Intrathalamic Interaction in the Medial Geniculate Body

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Ph.D
The Hong Kong Polytechnic University
2012

The Hong Kong Polytechnic University
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A thesis submitted in partial fulfillment of the requirements for the Degree of Doctor of Philosophy

July 2011

CERTIFICATE OF ORIGINALITY

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Guo Shanshan

Abstract of thesis entitled "Intrathalamic Interaction in the Medial Geniculate Body" submitted by Guo Shanshan for the degree of Doctor of Philosophy at the Hong Kong Polytechnic University in June 2011

Abstract

All sensory signals other than olfactory ones go through the thalamus before reaching to the cortex. The thalamus receives massive feedback from the cortex. Both thalamocortical and corticothalamic projects pass through a thin sheet structure in the ventral thalamus called thalamic reticular nucleus (TRN) and give collateral inputs to its neurons. It has been suggested that the thalamus together with the TRN is not a simple relay station but a complicated processor. Previous studies have shown that the corticofugal projections have a strong modulation on the thalamic relay neurons. In this study, we investigated the intrathalamic interaction between different nuclei in the auditory system of rats and guinea pigs.

Specifically, we investigated the gain adjustment in medial geniculate body (MGB) by TRN and the cross modality modulation via the TRN, and confirmed the pathway though which the MGB was modulated, by in-vivo extracellular and intracellular recording.

In the first experiment, we examined the modulating effect of electrical activation of one site in the MGB on neuronal responses to acoustic stimuli in another site of the same nucleus. The auditory cortex was ablated to minimize the recurrent

activation of the thalamocortical loop. Electrical activation of the MGB preceded the acoustic stimulus and would activate the corresponding TRN neurons, which in turns inhibited the MGB neuronal responses to the acoustic stimulus. Both facilitating and inhibitory modulation effects were found in the MGB, and the majority of the modulation was inhibition. The facilitation appeared as excitatory postsynaptic potentials or increased spike number in auditory responses. The inhibitory modulation appeared as inhibitory postsynaptic potentials (IPSPs) or decreased spike number in auditory responses.

In the second experiment, we inactivated TRN by lidocaine after inhibitory modulation was found in MGB, and then repeated the experimental procedures as in the first experiment. We found that the inhibitory modulation was diminished after TRN inactivation.

In the third experiment, we inactivated the inferior colliculus (IC) after we recorded the auditory responses of the MGB neurons. Electrical stimulation at the neighboring MGB site triggered similar IPSPs in the recorded MGB neuron. The IPSPs, the representation of inhibition modulation, still existed, which means that IC was not involved in this modulating pathway.

In the fourth experiment, we examined the cross modality modulating effect between the visual and auditory system. Auditory response of MGB neurons were modulated by preceding electrically stimulation of the lateral geniculate nuclei (LGN). Both inhibitory and facilitating modulations were observed in this experiment.

In the fifth experiment, we examined the spatial range in the MGB that was modulated by electrical stimulation in another MGB site. Modulations of auditory responses of MGB neurons on the same coronal plane were recorded when the electrical stimulation site in the MGB was fixed. We also investigated the modulations to a point of MGB unit from different stimulation sites of a coronal plane in the MGB. We found that in the randomly sampled coronal plane, the modulation range was 2.8-4.0mm laterally to the bregma and depth was from 5.0-6.5mm vertically to the brain surface. 52%-56% points of all points tested in the plane caused modulation effects. No tonotopic correlation in the modulation map was found.

The present results indicate that a strong intrathalamic modulation occurs in the auditory thalamus. The modulation is via the TRN in the guinea pig. The results suggest that intrathalamic interaction between the TRN and MGB is likely an additional gain processor in the auditory signal pathway. The modulation via the TRN has cross-modal influences. The cross-modal influences and the results that each MGB receives modulations from a large thalamic area within the MGB suggest that the intrathalamic interaction may perform a global modulation function on the top of gain adjustment.

Relevant Publications

Conference papers:

Guo Shanshan., Yu Xiongjie., HE Jufang. (2009) Intrathalamic Interaction in Medial Geniculate Body. *The 8th National Academic meeting of Chinese Neuroscience Society, Guangzhou, China, November 7-10, 2009*

Guo Shanshan., Yu Xiongjie., HE Jufang. (2010) Gain Adjustment by Intrathalamic Interaction in Medial Geniculate Body . *Society for Neuroscience 40th Annual Meeting San Diego, United States, November 14-18, 2010*

Acknowledgements

The lines of this text is to all those who helped to make this thesis possible.

Firstly, I would like to thank my supervisor, Prof. Jufang HE, for his constructive guidance and support for this research. Without his encouragement, knowledge and perceptiveness I would never have finished my study. Thanks to my examiners, for managing to read the whole manuscript so thoroughly and providing all the advice and suggestions.

I sincerely thank Dr. Yu Xiongjie, Ms. Liu Chunhua, Dr. Gao LiXia, Mr. Chen Xi, Dr. Guo Yiping and the other entire lab mates who provided me with so much help and inspiration throughout my PhD studies.

I heartily thank my experimental rats and guinea pigs which I used in this study. Their sacrifice is priceless in terms of the contribution to our understanding of the auditory thalamus and thalamic reticular nuclei, which has undoubtedly formed the foundation for future human studies.

Finally and most importantly I would like to thank my mother and my husband, for their love, patience and continuous support during the whole PhD period.

The study summarized in the present report was mainly supported by the Hong Kong Polytechnic University.

Guo Shanshan

July 2011

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List of abbreviations

AC: auditory cortex
AAF: anterior auditory cortex
AI: primary auditory cortex
AP: action potential
AN: auditory nerve
BF: best frequency
CAF: central animal facilities
CN: cochlear nucleus
DCN: dorsal cochlear nucleus
CNS: central nerve system
CT: corticothalamic
EPSP: excitatory postsynaptic potential
EEG: electroencephalography
GABA: γ-aminobutyric acid
IC: inferior colliculus
CIC: central nucleus
DCIC: dorsal nucleus
i.p.: intraperitoneal
IPSP: inhibitory postsynaptic potential
LGN: lateral geniculate nuclei
MGB: medial geniculate body
MGd: dorsal nucleus
MGm: medial nucleus
MGcm: caudomedial nucleus
MGrm: rostromedial nucleus
MGs: shell nucleus
MGv: ventral nucleus
PB: phosphate buffer
SC: superior colliculus
S.D.: standard deviation
TRN: thalamic reticular nucleus
TC: thalamocortical

Chapter 1

Introduction

1.1 Background of the study

Thalamus is the last relay station in the ascending pathway before afferent information reaches the cortex in all mammalian sensory systems. The auditory thalamus includes three parts, the medial geniculate body (MGB), and lateral part of the posterior nucleus group and the auditory sector of thalamic reticular nucleus (TRN) (Imig and Morel, 1983). The MGB is the principal auditory thalamic nucleus and the synaptic station for passing auditory information from the inferior colliculus (IC) to the auditory cortex (AC) (Imig and Morel, 1983).

MGB contains three independent parts: ventral part (MGv), dorsal part (MGd) and medial part (MGm). The ascending auditory pathways from the thalamus to the cortex are divided into two parallel systems physiologically, primary (lemniscal) and secondary (nonlemniscal) projections (Hu, 2003). The lemniscal division of the MGB is MGv and it is tonotopically organized. Non-lemniscal MGB is MGd and MGm. These two parts have no obvious tonotopic organization. Neurons in MGv share properties, including sharp frequency tuning curves, high level of spontaneous activities and the short-latency (8-15 ms) auditory responses. Neurons from MGm and MGd respond to acoustic stimuli with wide frequency tuning curve, variable firing patterns, and long-latency (Calford and Webster, 1981; Calford, 1983; Imig and Morel 1988; Hu, 1995; Yu et al., 2004b).

MGB receives strong projections from auditory cortex (Andersen et al., 1980; Winer and Larue, 1987). For the innervating subcortical neurons, the corticofugal projections from AC present as a highly-focused positive feedback; for the rest, unmatched subcortical neurons, it is a widespread negative feedback (lateral inhibition) (Liu et al., 1995b). GABAergic terminals are only found in the non-lemniscal MGB nuclei in cats (Winer et al., 1999a). The research in our lab indicated that the inhibition caused by activated auditory cortex occurred only in the non-lemniscal MGB neurons (He, 2003b). For the lemniscal MGB cells, a small inhibitory effect and a strong facilitation were obtained from the activated auditory cortex (He, 1997, 2002).

TRN also sends inhibitory projections back to MGB neurons. According to the results of morphological and physiological studies, TRN has a strong inhibitory effect on the relay neurons in the thalamus (Bartlett et al., 2000; Golshani et al., 2001). Additionally, Winer (1996) observed in cats and Peruzzi (1997) in rats that direct monosynaptic inhibitory projections came from the inferior colliculus into the MGB by its GABAergic terminals and the ascending GABAergic projections to thalamus had been only found in the auditory system.

GABAergic TRN neurons send projections to the ventroposterior thalamus widely and also receive projections from a wide cortical region (Liu et al., 1995a). Extracellular electrophysiological recordings are the method to investigate the neural activities of MGB neurons. In this manner, the signals are obtained from multi-units in the MGB. To measure the change of membrane potentials or spikes from a single MGB neuron, in vivo intracellular recording is adopted.

According to TRN's special organization and location, Crick (1984) commented that "If the thalamus is the gateway to the cortex, the reticular complex might be described as the guardian of the gateway." To prove Crick's hypothesis, lesion and histological studies were conducted. Weese and his colleagues demonstrated a link between TRN and attentional effects of visual cues (Weese et al., 1999). Other studies about the interactions within the modality-specific TRN sectors showed that neural activities of the Fos-positive TRN sector, which was associated with the modality of the attended stimulus, was selectively increased (Montero, 1997, 1999, 2000; McAlonan et al., 2000).

Based on these findings, Newman (1995) proposed a "gating theory" in details. In his theory, reticular formation (RF), the lowest level gate, modulates (facilitate or inhibit) the TRN's input flow by their robust projections. And then the second-level gate formed by TRN turns on or off the appropriate regions in the cortex.

Axons from different parts of cortex and thalamus send out branches into different layers in TRN when passing through it (Crabtree, 1992; Crabtree, 1996; Crabtree, 1998). Therefore the TRN can be divided into 5 distinct functional regions correspondingly, such as auditory, visual and motor parts (Crabtree, 1996).

TRN receives projections from multiple regions because of its broad dendritic field and giant cell bodies. Nerve tracts transmitting information of different modalities may project to the same region of the TRN, making the tonotopic organization of TRN not as distinct as that of cortex or thalamus (Crabtree, 1998; Crabtree et al., 1998).

Neurons of different TRN sectors serve for different sensory modalities. Crabtree and his colleagues indicated that "the interconnections between TRN and dorsal thalamus have cross-nucleus or cross-modality characteristics" (Crabtree et al., 1998; Crabtree, 1999; Crabtree and Isaac, 2002).

Cross-modality responses of TRN may provide the physiological basis for the attentional shift from one modality to another. In my study, the characteristic of cross-modality modulation between auditory and visual systems via TRN will be investigated.

1.2 Aims of the study

The objective of this study is to enhance our knowledge and understanding of intrathalamic interactions in MGB about its pathway, range, distribution, and the functional implications in the gate-control theory as well.

The first aim of this study is to fully explore the effect on the auditory responses of the MGB neurons by the prior stimulation of neighboring MGB regions. To further understand the inhibitory modulation which is the main phenomenon observed, inhibitory effect on single MGB neuron was studied by intracellular recording.

The second aim of this study is to identify the intrathalamic inhibitory pathway when the auditory cortex is ablated. We compared the inhibitory effect in MGB with and without the participation of TRN. We also excluded the role of IC in this inhibitory pathway.

The third aim of this study is to investigate the cross-modality modulation on MGB neurons arising from LGN.

The last aim of this study is to reveal the distribution regularity and the range of intrathalamic interactions in MGB. The study was conducted by recording auditory responses of all neurons in a coronal plane of MGB when the same site of MGB neurons from a different plane was electrically stimulated.

1.3 Significance of the study

The present study helps us to further understand the relationship between MGB and TRN when AC is removed. The intrathalamic interactions were observed by recording MGN neurons' responses to the acoustic stimuli when other MGB neurons were stimulated electrically. The intrathalamic interactions had two different modes. The major one was an inhibitory effect and the other was a facilitating effect. The inhibitory effect was also tested on single MGB neuron by intracellular recording. The subjects used in this study were rats and guinea pigs which have rare interneurons in the MGB. Therefore we thought these modulations were induced by other nucleus such as TRN. The pathway, through which the intrathalamic interactions occurred, was tested by lidocaine injection into TRN and IC respectively. By investigating the range and distribution of the intrathalamic modulations in MGB, we found that single point of MGB neurons could influence other MGB neurons on a large scale. That may provide another evidence for the gating function of the TRN. Since TRN has cross-modality receiving characteristics, the modulation on the MGB through TRN may also

arise from other modalities such as visual or motor systems. Cross-modality modulations were examined by moving the stimulating site from MGB into LGN. This phenomenon might be related with the attentional shift between the auditory and the visual systems.

1.4 Outline of the thesis

Chapter 1 introduces the background, the objectives and the significance of the study.

Chapter 2 provides a literature review about the basic anatomic and physiological knowledge of the auditory system and the gate control theory.

Chapter 3 describes the methodology employed in this study, including the data collection and analysis.

Chapter 4 presents the results of intrathalamic interactions especially the inhibitory modulation in the MGB, the pathway of the inhibitory modulation, the range and distribution of interactions, and the cross-modality modulation from LGN.

Chapter 5 explains the findings observed in the study based on the relevant theory and pilot researches, and also proposes new questions for the future work.

Chapter 6 summarizes the findings and the conclusions of the present study.

Chapter 2

Literature review

This chapter introduces the principles of anatomy, electrophysiological properties and the functional implications of medial geniculate body and thalamic reticular nuclei. Basic knowledge of other parts of auditory systems is also illustrated. The anatomy and physiology of the MGB are introduced firstly. The second section focuses on the introduction of the TRN. The third section gives a brief introduction on AC, LGN and IC. The fourth section examines the thalamocortical (TC) and corticothalamic (CT) projections between MGB and AC. Gate control theory is introduced in the last part. After illustrating the interaction between TRN and auditory thalamus, this chapter also introduces the cross-modality characteristics and possible functions of the intrathalamic interactions.

2.1 Anatomy and physiology of MGB

The Medial Geniculate Body (MGB), the critical part of the auditory thalamus, relays auditory information from the inferior colliculus (IC) to the auditory cortex (AC). MGB influences the maintenance of the attention. It is divided into three separated sub-nuclei according to their neuronal morphology and density. Neurons from different subdivisions are distinct in their efferent and afferent connections and also the coding properties. In all mammals and most vertebrates, the auditory

information directed towards the telencephalon is processed in the MGB which works as an obligatory synaptic station. (Rouiller and de Ribaupierre, 1985).

The ascending primary auditory pathway is made up of the cochlear nuclei, the superior olive, the IC, the MGB and the AC. The auditory pathway and all levels of relay stations in it are illustrated in Figure 1. As shown in the picture, cochlear nuclei located in the brain stem collect auditory information from the auditory nerves, functioning as the first relay. The superior olivary complex located in the brain stem as well is the second relay. The third relay is inferior colliculus in the roof of the midbrain and the fourth relay before reaching the auditory cortex is medial geniculate body. Auditory information is transmitted and finally passed into auditory cortex by this pathway.

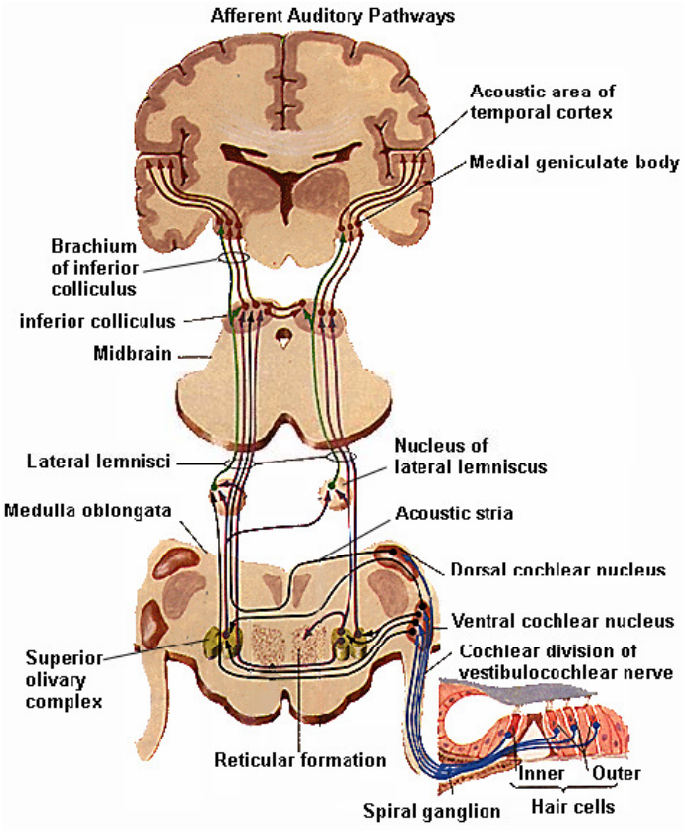

Figure1. Schematic diagram of auditory system

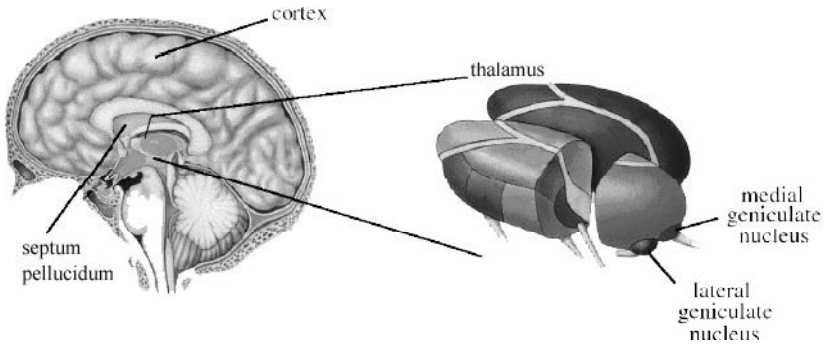

Figure2. The midline section (left panel) and the spatial model: showing the locations of thalamus, LGN and MGB in the human brain.

Generally speaking, the MGB is an ellipsoid protruding from the lateral edge of the brain stem, located at the border of the midbrain and diencephalons (Fig. 2.).

2.1.1 Structure and cellular morphology of MGB

Previous investigations showed that MGB in guinea pigs is an ovoid with the maximum mediolateral diameter of 3.5mm, a vertical diameter of 2-2.5mm and a length of 2.7-3mm rostrocaudally (Redies et al., 1991). Morest and Winer (Morest 1964, Winer, 1992) proposed that the MGB in cats mainly contained two typical neuron types. They are bushy and stellate neurons.

Morest (1964) divided the MGB into three different parts according to the dendritic morphology of their neuronal population. In terms of cellular morphology, the three main parts are MGv, MGd, MGm. Each of them has independent afferent fibers and cortical terminations. The neurons in MGv are mainly bushy neurons with tufted dendrite trees. The MGd consists of both stellate neurons and bushy neurons. The stellate neurons in MGd have extensive dendrite arbors. The dendrite branches of bushy neurons in MGd are less tufted than those in MGv (Morest, 1964). The neurons in MGm are typical stellate neurons with the largest soma comparing to the ones in previous two subdivisions. Besides, small tufted neurons are also observed in MGm (Winer, 1992).

The relative locations of these three parts in MGB are illustrated in Figure3.

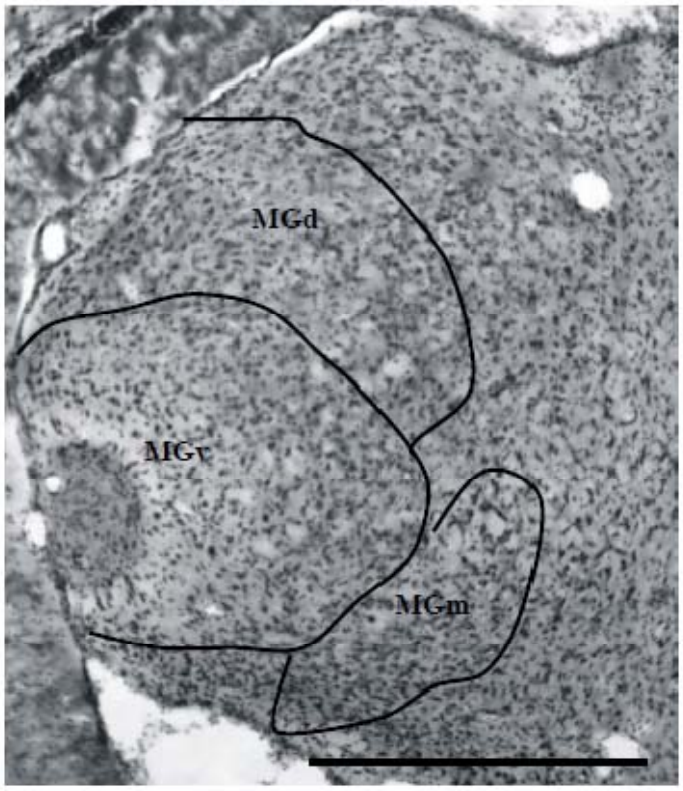

Figure3. The relative locations and the range of MGB subdivisions in the coronal plane of rats (Obtained from Dr YuXiongjie)

MGv which is the largest part in the MGB takes about half the volume of it. MGv is formed by neurons of the same type with medium and small sizes, which are divided into two categories (Aitkin and Webster 1971, Calford 1981). The first category is star-shaped neurons and the other one is dendrite-clustered neurons. Star-shaped neurons are smaller and have less collateral (Aitkin and Webster, 1972). The relay neurons, dendrite-clustered neurons have denser collaterals and larger sizes (Calford, 1983).

MGd and MGm each take 1/4 of the size of MGB. Different from MGv, MGd is constituted by regions with distinct anatomy and physiological characteristics. Unlike

MGv neurons, MGd neurons present no typical tonotopic organization. Star-shaped neurons can be widely observed in MGd and their collateral arrangement is not obviously correlated with directions. MGm also is divided into several regions. Neurons from MGm are quite different from the ones in the previous two parts. MGm has neurons of less density than the ones in MGv and MGd. Cell bodies of MGm neurons vary greatly. Neurons with large size, longer dendrites and fewer collaterals are thought to be the most auditory event-related. Both dendrite-clustered and star-shaped neurons with smaller size share the same physiological characteristics (Morest 1965, Winer 1992).

As introduced before, MGB receives ascending input from the inferior colliculus, inhibitory projections from the TRN and excitatory projections from the auditory cortex. In the following paragraphs, the precise efferent and afferent projections of each MGB subdivision will be illustrated.

Redies and his collegues (1991) divided the MGB of guinea pigs into four sub-nuclei. The first one is MGv which is located in the lateroventral part of the rostral two-thirds of the MGB. Projections from this part ascend to two fields with tonotopic organization. They are fields AI and dorsocaudal field (DC) of the auditory cortex. In neutral red preparations, MGv neurons are densely packed and not deeply stained. The second part is shell nucleus (MGs) surrounding the MGv. MGs with a continuous shell-shape is located laterally in the MGB. Neurons of this nuclei project to a ventrocaudal cortical area of auditory cortex without tonotopic organization. Although presenting similar cytoarchitectonics with the MGv neurons, MGs cells do not appear immediately in Nissl staining. The third division is the caudomedial nucleus (MGcm)

which projects to nearly the whole auditory cortex. Neurons in MGcm are deeply stained and less densely packed in Nissl stain. The last division is the rostromedial nucleus (MGrm), situated in the rostral MGB medially to the MGv. Projections from MGrm terminate in a small tonotopic cortical field called field S. In Nissl preparations, neurons of this nucleus show less densely packed and deeper-staining properties (Redies 1991).

2.1.2 Response properties and tonotopic organization of MGB

MGv neurons have largely similar properties. Most MGv neurons exhibit sharp frequency tuning, high levels of spontaneous activity and they are tonotopically organized. MGv neurons respond to acoustic stimuli with the shortest latency (8-15 ms), comparing to MGm and MGd neurons. The MGv is found tonotopically organized. In cats, the high-frequency area lies in the rostromedial part; the middle-frequency area occupy the caudomedial position; the low-frequency area is located laterally (Aitkin and Webster, 1972; Imig and Morel, 1984, 1985). The distribution in guinea pigs differs. The high-frequency area is located rostrally and the low-frequency area caudally (Redies and Brandner, 1991; He, 2002).

