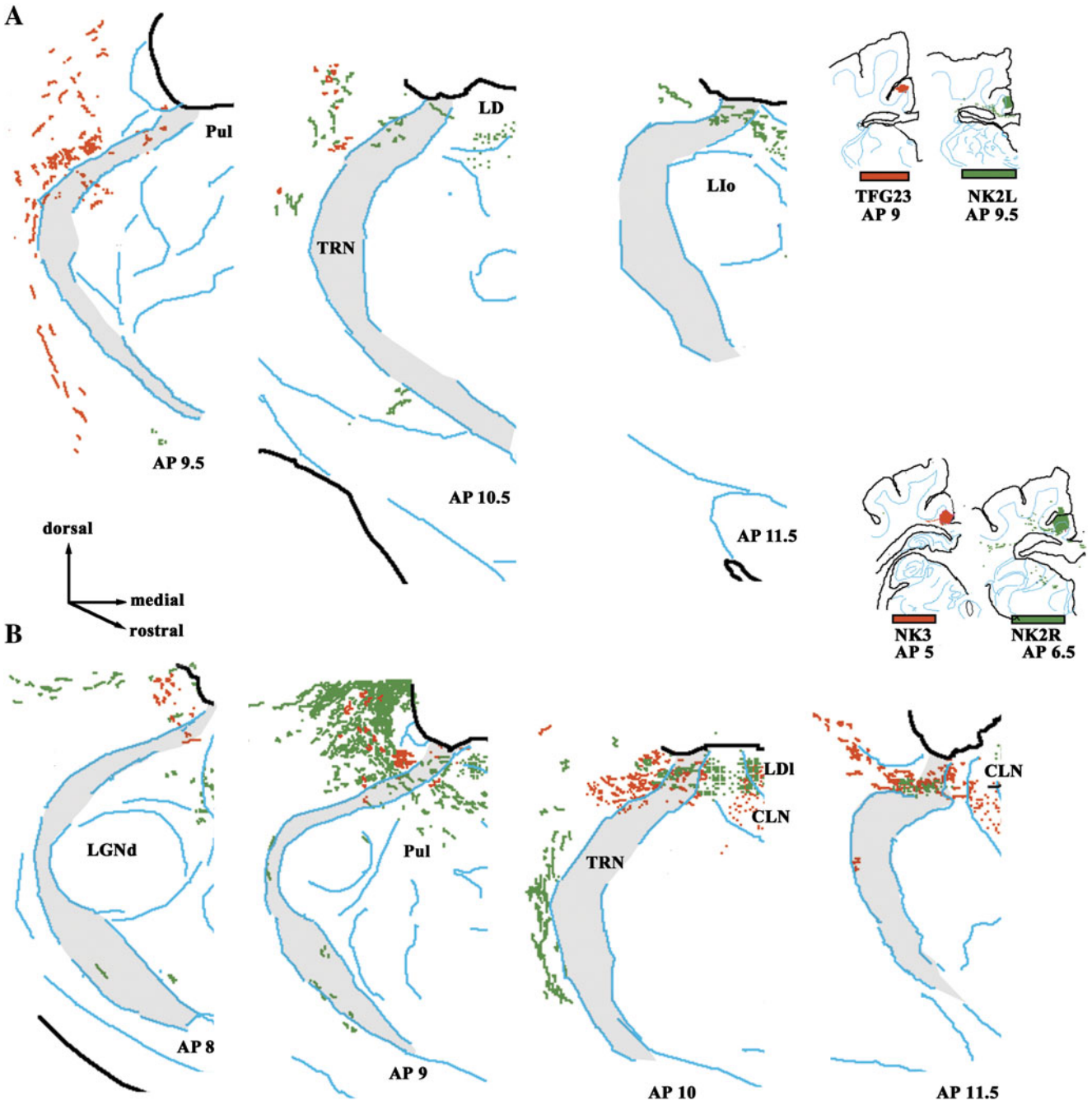


Fig. 5. Four separate injections are illustrated to show the distribution of labeled profiles with the TRN. Injections from rostral (**A**) and caudal (**B**) parts of CG can be compared. Sections were drawn, and then, the labeled distributions superimposed on sections at the same AP plane. The boundaries of the TRN are indicated by the shaded area. Drawings show the location of both labeled fibers and boutons. Previous reports have shown that location of labeled axons provides an accurate picture of the projection zone within the TRN when compared to plots of the boutons seen in BDA-labeled sections. Note that sections from rostral and caudal cat # NK2W (A and B, respectively) were taken from injections in opposite hemispheres. The drawings have been orientated for ease of comparison. Small injections such as that in cat # TFG23B tended to result in relatively light labeling in the TRN and thalamus. Abbreviations: CLN, central lateral nucleus; LIo, pars oralis of the intermediate nucleus of the lateral group; LPI, lateral division of the nucleus lateralis posterior.

Terminal labeling within the thalamus was characterized by numerous axonal swellings (*en passant* contacts) and small terminal boutons. Large boutons forming grape-like clusters were also evident in the thalamus (Robson, 1984; Paré & Smith, 1996; Guillery et al., 2001; for primates, see Rockland, 1996; Zikopoulos & Barbas, 2006; for rat, see Pinault, 2004;) but were not seen in the TRN. The densities of boutons, axon swellings, and terminal branches were clearly higher in thalamic areas compared with labeling observed in the TRN (Fig. 3).

