# Ocular motility consequences following lesions of the thalamus: a literature review

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## Abstract

*Aim:* **To summarise the anatomy and function of the thalamus and review the medical literature for types of thalamic lesions and resultant ocular motility deficits.**
*Methods:* **A literature search was undertaken using the PubMed and Web of Knowledge databases. Non-English-language studies were not included.**
*Results:* **Types of thalamic lesions included vascular infarct or haemorrhage, space-occupying lesions, birth trauma, and associated periventricular leucomalacia. Ocular motility deficits included vertical gaze palsies, skew deviation, convergence anomalies, third nerve palsy, nystagmus, pupil and lid anomalies, together with saccadic and smooth pursuit deficits.**
*Conclusion:* **Vascular pathology is the most common cause of thalamic lesions. The lesions may be partial or complete, and unilateral or bilateral. The predominant ocular motility deficit reported is that of vertical gaze palsy. Commonly involvement of the midbrain also occurs.**

**Key words:** Midbrain, Ocular motility, Thalamus, Vascular, Vertical gaze palsy

## Introduction

Within the current literature that addresses thalamic pathology, there are two schools of thought with regard to the aetiology of ocular movement deficits. Namely, whether such deficits are due to thalamic pathology alone, or whether the midbrain, and therefore the important eye movement centres, also become involved.

This review summarises the main discussions associated with these two proposals. In order to aid visualisation of the location of pathologies within the thalamus concerning ocular motor abnormalities, the review is subdivided into sections that cover anatomy and the vascular supply of the thalamus. The discussion then turns towards ocular abnormalities (including saccadic and smooth pursuit deficits) concerning paediatric and adult thalamic pathology. As the most common aetiology of thalamic lesions tends to be vascular, i.e. stroke, the review is focused particularly on this aspect. However, the more unusual aetiologies are briefly discussed.

For the purposes of this review a literature search was undertaken which identified English-language publications using the following databases: PubMed, Web of Knowledge, orthoptic journals and conference transactions (www.liv.ac.uk/orthoptics/research/search.htm). Search terms included 'thalamus', 'thalamic nuclei', 'gaze palsy', 'eye movement', 'ocular motility', 'strabismus', 'stroke', 'cerebrovascular accident', 'vascular', 'anatomy' and 'pathology', with the connectors 'and' and 'or'. The time period for this search ranged from 1939 to 2008. Thirty-two papers were identified that specifically addressed human pathology of the thalamus and the resultant ocular sequelae. A total of 599 patients were reported in these papers.

## Anatomy and function of the thalamus

The thalamus makes up four-fifths of the diencephalon structure; the remaining portion is the hypothalamus. The thalamus consists of two oval masses which are usually joined by a bridge of grey matter that crosses the third ventricle, known as the intermediate mass. Each oval mass measures approximately 3 cm in length and sits superior to the midbrain. The majority of the thalamus is grey matter which is organised into nuclei groups (Fig. 1). However, the internal medullary lamina (IML) is a strip of white matter which separates the grey matter masses into the anterior nuclear group, medial nuclear group and lateral nuclear group.[1]

There are several pathways that traverse the thalamus in order to link cortical regions to the brainstem. The thalamus is considered to be the principal relay station for sensory impulses from the spinal cord, brainstem, cerebellum and parts of the cerebrum that are destined for the cerebral cortex, i.e. spinal cortical tracts.[1,2] All afferent pathways, with the exception of the olfactory pathway, project to the last subcortical neuron present in the thalamus. They then extend forward to the cortex via the 'thalamocortical projection pathways'.[2] The vestibulo-ocular pathway is also thought to traverse the thalamus.[3] Several studies have concluded that the IML is connected to the frontal eye fields, supplementary eye fields and the posterior parietal cortex.[4,5] These studies were conducted on monkeys and cats, respectively, and therefore do not fully apply to the human anatomy.