Unlike MGv neurons, the role of MGd neurons is not to relay auditory information uniformly to AC. They presumably serve for more complex processing of auditory information. Therefore, the properties of MGd neurons show variations. Most MGd neurons are silent and they respond to acoustic stimuli inconsistently with extremely long latencies (up to 100ms) (Redies and Brandner, 1991). A small percentage of MGd neurons (about 15%) do not respond to acoustic stimuli (Calford,

1983). The firing of MGd neurons lasts for a relatively longer time. MGd neurons also are sensitive to novel stimuli. Reponses of MGd neurons are easily habituated and the habituation is easily relieved when the intensity or frequency of the stimulus are slightly changed. Without obvious best frequency (BF) in the tuning curve, MGd presents no tonotopic organization. The number of MGd neurons that show sustained responses is larger than the one of other MGB sub-nuclei. In MGm, the responses of 1/2 responsive neurons are sharply tuned with short latencies. Neurons from this half have best frequency curves similar as those of MGv neurons. The other half responds to the acoustic stimuli with long latencies and neurons from this part tune to a wide range of frequencies, similar as the MGd neurons (Popper and Fay, 1992). No tonotopic organization is observed in the non-lemniscal part of MGB. And neurons from the non-lemniscal part also respond to the stimuli from other sensory modalities similarly to auditory stimuli. (Wepsic, 1966; Calford and Aitkin, 1983; Winer and Morest, 1983a; Rouiller and de Ribaupierre, 1989; Winer et al., 1992; Kosaki et al., 1997; Rauschecker et al., 1997; Winer et al., 1999c) .

2.1.3 Electrophysiological properties of MGB

Extracellular recordings in cats, monkeys and rodents indicate that, MGv neurons represent a classical tonotopic organization and have a high level of spontaneous activities. MGv neurons share similar response characteristics and most of them have special frequency tuning range. The latency to the acoustic stimuli (about 8-15ms) is relatively short. The auditory responses are phasic-tonic as the ones of other thalamic relay neurons (Aitkin and Webster, 1971, 1972; Calford and Webster, 1981; Calford, 1983; Allon and Yeshurun, 1985; Imig and Morel, 1985; Edeline, 1999).

MGd neurons with multiple characteristics are not appropriate for information relay and discrimination of complex acoustic input. Spontaneous activity of MGd neurons is lower than that of MGv neurons. They have long latencies when responding to acoustic stimuli (about 100ms). The auditory responses are not enduring and fixed, comparing with the responses of the MGv neurons. And a part of MGd neurons even show no responses to noises (Aitkin and Webster, 1971; Allon and Yeshurun, 1985; Edeline, 1999; Aitkin and Prain, 1974; Rodrigues-Dagaeff et al., 1989; Bordi and LeDoux, 1994).

MGm has a complex composition. Half of the MGm neurons which respond to noises show narrow frequency tuning range, short latencies and similar tuning curves to the ones of MGv neurons. And the rest, which have no responses to noises, show inconsistent responses with long latencies and broad frequency tuning range as MGd neurons do. Compared with the MGm and MGd, MGv is more persistently responding to acoustic stimuli (Aitkin and Webster, 1971).

MGv neurons represent a conspicuous tonotopic organization. Low frequency responding neurons locate in the lateral side of MGv; high frequency one in the medial side of rostral MGv and middle frequency one in the medial side of caudal MGv (Aitki and Webster, 1972; Edeline, 1999; Imig and Morel, 1984). Neurons in other part of MGB with long latencies and wide frequency tuning range present no tonotopic organization (Calford, 1983; Rouiller et al., 1989). Many researches indicate that, parts of non-MGv neurons are not only sensitive to the acoustic stimuli but also respond to stimuli from other modalities (Aitkin and Webster, 1971; Rouiller et al., 1989; Calford, 1983; Winer and Morest, 1983). MGB neurons discharge in burst or tonic modes,

similar to TRN neurons, and also show oscillations of various types. Recent Studies show that on neurons and off neurons locate separately in the MGB. Off and on-off neurons mostly locate at the edge of MGv nucleus (He, J., 2001).

2.2 Thalamic reticular nucleus

2.2.1 Anatomy and physiology of TRN

TRN is located in the ventral thalamus. It is capsule-shaped which surrounds the thalamus laterally. An external medullar lamina separates TRN from the thalamus. However, recent researches on mice and fish propose a different definition that TRN is actually a dorsal thalamic structure (Scholpp et al., 2009; Vue et al., 2009).

TRN which is a shin sheet formed by GABAergic neurons is interfaced between the auditory cortex and the thalamus (Fig.3). TRN neurons send out inhibitory GABAergic input to the thalamic nuclei and receive excitatory afferents from them (Ahlsen et al., 1985; Arcelli et al., 1997). The MGB neurons which receive information from TRN have two kinds of receptors, GABA-A and B (Bartlett and Smith, 1999). By receiving the collaterals both from CT and TC axons that rise from layer VI pyramidal neurons, TRN also receives excitatory projections (glutamatergic) from AC (Jones, 1985; Murphy and Sillito, 1996; Pinault et al., 1997; Cox and Sherman, 1999). Although receiving regulation from auditory cortex, TRN sends no projections back to the cortex. (Crabtree, 1998; Guillery and Harting, 2003).

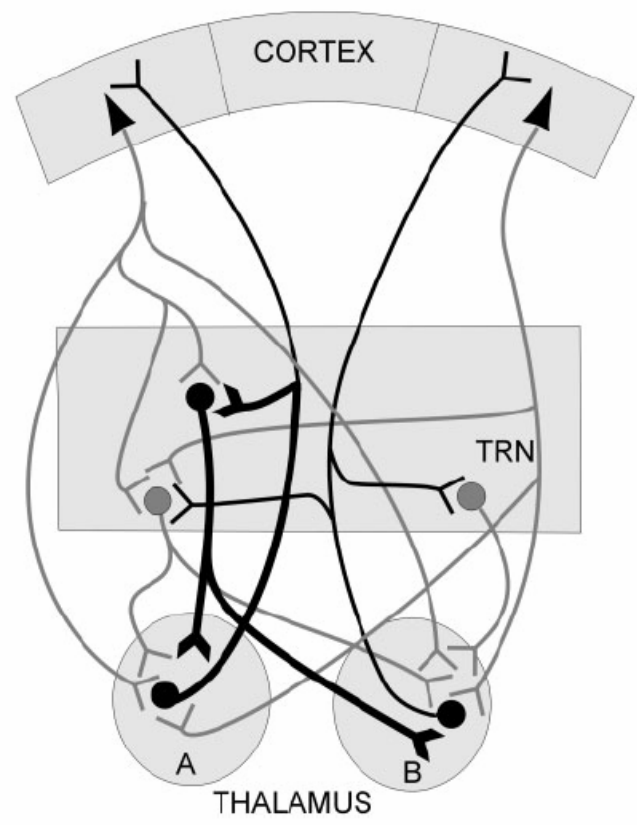

Figure4. Schematic diagram of connections within AC, thalamus and TRN.
The thin black lines indicate the possible connections which may be formed by the collaterals arising from CT projections. The thick black lines indicate that the same reticulothalamic axon can control more than one thalamic nucleus. And therefore a dis-synaptic inhibitory circuit among these thalamic nuclei is formed. The gray lines demonstrate the possible connections formed by CT projections coming from layer VI neurons. These links send out branches into two thalamic relay nuclei and a sector of the TRN. (From Guillery and Harting, 2003)

TRN can be divided into several subdivisions, each of which modifies a different sensory modality. The auditory division lies in the caudoventral TRN (Jones, 1975; Shosaku and Sumitomo, 1983). Crabree and his colleagues illustrated the cross-nucleus and cross-modality properties of the interconnections between dorsal thalamus and TRN (Crabtree et al., 1998; Crabtree, 1999; Crabtree and Isaac, 2002). Neurons in auditory TRN are topographically organized, corresponding with each MGB region

under their innervations (Crabtree, 1998). More than 60% auditory TRN neurons respond to acoustic stimuli (Simm et al., 1990; Villa, 1990). Through the inhibitory projections to the thalamus, activated TRN auditory neurons inhibit the auditory responses and spontaneous activity of MGB neurons (Yingling and Skinner, 1976; Shosaku and Sumitomo, 1983). In guinea pigs, activated AC neurons induce long-lasting and intense inhibitory effect on non-lemniscal MGB neurons. He and Xiong found that such intense inhibition was not coming from GABAergic neurons in IC but caused by the AC-TRN-MGB loop (He, 2003c; Xiong et al., 2004). As for lemniscal MGB neurons, activated AC leads them strongly facilitated and slightly inhibited (He, 2002; Xiong et al., 2004; Yu et al., 2004b).

In conclusion, the thalamic reticular nucleus receives axons from both cortical areas and dorsal thalamic nuclei. Information is transmitted into TRN from the collaterals of axons which pass through it. TRN efferent axons project to dorsal thalamic nuclei. But except the dorsomedial nucleus which projects to the prefrontal cortex, it is the only thalamic nucleus which never projects to the cerebral cortex. The organization of TRN may prepare it as a modulator, regulating the information flow from thalamus to the cortex. Besides regulating local information transmission, TRN is also proposed to function as a crucial nexus in modulating the global one. To understand the interactions between thalamus and auditory cortex or only intrathalamic interactions, further studies on functions and intrinsic circuits of TRN are necessary.

2.2.2 Cross-modality properties of TRN

Both corticothalamic and thalamocortical projections send out branches to modality-specific sectors in TRN when passing through it. Cortical fields and thalamic areas innervating different modalities project into different layers in TRN (Crabtree, 1992, 1996, 1998). The TRN is correspondingly divided into 5 functional regions, such as auditory, visual and motor sectors (Steriade, 1997).

TRN neurons with giant cell bodies and wide dendrite fields have a relatively large receptive field. The wide receptive field of TRN allows the same TRN neuron to possibly receive projections from target regions of different modalities. Therefore, the tonotopic organization of TRN is not as obvious as the ones of cortex and thalamus (Crabtree et al., 1998; Crabtree and Isaac, 2002). Neurons from different TRN subdivision mainly carry out information processing for one sensory modality. However, Crabtree and his colleagues found evidences, proving that the interconnections between TRN and dorsal thalamus had cross-nucleus or cross-modality properties (Crabtree et al., 1998; Crabtree and Isaac, 2002). Cross-modality characteristics of TRN make it possible to participate in the attention shift within modalities (Crabtree et al., 1998; Crabtree and Isaac, 2002). Scholpp (2009) proposed a searchlight and a gate control theory. The searchlight theory emphasized the relevant neural activities which are related to the present attention. TRN is thought to be functioning as the controller of the internal attentional searchlight. That means TRN, the GABAergic structure, has an important role at different states of consciousness. Additional questions about the validity of this speculative hypothesis were generalized from the present findings. However, the complex control functions of TRN were

supported by data collected from behavioral, electrophysiological, anatomical and neurochemical experiments over the last two decades.

2.3 Structure and tonotopic organization of auditory cortex

Many studies for understanding auditory cortex have been carried out in primates, rodents, cats, and bats. The number of auditory fields in different species varies. In carnivores and primates, six to more than eight fields are found. For rodents, the number is four to seven and for insectivores three or four (Morel and Kaas, 1992; Stiebler et al., 1997; Hackett et al., 1998).

In guinea pigs, Redies and Wallace divided the auditory cortex into several parts (Redies et al., 1989b; Wallace et al., 2000). The primary auditory cortex is composed of two parts, AI and DC. AI with narrow frequency tuning curves takes the anterior half volume of auditory cortex. When the acoustic stimuli are provided, AI presents strong responses with short latency. AI is tonotopically organized with high best frequencies observed on the caudal side and low best frequencies on the rostral side. There is another smaller tonotopic area, which is caudal to the first field. Primary auditory field (AI) is distinct for its unique cytoarchitecture and connections with the MGv. Besides, auditory cortex is divided into several functional subdivisions by its tonotopic organization (Winer et al., 2001). The majority of AI neurons are tuned to a narrow range of frequencies and the rest of AI neurons are tuned to a broad range when the subjects are anaesthetized or awake (Imig and Reale, 1980, 1981).

The dorsocaudal field (DC) is located in the dorsal part of the posterior auditory cortex, caudally to the first field. DC is smaller, but is also tonotopically organized.

The tonotopic organization of DC is more complex than AI, although neurons from DC share the same strong frequency specificity with the ones in AI. (Imig and Reale, 1980, 1981).

More than one other primary auditory field with tonotopy are observed besides AI in many species, and a mirror image is formed by adjacent tonotopic fields at their border which have the same range of frequency. Unlike AI, some mirror fields with reversed tonotopic characteristics may have no representation of the full audible frequency-range. One of this adjacent fields called secondary auditory cortical field (AII) are found in some mammals. AII, with multi-sensory association regions that receive visual and somatosensory in addition to auditory signals at its outer borders locates ventrally to AI (Berman, 1961b, a; Irvine and Huebner, 1979; Toldi et al., 1986; Clarey and Irvine, 1990a, b; Hofstetter and Ehret, 1992; Barth et al., 1993).

Caudally around AI and DC fields, there is a broad cortical area without tonotopic organization called auditory belt which is divided into two areas: the ventrocaudal and the dorsocaudal belt regions (Redies et al., 1989b). Neurons from auditory belt have broad tuning curves and longer response latency comparing with the ones from tonotopic cortical areas. Ventrocaudal belt responds to acoustic stimuli with tonic discharge frequently and the dorsocaudal belt reacts to pure tones with a phasic on-response. Rostral belt, another nontonotopic region, lies in the anterior auditory cortex, rostrally to AI and DC. Neurons from this part have wide tuning curves and respond to strong acoustic stimuli with short latencies because of its high thresholds.

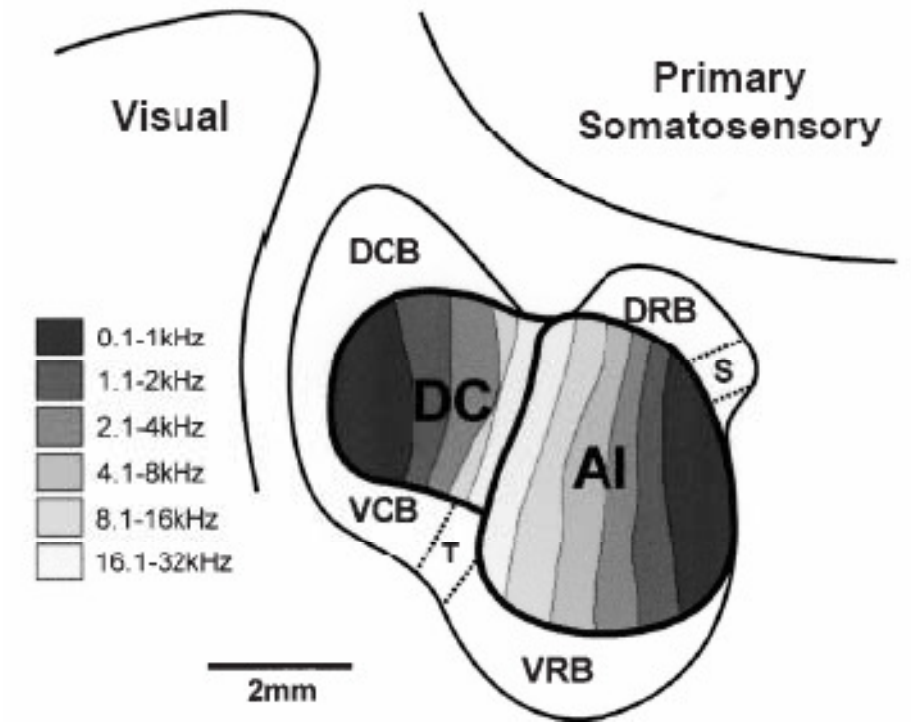

Figure5. A schematic diagram for illustrating the positions of the seven auditory fields. In AI and DC, different frequency areas are represented by shaded bands in different grey level (Wallace et al., 2000).

2.4 Lateral geniculate nucleus

The lateral geniculate nucleus (LGN) located in the thalamus is a critical relay station in the visual system, transmitting the visual signals collected from the retina to the visual cortex.

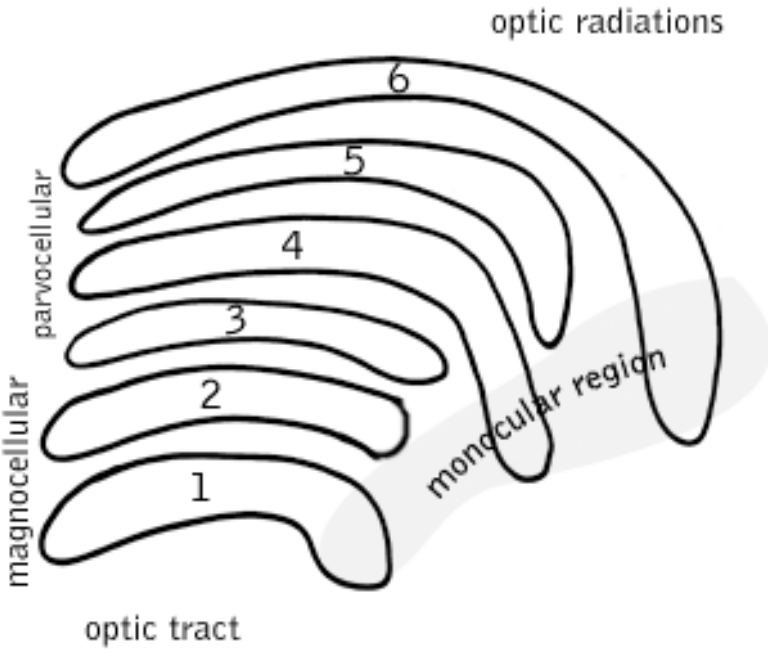

Figure6. A schematic diagram illustrating the layers of lateral geniculate nucleus.

Lateral geniculate nucleus is composed of several layers of cell bodies and layers of neuropil in between. Six layers are observed in the LGN of humans and macaques. As shown in Figure 6, magnocellular layers are formed by the inner two layers while parvocellular layers are formed by the outer four layers. In addition, the koniocellular sublayers lies ventrally to each of parvocellular and magnocellular layers. The structures of layers in LGN vary within species (Carlson, 2007).

Retinal ganglion cells input visual information to the LGN directly through the ascending optic tracts. The afferent fibers originated from the neurons of LGN go through the optic radiation and directly project into the primary visual cortex. Primary visual cortex in turns sends back descending axons into LGN, providing a strong feedback connection with it. In human beings and other mammals, there are two strongest ways to transmit the visual signals from eye into the cortical areas. One is

formed by the axons projected into the Superior Colliculus (SC) and the other is into LGNd (dorsal part of the LGN in the thalamus) (Goodale and Milner, 2004). In addition, the LGN also receives information from the optic tectum in some species as the superior colliculus (Wild, 1989; Hackett et al., 1998).

Axons from the LGN go through the optic radiations, a part of the retrolenticular limb of the internal capsule and then terminate in V1 of the visual cortex. Layer 4 in V1 receives inputs both from the magnocellular and the parvocellular layers. Layer 4cβ in V1 receives inputs from parvocellular layers, and layer 4cα receives inputs from magnocellular layers. In addition, layer 4a in V1 receives projections from the koniocellular layers (in between layers 1-6). LGN receives axons from layer 6 of visual cortex as the feedback (Schmid and Michael, 2010) Researches about blind-sight suggest that in addition to the primary visual cortex, LGN also projects to V2 and V3,which are higher cortical areas. When the contralateral primary visual cortex is injured in patients with blind-sight, patients suffer phenomenally blind in the certain visual field. Although, these patients still are capable of finishing certain motor tasks accurately in their blind field. This experiment provides evidences, proving that neurons of LGN project to visual cortex and other higher cortex regions of both sides (Schmid and Michael, 2010).

2.5 Inferior colliculus

The inferior colliculus (IC) is also a principal nucleus located in the midbrain in the auditory system. IC receives auditory information from several peripheral brainstem nuclei and feedback from projections of auditory cortex. The inferior

colliculus is composed of three parts. They are the external cortex (ICX), the dorsal cortex (DCIC) and the central nucleus (CIC). CIC is the principal station for relaying auditory information among these three subdivisions. Neurons in IC have bimodal properties. They receive information from somatosensory nuclei in addition to the auditory system, making IC possible to participate in the interactions between auditory and somatosensory systems (Shore, 2009).

The inferior colliculus and the superior colliculus constitute a part of tectal region in the midbrain. These two structures form the eminences of the corpora quadrigemina. The inferior colliculus lies below the superior colliculus which is the visual processing center. The exact location is above the trochlear nerve, at the base of axons coming from the lateral geniculate nucleus (LGN) and the medial geniculate nucleus (MGN). (Goodale and Milner, 2004).

The inferior colliculus is the first station in which fusiform cells in the dorsal cochlear nucleus can connect the vertical-orienting signals with horizontal-orienting ones (Shore, 2009).

2.5.1 Afferent and efferent connections of IC

Except the contralateral ventral nucleus of the lateral lemniscus (LL), all nuclei send ascending axons to the central nucleus (CIC) bilaterally. Most ascending auditory fibers in the lateral lemniscus are reported to terminate in CIC. IC receives descending information from superior colliculus (SC), medial geniculate body (MGB), and auditory cortex (Skottun, et al., 2001).

Although receiving input from cochlear nucleus bilaterally, IC still has lateralization. The dorsal axons, caring vertical data only project to the inferior colliculus from the contralateral side. The inferior colliculus receive most inputs from the contralateral ear and then projects to ipsilateral medial geniculate nucleus (Skottun, et al., 2001).

The medial geniculate body is the last sub-cortical relay station before auditory information from inferior colliculus reaches auditory cortex. Most auditory signals, coming from the central nucleus of IC (CIC), are input into the ventral division (MGv) (Gelfand and Stanley, 2004).

2.5.2 Functions of IC

IC is functioning as an integrator and switchboard for all the ascending auditory information. It is closely related with startle reflex and vestibulo-ocular reflex via integrating and routing sensory information from multiple modalities together. IC also responds to amplitude-specific modulating frequencies, making it possible for pitch detection. IC is involved in the spatial localization by binaural hearing as well (Gelfand and Stanley, 2004).

2.5.3 The connections between MGB and IC

MGB is a critical structure composed of several distinct nuclei in almost all mammals. Each subdivision in the MGB has its own pathways via which the auditory information is transmitted into auditory cortex (Imig and Morel, 1984). MGv of one

side receives information mostly from the central nucleus in the ipsilateral IC and also a small input flow from the contralateral IC. The information from the contralateral peripheral auditory apparatus is input into MGv in the most direct, oligosynaptic way. Therefore MGv responds to the acoustic stimuli with shortest latency and is highly topographic organized (Calford and Aitkin, 1983; Imig and Morel, 1984).

MGd receives afferents mainly from nucleus sagulum and ipsilateral pericentral nucleus of IC. The pathways from MGd to auditory cortex are not that direct as the ones from MGv to AC. Topographic organization in MGd is not such obvious. Axons arising from MGd mainly terminate in the cortical areas outside AI (Calford and Aitkin, 1983; Imig and Morel, 1984).

MGm receives afferents mainly from the external nucleus of IC, scattered neurons of the central nucleus (Calford and Aitkin, 1983) and the deep layers of superior colliculus (SC) as well (Graham, 1977). The information input into MGm is relatively complex, collected from a wide range, such as mixed auditory, somatosensory, vestibular signals and other input flows. MGm neurons may stay silent to acoustic stimuli or responds to it in multiple manners. Efferent fibers from MGm are widely distributed in the cortical areas (Calford and Aitkin, 1983).

2.6 Thalamocortical and corticothalamic projections

2.6.1 Thalamocortical projections

The thalamocortical pathways start from thalamic neurons, ascend and terminate in different cortical layers. The pathways from the MGB into the auditory cortex in

different mammals, such as cats, bats and monkeys, share the similar organization (Radtke-Schuller, 2004; Radtke-Schuller et al., 2004). MGv neurons in cats send out axons mainly terminated in AI and the anterior auditory field (AAF), which is AI's mirror region. For the MGv neurons in guinea pigs, the axons project mainly into AI and DC areas (Imig and Morel, 1984). MGd neurons send out axons into cortical areas around primary cortex. The projections from MGm neurons are distributed widely. MGm neurons project to almost all the auditory cortical areas as well as its association cortex (Winer et al., 1977; Niimi and Matsuoka, 1979; Andersen et al., 1980; Imig and Morel, 1983; Hashikawa et al., 1995). In addition to auditory system, MGm neurons send out axons projecting to somotosensory cortex, prefrontal cortex, amygdala and basal ganglia (Wepsic and Sutin, 1964; Russchen, 1982; LeDoux et al., 1990; Cruikshank et al., 1992; Shinonaga et al., 1994; Kimura et al., 2003).