Topography of labeled cortical profiles in the TRN

The locations of axons, boutons, and swellings within the TRN were plotted after BDA injections into SVA or CG (see Figs. 4–6),

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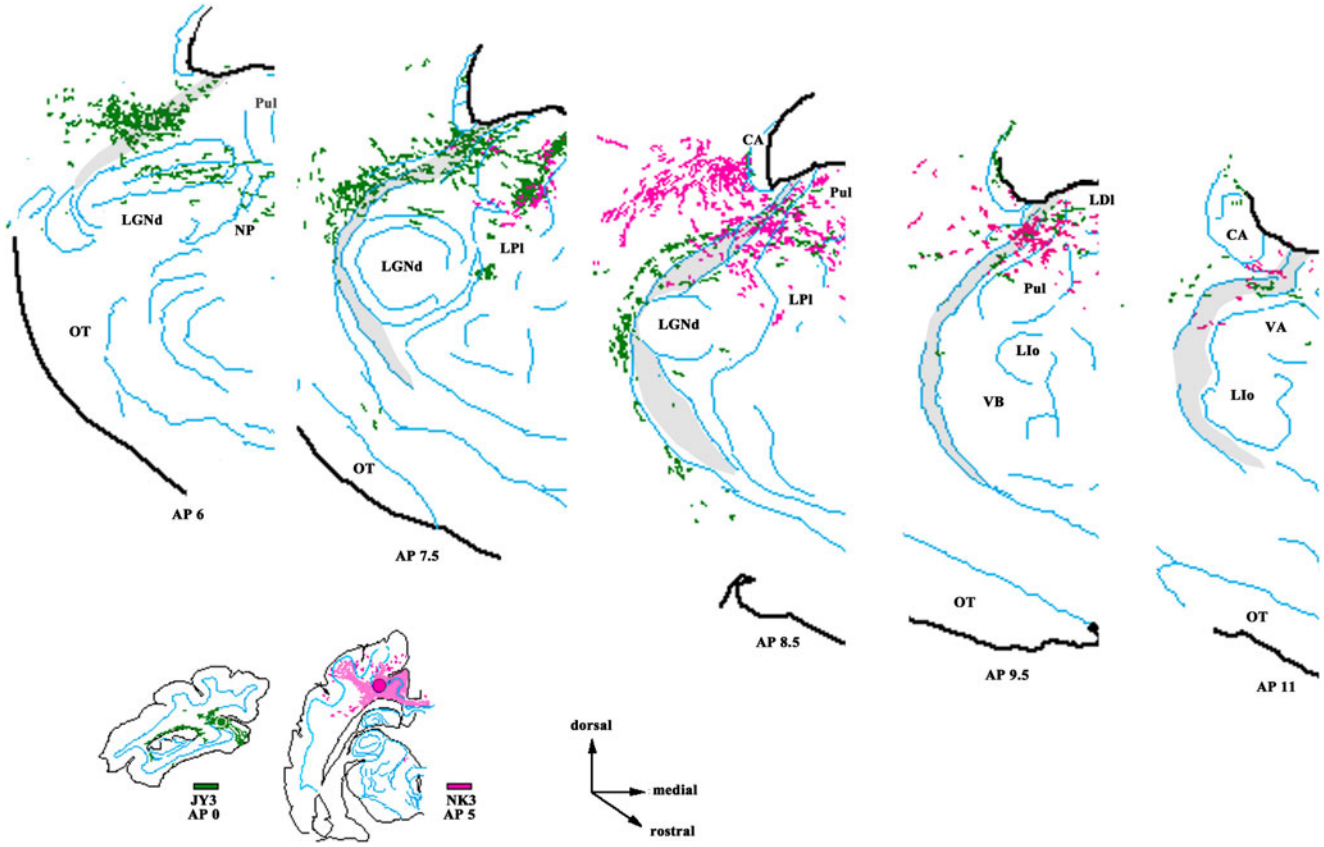


Fig. 6. Rostral and caudal injections within the SVA can be compared after overlapping the distribution of labeled profiles within the TRN. Note that the TRN labeling from the caudal SVA injection tends to spread more ventrally within the TRN compared to the rostral SVA injection, but both injection sites label the rostrodorsal aspect of the TRN. Abbreviations: NP, posterior nucleus of Rioch; OT, optic tract; VB, Ventrobasal complex.

whereas the locations of labeled axons and presumptive terminal fields were plotted after WGA-HRP injections. Previous reports have shown that location of labeled axons following WGA-HRP or BDA injections provides an accurate picture of the overall projection zone within the TRN (Figs. 5 and 6), such that a certain proportion of labeled axons throughout the projection zone are accompanied by boutons (BDA labeling). WGA-HRP injections provide sufficient detail to define the projection zone due to axonal labeling and may result in localized areas of higher density labeling; however, separating axonal labeling from terminal labeling in the TRN can be problematic. Therefore, BDA labeling has been used to determine the distribution of boutons within the TRN (Fig. 4). SVA and CG injections resulted in labeled TRN regions between ~AP 6.0 and ~AP 12.0 (i.e., extending from the rostral pole of the LGNd to the caudal aspect of the ventral anterior (VA) nucleus). Labeled profiles were largely confined to the dorsal half of the TRN (i.e., regions adjacent or dorsal to the LGNd), and labeling was particularly prominent in the rostral TRN regions close to the ventricles. Only a weak topographic organization was apparent with respect to the injection sites. Generally, a caudal to rostral shift of the injection site produced a similar caudal to rostral shift in the focus of labeled profiles. Medial to lateral shifts of the injection site within CG produced very little, if any, evidence for a mediolateral organization. The distribution of SVA contacts (cf. Figs. 5 and 6) overlapped those of the CG; the only difference being a tendency to have a greater dorsoventral spread in parts of the caudal TRN adjacent to the Pulvinar (Pul). Caudal injection sites labeled regions that tended to extend more ventrally within the TRN compared with rostral injection sites.