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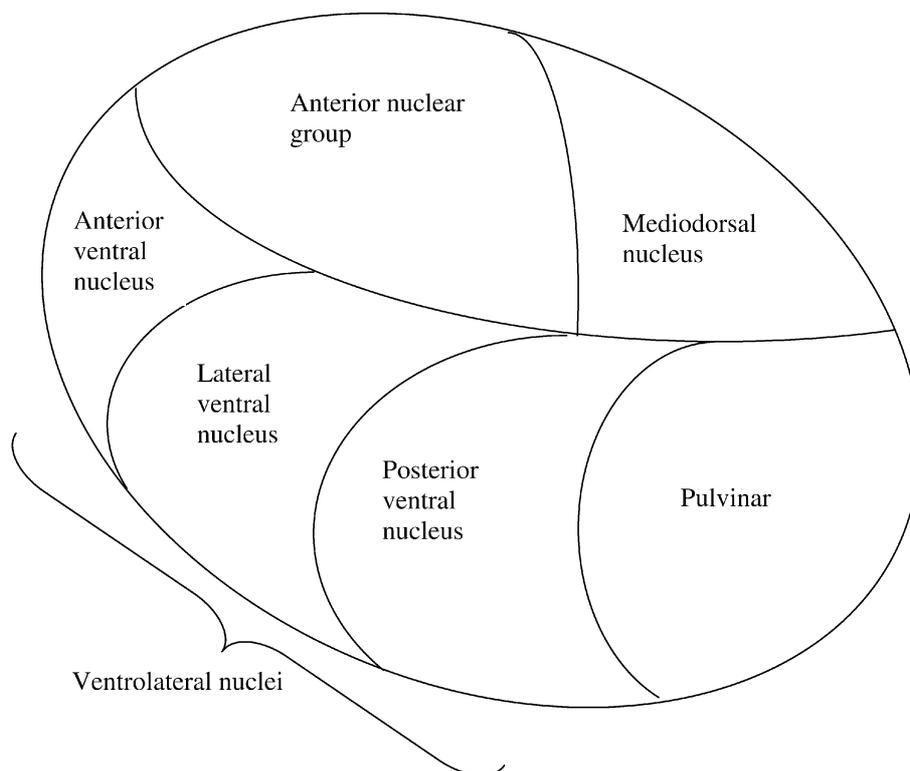
**Fig. 1.** Schematic outline of the thalamus nucleus.

The nucleus gracilis and the nucleus cuneatus located in the medulla play a role in visceral functions and coordination of automatic reflexes. These nuclei relay somatic sensory information to the thalamus.[6] Taste sensation, which occurs in the anterior two-thirds of the tongue, the floor of the mouth and the palate, is relayed to the sensory nucleus in the pons. These fibres in turn travel through the thalamus in order to reach the centre for taste in the cerebral cortex.[7]

Sensory information regarding saccadic generation, which descends to the superior colliculus and paramedian pontine reticular formation, also passes through the thalamus from the cerebral cortex. The inferior colliculus projects mainly auditory information to the medial geniculate body in the thalamus. In terms of smooth pursuit pathways, internal feedback pathways run through the central thalamus.[8] In the paramedian portion of the thalamus, pathways holding convergence information traverse the thalamus from cortical areas to the midbrain.[9,10] Contralateral pre-motor vergence neurons, which project to the medial rectus subnucleus on the same side, are inhibited by the convergence pathway.[9] The inhibitory descending pathways for convergence are thought to decussate in the subthalamic region. The posterior wing of the internal capsule flanks the thalamus on one side and the posterior surface of the lentiform nucleus on the other. It is, however, the anterior limb through which thalamo-cortical projections run. The internal capsule is a compact fibre bundle that serves as a major channel to and from the cerebral cortex.[11]