Primary TC pathways (also called lemniscal pathway) are formed by axons from MGv neurons to middle layers of AI. Correspondingly, non-primary TC (also called non-lemniscal) pathways are formed by axons arising from other thalamic nuclei, including MGd, MGm, peripeduncular nucleus (Ryugo and Killackey, 1974; Caviness and Frost, 1980; Herkenham, 1980; Arnault and Roger, 1990; Clerici and Coleman, 1990; Romanski and LeDoux, 1993; Linke and Schwegler, 2000). Axons from each MGB sub-nuclei terminate in more than one cortical fields in many species (guinea pig: Redies et al., 1989a; rat: Clerici and Coleman, 1990; cat: Huang and Winer, 2000). TC projections from relatively tonotopic areas in MGV mainly terminate in AAF and AI. Axons from non-topographic thalamic areas are observed projecting into frequency-specific areas in cats' auditory cortex (Lee et al., 2004). The corresponding projections

between thalamus and cortex may be involved in the signal presentation and neuronal plasticity in cortex (Winer JA, 2004). Unlike MGv, Axons from MGm project to nearly all auditory cortical areas. And MGm receives and processes information from other sensory modalities (Gerren and Weinberger, 1983). Limited by its wide distributed projecting areas, MGm is not functioning for selecting signals in terms of frequencies and spaces.

Different MGB subdivisions have different TC projections. In cats, MGv and parts of MGd send out axons mainly projecting to layer III-IV in auditory cortex. Axons from MGd mainly project to layer I. Axons from MGm with the largest size, which have the lowest density of labeling in the Nissl preparation project to layer I. Although independent for thalamic information, more than 10% of all thalamic inputs terminate in layer V of auditory cortex (Niimi et al., 1984; Mitani et al., 1985; Huang and Winer, 2000). The case in monkeys is slightly different. Axons from MGv mainly project to layer IV and part of deep layer III (IIIB). Axons from MGd project mainly to layer IIIB. And the target areas of MGm are still larger than the above two subdivisions. Axons from MGm project mainly to the middle layers and some to layer I (Hashikawa et al., 1995).

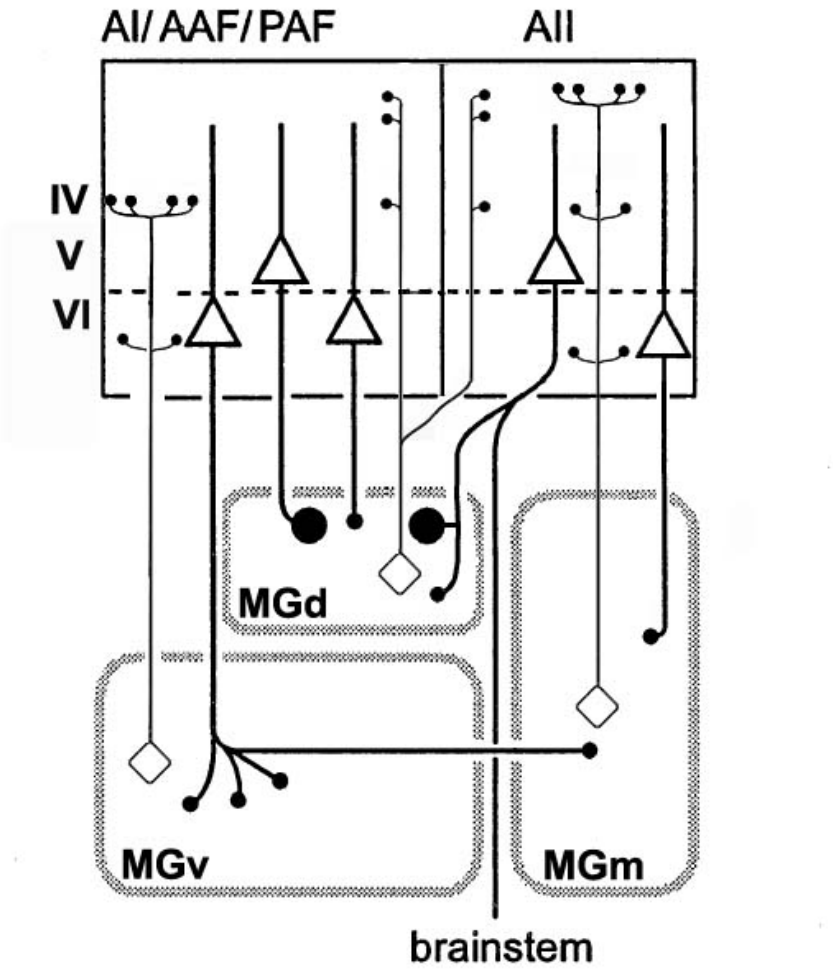

Figure7. A schematic diagram of cortico-thalamo-cortical projections in cats. Triangles represent the corticothalamic neurons and rectangles represent thalamocortical neurons. Filled circles of both large and small sizes represent axon terminals. (Rouiller and Welker, 2000; Winer et al., 2001)

2.6.2 Corticothalamic projections

The descending projections arising from auditory cortex to the thalamus are introduced in the following paragraphs. Divergent as thalamocortical (TC) projections, corticothalamic (CT) projections start from the heterogeneous pyramidal neurons in layer V and layer VI (Kelly and Wong, 1981; Mitani and Shimokouchi, 1985; Rouiller

et al., 1985; Hoogland et al., 1991; Schwartz et al., 1991; Guillery, 1995; Winer et al., 2001). CT projections have both corticofugal inhibitory and excitatory effects on the thalamic neurons. The polysynaptic connections with GABAergic neurons in TRN or the GABAergic interneurons in MGB cause the inhibitory effect (Stiebler et al., 1997). And strong monosynaptic connections with the distal part of thalamic dendrites cause the excitatory corticofugal effect (Liu et al., 1995b). In cats, MGB receives the inputs from every auditory cortical field. MGv receives projections from AI and AAF; MGd receives projections from AII and MGm from all auditory cortical fields. In total, half layer VI pyramidal neurons are involved in the corticothalamic projections (Andersen et al., 1980, Merzenich et al., 1982). Tracing experiments by He and Hashikawa show that MGm receives less cortical inputs, compared with MGv and MGd (He and Hashikawa, 1998). In addition, Winer and Prieto found that pyramidal neurons with long, well-filled apical dendrites from layer V also participated in the corticothalamic projections (Winer and Prieto, 2001). Researchers also found other compositions of corticothalamic projections. Other kinds of pyramidal neurons with intrinsic bursting characteristics participate in corticothalamic projections by forming the projections from layer V to MGB and IC (Hefti and Smith, 2000).

In most mammals, corticothalamic projections are divided into two functional categories. The corticothalamic projections with large terminals (2-10 μm), coming from pyramidal neurons in layer V, only innervate MGB (Rouiller and Welker, 1991; Ojima, 1994; Bartlett et al., 2000; Hefti and Smith, 2000). Thalamus is mainly driven by this pathway. One cortical field may influence other ones through thalamus and therefore the communications within cortical areas may be established via this feed-

forward mechanism (Sherman and Guillery, 1996; Sherman et al., 2006). The second category is the projections with small axon terminals (<1 μm) originated from layer VI (Liu et al., 1995b). These pathways project to both dorsal thalamus and TRN (Jones and Powell, 1969a, b). The second group transmits the neural activities of thalamus to auditory cortex, providing the feedback control from the cortical fields on their corresponding thalamic areas (Sherman and Guillery, 1996; Sherman et al., 2006).

2.7 Thalamus and the gate-control theory

Thalamic reticular nucleus is positioned between the cortex and thalamus. Both TC and CT projections connect with TRN (Jones, 1975; Steriade, 1997). Cortex sends out excitatory axons to the TRN and axons from the GABAergic neurons in TRN are sent into the thalamus. Both the efferent and afferent information are tonotopically organized (Jones, 1975; Steriade, 1997).

Many studies have been conducted for understanding the functions of TRN. Francis Crick (1984) commented that "If the thalamus is the gateway to the cortex, the reticular complex might be described as the guardian of the gateway" according to its special location and characteristics. Crick also proposed that the unique characteristics of the TRN prepared it a qualified "guardian" of the thalamic gateway where information was selected and transmitted to the cortex (Crick, 1984; Mayo, 2009). Crick's "guardian" is represented in two aspects. One is concerning whether the neuronal activities level is changed in TRN and LGN; the other one is concerning whether the activity change happens in TRN before in LGN (Mayo, 2009). Both two

questions were answered by McAlonan. The function of TRN as a guardian of thalamic gateway was proven (Kerry M. et al., 2008).

Further studies by lesion and histological methods were conducted by Weese and his colleagues. In their experiments, they damaged the visual TRN of one side. And then they found the primary effects associated with the contralateral cue were abolished. Therefore a link between TRN and the attentional effects of visual cues was founded (Weese et al., 1999). Montero and McAlonan also investigated the interactions within different modality-specific TRN sectors. When applied with the attended stimulus of one modality, fos-positive neurons in the corresponding TRN sector were selectively increased (Montero, 1997, 1999, 2000; McAlonan et al., 2000).

Francis Crick (1994) stated that cortico-thalamo-cortical loops were closely related with the awareness and TRN was functioning as the ‘‘searchlight’’ of attention. This attention searchlight hypothesis was supported by Kerry M. et al. (2006). They thought that TRN participated in the attention processing at a sub-cortical level. With the assistance of TRN, the relevant sensory signals were selected out and highlighted for additional processing by decreasing other irrelevant inputs.

The theories and studies introduced above are proposed and applied on the visual system. To understand the mechanisms of gate-control functions of TRN, the connections of TRN with structures in visual system are critical. Visual sector of the TRN receives collaterals both from ascending and descending projections between the lateral geniculate nucleus (LGN), the visual thalamic relay station and the primary visual cortex (V1) (Conley and Diamond, 1990; Harting et al., 1991; Uhlrich et al., 2003). All these collaterals received by TRN are excitatory while TRN sends back the

inhibitory information to LGN via its GABAergic neurons (Cox et al., 1997; Kim et al., 1997).

Two mechanisms are thought possibly involved in the gate control of visual system. The first one related with the feedback inhibition is close loop, formed by the GABAergic projections from TRN to LGN cells. The inhibitory feedback on LGN makes it firing in a rhythmic bursting manner. The visual cortex is eventually announced with this behaviorally relevant sensory input (Crick, 1984; Sherman and Guillery, 1996) and the signal transmission is strengthened when the visual target is obtained and fixed in the early stage (Guido and Weyand, 1995; Ramcharan et al., 2000).

In addition, Newman (1995) proposed a detailed "gate theory" based on the theory stated by Francis Crick. In this theory, reticular formation (RF) which is the lowest-level gate has strong projections to the TRN. It modulates the input flow of TRN. TRN as a second- level gate inhibits or facilitates the target areas in the cortex. When the attention is changed, reticular formation modulates the status of TRN by decreasing its activities. TRN's inhibitory effect on MGB neurons will therefore be reduced (Newman, 1995).

Chapter 3

Methodology

3.1 Introduction

The methods employed in the whole project consist of observational recordings and designed experiments. This chapter demonstrates the common content, including animal model, surgical procedures, recording techniques, stimulating signals, histological methods and data analysis, and the special methods used for each study as well. Some further information is described and supplemented in Chapter 4 to 5 if necessary.

3.2 Materials and methods

3.2.1 Animal preparation

Sprague-Dawley rats weighting from 220 to 370g and Hartley albino guinea pigs, Cavia porcellus, weighting from 400 to 700g, provided by central animal facilities (CAF), Hong Kong Polytechnic University, served as the subjects (Fig.8-9.). Anesthesia was initially induced with Urethane (Sigma, 1.5g/kg for rats and1.3g/kg for guinea pigs i.p., 20% solution in 0.9% saline) during the surgical preparations. Supplemental doses of the same anesthetic were administrated regularly during recording session (50 mg/kg/hr Urethane). Atropine sulphate (0.05 mg/kg initially and 0.01 mg/kg/hr, s.c.) was administrated 15 mins before anesthesia and at regular

intervals. Following the induction of anesthesia, subjects were mounted in a stereotaxic device. After making a midline incision in the scalp, we performed craniotomy performed for vertical access to the MGB, TRN, LGN and IC (Yu et al., 2004b). To eliminate the possibility of the involvement of the cortex in the genesis of inhibition or facilitation, we ablated the AC (5.0 × 4.0 mm^2) with a suction pump (REFCO, ROYAL-2). Cerebrospinal fluid was released to minimize the fluctuation through the foramen magnum. Throughout the recording, the electrocardiograph and the end-tidal carbon dioxide was monitored to evaluate the level of anesthesia. Core temperature was maintained at 37.6-38.5°C via a rectal probe and a heating blanket. Especially for intracellular recording, animal's body was suspended for reducing vibrations of the brain caused by intra-thoracic pressure. And the animal with the chest opened bilaterally, was provided with artificial respiration and their muscles were relaxed by administrating gallamine triethiodide (Sigma, 50 mg/kg initially 10 mg/kg/hr regularly, i.p.). A piggyback glass-pipette was inserted into the TRN or IC for drug injection if necessary. All the experimental protocols were approved by the Animal Subjects Ethics Sub-Committee of The Hong Kong Polytechnic University. License for using rats and guinea pigs in our lab is resumed every year.

Figure8. Sprague-Dawley rats

Figure9. Hartley albino guinea pig

3.2.2 Acoustic stimuli

The subject was placed in a double-walled soundproof room (NAP, Clayton, Australia). Acoustic stimuli were generated by a MALab system digitally (Kaiser Instruments, Irvine, CA, USA) (Semple and Kitzes, 1993; He, 1997), or TDT auditory physiology workstation (Tucker-Davis Technologies, Alachua, FL). Acoustic stimuli were delivered through sealed acoustic system. In my project, it is a calibrated earphone (Bayer DT-48 or TDT EC1) attached to the distal end of an ear bar that inserted into the one side of animals' auditory outer meatus. Repeated white noise

bursts with a 5 ms rise-fall time were used to examine the neuronal responses. A frequency range of 100 Hz to 35 kHz was controlled by computer through using a condenser microphone and the sound pressure level (SPL) of the earphone was calibrated over the white noise (Brüel and Kjær, 1/4 inch).

3.2.3 Electrical stimulation

Two kinds of stimulating electrode arrays were used in my study. The first one comprises a tungsten recording electrode with the impedance of 1-4MΩ, an electrode with very low impedance as stimulating ground and a tungsten stimulating electrode. The second is a tungsten electrode array consisting of five parallel low impedance electrodes with a constant inter-electrode distance of 0.3-0.5mm. They were implanted into MGB and LGN (Semple and Kitzes, 1993) ipsilaterally to the recording hemisphere.

Bi-phasic electrical stimuli of 0.5ms in width, 1-10 pulses with time interval of 5ms, were adopted activate MGB and LGN and they were applied 10-30ms before the noise bursts to allow that the signals were transmitted from MGB to TRN and then projected back from TRN into MGB. The number of the stimulations was set from 1 to 5, which could effectively activate the stimulating side according to previous studies in our lab. The amplitude of the electricity was chosen among 25μA, 50μA and100μA. The maximum amplitude adopted should not activate the recording sides directly. Once the electrode array was implanted, the skull opening was covered with paraffin. Electrical currents of 50-100μA were delivered through an isolator.

3.2.4 Visual stimulation

Visual stimuli were generated digitally by a MALab system (Kaiser Instruments, Irvine, CA, USA) (Semple and Kitzes, 1993; He, 1997), or TDT system (Tucker-Davis Technologies, Alachua, FL). Visual stimuli were delivered through a row of glittering diodes triggered by the TDT system. The diode was located closely to the contralateral eye. The light duration was 100ms.

3.2.5 Extracellular recording

The majority of the data was collected by extracellular recordings. For extracellular recording, a 6-electrode array with tips offset of 250μm and impedance of 1.0-4.0 MΩ (FHC, U.S.A.) was used to record the neural activities of different divisions in MGB. The electrode was advanced vertically from brain surface by a stepping motor (Narishiga, Japan). The electrodes were lowered to a depth of 3-4mm to get close to the target areas, followed by slowly advancement at 1 or 2μm steps. After physiological study, an electrical current was applied to one of the electrodes to lesion the tissue around the recorded side. The recording positions were confirmed morphologically using Nissl materials. Neuronal activities from multiple units near the recording arrays were recorded.

3.2.6 Intracellular recording

A glass-pipette filled with 3.0 M KAc or 1.0 M KCl was used to record the membrane potential of MGB neurons. The resistance of this electrode was 40-90 MΩ.

The electrode was advanced vertically from the brain surface by a stepping motor (Narishiga, Japan). After the electrode was lowered to a depth of 3-4 mm, cortical exposure was sealed by using low-melting temperature paraffin (Wako). When the electrode was close to the target area, it was then slowly advanced at 1 or 2μm steps. Neurons, with spikes that overshot the baseline and a resting membrane potential (mV) < -50 mV, were collected and analyzed in the present studies.

3.2.7 Anatomical confirmation

At the end of the experiment, the positions of the extracellular recording and electrical stimulating electrodes were marked via electrical lesions. The tracks and lesions were both used to confirm the locations of electrodes.

The subjects were deeply anesthetized after the recording session with overdose of sodium pentobarbital (0.1 ml/100 g, 60 mg/ml, i.p.; Sigma) and perfused trans-cardiac with 200ml 0.9% saline followed by a mixture of 2.5% glutaraldehydein 0.1 M phosphate buffer (pH 7.3) and 0.4% paraformaldehyde. The brains were removed quickly from the skull and post-fixed for 4 hours in the same fixative. The brains were then cryoprotected in 25% sucrose in PB (0.1 M, pH 7.4, 4°C) for 2 days. After cryprotection, the thalamus, LGN and TRN were cut into coronal section (with a thickness of 60 or 90μm) with a freezing microtome. The sections, containing stimulation tracks and labeled neurons, were mounted on gelatin-coated slides. Those sections were then all stained by using the Nissl method. The stained sections were then capable of presenting as the physiology map, guiding us by the lesions or the electrode tracks. The sections were examined under the microscope before they were

photographed. After the Nissl procedures, the sections were usually shrunk about 10-13%. Therefore, to match them to the physiology status, enlargements of 10-13% of the images were made during the data analysis.

3.2.6 Data acquisition and analysis

After amplification, extracellular neuronal activities, intracellular membrane potential signals and stimulus signals as well were presented and stored in the computer with the assistance of software (AxoScope, Axon). No manipulations of spike rate and membrane potentials of the neurons were made unless specially stated. The spike numbers (rate) and amplitudes of IPSPs were calculated as the change of neuronal activities evoked by acoustic or electrical stimulation. The calculating method will be illustrated in details in chapter 4. Numerical results are expressed as mean ± standard deviation (S.D.). Comparison of spike numbers and IPSP amplitude between control and experimental conditions was made by using paired t-test or t-test. Nighty-five percent confidence was set as the statistical significance.

3.3 experimental designs

3.3.1 The responses of auditory neurons in MGB to the electrical stimulation in MGB

S-D rats were used as subjects in this study. Repeated noise bursts (60dB, 100ms duration and 2000ms interval) were used to examine the neuronal responses. The parameters of the electrical stimulation were the same as described above.

The stimulating electrode arrays were implanted into caudal or rostral MGB firstly and fixed there. The recording array was implanted into rostral or caudal MGB, 0.5-1.5mm rostrocaudally apart from the stimulating site. The array was advanced gradually from superficial to deep MGB to record all auditory neurons in this coronal section. The depth of each electrode in the array when touching the brain surface was recorded and it was subtracted to obtain net depth of each neuron recorded in the plane.

The auditory responses of MGB neurons to noises only were recorded in the control group. In the experimental condition, electrical stimulation was applied 10-30ms before noises in each trial on the stimulation site. Then auditory responses of the same MGB neurons to noise were recorded again.

Spike numbers for 20-30 trials of both control and experimental conditions were calculated by software Brainware. Degree of change was calculated by [SR (spike rate) (experimental) - SR (spike rate) (control)] / SR (spike rate) (control)*100%.

3.3.2 The response of auditory neurons in MGB to the electrical stimulation in MGB by intracellular recording

Guinea pigs were used as subjects in this study for they are lack of MGB interneurons. To further understand the inhibitory effect observed in study 1, intracellular recording was conducted. The stimulating electrode arrays was implanted into MGB firstly and fixed there. A glass-pipette filled with 3.0 M KAc or 1.0 M KCl was then used to record the membrane potential of other MGB neurons. Parameters of acoustic and electrical stimuli were the same as study 1.

3.3.3 The participation of TRN in the intrathalamic inhibition

S-D rats were used as subjects in this study. The electrode arrays, consisting of a recording electrode, a glass-pipette (d=20μm) full of lidocaine for local anesthetization was implanted into TRN. Acoustic stimuli were applied and auditory responses of TRN were used to place the electrode arrays. MGB neurons with inhibitory effect were then found by extracellular recording. 10-50μl (20mg/ml) lidocaine was injected into TRN to temporarily inactivate TRN. The effect was monitored by recording the neural activities of TRN. After TRN inactivation, the examination of the same point of MGB units to noises and the combination of noises and electrical stimuli was repeated. The inhibitory rate of MGB neurons before and after TRN inactivation was compared to test the role of TRN in the inhibitory effect.

3.3.4 The elimination of IC in the intrathalamic inhibition

The injection electrode arrays was implanted and fixed in IC. Acoustic stimuli were applied and auditory responses of IC were found to locate the electrode arrays. A MGB neuron with inhibitory effect was found by intracellular recording. 50μl lidocaine was injected into IC to temporarily inactivate it. The effect was monitored by recording the neuronal activities of IC. After inactivation, the transmission of auditory information was terminated at the level of IC and therefore MGB neurons had no responses to noises. In this case, IPSPs as the critical indicator of the inhibitory effect could still be observed if IC did not participate in the inhibitory effect.

3.3.5 The cross modalities effect between LGN and MGB

The stimulating arrays, consisting of a recording electrode, and a bipolar stimulating electrode were implanted in LGN. Visual stimuli were applied and visual responses of LGN were used to place the stimulating arrays. The recording array was then implanted into MGB. The array was advanced gradually from superficial to deep MGB to record auditory neurons in the same coronal section. The auditory responses of MGB neurons to noises only were recorded in the control group. In the experimental group, electrical stimulation was applied to LGN 10-30ms before noises for each trial. Auditory responses of the same MGB neurons to noises were recorded again.

Spike numbers for 20-30 trials of both control and experimental groups were calculated by the software Brainware. Degree of change was calculated by the formula listed above.

3.3.6 Distribution of the intrathalamic interactions in a coronal plane of MGB

Distribution regularities of all kinds of intrathalamic interactions in a coronal plane of MGB were detected in two manners.

The first way was recording the responses from auditory neurons in a coronal plane of MGB, when single point of MGB units from another coronal plane were electrically stimulated. Auditory responses of MGB were identified in order to locate the stimulating arrays. A recording array with 5-6 electrodes was removed from superficial to deep MGB.

The second way was the reverse one by fixing the recording electrode and removing the stimulating array with 5-6 stimulating electrodes. The stimulating array was advanced from superficial to deep MGB. A single recording electrode was implanted into MGB to collect responses of the same MGB units when different MGB neurons on another coronal plane were electrically stimulated.

An electrical current (9v, 45secs or 1μA, 1min) was applied to lesion the tissue around the last recording point or stimulation site recorded. The positions were confirmed morphologically. Locations of other neurons were estimated according to the marked points.

Chapter 4

Results

This chapter presents the results of the whole study, which consists of six parts. Study 1 illustrates responses of auditory neurons in MGB to the electrical stimulation in other MGB neurons. Study 2 further investigates the major phenomenon observed in study 1, which is the inhibitory modulation. Study 3 focuses on the participation of TRN in the inhibitory effect. By study 4, the role of IC is eliminated in the loop, from which the inhibitory effect arises. In study 5, cross-modality effect arising from LGN via TRN on auditory neurons in MGB is examined. And the last study investigates the range and distribution regularities of intrathalamic interactions in the same coronal MGB plane.

4.1 Study 1: The responses of auditory neurons in MGB to the electrical stimulation in other MGB neurons

4.1.1 Conclusion of the intrathalamic interactions from all MGB neurons recorded.

In this study, 238 auditory neurons were recorded in total. Three kinds of phenomenon were observed. They were inhibitory effect, facilitating effect and no significant change.