Discussion

Organization of CG/SVA projections to TRN

Our results show that CG and SVA project to the same area of the TRN, and that this projection zone partially overlaps dorsorostral areas of the larger projection zone defined by visuocortical input (Fig. 7A2). The projection zone also extends to more rostral parts of the TRN that receive information from cortices traditionally classified as nonvisual, for example, area 5 (Fig. 7A3; Robertson & Cunnigham, 1981). The location of the CG/SVA projection within the TRN is in general agreement with previous autoradiographic results (Kaitz & Robertson, 1981), although earlier schematic figures show a more localized projection compared to the more extensive projection zone seen with BDA. The rostrocaudal extent of CG/SVA is only roughly mapped along the rostrocaudal axis of the TRN and is similar to the crude maps described for area 7 (Fig. 7A4; FitzGibbon et al., 1999; FitzGibbon, 2000).

The anatomical nature of the CG/SVA profiles indicates that this input arises from layer VI and is thus a "modulator" rather than a "driver" of the TRN (Sherman & Guillery, 1998; see also Guillery et al., 2001; Gentet & Ulrich, 2004; Reichova & Sherman, 2004; Lam & Sherman, 2007; but cf. Montero, 1999). Zikopoulos and

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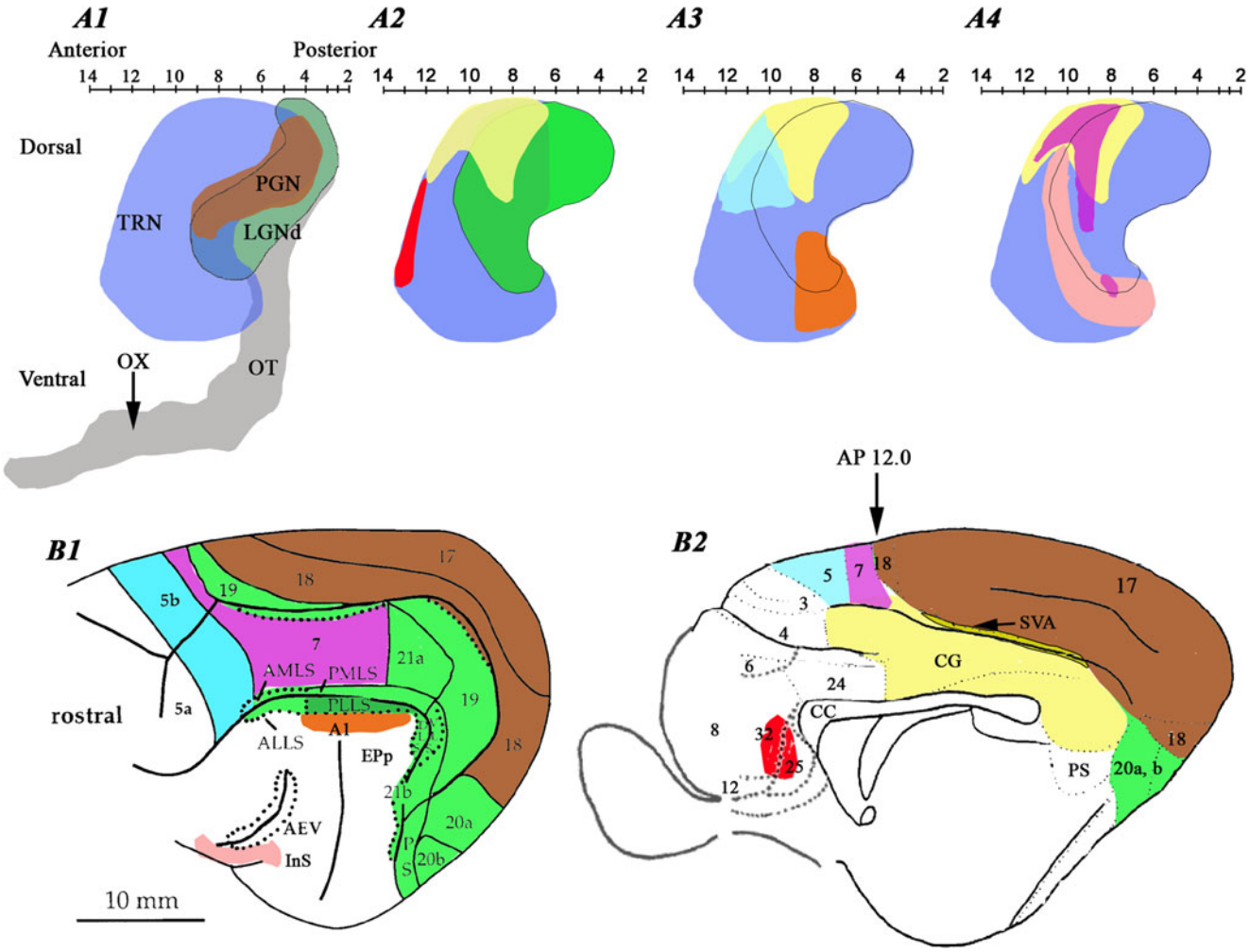