The pulvinar is the largest portion of the thalamus and is situated in the posterior aspect. Communications exist to and from the pulvinar from the striate, frontal, parietal cortex and the superior colliculus.[12] The nuclei that make up the thalamus can be divided into specific and non-specific nuclei, according to their functional ability. Specific nuclei are classed as those that relay fibres to primary, secondary or tertiary cortical fields. The nuclei that do not project fibres to the cortex but are still communicating with the brainstem, basal ganglia or the reticular formation are known as non-specific nuclei.[1]

The most important of these specific nuclei regions contains the ventroposterior and posteromedial nuclear complexes and connects to the primary cortical fields. The somatosensory neurons, spinothalamic tract and trigeminothalamic tract are then relayed further to the primary sensory cortex.[2]

The mediodorsal nuclei sit to one side of the IML and form the largest of the medial nuclei group. Extensive connections connecting the mediodorsal nucleus to other thalamic nuclei exist.[8] The mediodorsal nuclei group is also thought to communicate with the superior colliculus and may therefore play a role in saccadic activity.[13–16] The medial geniculate nuclei, lateral geniculate nuclei and ventral posterior nuclei are involved with hearing, vision, and taste and somatic sensations (i.e. heat, pain, pressure), respectively. These nuclei relay sensory information to the cerebral cortex.

It has been suggested that the ventrolateral neurons of the thalamus are involved with smooth pursuit activity, possibly concerning direction-specific and velocity aspects.[8] Ventrolateral neurons project to the frontal eye fields and the supplementary eye fields. Other neurons such as the paralaminar regions of the mediodorsal and ventroanterior nuclei also project to these regions.[8,17,18]

Nuclei of the thalamus act as centres for synapses in the somatic motor system; these include the ventral lateral nuclei and ventral anterior nuclei which are involved with voluntary motor actions and arousal. The floor of the lateral ventricle holds the anterior nucleus, which plays a role in emotions and memory.[1]

## Vascular supply

Several small arterial branches supply the thalamus, and a lesion to each division can cause a different manifestation clinically.[19] The thalamotuberal artery arises from the middle third of the posterior communicating artery.[2,20,21] It supplies the posterior section of the hypothalamus. Within the thalamus, areas that are supplied by this artery are the anterior thalamic nuclei along with the ventral section of the IML. The ventral pole of the medial dorsal nucleus and the rostral part of the ventrolateral nucleus also receive their blood supply from this artery.[21] The reported prevalence of the absence of the thalamotuberal artery in the general population varies. Barkhof and Valk[20] cite a 50–75% absence whilst Bogousslavsky *et al.*[22] quote an absence of 30–40%.

If the thalamotuberal artery is not present, its function is taken on by the paramedian artery. This artery arises from the first segment of the posterior cerebral artery merging later with posterior communicating arteries. This artery irrigates the dorsomedial part of the thalamus and the paramedian part of the upper midbrain. There is often a connection between the right and left paramedian arteries.[22]

The posterior cerebral artery gives rise to the thalamogeniculate (peduncle) artery, after merging with the posterior communicating artery. This also includes the branches known as the thalamic inferolateral arteries and the pulvinarian inferolateral arteries. The areas supplied are a section of the ventral lateral nucleus and the pulvinar, along with the majority of the ventral posterior nucleus.[20,22]

The posterior cerebral artery also branches into the posterior choroidal arteries, at the same level as the thalamogeniculate (peduncle) artery. The posterior choroidal arteries then split into two systems: the mesencephalo-posteromedial system and the hippocampo-posterolateral system. These systems supply the dorsolateral aspect of the thalamus, along with the area of the substantia nigra, pulvinar and the lateral and medial geniculate bodies.[20,22,23]

## Pathology

Several studies have indicated that vascular pathology may be the most frequent cause of thalamic lesions: cardio-embolism, artery-to-artery embolism and small artery disease are known to be the main causes. Risk factors are hypertension, diabetes and smoking.[22,24,25] Unusual aetiologies include migraine,[22,25] thiamine deficiency, cerebral lupus, infective abscesses (most likely to be caused by fungi or toxoplasmosis), cerebral syphilitic gumma and tumours.[26]

### Atypical pathology

Papayannis *et al.*[27] report a case study of presentation with upgaze palsy, nystagmus and poor convergence. Multiple cystic lesions were found using magnetic resonance imaging (MRI), one of which had extended from the thalamus to the midbrain and the pons. These cysts are not usually symptomatic; however, in this case the size of the cyst acted as a space-occupying lesion, causing compression of the midbrain giving ocular abnormalities and ultimately causing hydrocephalus.