The spike rate of MGB neurons to noise was recorded in the control condition. In the experimental condition, electrical stimuli (20-100μA) were applied to other point of MGB units 15-30ms before noises. The spike rate of the same MGB neurons

in the recording site to the combination of electrical stimuli and noises was recorded. Degree of change was calculated by [SR (spike rate) e (experimental) - SR (spike rate) c (control)] / SR (spike rate) c (control)*100%.

The degree of change of every auditory MGB units was calculated. The results were summarized in Figure 10.

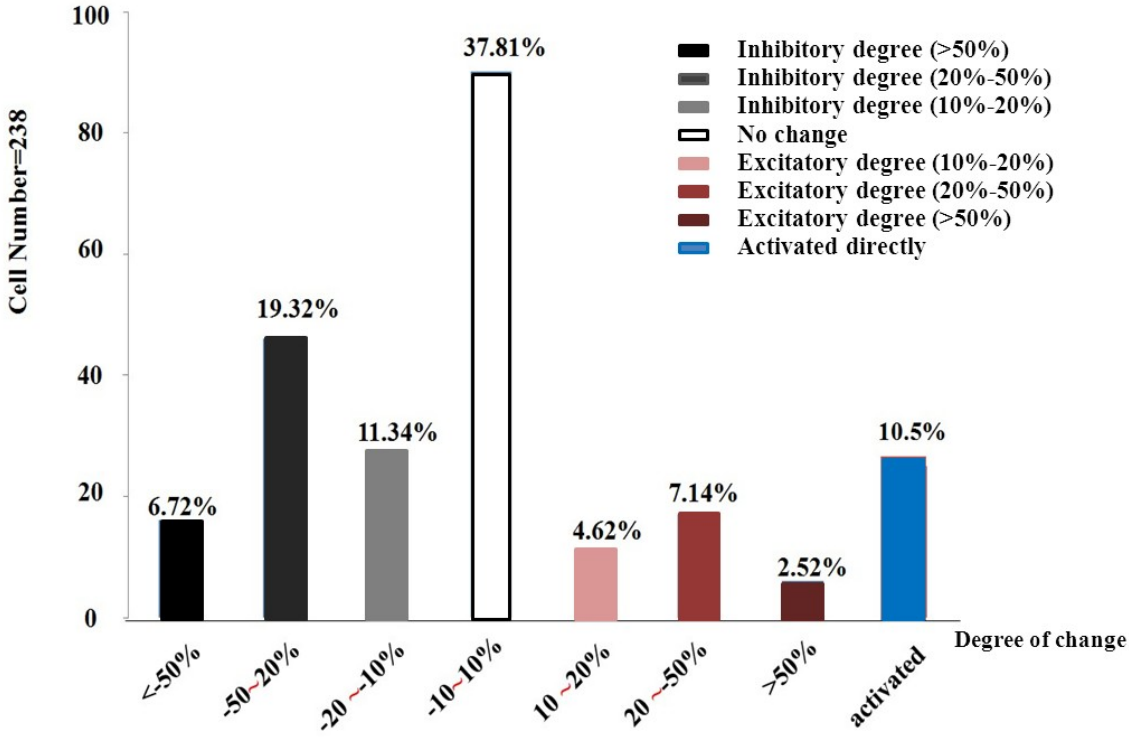

Figure10. Summary of the intrathalamic interactions from all MGB neurons recorded.

The first column (from left to right), presents the percentage of the neurons with the inhibitory rate larger than 50%, which is 6.7%. The total number of neurons in this group is 16.The second column, presents the percentage of the neurons with the inhibitory rate from 20% to 50%,which is 19.3%. The total number of neurons in this

group is 46. The third column, presents the percentage of the neurons with an inhibition from 10% to 20%,which is 11.3%. The total number in this group is 27.

By recording the auditory responses of MGB neurons to noises only, we found that natural deviation degree of neuron activities was ranged from -10% to 10%. -10% to 10% was then set as the criteria for no significant change. As presented in the fourth column, 90 cases belong to this group, comprising 19.3% of all the ones recorded.

The fifth column, presents the percentage of the neurons with an facilitating degree from 10% to 20%,which is 4.62%. The total number in this group is 11.The sixth column, presents the percentage of the neurons with an facilitating degree from 20% to 50%,which is 7.14%. The total number of this group is 17. The seventh column, presents the percentage of neurons with the facilitaing rate larger than 50%,which is 2.52%. The total number of this group is 6.

The last group, taking 10.5% of the whole neurons, are the ones directly activated by the electrical stimuli. For these cases, immediate neural responses with the latency less then 10ms were observed in the studies. This phenomenon may be caused by the electrical stimuli with excessive amplitudes. For another reason, the dendrites of the neurons recorded may possibly pass by the stimulation points, inducing the direct activation. The strong activation forced neurons into a refractory period, leading the significant decrease of spikes in the responding period. Although this decrease was not caused by the inhibitory loop we were investigating and they were not accounted in the data that would be further studied.

For the rest 213 neurons without direct activation, the information was summarized in a table presented as follows.

Table 1

	Inhibitory effect	<-50%	-50~-20%	-20~-10%	-10~10%	10~20%	20~50%	>50%	Excitatory effect
Neurons numbers	89	16	46	27	90	11	17	6	34
percentage	41.8%	7.51%	21.6%	12.7%	42.3%	5.16%	8%	2.81%	15.9%

(Total cell number = 213)

4.1.2 Three types of intrathalamic interactions in the MGB neurons

As representative examples, 3 neuron clusters with different kinds of intrathalamic interactions are presented as follows.

Figure 11 shows a neuron cluster in MGB with a typical inhibitory effect. In this figure, spike rate of 30 trials to noises only and to the combined stimulation of noises and electrical stimuli are displayed respectively. In this case, the electrical stimulus, of which the artifacts are marked with red arrows, are applied at 0ms, 15ms before noises. Its amplitude was 50μA. In the same time window from 27ms to 80ms, which is the response period of this neuron cluster, the spike rate with electrical stimuli was significantly decreased, compared with the ones to noises only. The interval between two dashed red lines indicated the response period. Data from two conditions were analyzed and the results are presented in Fig. 12. Spike rate (spike number/sec) of control condition is 1.97 and the one of experimental condition is 0.90. According to the formula listed above, the inhibitory degree is 54.3%. Accurate spike numbers of 30 trials from two conditions were compared via T-Test. The P value is

0.002 (<0.05), which means that data from these two conditions are significantly different.

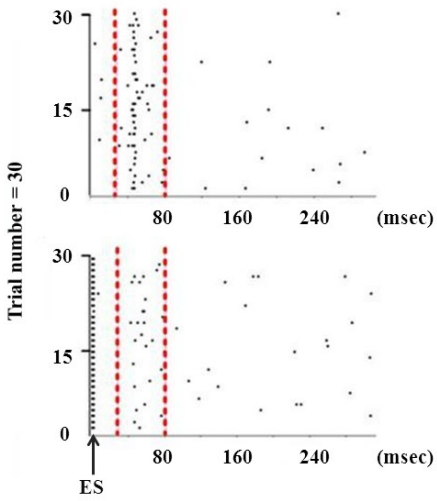

Figure11. The inhibitory interaction: auditory responses of the same group of MGB neurons for 30 trials between control (responses to noises only) and experimental (electrical stimuli were applied 15ms before noises) conditions are displayed by raster plots and compared via T-Test.

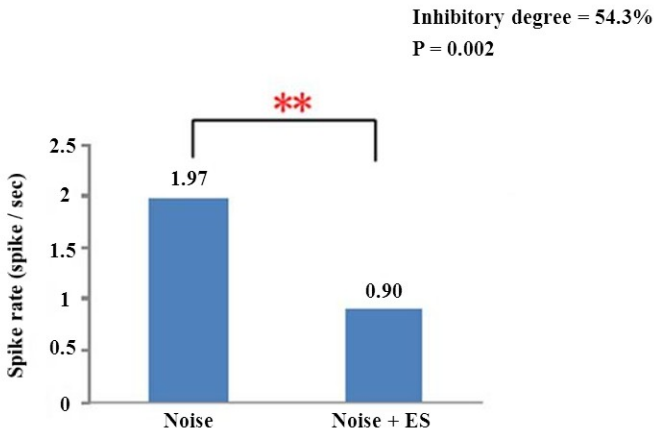

Figure12. The inhibitory interaction: spike rate (spikes / sec) for 30 trials of two conditions are compared through T-Test.

Figure 13 shows a neuron cluster in MGB with a typical facilitating effect. In this case, the electrical stimuli were applied 15ms before noises and its amplitude was 100μA. The recording method was the same as the previous one. The response period of this neuron cluster was from 25ms to 160ms, in which the neurons responded to noises intensively. The spike rate of experimental condition was increased, compared with the one of control condition. As shown in Figure 14, the spike rate of control condition is 1.93/sec and the one of experimental condition is 3.93/sec. According to the formula listed above, the degree of facilitation is 103.6%. The P value is 0.000055 (<0.05), which means that data from these two conditions have significant differences.

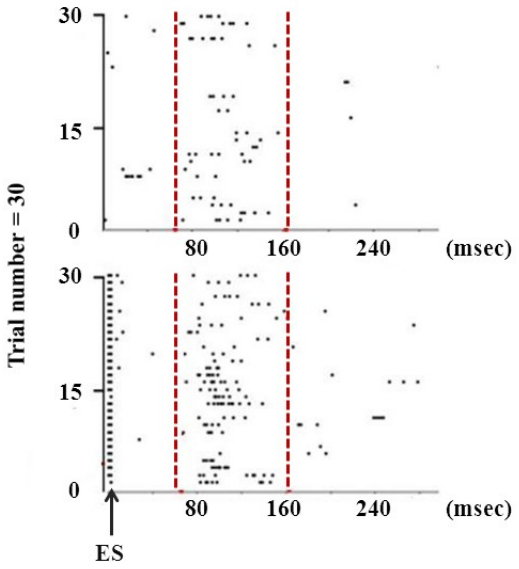

Figure13. The facilitating interaction: auditory responses of the same group of MGB neurons for 30 trials of control and experimental conditions are displayed by raster plots.

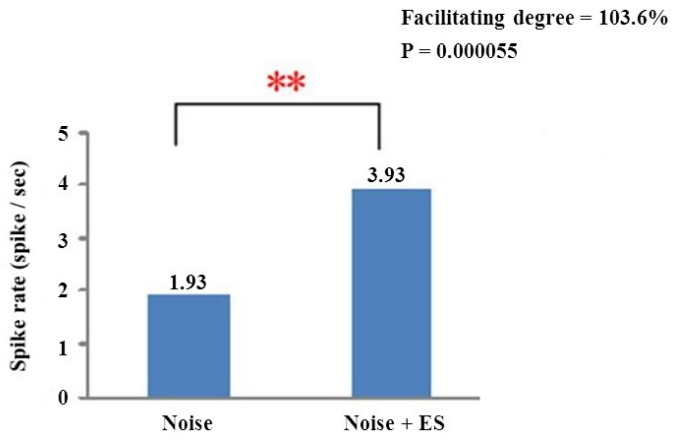

Figure14. The facilitating interaction: spike rate (spikes / sec) for 30 trials of two conditions are compared through T-Test.

42.3% neuron clusters have no significant change between control and experimental conditions. A neuron cluster representative for this type is shown in figure 15 and 16. In this case, the electrical stimuli were applied 15ms before noises and its amplitude was 50μA. The response period of this neuron cluster is from 35ms to 65ms. No significant change was observed between the two conditions. Figure 15 shows that the spike rate of control group is 9.03 and the one of experimental group is 8.30. The degree of change is -8.08%. The P value is 0.255 (>0.05), which means that data from these two groups have no significant difference.

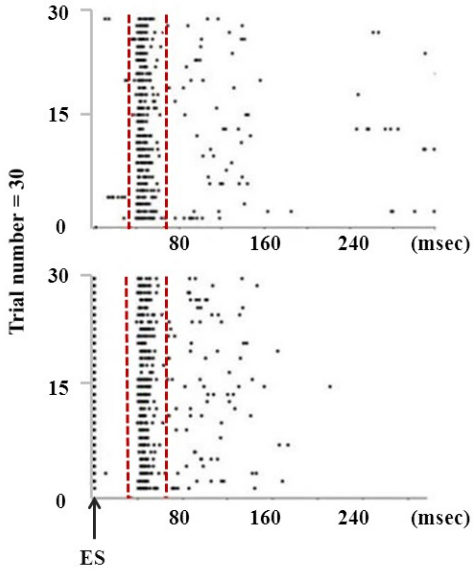

Figure15. No significant interaction: auditory responses of the same group of MGB neurons for 30 trials of control and experimental conditions are displayed by raster plots.

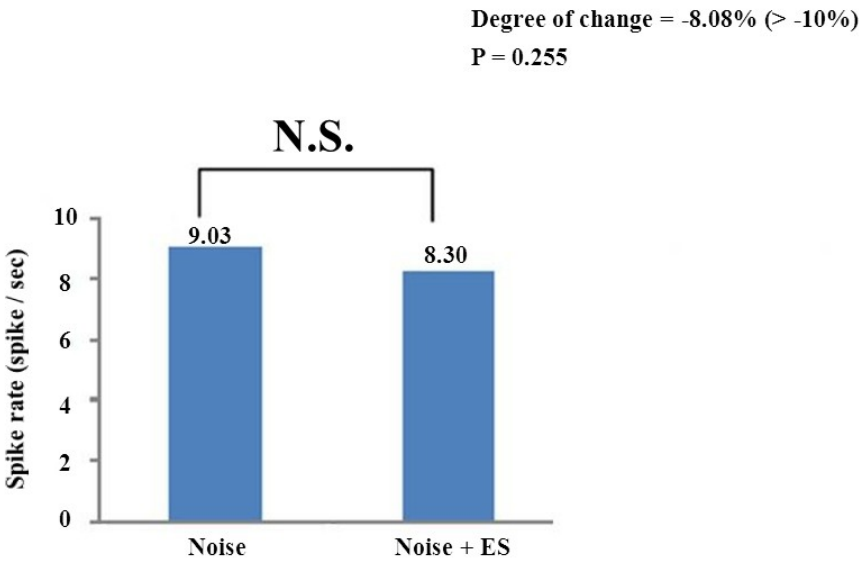

Figure16. No significant interaction: spike rate (spikes / sec) for 30 trials of two conditions are compared through T-Test, the spike rate of two conditions is compared.

4.2 Inhibitory interaction in the Medial Geniculate Body

Inhibitory effects were observed in 41.8% of all neuron clusters analyzed by extracellular recording. In this way, data were collected from the multiple units all around the recording electrode. To provide further information about the inhibitory modulation, intracellular recording was conducted. Auditory responses of single MGB neuron were investigated via this method.

4.2.1 Inhibitory interaction in the MGB by extracellular recording

Through the preparative experiments, we found that 15-30ms was easy to observe the inhibitory effect. 15ms-30ms was theoretically suitable for information transmitted from MGB to TRN and then back to MGB. Therefore, 15ms-30ms was chosen as the time delay between electrical stimuli and noises. Figure 17 shows an example with inhibitory effect. In this case, the electrical stimuli were applied at 0ms and noises were given at 15ms. Its amplitude was 100μA. The spike rate indicated by the raster plots for 30 trials was presented in Fig.17. The spike rate of control condition is 4.27 and the one of experimental condition is 2.93. The inhibitory rate is 31.4% ($P=0.0177<0.05$).

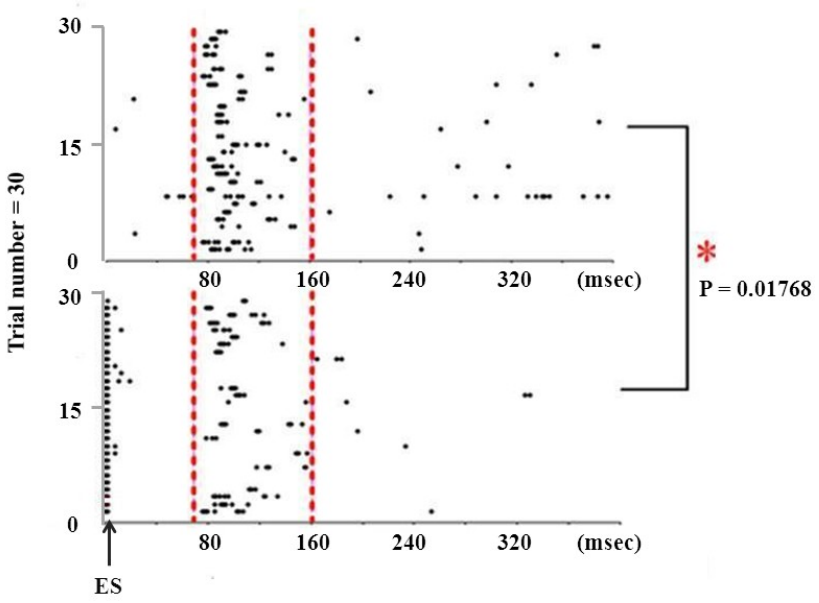

Figure17. The inhibitory interaction.

The original data of this neuron cluster are shown in Figure 18. The upper trace in this picture presents the auditory responses to noises only. The lower trace presents the auditory responses of the same neuron cluster when another MGB point was electrically stimulated 15ms before noises. Red line in this row indicates the artifact of the electrical stimuli. No auditory responses observed in the response period of this neuron cluster in the experimental condition.

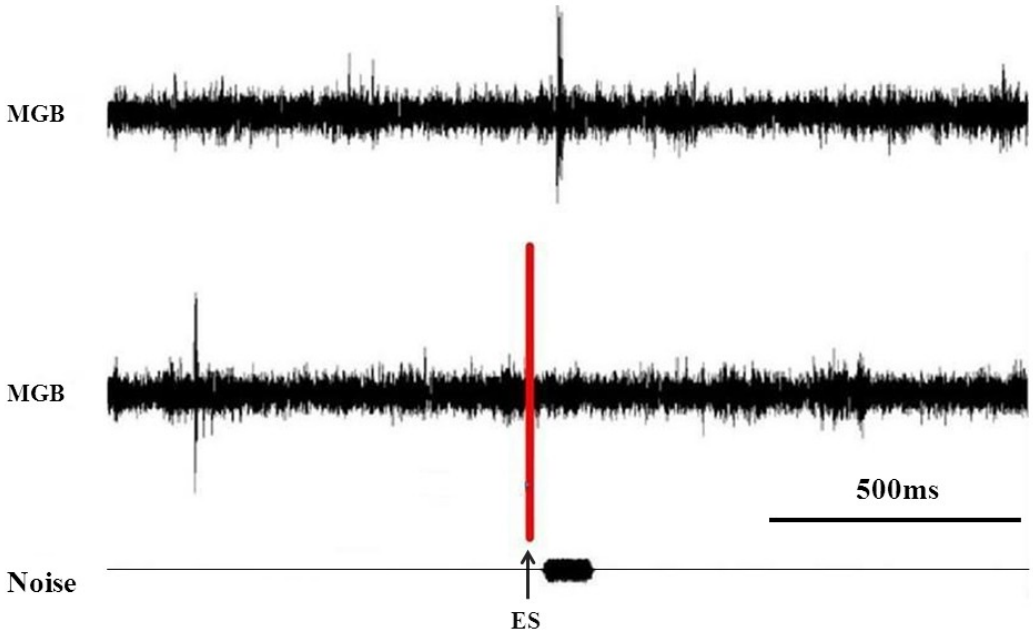

Figure18. Original data for inhibitory interaction are presented by the software Axon.

4.2.2 Inhibitory interaction in the MGB by intracellular recording

To understand responses change of a single MGB neuron, intracellular recording was conducted. There are 4 neurons in total that were recorded with the inhibitory interaction. Figure 19-20 shows the results from two MGB neurons. These two neurons received inhibitory modulation when another MGB points were electrically stimulated.

Neuron A in figure 19 had a resting membrane potential of -75mV. The electrical stimulation was a single pulse with the amplitude of 50μA, which was applied in MGB 20ms before noises. The noise signals presented in the last row were applied to both conditions. Neuron A received the inhibitory modulation with IPSPs of

-7mV. As presented in the picture, the membrane potential of neuron A was hyperpolarized to -82mV by the electrical stimulation in other MGB neurons.

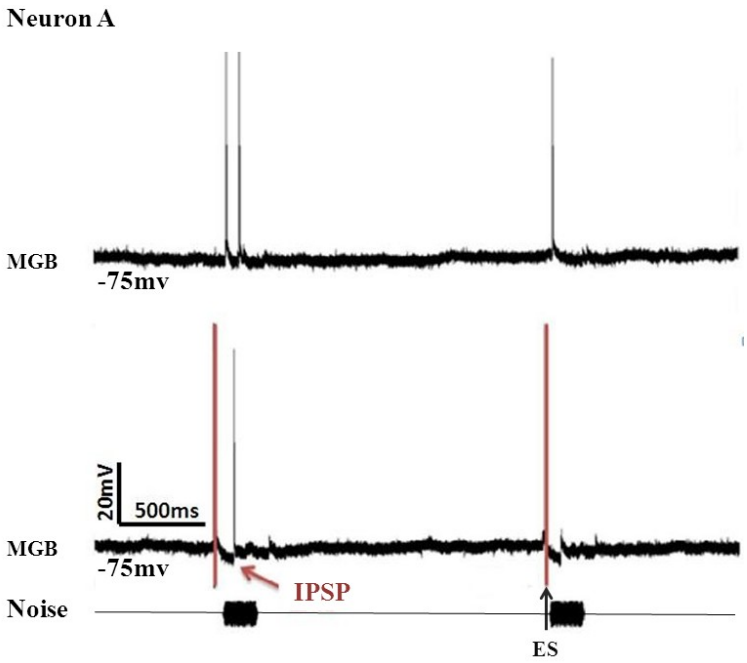

Figure19. The inhibitory modulation on neuron A by intracellular recording: IPSPs and electrical stimuli were marked by arrows with different colors.

Neuron B had a resting membrane potential of -52mV. The electrical stimulation was a single pulse with the amplitude of 25μA, which was applied in MGB 10ms before noises. This neuron responded to noises with spikes followed by prolonged IPSPs. Compared to the ones of control condition, the amplitude of IPSPs insignificantly changed in the experimental condition, although the spikes were inhibited by the electrical stimulation.

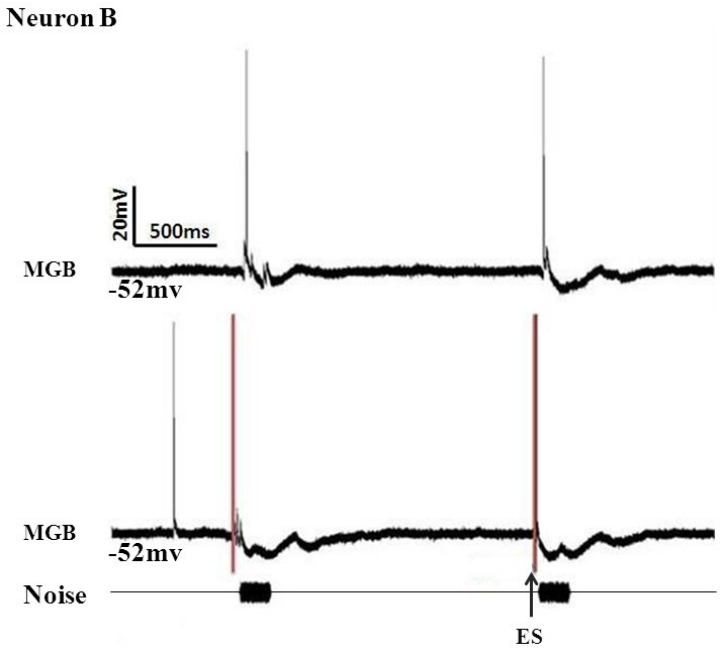

Figure20. The inhibitory modulation on neuron B recorded intracellularly: electrical stimuli were marked by arrows.

4.3 The participation of TRN in the intrathalamic interactions in MGB neurons

In this study, we investigated the role of TRN in the inhibitory modulation. Firstly, the location of TRN was identified by measuring its auditory responses. Then a neuron cluster in MGB with inhibitory effect induced by the electrical stimulation was identified. TRN was subsequently inactivated by lidocaine injection. The inhibitory effect was examined for the same neuron cluster again.