Fig. 7. Summary schematic diagram to illustrate cortical projections zones within the TRN. Sagittal sections of the TRN were traced (Berman & Jones, 1982), and the AP and dorsoventral extent of the TRN reconstructed (light blue in A1–A4; viewed from the side); the LGNd (dark green with outline in A1) and optic tract (gray) and position of the chiasm are shown for additional reference points. Each colored region represents a different cortical projection zone (note that some regions overlap resulting in a mixed color). The cortices projecting to these regions are similarly colored in the lateral (B1) and medial (B2) views of the cortex. The projection to the PGN (brown in A1) constitutes the first-order region of the TRN and receives prominent projections from primary visual cortex (areas 17 and 18). The TRN also receives projections from striate cortex in addition to a number of other higher-order visuotopically organized cortices (green, A2 and outlined in A3 and A4; the colors are partially overlapped by areas 17 and 18 in B). The projection from CG/SVA (yellow) is shown in A2–A4 for comparison with other projections zones. Note the extensive overlap of CG/SVA with area 5–7 but lack of overlap with rostroventral cortical areas associated with visual tasks. The higher-order visuotopically organized cortices of the suprasylvian area have a more rostrally placed projection zone within the TRN visual sector and overlap nonvisual projections (e.g., auditory area A1; A3). The location of the projection zones was deduced from figures found in previous reports (Jones, 1975; Kaitz & Robertson, 1981; Robertson & Cunnigham, 1981; Room et al., 1985; Yen et al., 1985; Crabtree, 1992*a*, 1996, 1998; Bajo et al., 1995; Clascá et al., 1997; FitzGibbon et al., 1999; FitzGibbon, 2000). Abbreviations: AEV, anterior ectosylvian sulcus; DLS, dorsal suprasylvian areas; VLS, ventral suprasylvian areas; EPp, posterior part of posterior ectosylvian gyrus; InS, insular cortex; PS, posterior suprasylvian area; AMLS, anteriomedial lateral suprasylvian area; ALLS, anteriolateral lateral suprasylvian area; PMLS, posteriomedial lateral suprasylvian area; PLLs, posteriolateral lateral suprasylvian area; PS, posterior suprasylvian area; Ps, postsubicular area (for references, see Scannell et al., 1999).

Barbas (2006) have shown that projections from frontal cortices to the TRN in primates contains a mixture of large and small synaptic boutons. This could indicate that the TRN receives some layer V input (a driver) and thus casts doubt on the assumption that only cortical layer VI projects to the TRN.

CG/SVA does not appear to target-specific TRN tiers (cf. Conley & Diamond, 1990; Conley et al., 1991; Crabtree, 1992*a*, 1996, 1998; Lozsádi, 1994; Lozsádi et al., 1996; Kimura et al., 2005) and in this respect is similar to projections from area 7 (FitzGibbon et al., 1999; FitzGibbon, 2000). This seems to be in marked contrast to insular and anterior sylvian cortical projections that target specific mediolateral TRN tiers that are rostroventral to the CG/SVA projection zone (Clascá et al., 1997).

CG/SVA, thalamus, and TRN sectors

The cat's posterior CG, although not visutopically organized (Kalia & Whitteridge, 1973), has extensive connections with multiple visual cortices (Symonds & Rosenquist, 1984; Rosenquist, 1985; Olson & Musil, 1992; for references, see Scannell et al., 1999).

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Olson and Musil (1992) indicated that the major connections to posterior CG arise from frontal (36%), visual (30%), anterior cingulate (16%), and parahippocampal (14%) cortices. They proposed that CG could be subdivided into somatic, ocular, and complex subregions. The thalamus and CG have a crude topographic relationship (caudal CG to mediodorsal thalamus, rostral CG to ventrorostral thalamus; for details, see Kaitz & Robertson, 1981; Robertson & Kaitz, 1981; Niimi et al., 1983; Raczkowski & Rosenquist, 1983; Room et al., 1985; Olson & Musil, 1992; Rodrigo-Angulo & Reinoso-Suarez, 1995), and this organization also appears to be reflected in the rostrocaudal connections with the TRN (rostral TRN–intralaminar complex; dorsocaudal TRN–LP-Pul complex; Jones, 1975; Steriade et al., 1984; Rodrigo-Angulo & Reinoso-Suárez, 1988; FitzGibbon, 1994; FitzGibbon et al., 1995; Sakoda et al., 2004).

Can CG/SVA affect auditory function via *the TRN?*

Based on anatomical studies, one could argue that, at least in the cat, CG may be more closely associated with visual than auditory processing. This is also reflected in the projections from CG/SVA to the TRN regions that predominately project to nuclei associated with visual or visuomotor processing (e.g., LP-Pul and intralaminar complexes; FitzGibbon, 1994; FitzGibbon et al., 1995). Nevertheless, CG/SVA/TRN may affect auditory processing *via* connections with thalamic areas such as the medial division of the lateralis posterior nucleus and the medial division of the lateralis suprageniculate nucleus that have marked multimodal responses (Norita et al., 1986; Benedek et al., 1997; Sakoda et al., 2004). Anatomical and physiological studies have shown that there is a lack of strict reciprocity between cells of the TRN and the thalamus creating the possibility for a number of "open loops" (Rodrigo-Angulo & Reinoso-Suárez, 1988; FitzGibbon, 1994; FitzGibbon et al., 1995; Deschênes et al., 1998; Kolmac & Mitrofanis, 1998; Pinault & Deschênes, 1998; Crabtree & Isaac, 2002; Gentet & Ulrich, 2003; Pinault, 2004; Kimura et al., 2007; Lam & Sherman, 2007), which can initiate crossmodal inhibition or modulation between different thalamic nuclei (Crabtree & Isaac, 2002). Interestingly, insular cortex and the anterior ectosylvian sulcus, considered to be an extrastriate visual or auditory–visual field (for references, see Norita et al., 1986; Clascá et al., 1997; Scannell et al., 1999), have projection zones in the TRN that differ from the projections zones of the striate visual cortices and CG/SVA (cf. FitzGibbon et al., 1999; FitzGibbon, 2000; Clascá et al., 1997). It would be of interest to determine if the CG targets auditory sectors of the TRN at the expense of the visual sector in animals, such as bats, that are highly dependent on a different modality for orientation.