Thalamic tumours are uncommon and tend to be unilateral astrocytomas, in which sensory and motor functions are usually intact with patients complaining more of personality change with some cognitive ability loss.[2,28]

Deep brain stimulation has been used for improvement of motor impairments in conditions such as Parkinson's disease, progressive supranuclear palsy, epilepsy and Tourette's syndrome.[29–31] A number of ocular signs have been reported in association with deep brain stimulation of the thalamic nuclei. These may often be due to the small size of the nuclei and their proximity to axonal projections, which result in multiple side effects.[29] Such induced ocular signs include central nystagmus and contralateral conjugate eye deviation.[29,30] Wark *et al.*[31] reported that the frequency of fixation instability due to interruptive saccades improved following deep brain stimulation in the subthalamic nuclei.

## Paediatric pathology

There are some reports of infants with thalamic lesions resulting in ocular motor dysfunctions. In a case report of a 10-month-old infant with vertical ocular motor apraxia, birth trauma was reported to be the most likely cause of thalamic and cerebellar ischemia.[32] Furthermore, Garbutt and Harris[33] reported 3 children with lesions of the thalamus who had normal vertical smooth pursuit movements but absent vertical ocular kinetic nystagmus (OKN). The authors attributed the cause to possible rostral midbrain involvement, but this was speculation. This study, however, was the first of its kind in terms of investigating vertical OKN in a group of infants with visual pathway pathology.

Profound asphyxia in 5 infants at post-conceptional ages of 27 to 32 weeks resulted in characteristic neuroimaging findings, abnormal basal ganglia and apparent bilateral calcification of the thalami.[34] Brainstem structures and cerebelli were also shown to be affected. This study, however, did not identify whether abnormal eye movements occurred. At the time of the imaging the infants ranged in age from 1 day to 4 months.

Among 44 infants with periventricular leucomalacia (PVL), 50% had thalamic lesions which involved the posterior part of the thalamus bilaterally and the pulvinar.[35] Lesions generally also involved the posterior limb of the internal capsule, situated adjacently. A paroxysmal ocular downward deviation was found to be a frequent feature in these patients, and this was combined with the presence of an IQ less than 70. This study also compared patients with PVL who had

associated thalamic lesions and those without thalamic involvement.[35] The authors suggested that the lesion occurring in the thalamus was secondary to a cerebral lesion and was generally associated with more severe types of PVL. Fewer saccadic deficits are reported in infants and this is proposed to be due to adaptation mechanisms related to the neural plasticity of the infant visual system.[36]

### Adult vascular pathology

#### Paramedian vascular territory

Unilateral infarcts mainly cause upgaze palsies. Bilateral infarcts have been found to cause upgaze, downgaze or combined vertical palsies.[22,37–40] Recovery has been recorded in some patients. Swanson and Schmidley[39] reported one case where the palsy was noted to have resolved within 2 weeks and the skew deviation that was seen at hospitalisation had resolved within 24 hours, which coincided with an improvement in the patient's comatose state.