4.3.1 TRN identification and inactivation

Auditory responses of TRN neurons are indicated in the first column in Figure 21. After identifying the MGB neurons with inhibitory effect by MGB stimulation, lidocaine was injected into TRN. The auditory responses of TRN during the whole process of lidocaine injection were recorded to monitor the effect of TRN inactivation. After lidocaine injection, the TRN presented no responses to noises, as shown in the second row in Figure 21. The activation of TRN neurons to noises for 30 trials before and after inactivation was recorded respectively. The spike presented by raster plots of these two conditions are illustrated in Figure 22. The upper trace presents the responses of TRN units to noises before inactivation. The lower trace presents the data after inactivation. In the same response period, no activities were recorded after inactivation.

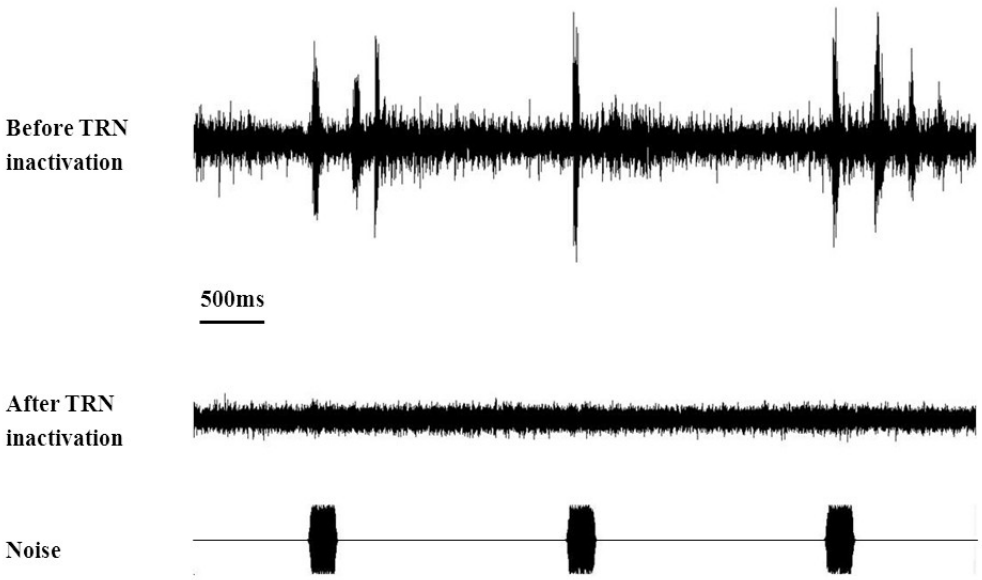

Figure21. Original data presented by software Axon: the auditory responses of TRN units before and after inactivation.

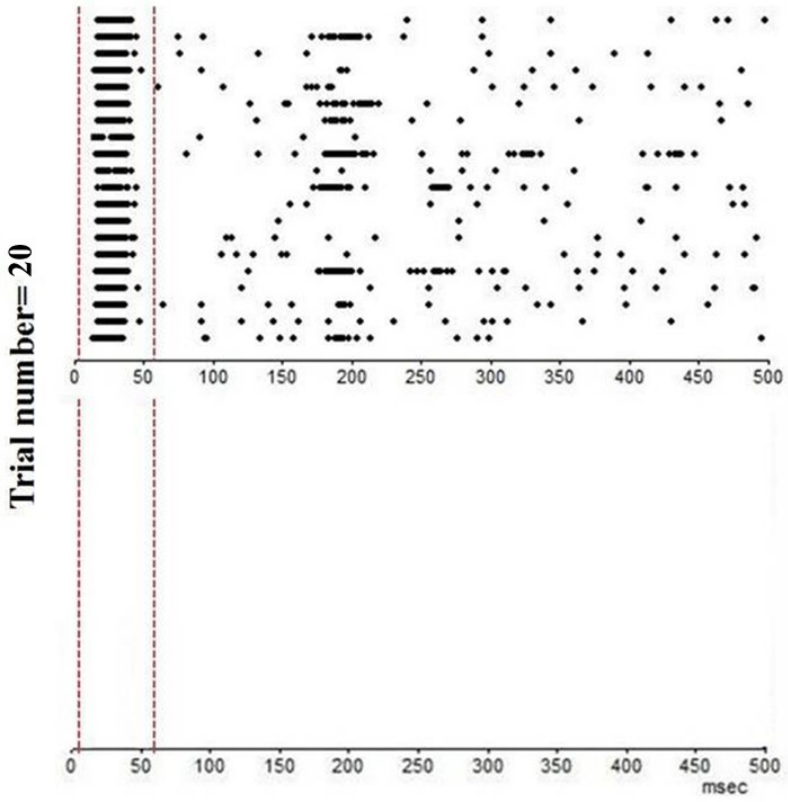

Figure22. Auditory responses of TRN units before and after inactivation presented by spike raster plots.

4.3.2 The elimination of inhibitory modulation in MGB after TRN inactivation

After the identification of TRN neurons, a MGB cluster with inhibitory effect was identified. Figure 23 shows the results collected from this MGB neuron cluster. The electrical stimulation was 5 pulses with the amplitude of 50μA, which was applied to MGB 15ms before noises. Figure 23 shows the original data of neural responses collected from both control and experimental conditions. To provide further information, the middle response circulated by the purple rectangle was resolved in

Fig. 24. As indicated by Fig.24, the spike rate was obviously inhibited in the experimental condition. Data from 20 trials were presented in Fig.25. In picture A, the upper part shows neural responses of the control condition and the lower one from experimental condition. In picture B, data of 20 trials from the same neuron unit were analyzed. The inhibitory rate of this cluster is 61%.

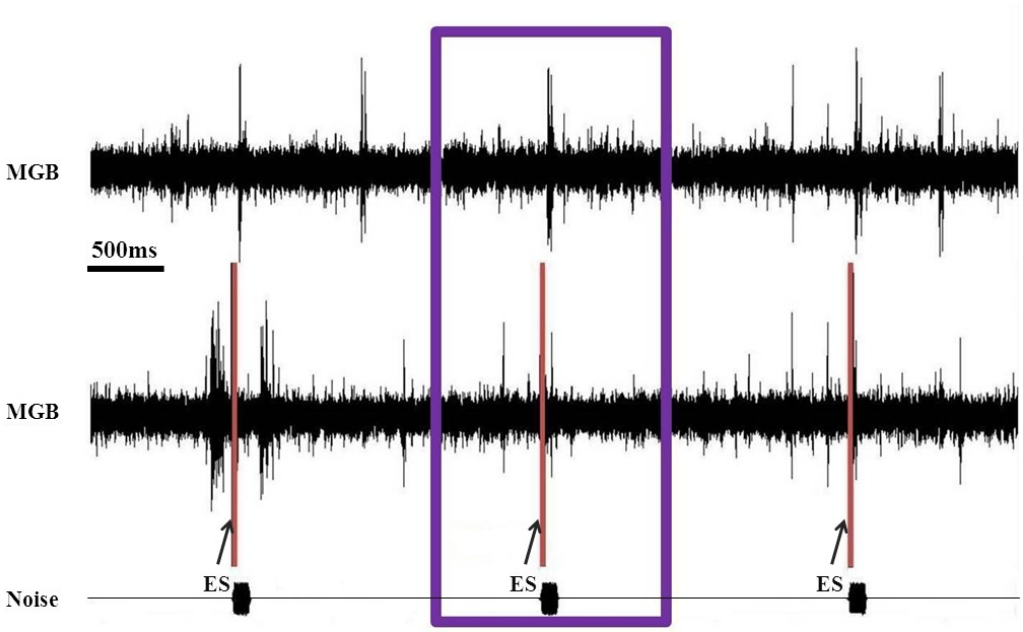

Figure23. Before TRN inactivation: auditory responses of MGB units to auditory stimuli alone and auditory plus electrical stimulation.

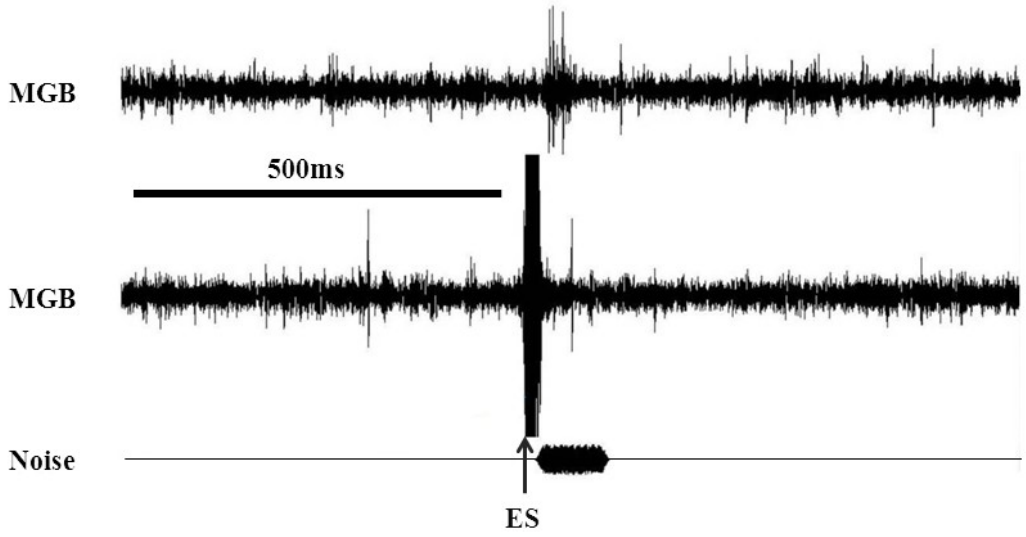

Figure24. Higher resolution of Figure 23.

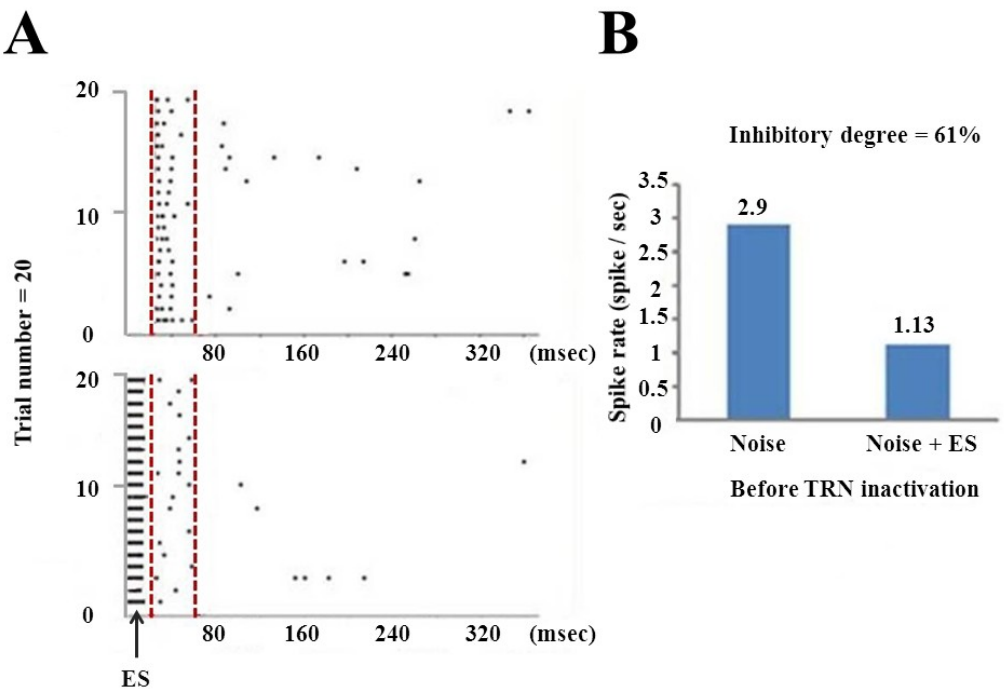

Figure25. Analyzed data for the inhibitory interaction on the same MGB units before TRN inactivation.

After the auditory responses of TRN disappeared, the TRN was inactivated by lidocaine injection. Then, the same experimental procedures were repeated to this MGB neuron cluster. All parameters remained the same as the previous one. The results are presented in the Figure 26-28. In figure 26, the upper trace is responses collected from auditory stimulation and the lower trace from combined stimuli of electrical and auditory stimulation. The middle response circulated by the purple rectangle was more resolved in Figure 27. As shown in Figure 26-27, the spike rate showed no significant change between two conditions. Data from 20 trials were presented in Figure 28, further confirming that no significant inhibition was observed in this MGB cluster after TRN inactivation. Picture B in Figure 28 presents the analyzed data from 20 trials. The inhibitory rate of this neuron cluster is -0.7%.

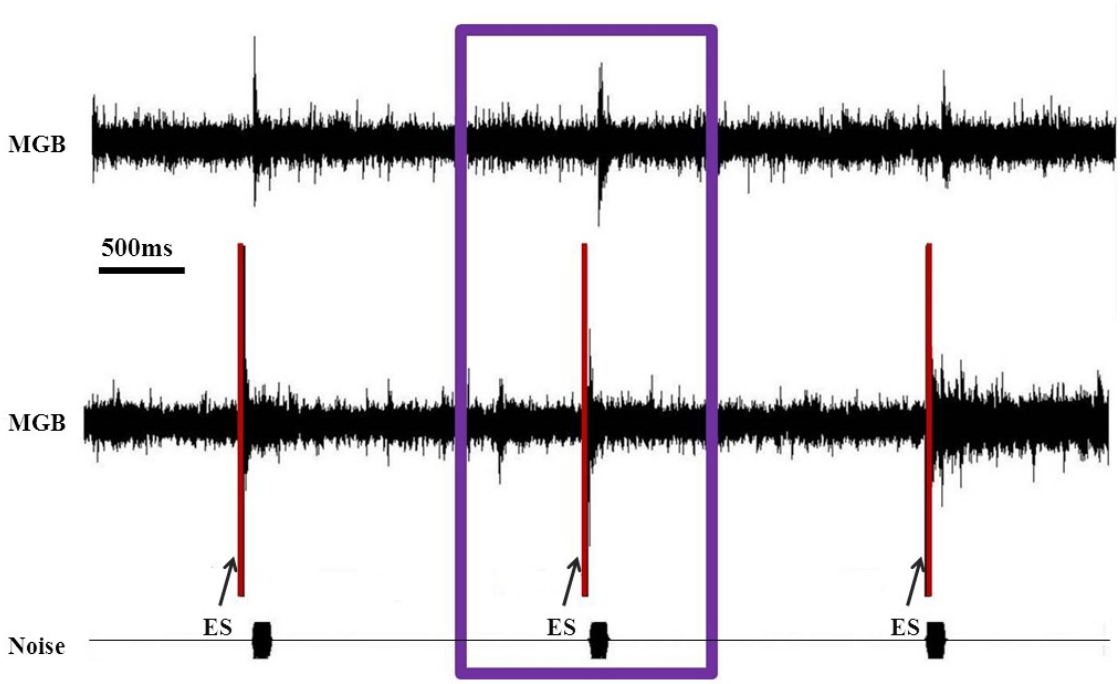

Figure26. Auditory responses of the same MGB units to auditory stimuli alone and auditory plus electrical stimulation after TRN inactivation.

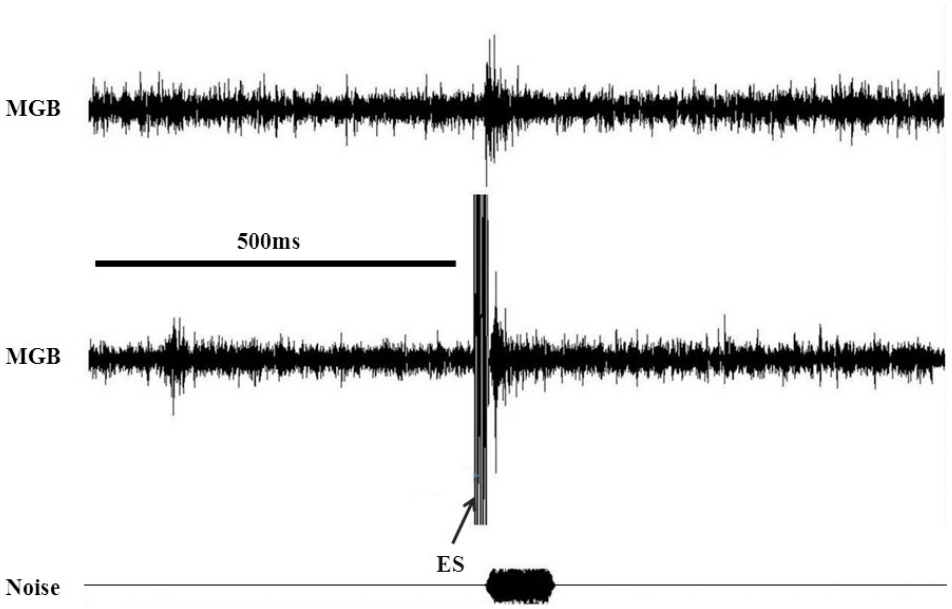

Figure27. Higher resolved picture of Figure 26.

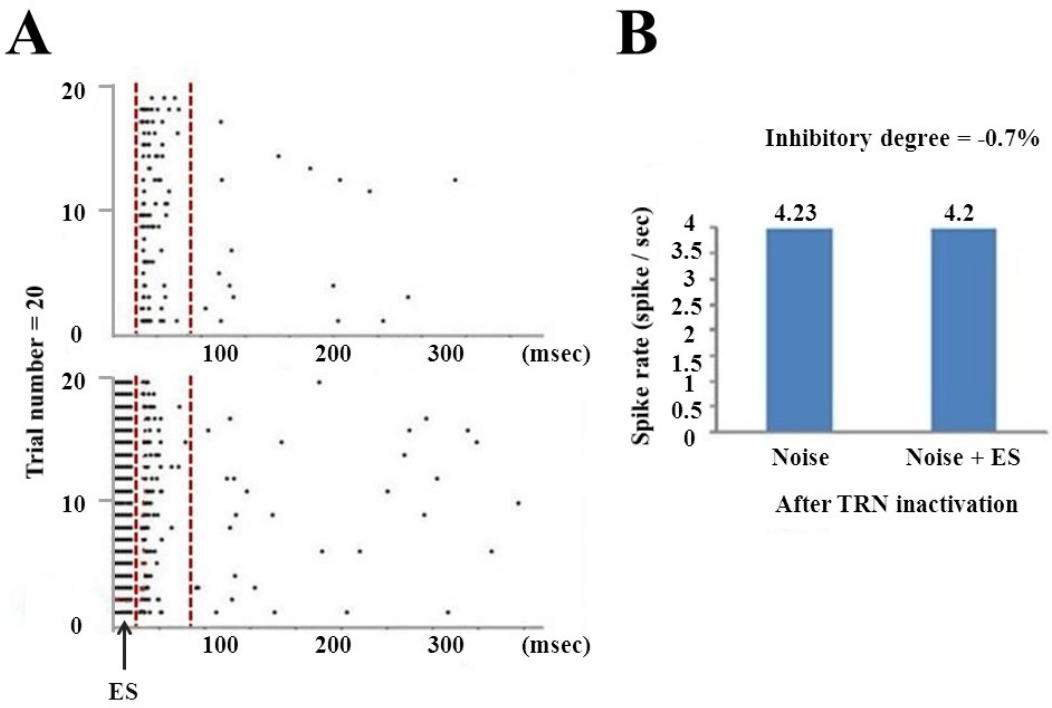

Figure28. No inhibitory interaction on the same MGB units observed after TRN inactivation.

4.3.3The role of TRN in the inhibitory effects in MGB neurons

10 experiments were completed for this study in total. In 5 experiments, the inhibitory effects were diminished after the TRN inactivation, the similar as the example shown in the last section. In 3 experiments, the MGB units received inhibitory interactions before TRN inactivation. After TRN inactivation, the same MGB units became more sensitive and they were directly activated when the electrical stimulation with the same parameters was applied to MGB. Therefore，this part of data could not be accounted in because of its incomparability. In 2 experiments, the inhibitory degree was not significantly changed, compared with the one before TRN inactivation.

The results of 5 experiments, in which the inhibitory effects were diminished by TRN inactivation, were demonstrated in table 2 in details. The results of trial 1 have been demonstrated in Figure 21-28. Trials 3, 4, 5 received the similar diminishment of the inhibitory interactions after TRN inactivation. For trial 2, the inhibitory interaction was not diminished completely, but the inhibitory degree was decreased after TRN inactivation. It was changed from 33.6% to 16.8%. To provide more information, these 5 pairs of data were summarized in Figure 29. The p-value via paired T –Test is 0.011 (<0.05), proving that the groups with intact TRN have significant difference comparing to the ones after TRN inactivation.

Table 2

	Spike rate (spike number/sec) (N)	Spike rate (spike number/sec) (N+ES)	Inhibitory degree	Spike rate (spike number/sec) (N)	Spike rate (spike number/sec) (N+ES)	Inhibitory degree
Trial 1	2.9	1.1	6%	4.23	4.1	-0.7%
Trial 2	4.37	2.9	33.6%	10.3	8.57	16.8%
Trial 3	6.03	4.37	27.5%	4.1	4.17	-1.8%
Trial 4	5.07	2.87	43.3%	12.27	12.47	-1.6%
Trial 5	1.47	0.33	77.6%	2.67	2.47	7.5%

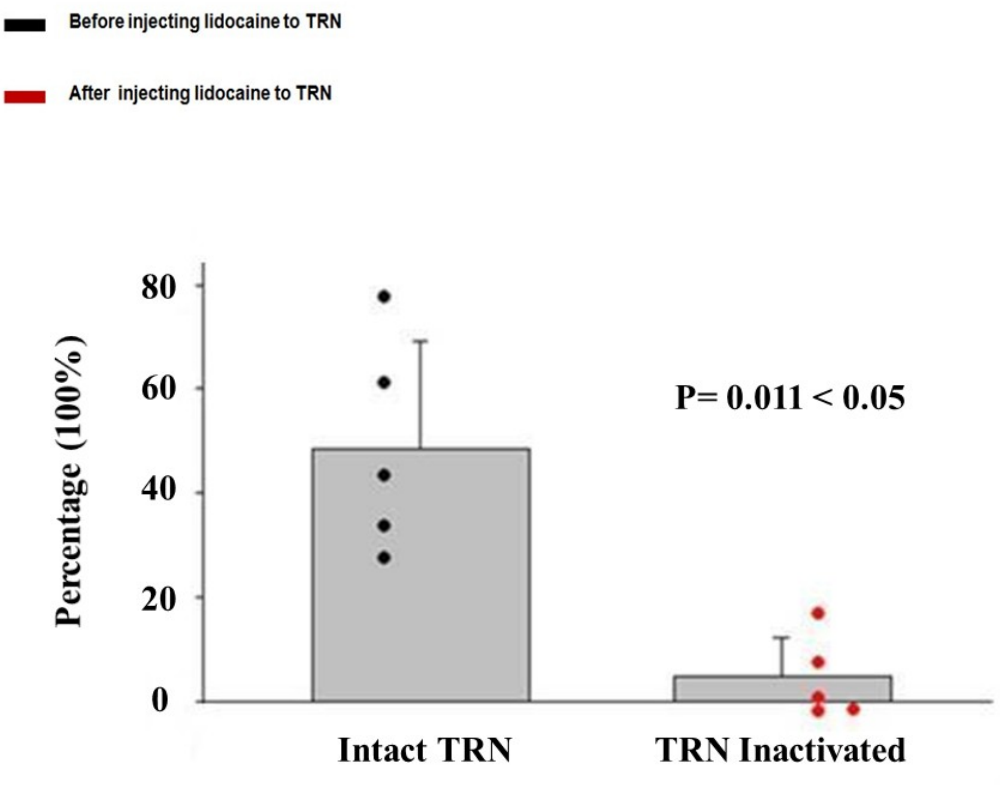

Figure29. Summary of 5 successful trials for TRN inactivating experiments.

4.4 Intrathalamic interactions in MGB neurons after IC ablation

In this study, the role of IC in the inhibitory modulation was investigated. Firstly, location of IC was identified. A neuron in MGB with inhibitory effect elicited by electrical stimulation was identified. And then, IC was temporarily inactivated by lidocaine injection. The inhibitory effect was examined again for the same neuron. We found the inhibitory effect still existed after IC inactivation. 2 neurons were successfully recorded for this experiment.

4.4.1 IC identification and inactivation

Auditory responses of IC neurons are illustrated by the upper trace in Figure 30. After identifying the MGB neurons with intracellular inhibitory effect, lidocaine was injected into IC. Then, MGB presented no responses to noises, as shown in Figure 31. The MGB responses to noises before, during and after inactivation were recorded to monitor the effect of inactivation. They are illustrated in the Figure 31 in the time order. The first row indicated the data collected at the beginning of lidocaine injection, and the second row in the intermediate stage and the third row at the last stage.