Functional considerations

Posterior CG may be involved in processes that depend on the integration of hippocampal output (*via* anterior thalamic nuclei) and sensory information, in particular, the involvement of spatial orientation and memory (monkeys, Murray et al., 1989; rats, Sutherland et al., 1988; Cooper et al., 2001). Area 7 has strong reciprocal connections with CG/SVA (Joseph & Giroud, 1986; Olson & Lawler, 1987; Olson & Musil, 1992; for functions, see Ventre, 1985; Joseph & Giroud, 1986) and has a TRN projection zone that overlaps that formed by the CG/SVA (Fig 6A4). The LP-Pul complex, which also has connections with the CG/SVA projection zone in the TRN, is also an area of multimodal convergence and may play a role in eye movement and orientation, visual salience, and attention (Avanzini et al., 1980, 2000; Motles et al., 1980; Shumikhina & Maiskii, 1991; Robinson & Petersen, 1992; Shipp, 2004).

The CG/SVA, in combination with area 7, may provide an important element of behavioral relevance to thalamic function (eye movement/orientation). Previous work (cf. Zhang & Jones, 2003; Deleuze & Huguenard, 2006; Lam et al., 2006) suggests two possibilities concerning the effect of CG/SVA input to TRN. On the one hand, CG/SVA may initiate a spread of inhibition to the adjacent visual and somatic recipient zones of the TRN causing disinhibition of visually related regions of the thalamus prior to affecting auditory regions. On the other hand, CG/SVA effects may remain highly localized within the TRN and enhance signal-to-noise ratios or sharpen sensory processing (Funke & Eysel, 1998; Lam & Sherman, 2005) in a small subset of thalamic cells or areas tuned to visual orientation-specific tasks (Motles et al., 1980).

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References

Asanuma, C. (1992). Noradrenergic innervation of the thalamic reticular nucleus: A light and electron microscope immunohistochemical study in rats. *The Journal of Comparative Neurology* **319**, 299–311.

Avanzini, G., Broggi, G., Franceschetti, S. & Spreafico, R. (1980). Multisensory convergence and interaction in the pulvinar-lateralis posterior complex of the cat's thalamus. *Neuroscience Letters* **19**, 27–32.

Avanzini, G., Panzica, F. & de Curtis, M. (2000). The role of the thalamus in vigilance and epileptogenic mechanisms. *Clinical Neurophysiology* **111**, s19–s26.

Bajo, V.M., Rouiller, E.M., Welker, E., Clarke, S., Villa, A., Deribaupierre, Y. & Deribaupierre, F. (1995). Morphology and spatial-distribution of corticothalamic terminals originating from the cat auditory-cortex. *Hearing Research* **83**, 161–174.

Benedek, G., Perény, J., Kovács, G., Fischer-Szátmári, L. & Katoh, Y.Y. (1997). Visual, somatosensory, auditory and nociceptive modality properties in the feline suprageniculate nucleus. *Neuroscience* **78**, 179–189.

Berman, A.L. & Jones, E.G. (1982). The Thalamus and Basal Telencephalon of the Cat. A Cytoarchitectonic Atlas with Stereotaxic Coordinates. Madison, WI: University of Wisconsin Press.

Clascá, F., llamas, A. & Reinoso-Suárez, F. (1997). Insular cortex and neighboring fields in the cat: A redefinition based on cortical microarchitecture and connections with the thalamus. *The Journal of Comparative Neurology* **384**, 456–482.

Coleman, K.A. & Mitrofanis, J. (1996). Organization of the visual reticular thalamic nucleus of the rat. *The European Journal of Neuroscience* **8**, 388–404.

Conley, M. & Diamond, I.T. (1990). Organization of the visual sector of the thalamic reticular nucleus in *Galago*—Evidence that the dorsal lateral geniculate and pulvinar nuclei occupy separate parallel tiers. *The European Journal of Neuroscience* **2**, 211–226.

Conley, M., Kupersmith, A.C. & Diamond, I.T. (1991). The organization of projections from subdivisions of the auditory cortex and thalamus to the auditory sector of the thalamic reticular nucleus in *Galago*. *The European Journal of Neuroscience* **3**, 1089–1103.

Cooper, B.G., Manka, T.F. & Mizumori, S.J.Y. (2001). Finding your way in the dark: The retrospinal cortex contributes to spatial memory and navigation without visual cues. *Behavioral Neuroscience* **115**, 1012–1028.

Crabtree, J.W. (1992*a*). The somatotopic organization within the cat's thalamic reticular nucleus. *The European Journal of Neuroscience* **4**, 1352–1361.

Crabtree, J.W. (1992*b*). The somatotopic organization within the rabbit's thalamic reticular nucleus. *The European Journal of Neuroscience* **4**, 1343–1351.

https://doi.org/10.1017/S0952523811000319 Published online by Cambridge University Press

Crabtree, J.W. (1996). Organization in the somatosensory sector of the cat's thalamic reticular nucleus. *The Journal of Comparative Neurology* **366**, 207–222.

Crabtree, J.W. (1998). Organization in the auditory sector of the cat's thalamic reticular nucleus. *The Journal of Comparative Neurology* **390**, 167–182.

Crabtree, J.W., Collingridge, G.L. & Isaac, J.T.R. (1998). A new intrathalamic pathway linking modality-related nuclei in the dorsal thalamus. *Nature Neuroscience* **1**, 389–394.

Crabtree, J.W. & Isaac, J.T.R. (2002). New intrathalamic pathways allowing modality-related and cross modality switching in the dorsal thalamus. *The Journal of Neuroscience* **22**, 8754–8761.

Crabtree, J.W. & Killackey, H.P. (1989). The topographic organization and axis of projection within the visual sector of the rabbit's thalamic reticular nucleus. *The European Journal of Neuroscience* **1**, 94–109.

Crick, F. & Koch, C. (1990). Some reflections on visual awareness. *Cold Spring Harbor Symposia on Quantitative Biology* **55**, 953–962.

Deleuze, C. & Huguenard, J.R. (2006). Distinct electrical and chemical connectivity maps in the thalamic reticular nucleus: Potential roles in synchronization and sensation. *The Journal of Neuroscience* **26**, 8633–8645.

Deschênes, M., Veinante, P. & Zhang, Z.-W. (1998). The organization of corticothalamic projections: Reciprocity versus parity. *Brain Research Reviews* **28**, 286–308.

FitzGibbon, T. (1994). Rostral reticular nucleus of the thalamus sends a patchy projection to the pulvinar lateralis-posterior complex of the cat. *Experimental Neurology* **129**, 266–278.

FitzGibbon, T. (2000). Cortical projections from the suprasylvian gyrus to the reticular thalamic nucleus in the cat. *Neuroscience* **97**, 643–655.

FitzGibbon, T., Bittar, R.G. & Dreher, B. (1999). Projections from striate and extrastriate visual cortices of the cat to the reticular thalamic nucleus. *The Journal of Comparative Neurology* **410**, 467–488.

FitzGibbon, T., Tevah, L.V. & Sefton, A.J. (1995). Connections between the reticular nucleus of the thalamus and pulvinar-lateralis posterior complex: A WGA-HRP study. *The Journal of Comparative Neurology* **363**, 489–504.

Funke, K. & Eysel, U.T. (1998). Inverse correlation of firing of single topographically matched perigeniculate neurons and cat dorsal lateral geniculate relay cells. *Visual Neuroscience* **15**, 711–729.

Gentet, L.J. & Ulrich, D. (2003). Strong, reliable and precise synaptic connections between thalamic relay cells and neurones of the nucleus reticularis in juvenile rats. *The Journal of Physiology* **546**, 801–811.

Gentet, L.J. & Ulrich, D. (2004). Electrophysiological characterization of synaptic connections between layer VI cortical cells and neurons of the nucleus reticularis thalami in juvenile rats. *The European Journal of Neuroscience* **19**, 625–633.

Graybiel, A.M. & Berson, D.M. (1980). Histochemical identification and afferent connections of subdivisions in the lateralis posterior-pulvinar complex and related thalamic nuclei in the cat. *Neuroscience* **5**, 1175–1238.

Guillery, R.W., Feig, S.L. & Lozsádi, D.A. (1998). Paying attention to the thalamic reticular nucleus. *Trends in Neurosciences* **21**, 28–32.

Guillery, R.W., Feig, S.L. & Van Lieshout, D.P. (2001). Connections of higher order visual relays in the thalamus: A study of corticothalamic pathways in cats. *The Journal of Comparative Neurology* **438**, 66–85.

Guillery, R.W. & Sherman, S.M. (2002). Thalamic relay functions and their role in corticocortical communication: Generalizations from the visual system. *Neuron* **33**, 163–175.

Heath, C.J. & Jones, E.G. (1971). An experimental study of ascending connections from the posterior group of thalamic nuclei in the cat. *The Journal of Comparative Neurology* **141**, 397–426.

Jones, E.G. (1975). Some aspects of the organization of the thalamic reticular complex. *The Journal of Comparative Neurology* **162**, 258–308.

Joseph, J.P. & Giroud, P. (1986). Visuomotor properties of neurons in the anterior suprasylvian gyrus in the awake cat. *Experimental Brain Research* **62**, 355–362.

Kaitz, S.S. & Robertson, R.T. (1981). Thalamic connections with limbic cortex. II Corticothalamic projections. *The Journal of Comparative Neurology* **195**, 527–545.

Kalia, M. & Whitteridge, D. (1973). The visual areas in the splenial sulcus of the cat. *The Journal of Physiology* **232**, 275–283.

Kimura, A., Donishi, T., Okamoto, K. & Tamai, Y. (2005). Topography of projections from the primary and non-primary auditory cortical area to the medial geniculate body and thalamic reticular nucleus in the rat. *Neuroscience* **135**, 1325–1342.

Kimura, A., Imbe, H., Donishi, T. & Tamai, Y. (2007). Axonal projections of single auditory neurons in the thalamic reticular nucleus: Implications for tonotopy-related gating function and cross modulation. *The European Journal of Neuroscience* **26**, 3524–3535

Kolmac, C.I. & Mitrofanis, J. (1998). Patterns of brainstem projection to the thalamic reticular nucleus. *The Journal of Comparative Neurology* **396**, 531–543.