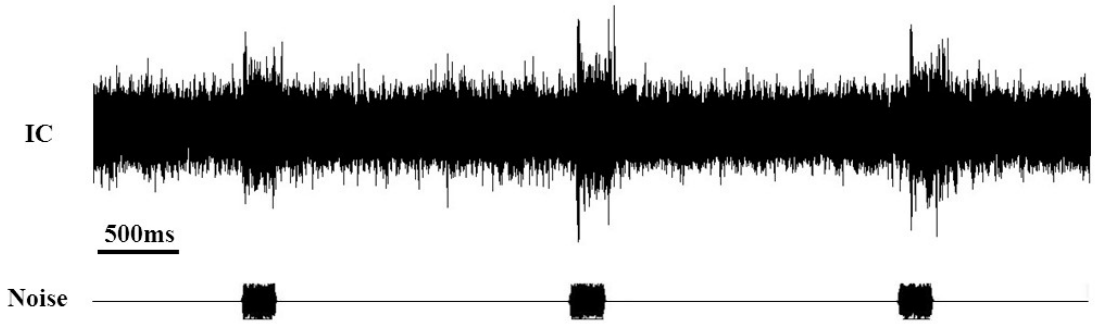

Figure30. Auditory responses of IC neurons.

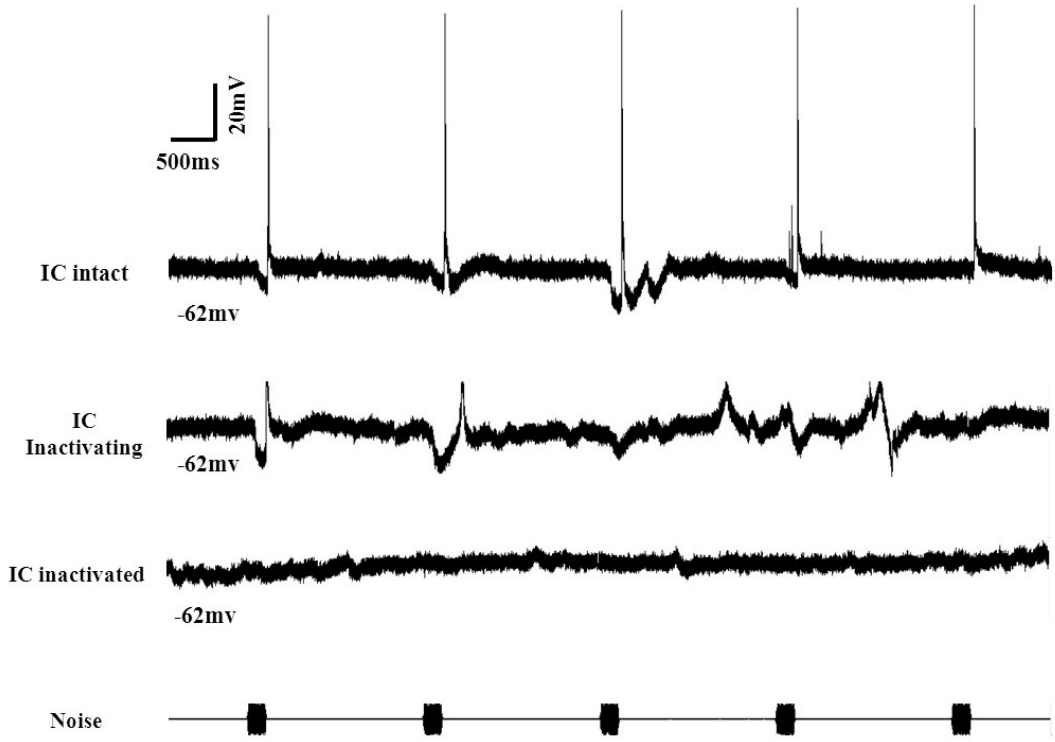

Figure31. Auditory responses of the MGB neuron during IC inactivation.

4.4.2 The disassociation of IC with the inhibitory modulation in MGB neurons

After the identification of IC neurons, a MGB neuron with inhibitory effect was detected. Figure 32-33 shows the results collected from this MGB neuron. The electrical stimulation was one pulse with the amplitude of 50μA, which was applied to the MGB 15ms before noises. Picture A of Figure 32 shows the original data of neural responses from both control and experimental conditions. The neuron had a resting potential of 64mV. When MGB was electrically stimulated, the membrane potential was hyperpolarized for the average 11.4mV. The amplitude of IPSPs of the same

neuron for both conditions is listed in table 3. Picture B illustrates the difference for 5 trials of the same MGB neuron between these two conditions.

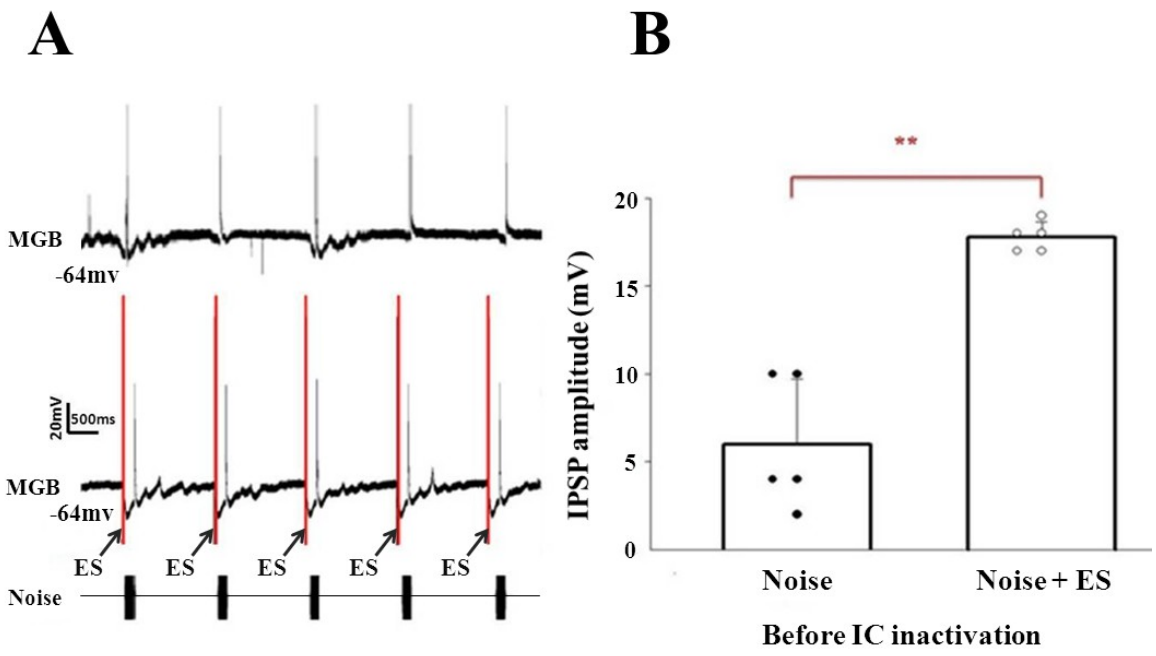

Figure32. Inhibitory interaction on a MGB neuron before IC inactivation.

Table 3

Conditions IPSP Amplitude (mV)	Trial 1	Trial 2	Trial 3	Trial 4	Trial 5
Control (Noise)	10	4	10	2	4
Experimental (Noise + ES)	19	18	17	18	17

4.4.3The inhibitory effects in MGB neurons after IC inactivation

After the inactivation of IC, the same experimental procedures were repeated to this neuron. All parameters remained the same as the previous one. When MGB was electrically stimulated, the membrane potential was hyperpolarized for 16.4mV. The amplitude of the IPSPs for both conditions was listed in table 4. The IPSPs of the experimental condition after IC inactivation and the experimental condition before IC inactivation were compared. And the results indicated by Figure 34, show that there is no significant difference between the conditions with IC and without IC.

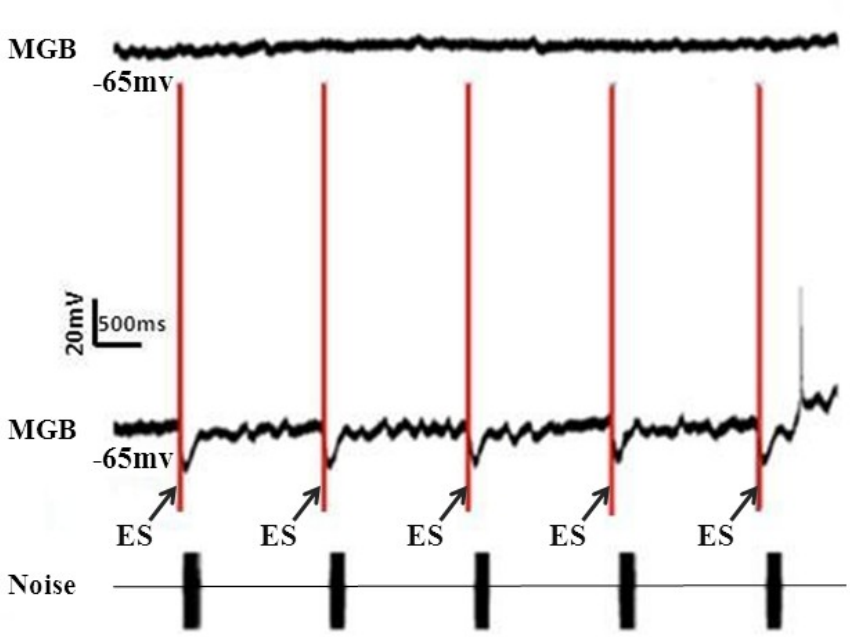

Figure33. Inhibitory modulation on the MGB neuron after IC inactivation.

Table 4

Conditions IPSP Amplitude (mV)	Trial 1	Trial 2	Trial 3	Trial 4	Trial 5
Control (Noise)	0	0	0	0	0
Experimental (Noise + ES)	18	17	17	15	15

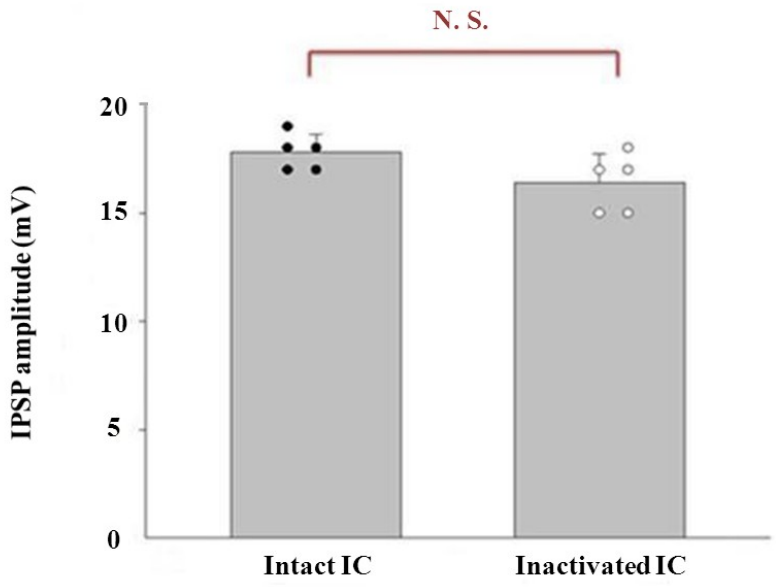

Figure34. The comparison of inhibitory modulation before and after IC inactivation via T-Test. Left panel shows the IPSP amplitude of the experimental condition before IC inactivation and the right panel shows the ones of the experimental condition after IC inactivation.

4.5 Cross-modality effect arising from LGN via TRN on auditory neurons in MGB

In this study, the cross modality effect was examined. The electrical stimulation was applied into lateral geniculate nuclei (LGN) instead of MGB. The recording sites remained in MGB. Firstly, visual units in LGN were identified. Visual responses to the light are presented in Figure 35. The light was given at the beginning of each trial.

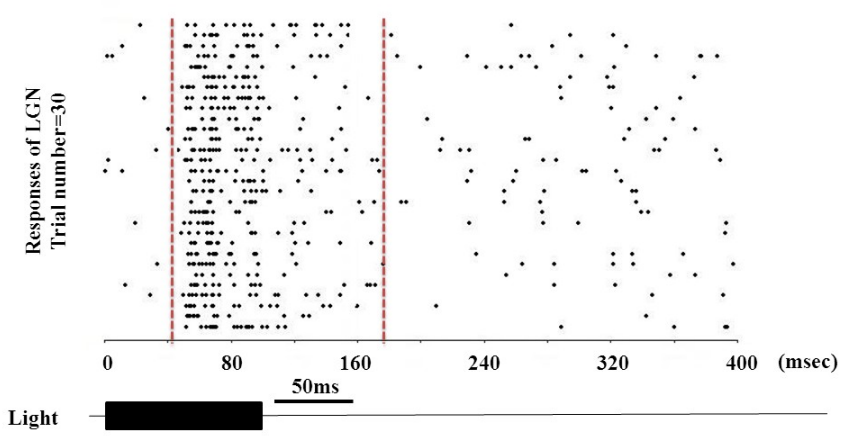

Figure35. Visual responses of LGN neurons (by raster plots).

3 kinds of effect were observed. They were inhibitory effect (17 neuron clusters), excitatory effect (13 neuron clusters) and no significant change (25 neuron clusters), similar to the ones observed in study 1.

The responses of MGB units to noises only were recorded as the control condition. In the experimental condition, electrical stimuli (20-100μA) of 1-5 pulses were applied to the neurons in LGN 15ms before the noise.

Picture A in Figure 36 shows a MGB cluster with the inhibitory effect. The responses of 30 trials from both control and experimental conditions were recorded.

In this case, the electrical stimuli were 2 pulses with the amplitude of 50μA, which were marked by the red arrow. They were delivered at 0ms, 15ms before the noises. In the same time window from 45ms to 95ms, which was the response period of this neuron, the spike rate of experimental condition was significantly decreased, compared with the one of control condition. The data from two groups were analyzed and the results were presented in the Figure 36. The spike of control condition is 5.87 and the one of experimental condition is 4.37. The inhibitory degree is 25.6%. Exact spike numbers of 30 trials from two conditions were compared via T-Test. The P value is 0.0198 (<0.05), which means that data from these two conditions have significant difference.

Picture B in Figure 36 shows the MGB units with the facilitating effect. The electrical stimuli were applied 15ms before noises and it was 1 pulse with the amplitude of 100μA. The response period of this neuron cluster is from 45ms to 70ms. The spike rate of control condition is 0.93 and the one of experimental condition is 1.63. The facilitating degree is 75.2%. The P value is 0.008 (<0.05), which means that data from these two groups have significant difference.

Neurons without any significant change between control and experimental conditions were also observed in this study. The neuron cluster representative for this part is shown in picture C. In this case, the electrical stimuli were applied 15ms before noises and it was 1 pulse with the amplitude of 50μA. The response period of this neuron cluster is from 35ms to 70ms. No significant change was observed between two conditions. The spike of control condition is 9.0 and the one of experimental

condition is 8.50. The degree of change is -5.6%. The P value is 0.39 (>0.05), which means that the data from these two groups have no significant difference.

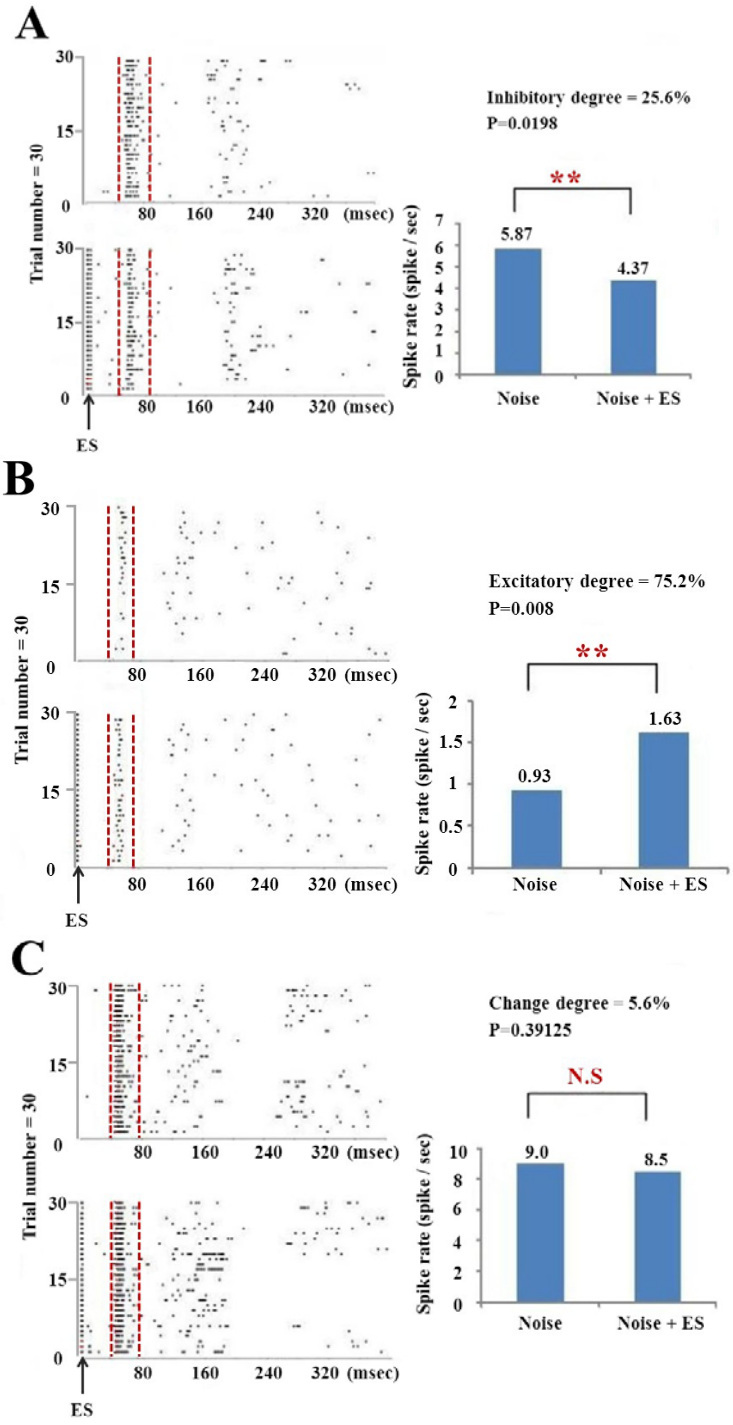

Figure36. Cross-modality modulation arising from LGN on MGB neurons.

4.6 The distribution and regularity of intrathalamic interactions on the coronal MGB plane

To study the anatomical relationship between effective and ineffective points in the MGB to elicit inhibitory and / or facilitating interactions, I varied the stimulating and recording sites in two ways. In the first group, the stimulating point in MGB is fixed. Intrathalamic interactions from auditory neurons on a coronal plane in MGB are recorded when a single point in the MGB on different plane is electrically stimulated. In the second group, the recording point in MGB is fixed. The responses of this neuron cluster are recorded when different points on another MGB coronal plane are electrically stimulated. Together with the work of histogram confirmation, the distribution and the regularity of the intrathalamic interactions are evaluated.

4.6.1The influences of a MGB neuron on other MGB neurons

In this study, the stimulating electrode array was located firstly on one point of MGB, which is in the different plane from the recording plane. Figure 37 shows the stimulating point. The terminal and tract of the stimulating electrode are clearly presented on the picture.

Figure 38-39 shows the positions of all MGB neurons recorded from another different coronal plane. Figure 38 displays the entire vision of the left coronal section of MGB recorded. The red cubic indicates the area where neurons recorded assemble. And Figure 39 is the more resolved picture of the red cubic area. The horizontal

coordinates mean the lateral distance from bregma and the vertical coordinates mean the depth of the recording sites from the brain surface.

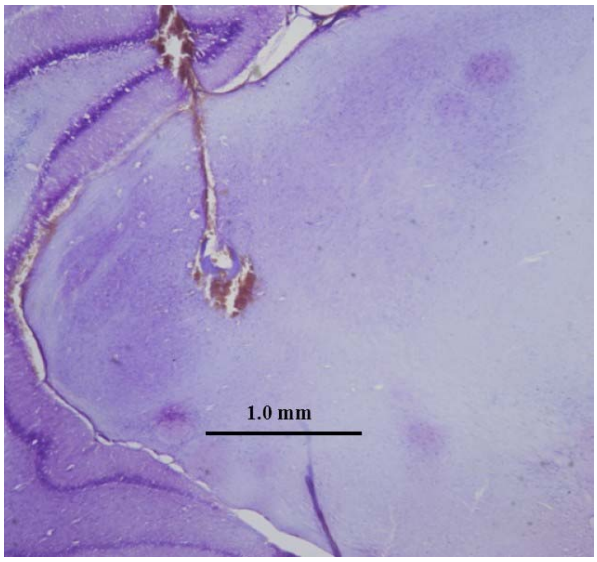

Figure37. The position of the stimulating site in MGB.

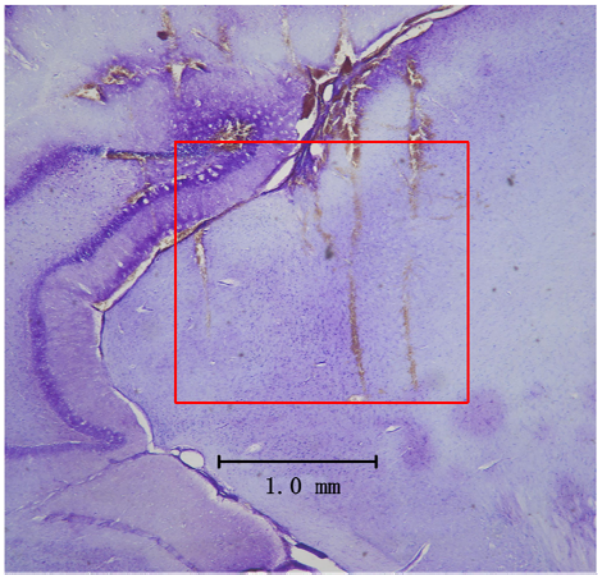

Figure38. The location of the recording site on the left coronal section of MGB.

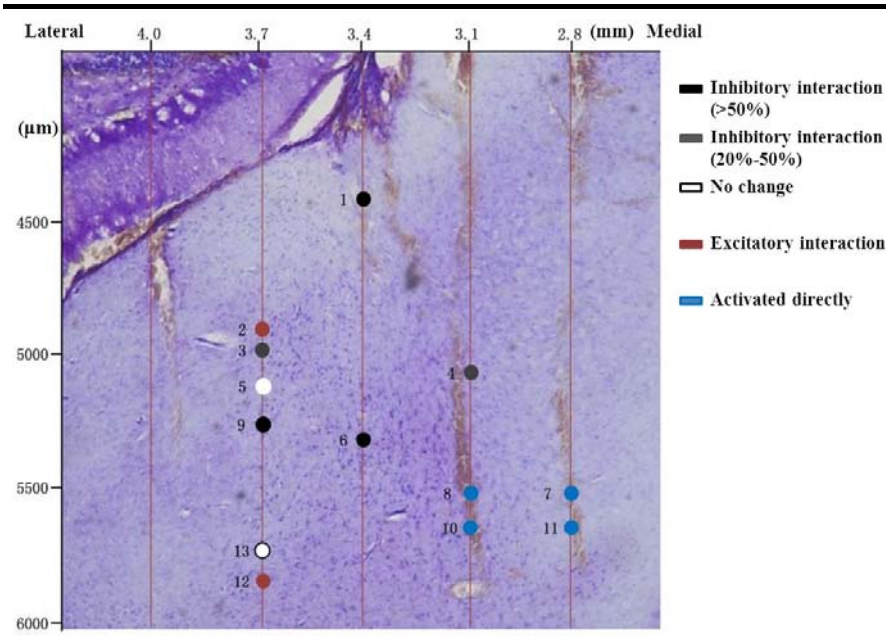

Figure39. All MGB neurons recorded on this coronal plane. Dark circles represent neurons with inhibitory modulation. Red circles represent neurons with facilitating modulation. White circles represent neurons without modulation. Blue circles represent neurons that were activated directly.

There are 11 neuron clusters recorded in total. Black color indicates the neurons of which the auditory responses are inhibited when other MGB neurons are electrically stimulated. The darker the color is, the higher the inhibitory degree is. Red color indicates the neurons that have facilitating effect. White color indicates the neurons without significant modulation. Blue color indicates the neurons that are directly activated. This picture implies the stimulation on a point of MGB influence other MGB neurons from a relative wild range, about 1.4mm in depth and 0.9mm in lateral distance.