Lam, Y.-W., Nelson, C.S. & Sherman, S.M. (2006). Mapping of the functional interconnections between thalamic reticular neurons using photostimulation. *Journal of Neurophysiology* **96**, 2593–2600.

Lam, Y.-W. & Sherman, S.M. (2005). Mapping by laser photostimulation of connections between the thalamic reticular and ventral posterior lateral nuclei in the rat. *Journal of Neurophysiology* **94**, 2472–2483.

Lam, Y.-W. & Sherman, S.M. (2007). Different topography of the reticular thalamic inputs to first- and higher-order somatosensory thalamic relays revealed using photostimulation. *Journal of Neurophysiology* **98**, 2093–2909.

Lozsádi, D.A. (1994). Organization of cortical afferents to the rostral, limbic sector of the rat thalamic reticular nucleus. *The Journal of Comparative Neurology* **341**, 520–533.

Lozsádi, D.A., Gonzalez-Soriano, J. & Guillery, R.W. (1996). The course and termination of corticothalamic fibres arising in the visual cortex of the rat. *The European Journal of Neuroscience* **8**, 2416–2427.

McAlonan, K., Cavanaugh, J. & Wurtz, R.H. (2006). Attentional modulation of thalamic reticular neurons. *The Journal of Neuroscience* **26**, 4444–4450.

McAlonan, K., Cavanaugh, J. & Wurtz, R.H. (2008). Guarding the gateway to cortex with attention in visual thalamus. *Nature* **456**, 391–394.

McCormick, D.A. & Bal, T. (1997). Sleep and arousal. *Annual Review of Neuroscience* **20**, 185–215.

Montero, V.M. (1997). C-fos induction in sensory pathway of rats exploring a novel complex environment: Shifts of active thalamic reticular sectors by predominant sensory cues. *Neuroscience* **76**, 1069–1081.

Montero, V.M. (1999). Amblyopia decreases activation of the cortico-geniculate pathway and visual thalamic reticularis in attentive rats: A 'focal attention' hypothesis. *Neuroscience* **91**, 805–817.

Motles, E., Ely, Y. & Elazar, Z. (1980). Role of the pulvinar-lateral posterior nucleus complex in turning behaviour. *Physiology and Behavior* **25**, 921–929.

Murray, E.A., Davidson, M., Gaffan, D., Olton, D.S. & Suomi, S. (1989). Effects of fornix transection and cingulate cortical ablation on spatial memory in rhesus monkeys. *Experimental Brain Research* **74**, 173–186.

Niimi, K., Niimi, M., Matsuoka, H., Yanagihara, M. & Katayama, T. (1983). The laminar arrangement of limbic thalamocortical neurons in the lateropulvinar nuclei of the cat thalamus. *Neuroscience Letters* **38**, 215–219.

Norita, M., Mucke, L., Benedek, G., Albowitz, B., Katoh, Y. & Creutzfeldt, O.D. (1986). Connections of the anterior ectosylvian visual area (AEV). *Experimental Brain Research* **62**, 225–240.

Olson, C.R. & Lawler, K. (1987). Cortical and subcortical afferent connections of a posterior division of feline area 7 (area 7p). *The Journal of Comparative Neurology* **259**, 13–30.

Olson, C.R. & Musil, S.Y. (1992). Topographic organization of cortical and subcortical projections to posterior cingulate cortex in the cat: Evidence for somatic, ocular, and complex subregions. *The Journal of Comparative Neurology* **324**, 237–260.

Paré, D. & Smith, Y. (1996). Thalamic collaterals of corticostriatal axons: Their termination field and synaptic targets in cats. *The Journal of Comparative Neurology* **372**, 551–567.

Pinault, D. (2004). The thalamic reticular nucleus: Structure, function and concept. *Brain Research Reviews* **46**, 1–31.

Pinault, D. & Deschênes, M. (1998). Projection and innervation patterns of individual thalamic reticular axons in the thalamus of the adult rat: A three dimensional, graphic, and morphometric analysis. *The Journal of Comparative Neurology* **391**, 180–203.

Raczkowski, D. & Rosenquist, A.C. (1983). Connection of the multiple visual cortical areas with the lateral posterior-pulvinar complex and

https://doi.org/10.1017/S0952523811000319 Published online by Cambridge University Press

adjacent thalamic nuclei in the cat. *The Journal of Neuroscience* **3**, 1912–1942.

Raeva, S. & Lukashev, A. (1993). Unit activity in human thalamic reticularis neurons II. Activity evoked by significant and non-significant verbal or sensory stimuli. *Electroencephalography and Clinical Neurophysiology* **86**, 110–122.

Reichova, I. & Sherman, S.M. (2004). Somatosensory corticothalamic projections: Distinguishing drivers from modulators. *Journal of Neurophysiology* **92**, 2185–2197.

Robertson, R.T. & Cunningham, T.J. (1981). Organization of corticothalamic projections from parietal cortex in cat. *The Journal of Comparative Neurology* **199**, 569–585.

Robertson, R.T. & Kaitz, S.S. (1981). Thalamic connections with limbic cortex. I. Thalamocortical projections. *The Journal of Comparative Neurology* **195**, 501–525.

Robinson, D.L. & Petersen, S.E. (1992). The pulvinar and visual salience. *Trends in Neurosciences* **15**, 127–132.

Robson, J.A. (1983). The morphology of corticofugal axons to the dorsal lateral geniculate nucleus in the cat. *The Journal of Comparative Neurology* **216**, 89–103.

Rockland, K.S. (1996). Two types of corticopulvinar terminations: Round (type 2) and elongate (type 1). *The Journal of Comparative Neurology* **368**, 57–87.

Rodrigo-Angulo, M.L. & Reinoso-Suárez, F. (1988). Connections to the lateral posterior-pulvinar complex from the reticular and ventral lateral geniculate thalamic nuclei: A topographical study in the cat. *Neuroscience* **26**, 449–459.

Rodrigo-Angulo, M.L. & Reinoso-Suarez, F. (1995). Afferent connections of the lateralis medialis thalamic nucleus in the cat. *Brain Research Bulletin* **38**, 53–67.

Room, P., Russchen, F.T., Groenewegen, H.J. & Lohmann, H. (1985). Efferent connections of the prelimbic (Area 32) and the infralimbic (Area 25) cortices: An anterograde tracing study in the cat. *The Journal of Comparative Neurology* **242**, 40–55.

Rosenquist, A.C. (1985). Connections of visual cortex in the cat. In *Cerebral Cortex*, ed. Peters, A. & Jones, E.G., pp. 81–117. Plenum Publishing Corporation, New York.

Sakoda, T., Kimura, A., Donishi, T., Kitano, H. & Tamai, Y. (2004). Presence and connections of auditory neurons in the rostrodorsal and rostrolateral parts of the thalamic reticular nucleus. *Acta Oto-laryngologica. Supplementum* **553**, 36–42.

Scannell, J.W., Burns, G.A.P.C., Hilgetag, C.C., O'Neil, M.A. & Young, M.P. (1999). The connectional organization of the corticothalamic system of the cat. *Cerebral Cortex* **9**, 277–299.

Sherman, S.M. & Guillery, R.W. (1998). On the actions that one nerve cell can have on another: Distinguishing "drivers" from "modulators". *Proceedings of the National Academy of Sciences of the United States of America* **95**, 7121–7126.

Sherman, S.M. & Koch, C. (1986). The control of retinogeniculate transmission in the mammalian lateral geniculate nucleus. *Experimental Brain Research* **63**, 1–20.

Shipp, S. (2004). The brain circuitry of attention. *Trends in Cognitive Sciences* **8**, 223–230.

Shosaku, A. & Sumitomo, I. (1983). Auditory neurons in the rat thalamic reticular nucleus. *Experimental Brain Research* **49**, 432–442.

Shumikhina, S.I. & Maiskii, V.A. (1991). Relationship between thalamic projections and different areas of the parietal association cortex in cats. *Neurophysiology* **23**, 100–106.

Steriade, M., Jones, E.G. & McCormick, D.A. (1997). *Thalamus*, Vol. **1**. Amsterdam, The Netherlands: Elsevier.

Steriade, M. & Llinas, R.R. (1988). The functional states of the thalamus and the associated neuronal interplay. *Physiological Reviews* **68**, 649–742.

Steriade, M., Parent, A. & Hada, J. (1984). Thalamic projections of nucleus reticularis thalami of cat: A study using retrograde transport of horseradish peroxidase and fluorescent tracers. *The Journal of Comparative Neurology* **229**, 531–547.

Sugitani, M. (1979). Electrophysiological and sensory properties of the thalamic reticular neurones related to somatic sensation in rats. *The Journal of Physiology* **290**, 79–95.

Sutherland, R.J., Whishaw, I.Q. & Kolb, B. (1988). Contributions of cingulate cortex to two forms of spatial learning and memory. *The Journal of Neuroscience* **8**, 1863–1872.

Symonds, L.L. & Rosenquist, A.C. (1984). Corticocortical connections among visual areas in the cat. *The Journal of Comparative Neurology* **229**, 1–38.

Tusa, R.J., Palmer, L.A. & Rosenquist, A.C. (1978). The retinotopic organization of area 17 (striate cortex) in the cat. *The Journal of Comparative Neurology* **177**, 213–236.

Tusa, R.J., Palmer, L.A. & Rosenquist, A.C. (1981). Multiple cortical visual areas. Visual field topography in the cat. In *Cortical Sensory Organization*, ed. Woolsey, C.N., pp. 1–31. New Jersey, NJ: Humana Press.

Tusa, R.J., Rosenquist, A.C. & Palmer, L.A. (1979). Retinotopic organization of areas 18 and 19 in the cat. *The Journal of Comparative Neurology* **185**, 657–678.

Ventre, J. (1985). Cortical control of oculomotor functions. I Optokinetic nystagmus. *Behavioural Brain Research* **15**, 211–226.

Yen, C.T., Conley, M., Hendry, S.H.C. & Jones, E.G. (1985). The morphology of physiologically identified GABAergic neurons in the somatic sensory part of the thalamic reticular nucleus in the cat. *The Journal of Neuroscience* **5**, 2254–2268.

Yingling, C.D. & Skinner, J.E. (1975). Regulation of unit activity in nucleus reticularis thalami by the mesencephalic reticular formation and the frontal granular cortex. *Electroencephalography and Clinical Neurophysiology* **39**, 635–642.

Zhang, L. & Jones, E.G. (2003). Corticothalamic inhibition in the thalamic reticular nucleus. *Journal of Neurophysiology* **91**, 759–766.

Zikopoulos, B. & Barbas, H. (2006). Prefrontal projections to the thalamic reticular nucleus form a unique circuit for attentional mechanisms. *The Journal of Neuroscience* **26**, 7348–7361.

https://doi.org/10.1017/S0952523811000319 Published online by Cambridge University Press