4.6.2 The influences on a MGB neuron from other neurons in MGB

The recording site is located and fixed on a MGB neuron. Figure 40 shows the recording side.

Figure 41 shows the positions of MGB neurons stimulated on the right coronal plane. The horizontal and vertical coordinates mean the lateral distance from the bregma and the depth of the stimulating sites from the brain surface respectively. When stimulating the points shown in the Figure 41, the auditory responses of the same MGB units are recorded. The data are listed in table 5. From this study, MGB neurons receive influences from other MGB neurons of a wide range. Presented on this coronal section, the range is about 1mm in depth and 1.2mm in lateral distance.

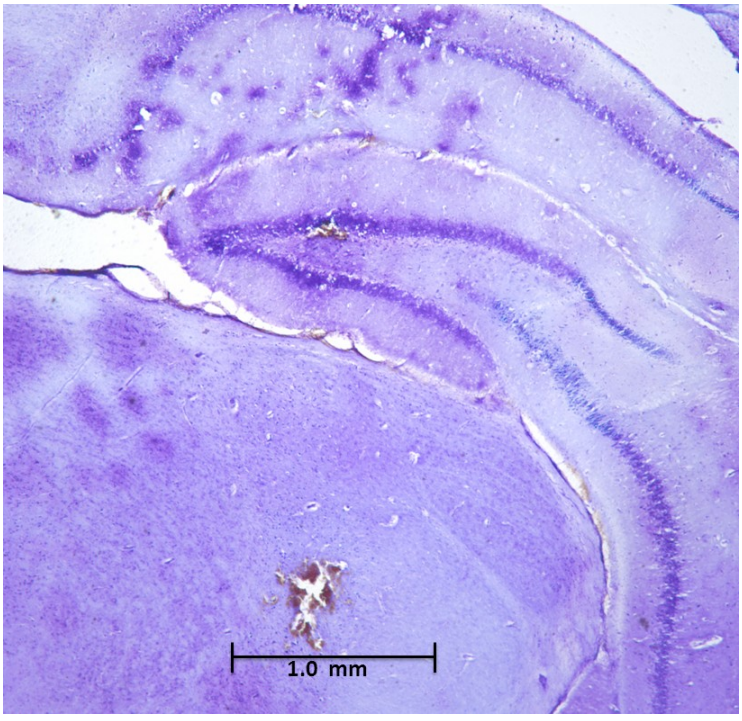

Figure40. The position of the MGB units recorded.

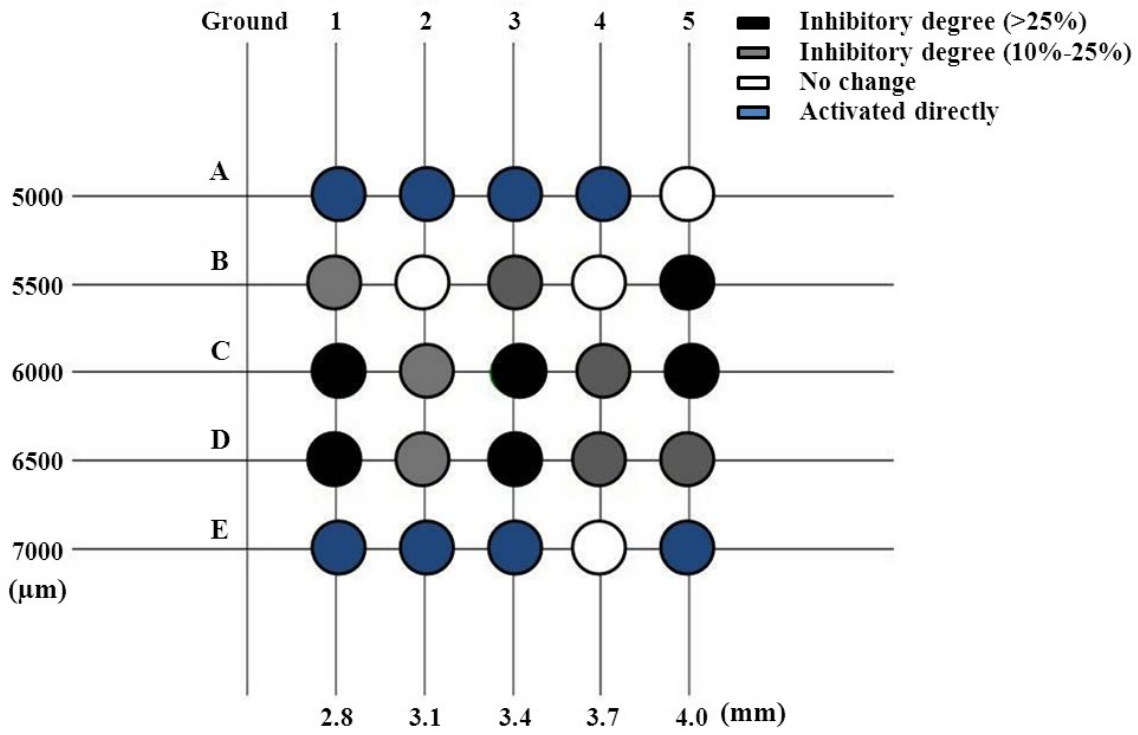

Figure41. The positions of the stimulating points in MGB.

Table 5

	1	2	3	4	5
A	*	*	*	*	-9.09%
B	-14.3%	-8.1%	-12.9%	-1.1%	-26.3%
C	-47.8%	-17.3%	-34.50%	-14.3%	-28.2%
D	-34.8%	-14.50%	-34%	-12.6%	-11.1%
E	*	*	*	-7.6%	*

(*: activated directly by the electrical stimulation)

Chapter5

Discussion and conclusions

5.1The intrathalamic interactions in MGB

Thalamic reticular nucleus (TRN) between cortex and thalamus makes connections with CT and TC projections. TRN receives topographically organized excitatory projections from both cortex and thalamus and sends inhibitory projections back to thalamus by its GABAergic neurons (Jones, 1975; Steriade, 1997).

Based on the special organization and location of TRN, Francis Crick (1984) proposed that "If the thalamus is the gateway to the cortex, the reticular complex might be described as the guardian of the gateway." Lesion and histological studies by Weese and his colleagues demonstrated a link between the TRN and the attentional effects of visual cues (Weese et al., 1999). The gating theories and the experiments were conducted in the visual system. To understand the gate-control function of TRN in the auditory system, we need to figure out the interactions between TRN, AC and MGB. The corticofugal inhibition on MGB has been studied in our lab (Zhang Z. et al., 2004/2005). Therefore my study focuses on the modulation of TRN on MGB.

5.1.1The inhibitory modulations in MGB

When MGB neurons were electrically stimulated, auditory responses of other MGB neurons were influenced. The inhibitory modulation occurred mostly, taking 37.38% (6.72%+19.32%+11.34%) of all neurons recorded as illustrated in Figure 10.

In study 1, the spikes of the MGB units to noises only and to the combination of noises and electrical stimuli to adjacent units were recorded and compared. Significant decrease of the spikes was observed in some MGB neurons. How does this inhibition happen? We believe that it takes place by the "open loop" formed between MGB and TRN. The electrical stimuli make MGB neurons at the stimulation sites robustly activated. The excitatory projections from these MGB neurons send the strengthened signals to the corresponding TRN units, activating these TRN units. Excited TRN neurons send back inhibitory projections to adjacent MGB neurons in turns, leading to inhibition of these units (control formation).

The signal ratio at the stimulation sites is consequently elevated by this control formation. This is an important way for TRN to select relevant information out and strengthen the signal relay into AC. Irrelevant information is terminated by lateral inhibition at TRN. Spreafico et al. (1994) and Bickford et al. (1994) suggested that TRN neurons formed a negative feedback by inhibiting the firing of relay cells. These findings support our explanations for the inhibitory effect observed in MGB neurons.

5.1.2 The facilitating modulations in MGB

Notably, 14.28% MGB neurons present facilitating effect when other MGB neurons are electrically stimulated in the study. TRN projects to MGB with its GABAergic tracts, making the inhibitory modulation in MGB easily explained. How does the facilitation happen?

As mentioned above, Crick (1984) argued for TRN's inhibitory modulation on LGN and suggested that TRN might be the guardian of the thalamic gateway. Based

on Crick's idea, Newman (1995) proposed another "gating theory" in details. In his theory, reticular formation (RF) as the lowest level gate modulates the input flow of TRN by their robust projections. And a second- level gate formed by TRN turns on or off the appropriate regions in the cortex. According to him, when the attention is changed, the activities of TRN would then be changed, modulated by the reticular formation. This change could be presented as a decrease of the neuronal activities in TRN. Therefore, the inhibition or less excitation of TRN may reduce its inhibition to MGB neurons. The electrical stimuli in MGB may possibly induce the attentional change and initiate this pathway, making the TRN inhibited. The increasing activities of MGB neurons may possibly be induced by this dis-inhibition through this pathway.

La Berge (1990) and Steriade et al. (1986) stated that as another important connection of TRN, the positive feedback was mediated by the involvement of the interneurons. Besides the simple input switch, TRN also facilitates relevant inputs through the thalamus by modulating ''high-frequency patterns of activation'' (<40-Hz rhythms) (Newman, 1995). Consequently, John Smythies (1997) suggested that "the TRN might have more to do with the overall organization of 'binding' than with selective attention". In the light of his work, we propose another hypothesis for the excitations of MGB neurons. The MGB neurons activated by electrical stimuli may facilitate relevant TRN neurons. The activated TRN neurons may inhibit the neural activities of other TRN neurons nearby, whose inhibitory modulation to the MGB neurons under their innervation could be reduced. The facilitating phenomenon we observed happens ultimately. In other words, the facilitations may be the outcome of the dis-inhibition on the MGB neurons.

The reasons for the facilitation of MGB neurons have not been proven in my studies. Whether the facilitation is coming from other loop, such as the loop between IC and MGB is still unknown. Further works are necessary to reveal the mechanisms of the selective excitation in MGB neurons.

5.2 The inhibitory effects in MGB by intracellular recording

From study 1, we think that the major effect, the inhibition in MGB is the modulating effect originated from TRN.

The data of study 1 were collected by extracellular recordings. The results showed that significant decrease of the firing occurred when electrical stimulation was applied into MGB.

To further understand the inhibitory effect, intracellular recording was conducted. In this manner, responses from single MGB neuron instead of multi-units to noises could be investigated. The results showed us two kinds of inhibitory interactions.

When other MGB neurons were electrically stimulated, the membrane potential of the recorded MGB neuron was hyper-polarized, forming IPSPs which were the indicators of the inhibitory interactions. Secondly, the firing of MGB neurons was reduced when other MGB neurons were applied with electrical stimulation. This is the other manifestation of inhibitory interactions.

5.3 The participation of TRN in the intrathalamic interactions in MGB

Anatomically, TRN is situated between MGB and cortex, receiving collaterals from both CT and TC projections. These imply that TRN may receive information

from a large scale of MGB and cortical areas. Functionally, TRN is thought to be the gate guardian of the tracts from thalamus to cortex and also the searchlight of the selective attention. Therefore, adequate information should be collected from cortex and MGB to execute its gating duties.

The experiments of inactivating TRN and IC were designed for investigating the source of inhibitory modulation on MGB. Studies of this part help us to understand the modulating functions of TRN.

According to Crick's "guardian" hypothesis, two physiological predictions were made. First one is regarding the neural activities, that is, increased activities in TRN occur together with decreased activities in the LGN and vice versa. Second one is regarding the timing of activity change, that is, change happens firstly in TRN and then in LGN (J. P. Mayo, 2009). These two aspects were proved by McAlonan et al. (2006).

In addition, Francis Crick (1984, 1994) believed that corticothalamic loops were essential to the awareness (Crick, 1994) and TRN controlled the ''searchlight'' of attention. McAlonan's (2006) results support Crick's attentional searchlight hypothesis. They indicated that TRN was involved in sub-cortical stages of attentional processing. And assisted by TRN, relevant sensory input was selected out and was additionally processed by sacrificing the irrelevant inputs.

Two mechanisms might be involved in the gate control, which were illustrated in visual system. Close loop, related with feedback inhibition, is formed when TRN sends back the GABAergic drives to the LGN cells where it receives information from. And inhibitory feedback initiates a rhythmic bursting firing in the LGN, alerting the

visual cortex about the behaviorally relevant sensory inputs (Crick, 1984; Sherman and Guillery, 1996). Such inhibition facilitates signal transmission during visual target acquisition and early phases of fixation (Guido and Weyand, 1995; also see Ramcharan et al., 2000). Alternatively the open loop is formed by TRN's inhibitory projections to the adjacent areas in LGN. In this case, lateral or surrounding inhibition rather than firing mode change happens when TRN activities are increased. The signal-to-noise ratio in LGN is elevated, improving initial detectability and discriminability consequently. The relevant information would then be made more salient by inhibition of the irrelevant inputs nearby (K. McAlonan et al., 2006). Lateral or surrounding inhibition is proved to be the primary way of TRN's attentional modulation on LGN neurons (Pinault and Deschenes, 1998).

In study 3 and 4, we investigated the pathway involved in the inhibitory modulation. The inhibitory degree of MGB neurons before and after the TRN inactivation was compared. We found that the inhibitory degree was significantly decreased by inactivating the TRN, implying that the TRN play an important role in the inhibitory modulation.

TRN, auditory cortex (AC) and inferior colliculus (IC) all have inhibitory projections to MGB. Since AC was removed before the experiments, the exclusion of IC was essential in the inhibitory modulating pathway. IC is a lower level nucleus in the auditory system. Inactivation of this part leads no auditory responses of MGB immediately. Thus, intracellular recording was applied in study 4. The MGB neurons displayed in chapter 4 had IPSPs as the indicator of inhibitory interactions. Data shows that auditory responses of MGB disappear after successful IC inactivation. But IPSPs

are still observed when other MGB points are applied with electrical stimuli. No significant difference is found by comparing the amplitude of IPSPs with and without IC inactivation.

These studies confirm that the inhibitory interactions arise from the loop between TRN and MGB. Enlightened by previous works on TRN, we believe that MGB neurons selectively process the relevant auditory information by depressing the activities of other irrelevant MGB neurons through the inhibitory modulation of TRN. And they might facilitate the signals of other relevant MGB neurons through the de-inhibition effect of TRN as well.

The primary function of TRN is gate control, which is serving for the attentional modulation. The following paragraphs will focus on the mechanisms of the attention associated with TRN and its manner of modulating. Kimura conducted attending experiments and found that visual signals were modulated by attention before they reached cortex. When the attention of monkeys was changed, researchers detected a decrease of activities in TRN and an increase of activities in LGN. The lateral inhibition of TRN on LGN neurons was reduced by its decreased activities, leading to the facilitation of LGN neurons consequently (Kimura, A. et al., 2007). In addition, intrinsic inter-TRN connections were revealed by various anatomical and functional studies. TRN neurons connect with each other by dendro-dendritic or axo-dendritic synapses. Inhibitory interactions among TRN neurons in the visual TRN sector were firstly observed in anaesthetized adult cats (G. Ahlsen et al., 1982).

In the summary, TRN modulates the receptive fields of multiple modalities by its negative feedback. For the species without inter-neurons which are lack of lateral

inhibition and contrasting modulation, TRN also functions as the compensation by its inhibitory projections (Sherman and Guillery, 1987). TRN may participate in the change of awareness and coordination for a wide range of brain activities (Llinás, R. et al., 1997).

5.4 Cross-modality effects arising from LGN via TRN on MGB neurons

5.4 .1The subdivisions of TRN

Nerve tracts between specific cortex and thalamus send out branches to different layers of TRN. The corresponding TRN has relevant functions and can be divided into 5 functional regions (Crabtree, 1992, 1996, 1998). Neurons of different TRN sectors serve for different sensory modalities. However, Crabtree and his colleagues indicated that the interconnections between TRN and dorsal thalamus were cross-nucleus and cross-modality (Crabtree, 1998, 1999; Crabtree and Isaac, 2002).

Cross-modality properties of TRN may provide the basis for the attentional shift from one modality to another. In this section, the characteristic of cross-modality (between auditory and visual systems) in TRN will be discussed. The relationship between TRN and MGB has been illustrated previously. The participation of TRN in the visual system is briefly introduced as follows. Visual TRN receives projections from the LGN which is the visual relay station. Both the projections from LGN to primary visual cortex (V1) and the ones from V1 layer 6 back to LGN send out projections to the TRN (Conley and Diamond, 1990; Harting et al., 1991; Uhlrich et

al., 2003). Except for the projections from TRN back to LGN are inhibitory, the remaining inputs projecting to TRN are excitatory (Cox et al., 1997; Kim et al., 1997).

Dendrite system of TRN spread along the thin layers, making TRN possibly receive sensory input from different modalities. As mentioned above, Crabtree's work indicated that TRN neurons were involved in the integration across multi-modalities (Crabtree et al., 1998; Crabtree, 1999; Crabtree and Isaac, 2002). The works in our lab by Dr Yu agree with it by finding out that the same TRN neuron responds to both acoustic and visual stimuli. In addition, TRN acted as an "attentional searchlight" (K. McAlonan, 2006). Therefore, TRN responses to visual stimuli could be modulated when attention was shifted from the auditory system to the visual one. On the contrary, could TRN responses to auditory stimuli be modulated when attention is shifted from the visual system to the auditory one? Or could the auditory responses of MGB neurons be modulated when the attention is shifted from the visual system to the auditory one? To answer these questions, study 5 was designed.

5.4 .2 Cross-modality effects arising from LGN via TRN on MGB neurons

In study 5, the stimulating side was located in LGN instead of MGB. The same experimental procedures as study 1 were carried out. We found that the inhibitory and excitatory effects occurred in the MGB when visual neurons in the LGN were electrically stimulated.

We think that the inhibitory interactions observed in study 5 happen through the similar pathway with the one when electrical stimuli are applied to MGB. The excited LGN neurons make the relevant TRN neurons activated. These excited TRN

neurons which receive projections from both visual and auditory systems may send inhibitory projections back into MGB neurons, making the latter ones inhibited.

Through the inhibition, the visual system competes with the auditory one and makes the visual information superior in the signal processing, which may be another presentation of TRN's gating function. With respect to the facilitation of MGB neurons, whether LGN neurons select out and strengthen the appropriate auditory inputs to facilitate the united signal processing is still unknown. Or possibly it is only the consequence of dis-inhibition effect via the similar loop as the one described in study 1. Activated LGN neurons excite relevant TRN neurons, which then inhibit the adjacent TRN neurons. The inhibited TRN neurons induce the dis-inhibition effect on the MGB neurons under their innervations ultimately.

Possible reasons illustrated above for the inhibitory or facilitating interactions from LGN to MGB are proposed on the basis of intrathalamic interactions between MGB and TRN. The structures and the possible loops involved in the cross-modality modulations have not been investigated in my project. To further understand the interactions within MGB, TRN and LGN or relay nuclei of other modalities, more works need to be focused on this issue in the future.

5.5 The distribution and regularity of the intrathalamic interactions in MGB

MGB contains three different subdivisions. MGv neurons present a conspicuous tonotopic organization (Aitkin and Webster, 1972; Morest, 1966). Other MGB neurons respond with long latencies and wide frequency tuning curves, presenting no tonotopic organization (Calford, 1983; Rouiller, E.M., et al., 1989). The

auditory TRN sector locates in the caudoventral area (Jones, 1975; Shosaku and Sumitomo, 1983). These neurons are topographically organized according to the MGB subdivision under its innervation (Crabtree, 1998). Based on the topographical organization of the MGB and the auditory TRN, the distributing regularity of the intrathalamic interactions in MGB is investigated in study 6.

From Dr Yu Xiongjie's work, the capture area in the MGB of a single TRN neuron is about 1.1mm mediolaterally and 1.7mm superioinferiorly, almost covering the whole MGB. His work implied us that a TRN neuron received projections from a large scale of MGB and auditory cortex. In my study, no obvious distributing regularities of intrathalamic interactions were found in the MGB. As introduced above, a MGB neuron may influence a large scale of TRN neurons. The non-biunique correspondence between the TRN and MGB neurons may be the possible reason for the irregularity observed in my experiments.

Additionally, we found that MGB neurons influence each other in a relatively large scale via TRN. It was presented in two directions. A MGB neuron is able to interact with other MGB neurons and receive their influences reciprocally from a wide range.

Chapter 6

Summary of findings and conclusions

The present study investigated the intrathalamic interactions in the medial geniculate body. To minimize the influences from auditory cortex, AC was removed for all experiments. The auditory responses of MGB neurons were examined when electrical stimuli were applied to other MGB neurons through both in-vivo extracellular and intracellular recordings in anaesthetized rats and guinea pigs. The pathways of intrathalamic interactions in MGB were investigated. Participations of TRN and IC in the inhibitory modulation were examined respectively. Cross-modality effects arising from LGN on the MGB neurons were studied as well. The physiological properties were examined in relation to the locations of the recorded neurons by anatomical confirmation.

The whole studies contain six parts. Results in study 1 illuminated the auditory responses of MGB neurons when electrical stimuli were applied to other MGB neurons by extracellular recordings. Three types of effects were observed, inhibitory modulation, facilitating one and no significant change. The inhibitory modulation was the primary modulation observed in the MGB.

To further understand the major phenomenon in study 1, the inhibitory effect was also examined by intracellular recording. IPSPs or reduced spikes, indicating the inhibitory effect, from a single MGB neuron were observed in study 2.

Study 3 investigated the pathway of the inhibitory effect on MGB neurons. The inhibition is eliminated after TRN inactivation, proving that TRN is one of the components in the pathway.

To confirm other structures in the inhibitory pathway, study 4 tested the role of IC. Intracellular recordings showed that IPSPs as the indicator of the inhibition still appeared after IC inactivation. IC was eliminated of the inhibitory pathway.

Study 5 examined cross-modality effect arising from LGN via TRN on the auditory neurons in the MGB. Electrical stimulation on LGN neurons influenced the auditory neural activities of MGB neurons. Both inhibition and facilitation were found in the experiments. Inhibition on MGB neurons by stimulating LGN was still most frequently observed.

And the last study investigated the range and distribution regularity of the intrathalamic interactions in MGB. Results in this section showed that a MGB neuron influences a wide range of other MGB neurons and is affected by them reciprocally. No obvious topographic organization is found in these corresponding relationships.

As a whole, the thesis indicates the intrathalamic interactions in medial geniculate body and identifies the participation of thalamic reticular nuclei in the major interaction, inhibitory effect. It also illustrates the range and distribution regularity of the intrathalamic interactions in MGB and clarifies the cross-modality effects on MGB from LGN. The mechanisms of the facilitation and the identification of TRN in the cross-modality effects need to be further studied.

References

Ahlsen G, Lindstrom S, Lo FS (1985) Interaction between inhibitory pathways to principal cells in the lateral geniculate nucleus of the cat. Exp Brain Res 58:134-143.

Aitkin, L.M. and S.M. Prain, Medial geniculate body: unit responses in the awake cat. J Neurophysiol, 1974. 37(3): p. 512-21.

Aitkin, L.M. and W.R. Webster (1971), Tonotopic organization in the medial geniculate body of the cat. Brain Res, 26(2): p. 402-5.

Aitkin, L.M. and W.R. Webster (1972), Medial geniculate body of the cat: organization and responses to tonal stimuli of neurons in ventral division. J Neurophysiol, 35(3): p. 365-80.

Allon, N. and Y. Yeshurun (1985), Functional organization of the medial geniculate body's subdivisions of the awake squirrel monkey. Brain Res, 360(1-2): p. 75-82.

Bordi, F. and J.E. LeDoux, Response properties of single units in areas of rat auditory thalamus that project to the amygdala. I. Acoustic discharge patterns and frequency receptive fields. Exp Brain Res, 1994. 98(2): p. 261-74.

Andersen RA, Knight PL, Merzenich MM (1980) The thalamocortical and corticothalamic connections of AI, AII, and the anterior auditory field (AAF) in the cat: evidence for two largely segregated systems of connections. J Comp Neurol 194:663-701.

Arcelli P, Frassoni C, Regondi MC, De Biasi S, Spreafico R (1997) GABAergic neurons in mammalian thalamus: a marker of thalamic complexity Brain Res Bull 42:27-37.

Arnault P, Roger M (1990) Ventral temporal cortex in the rat: connections of secondary auditory areas Te2 and Te3. J Comp Neurol 302:110-123.

Bartlett EL, Smith PH (1999) Anatomic, intrinsic, and synaptic properties of dorsal and ventral division neurons in rat medial geniculate body. J Neurophysiol 81:1999-2016.

Barth DS, Kithas J, Di S (1993) Anatomic organization of evoked potentials in rat parietotemporal cortex: somatosensory and auditory responses. J Neurophysiol 69:1837-1849.

Berman AL (1961a) Interaction of cortical responses to somatic and auditory stimuli in anterior ectosylvian gyrus of cat. J Neurophysiol 24:608-620.

Berman AL (1961b) Overlap of somatic and auditory cortical response fields in anterior ectosylvian gyrus of cat. J Neurophysiol 24:595-607.

Bickford, M. E., Gunluk, A. E., Van Horn, S. C., & Sherman, S. M. (1994). GABAergic projection from the basal forebrain to the visual sector of the thalamic reticular nucleus in the cat. Journal of Comparative Neurology, 348, 481–510.

Calford, M.B. and W.R. Webster, Auditory representation within principal division of cat medial geniculate body: an electrophysiology study. J Neurophysiol, 1981. 45(6): p. 1013-28.

Calford, M.B., The parcellation of the medial geniculate body of the cat defined by the auditory response properties of single units. J Neurosci, 1983. 3(11): p. 2350-64.

Calford MB, Aitkin LM (1983) Ascending projections to the medial geniculate body of the cat: evidence for multiple, parallel auditory pathways through thalamus. J Neurosci 3:2365-2380.

Carlson, N. R. (2007) Physiology of Behavior: ninth edition.Pearson Education, Inc.: Bosto

Caviness VS, Jr., Frost DO (1980) Tangential organization of thalamic projections to the neocortex in the mouse. J Comp Neurol 194:335-367.

Clarey JC, Irvine DR (1990a) The anterior ectosylvian sulcal auditory field in the cat: I. An electrophysiological study of its relationship to surrounding auditory cortical fields. J Comp Neurol 301:289-303.

Clarey JC, Irvine DR (1990b) The anterior ectosylvian sulcal auditory field in the cat: II. A horseradish peroxidase study of its thalamic and cortical connections. J Comp Neurol 301:304-324.

Crabtree JW (1998) Organization in the auditory sector of the cat's thalamic reticular nucleus. J Comp Neurol 390:167-182.

Crabtree JW (1999) Intrathalamic sensory connections mediated by the thalamic reticular nucleus. Cell Mol Life Sci 56:683-700.

Crabtree JW, Isaac JT (2002) New intrathalamic pathways allowing modality-related and cross-modality switching in the dorsal thalamus. J Neurosci 22:8754-8761.

Crick F. (1984), Function of the thalamic reticular complex: The searchlight hypothesis, Proc. Natl. Acad. Sci. USA Vol. 81, pp. 4586-4590, Neurobiology.

Crick, F. (1994). The astonishing hypothesis. New York: Scribner.

Cruikshank SJ, Edeline JM, Weinberger NM (1992) Stimulation at a site of auditory-somatosensory convergence in the medial geniculate nucleus is an effective unconditioned stimulus for fear conditioning. Behav Neurosci 106:471-483.

Clerici WJ, Coleman JR (1990) Anatomy of the rat medial geniculate body: I. Cytoarchitecture, myeloarchitecture, and neocortical connectivity. J Comp Neurol 297:14-31.

Conley M, Diamond IT (1990) Organization of the visual sector of the thalamic reticular nucleus in Galago. Eur J Neurosci 2:211–226.

Cotillon, N. and J.M. Edeline, Tone-evoked oscillations in the rat auditory cortex result from interactions between the thalamus and reticular nucleus. Eur J Neurosci, 2000. 12(10): p. 3637-50.

Cox CL, Sherman SM (1999) Glutamate inhibits thalamic reticular neurons. J Neurosci 19:6694-6699.

Edeline, J.M., et al., Do auditory responses recorded from awake animals reflect the anatomical parcellation of the auditory thalamus? Hear Res, 1999. 131(1-2): p. 135-52.

Gelfand, Stanley A. (2004) Hearing, an Introduction to Psychological and Physiological Acoustics, 4th Ed., Marcel Dekker, pp. 71-75.

Gerren RA, Weinberger NM (1983) Long term potentiation in the magnocellular medial geniculate nucleus of the anesthetized cat. Brain Res 265:138-142.

Guido W, Weyand T (1995) Burst responses in thalamic relay cells of the awake behaving cat. J Neurophysiol 74:1782–1786.

Goodale, M., Milner, D. (2004) Sight unseen.Oxford University Press, Inc.: New York.

Graham J (1977) An autoradiographic study of the efferent connections of the superior colliculus in the cat. J Comp Neurol 173:629-654.

Guillery RW (1995) Anatomical evidence concerning the role of the thalamus in corticocortical communication: a brief review. J Anat 187 (Pt 3):583-592.

Guillery RW, Harting JK (2003) Structure and connections of the thalamic reticular nucleus: Advancing views over half a century. J Comp Neurol 463:360-371.

G. Ahlsen, S. Lindstrom, Mutual inhibition between perigeniculate neurones, Brain Res. 236 (1982) 482– 486.

Hackett TA, Stepniewska I, Kaas JH (1998) Thalamocortical connections of the parabelt auditory cortex in macaque monkeys. J Comp Neurol 400:271-286.

Harting JK, Van Lieshout DP, Feig S (1991) Connectional studies of the primate lateral geniculate nucleus: distribution of axons arising from the thalamic reticular nucleus of Galago crassicaudatus. J Comp Neurol 310:411– 427.

Hashikawa T, Molinari M, Rausell E, Jones EG (1995) Patchy and laminar terminations of medial geniculate axons in monkey auditory cortex. J Comp Neurol 362:195-208.

He, J., Modulatory effects of regional cortical activation on the onset responses of the cat medial geniculate neurons. J Neurophysiol, 1997. 77(2): p. 896-908.

He, J., On and off pathways segregated at the auditory thalamus of the guinea pig. J Neurosci, 2001. 21(21): p. 8672-9.

He J (2002) OFF responses in the auditory thalamus of the guinea pig. J Neurophysiol 88:2377-2386.

He J (2003a) Corticofugal modulation on both ON and OFF responses in the nonlemniscal auditory thalamus of the guinea pig. J Neurophysiol 89:367-381.

He J (2003b) Slow oscillation in non-lemniscal auditory thalamus. J Neurosci 23:8281-8290.

He J (2003c) Corticofugal modulation of the auditory thalamus. Exp Brain Res 153:579-590.

He J, Hashikawa T (1998) Connections of the dorsal zone of cat auditory cortex. J Comp Neurol 400:334-348.

Hefti BJ, Smith PH (2000) Anatomy, physiology, and synaptic responses of rat layer V auditory cortical cells and effects of intracellular GABA(A) blockade. J Neurophysiol 83:2626-2638.

Herkenham M (1980) Laminar organization of thalamic projections to the rat neocortex. Science 207:532-535.

Hofstetter KM, Ehret G (1992) The auditory cortex of the mouse: connections of the ultrasonic field. J Comp Neurol 323:370-386.

Hoogland PV, Wouterlood FG, Welker E, Van der Loos H (1991) Ultrastructure of giant and small thalamic terminals of cortical origin: a study of the projections from the barrel cortex in mice using Phaseolus vulgaris leuco-agglutinin (PHA-L). Exp Brain Res 87:159-172.

Hu B (1995) Cellular basis of temporal synaptic signalling: an in vitro electrophysiological study in rat auditory thalamus. J Physiol 483 (Pt 1):167-182.
Hu B (2003) Functional organization of lemniscal and nonlemniscal auditory thalamus. Exp Brain Res 153:543-549.
Hu B, Senatorov V, Mooney D (1994) Lemniscal and non-lemniscal synaptic transmission in rat auditory thalamus. J Physiol 479 (Pt 2):217-231.
Huang CL, Winer JA (2000) Auditory thalamocortical projections in the cat: laminar and areal patterns of input. J Comp Neurol 427:302-331.

Imig TJ, Reale RA (1980) Patterns of cortico-cortical connections related to tonotopic maps in cat auditory cortex. J Comp Neurol 192:293-332.

Imig TJ, Reale RA (1981) Ipsilateral corticocortical projections related to binaural columns in cat primary auditory cortex. J Comp Neurol 203:1-14.

Imig TJ, Morel A (1984) Topographic and cytoarchitectonic organization of thalamic neurons related to their targets in low-, middle-, and high-frequency representations in cat auditory cortex. J Comp Neurol 227:511-539.

Imig TJ, Morel A (1985) Tonotopic organization in ventral nucleus of medial geniculate body in the cat. J Neurophysiol 53:309-340.

Irvine DR, Huebner H (1979) Acoustic response characteristics of neurons in nonspecific areas of cat cerebral cortex. J Neurophysiol 42:107-122.

John Smythies (1997), The Functional Neuroanatomy of Awareness: With a Focus on the Role of Various Anatomical Systems in the Control of Intermodal Attention, CONSCIOUSNESS AND COGNITION 6, 455–481.

Jones EG (1975) Some aspects of the organization of the thalamic reticular complex. J Comp Neurol 162:285-308.

Jones EG, Powell TP (1969a) An electron microscopic study of the mode of termination of cortico-thalamic fibres within the sensory relay nuclei of the thalamus. Proc R Soc Lond B Biol Sci 172:173-185.

Jones EG, Powell TP (1969b) Electron microscopy of synaptic glomeruli in the thalamic relay nuclei of the cat. Proc R Soc Lond B Biol Sci 172:153-171.

J. P. Mayo (2009), Intrathalamic Mechanisms of Visual Attention, J Neurophysiol 101: 1123–1125, doi:10.1152/jn.91369.2008.

Kaas, J.H., and Huerta, M.F. (1988). The subcortical visual system of primates. In: Steklis H. D., Erwin J., editors. Comparative primate biology, vol 4: neurosciences. New York: Alan Liss, pp. 327-391.

Kelly JP, Wong D (1981) Laminar connections of the cat's auditory cortex. Brain Res 212:1-15.

Kerry M., James C., and Robert H. W., (1998): Attentional Modulation of Thalamic Reticular Neurons, The Journal of Neuroscience, 26(16):4444–4450.

Kerry M., James C., and Robert H. W., (2008): Guarding the gateway to cortex: attention in visual thalamus, Nature. 456(7220): 391–394. doi:10.1038/nature07382.

Kim U, Sanchez-Vives MV, McCormick DA (1997) Functional dynamics of GABAergic inhibition in the thalamus. Science 278:130 –134.

Kimura A, Donishi T, Sakoda T, Hazama M, Tamai Y (2003) Auditory thalamic nuclei projections to the temporal cortex in the rat. Neuroscience 117:1003-1016.

Kimura, A., Imbe, H., Donishi, T. & Tamai, Y. Axonal projections of single auditory neurons in the thalamic reticular nucleus: implications for tonotopy-related gating function and cross-modal modulation. Eur J Neurosci 26, 3524-35 (2007).

Kosaki H, Hashikawa T, He J, Jones EG (1997) Tonotopic organization of auditory cortical fields delineated by parvalbumin immunoreactivity in macaque monkeys. J Comp Neurol 386:304-316.

Krause, M., W.E. Hoffmann, and M. Hajos, Auditory sensory gating in hippocampus and reticular thalamic neurons in anesthetized rats. Biol Psychiatry, 2003. 53(3): p. 244-53.

Lee CC, Schreiner CE, Imaizumi K, Winer JA (2004) Tonotopic and heterotopic projection systems in physiologically defined auditory cortex. Neuroscience 128:871-887.

Linke R, Schwegler H (2000) Convergent and complementary projections of the caudal paralaminar thalamic nuclei to rat temporal and insular cortex. Cereb Cortex 10:753-771.

Liu XB, Warren RA, Jones EG (1995a) Synaptic distribution of afferents from reticular nucleus in ventroposterior nucleus of cat thalamus. J Comp Neurol 352:187-202.

Liu XB, Honda CN, Jones EG (1995b) Distribution of four types of synapse on physiologically identified relay neurons in the ventral posterior thalamic nucleus of the cat. J Comp Neurol 352:69-91.

LeDoux JE, Cicchetti P, Xagoraris A, Romanski LM (1990) The lateral amygdaloid nucleus: sensory interface of the amygdala in fear conditioning. J Neurosci 10:1062-1069.

Llinás, R., Paré D, Coherent Oscillations in Specific and Nonspecific Thalamocortical Networks and Their Role in Cognition, in Thalamus J.E. Steriade M, McCormick DA, Editor. 1997, Plenum,: New York. p. 501-516.

McAlonan K, Brown VJ, Bowman EM (2000) Thalamic reticular nucleus activation reflects attentional gating during classical conditioning. J Neurosci 20:8897– 8901.

McAlonan, K., Cavanaugh, J. & Wurtz, R. H. Attentional modulation of thalamic reticular neurons. J Neurosci 26, 4444-50 (2006).

Mitani A, Shimokouchi M (1985) Neuronal connections in the primary auditory cortex: an electrophysiological study in the cat. J Comp Neurol 235:417-429.

MonteroVM (1997) c-fos induction in sensory pathways of rats exploring a novel complex environment: shifts of active thalamic reticular sectors by predominant sensory cues. Neuroscience 76:1069 –1081.

Montero VM (1999) Amblyopia decreases activation of the corticogeniculate pathway and visual thalamic reticularis in attentive rats: a ‘focal attention’ hypothesis. Neuroscience 91:805– 817.

Montero VM (2000) Attentional activation of the visual thalamic reticular nucleus depends on “top-down” inputs from the primary visual cortex via corticogeniculate pathways. Brain Res 864:95–104.

Morel, A., et al., Tonotopic organization in the medial geniculate body (MGB) of lightly anesthetized cats. Exp Brain Res, 1987. 69(1): p. 24-42.

Morel A, Kaas JH (1992) Subdivisions and connections of auditory cortex in owl monkeys. J Comp Neurol 318:27-63.

Morest DK (1964) The Neuronal Architecture of the Medial Geniculate Body of the Cat. J Anat 98:611-630.

Morest, D.K., The lateral tegmental system of the midbrain and the medial geniculate body: Study with Golgi and Nauta methods in cat. J Anat, 1965. 99(Pt 3): p. 611-34.

Murphy PC, Sillito AM (1996) Functional morphology of the feedback pathway from area 17 of the cat visual cortex to the lateral geniculate nucleus. J Neurosci 16:1180-1192.

Newman, J. (1995). Thalamic contributions to attention and consciousness. Consciousness and Cognition, 4, 172–193.

Niimi K, Matsuoka H (1979) Thalamocortical organization of the auditory system in the cat studied by retrograde axonal transport of horseradish peroxidase. Adv Anat Embryol Cell Biol 57:1-56.

Peruzzi D, Bartlett E, Smith PH, Oliver DL (1997) A monosynaptic GABAergic input from the inferior colliculus to the medial geniculate body in rat. J Neurosci. 1997 May 15;17(10):3766-77.

Pinault D, Smith Y, Deschenes M (1997) Dendrodendritic and axoaxonic synapses in the thalamic reticular nucleus of the adult rat. J Neurosci 17:3215-3233.

Pinault D, Deschenes M (1998) Anatomical evidence for a mechanism of lateral inhibition in the rat thalamus. Eur J Neurosci 10:3462–3469.

Popper AN, Fay RR (1992) The Mammalian auditory pathway : neurophysiology. New York: Springer-Verlag.

Radtke-Schuller S (2004) Cytoarchitecture of the medial geniculate body and thalamic projections to the auditory cortex in the rufous horseshoe bat (Rhinolophus rouxi). I. Temporal fields. Anat Embryol (Berl) 209:59-76.

Radtke-Schuller S, Schuller G, O'Neill WE (2004) Thalamic projections to the auditory cortex in the rufous horseshoe bat (Rhinolophus rouxi). II. Dorsal fields. Anat Embryol (Berl) 209:77-91.

Ramcharan EJ, Gnadt JW, Sherman SM (2000) Burst and tonic firing in thalamic cells of unanesthetized, behaving monkeys. Vis Neurosci 17:55– 62.

Rauschecker JP, Tian B, Pons T, Mishkin M (1997) Serial and parallel processing in rhesus monkey auditory cortex. J Comp Neurol 382:89-103.

Redies H, Brandner S, Creutzfeldt OD (1989a) Anatomy of the auditory thalamocortical system of the guinea pig. J Comp Neurol 282:489-511.

Redies H, Sieben U, Creutzfeldt OD (1989b) Functional subdivisions in the auditory cortex of the guinea pig. J Comp Neurol 282:473-488.

Redies H, Brandner S (1991) Functional organization of the auditory thalamus in the guinea pig. Exp Brain Res 86:384-392.

Romanski LM, LeDoux JE (1993) Organization of rodent auditory cortex: anterograde transport of PHA-L from MGv to temporal neocortex. Cereb Cortex 3:499-514.

Rouiller EM, de Ribaupierre F (1985) Origin of afferents to physiologically defined regions of the medial geniculate body of the cat: ventral and dorsal divisions. Hear Res 19:97-114.

Rouiller EM, de Ribaupierre F (1989) Note on the tonotopic organization in the cat medial geniculate body: influence of sampling of units. Exp Brain Res 74:220-226.

Rouiller, E.M., et al., Functional organization of the medial division of the medial geniculate body of the cat: tonotopic organization, spatial distribution of response properties and cortical connections. Hear Res, 1989. 39(1-2): p. 127-42.

Rodrigues-Dagaeff, C., et al., Functional organization of the ventral division of the medial geniculate body of the cat: evidence for a rostro-caudal gradient of response properties and cortical projections. Hear Res, 1989. 39(1-2): p. 103-25.

Russchen FT (1982) Amygdalopetal projections in the cat. I. Cortical afferent connections. A study with retrograde and anterograde tracing techniques. J Comp Neurol 206:159-179.

Ryugo DK, Killackey HP (1974) Differential telencephalic projections of the medial and ventral divisions of the medial geniculate body of the rat. Brain Res 82:173-177.

Scholpp S, Delogu A, Gilthorpe J, Peukert D, Schindler S, Lumsden A (November 2009). "Her6 regulates the neurogenetic gradient and neuronal identity in the thalamus". Proc. Natl. Acad. Sci. U.S.A. 106 (47): 19895–900.

Schmid, Michael C., Mrowka, Sylwia W., Turchi, Janita et al. (2010). "Blindsight depends on the lateral geniculate nucleus". Nature 466 (7304): 373–377. doi:10.1038/nature09179.

Schwartz ML, Dekker JJ, Goldman-Rakic PS (1991) Dual mode of corticothalamic synaptic termination in the mediodorsal nucleus of the rhesus monkey. J Comp Neurol 309:289-304.

Sherman SM, Guillery RW (1996) Functional organization of thalamocortical relays. J Neurophysiol 76:1367-1395.

Sherman SM, Guillery RW, Sherman SM (2006) Exploring the thalamus and its role in cortical function, 2nd Edition. Cambridge, Mass.: MIT Press.

Shore, S. E. (2009) Auditory/Somatosensory Interactions. In: Squire (Ed.): Encyclopedia of Neuroscience, Academic Press, pp. 691–695.

Shosaku A, Sumitomo I (1983) Auditory neurons in the rat thalamic reticular nucleus. Exp Brain Res 49:432-442.

Shinonaga Y, Takada M, Mizuno N (1994) Direct projections from the non-laminated divisions of the medial geniculate nucleus to the temporal polar cortex and amygdala in the cat. J Comp Neurol 340:405-426.

Simm GM, de Ribaupierre F, de Ribaupierre Y, Rouiller EM (1990) Discharge properties of single units in auditory part of reticular nucleus of thalamus in cat. J Neurophysiol 63:1010-1021.

Skottun, Bernt C. et al.(2001): The ability of inferior colliculus neurons to signal differences in interaural delay. PNAS November 20,vol. 98, no. 24, pp. 14050-14054.

Spreafico, R., Frassoni, C., Arcelli, P., & De Biasi, S. (1994). GABAergic interneurons in the somatosensory thalamus of the guinea-pig: A light and ultrastructural immunocytochemical investigation. Neuroscience, 59, 961–973.

Stiebler I, Neulist R, Fichtel I, Ehret G (1997) The auditory cortex of the house mouse: left-right differences, tonotopic organization and quantitative analysis of frequency representation. J Comp Physiol [A] 181:559-571.

Steriade, M., E. Jones, and D. McCormick, Thalamus (1997): Organisation and Function. . Vol. 1, Oxford: Elsevier Science.

Toldi J, Feher O, Wolff JR (1986) Sensory interactive zones in the rat cerebral cortex. Neuroscience 18:461-465.

Uhlrich DJ, Manning KA, Feig SL (2003) Laminar and cellular targets of individual thalamic reticular nucleus axons in the lateral geniculate nucleus in the prosimian primate Galago. J Comp Neurol 458:128 –143.

Villa AE (1990) Physiological differentiation within the auditory part of the thalamic reticular nucleus of the cat. Brain Res Brain Res Rev 15:25-40.

Vue TY, Bluske K, Alishahi A, et al. (April 2009). "Sonic hedgehog signaling controls thalamic progenitor identity and nuclei specification in mice". J. Neurosci. 29 (14): 4484–97.

Wallace MN, Rutkowski RG, Palmer AR (2000) Identification and localization of auditory areas in guinea pig cortex. Exp Brain Res 132:445-456.

Weese GD, Phillips JM, Brown VJ (1999) Attentional orienting is impaired by unilateral lesions of the thalamic reticular nucleus in the rat. J Neurosci 19:10135–10139.

Wepsic JG, Sutin J (1964) Posterior Thalamic and Septal Influence Upon Pallidal and Amygdaloid Slow-Wave and Unitary Activity. Exp Neurol 10:67-80.

Winer JA, Diamond IT, Raczkowski D (1977) Subdivisions of the auditory cortex of the cat: the retrograde transport of horseradish peroxidase to the medial geniculate body and posterior thalamic nuclei. J Comp Neurol 176:387-417.

Winer JA, Morest DK (1983a) The medial division of the medial geniculate body of the cat: implications for thalamic organization. J Neurosci 3:2629-2651.

Winer JA, Morest DK (1983b) The neuronal architecture of the dorsal division of the medial geniculate body of the cat. A study with the rapid Golgi method. J Comp Neurol 221:1-30.

Winer JA, Wenstrup JJ, Larue DT (1992) Patterns of GABAergic immunoreactivity define subdivisions of the mustached bat's medial geniculate body. J Comp Neurol 319:172-190.

Winer JA, Saint Marie RL, Larue DT, Oliver DL (1996) GABAergic feedforward projections from the inferior colliculus to the medial geniculate body. Proc Natl Acad Sci U S A 93:8005-8010.

Winer JA, Wenstrup JJ, Larue DT (1992) Patterns of GABAergic immunoreactivity define subdivisions of the mustached bat's medial geniculate body. J Comp Neurol 319:172-190.

Winer JA, Larue DT, Huang CL (1999a) Two systems of giant axon terminals in the cat medial geniculate body: convergence of cortical and GABAergic inputs. J Comp Neurol 413:181-197.

Winer JA, Diehl JJ, Larue DT (2001) Projections of auditory cortex to the medial geniculate body of the cat. J Comp Neurol 430:27-55.

Winer JA, Prieto JJ (2001) Layer V in cat primary auditory cortex (AI): cellular architecture and identification of projection neurons. J Comp Neurol 434:379-412.

Winer JA LC, Imaizumi K, Schreiner CE (2004) Challenges to a neuroanatomical theory of forebrain auditory plasticity. In: Plasticity and signal representation in the auditory system (Merzenich MM, eds).91–106.

Wild, J.M. (1989) Pretectal and tectal projections to the homolog of the dorsal lateral geniculate nucleus in the pigeon - an anterograde and retrograde tracing study with cholera-toxin conjugated to horseradish-peroxidase. Brain Res 489: 130-137.

Xiong Y, Yu YQ, Chan YS, He J (2004) Effects of cortical stimulation on auditory-responsive thalamic neurones in anaesthetized guinea pigs. J Physiol 560:207-217.

Yingling CD, Skinner JE (1976) Selective regulation of thalamic sensory relay nuclei by nucleus reticularis thalami. Electroencephalogr Clin Neurophysiol 41:476-482.

Wepsic JG (1966) Multimodal sensory activation of cells in the magnocellular medial geniculate nucleus. Exp Neurol 15:299-318.

Yu YQ, Xiong Y, Chan YS, He J (2004a) Corticofugal gating of auditory information in the thalamus: an in vivo intracellular recording study. J Neurosci 24:3060-3069.

Yu YQ, Xiong Y, Chan YS, He J (2004b) In vivo intracellular responses of the medial geniculate neurones to acoustic stimuli in anaesthetized guinea pigs. J Physiol 560:191-205.

Zhang Z., Chen Y., He J.(2004/2005) Thalamocorical and Corticothalamic Interaction in the Auditory System. Neuriembryology and Aging 3:239-248.