There have been several reports in the literature regarding bilateral paramedian thalamic infarction.[40,41] Abnormalities include convergence paralysis, bilateral internuclear ophthalmoplegia (6%; 1/16 patients) and involvement of the III nerve nucleus with ptosis (12%; 2/16 patients). A vertical gaze palsy and abnormal convergence was present in 88% of patients (14/16) with bilateral paramedian thalamic infarction.[40]

Reilly et al.[41] reported vertical gaze palsies in all 6 of their patients with thalamic infarction. In this study, only half (3/6) of the patients received MRI scans. These showed isolated bilateral medial thalamic infarctions, and unilateral infarction was seen in only the minority of cases. This prospective study was conducted over a 4-year period in a hospital setting. Clinical manifestations included lid retraction, bilateral ptosis, convergence retraction nystagmus and light-near dissociation.

Several authors have reported that a variant blood supply may in some individuals lead to midbrain involvement. Obstruction will cause a bilateral paramedian thalamic infarction; the midbrain will only be involved if the superior and inferior paramedian mesencephalic arteries arise from a common trunk along with the paramedian thalamic artery. The midbrain will be spared if the paramedian thalamic artery arises separately.[39,41]

Clark and Albers[42] utilised scanning techniques and used repeated MRI to exclude midbrain involvement. This study reported 3 cases of vertical gaze palsy, which were attributed to infarcts in the paramedian thalamic and polar artery territories. The authors did acknowledge that they could not fully state the midbrain was uninvolved in these cases. This was because limited sagittal T2-weighted images were used which may have missed small infarcts of the midbrain.

In a study by Chung et al.[19] 175 patients were analysed retrospectively. More detailed imaging was undertaken utilising both computed tomography (CT) and MRI to identify isolated thalamus pathology or combined thalamus and midbrain involvement. The authors were able to divide pathology into specific regions of the thalamus. Haematomas located in the medial thalamic region were present in 14% (24/175) of patients; they were small in size if restricted to the medial thalamus. It was reported that the haematomas often ruptured into the third ventricle, which caused obstructive hydrocephalus that produced a severe mass effect. The haematomas often extended mediocaudally into the midbrain. Patients with haematoma causing midbrain involvement (19/175) presented with marked motor abnormalities, due to the involvement of the cerebral peduncles. Oculomotor deficits were frequent in these patients, with 'wrong-way eyes' being noted in 32% (6/19 patients), and case fatality was high at 68% (13/19 patients). ('Wrong way eyes' describes a conjugate deviation of the eyes to the side contralateral to the lesion.) 'Wrong-way eyes' have been documented in medial haemorrhage; whilst explanations for this have been suggested, these have not been proven.[12]

#### Dorsal territory

Involvement of the dorsal territory was identified in 32 of the 175 patients reported by Chung et al. (18%).[19] In some patients the haematoma remained localised and transient uncharacteristic diplopia was recorded at onset. It is not clear whether horizontal or vertical diplopia was experienced. In support of this are other studies that have reported transient vertical diplopia.[3,41] This was proposed to be due to a transient lesion which affected the vestibulo-ocular pathway that traverses the thalamus.[3]

#### Posterolateral territory

Chung et al.[19] reported 77 patients with haematomas that involved the posterolateral aspect of the thalamus and demonstrated that 10 of the 175 patients (13%) with large haematomas in this area had ipsilateral Horner's syndrome. This clinical finding is in accordance with the observations of Gaymard et al.,[43] who also reported 2 cases of ipsilateral Horner's syndrome, with lesions involving the ventral posterolateral nuclei. Vertical gaze palsies, however, were only noted in patients with haematomas that were large enough to extend to the upper brainstem. The authors therefore suggest a correlation between the haematoma size and clinical findings, in this region.

Caudal lesions have been shown to cause what is known as 'thalamic esotropia' or pseudo-abducens palsy. Features include abnormal convergence (excessive or sustained) and slow or restricted abduction. The esotropia maybe marked and it has been hypothesised that vergence inputs to the oculomotor nuclei are disturbed.[44]

#### Anterior lateral territory

Haematoma in the thalamotuberal (polar) territory is reported as the least common type of thalamic haemorrhage. It was found in 11 of the 175 cases reported by Chung et al. (6%).[19] MRI and CT scans revealed that some of the haematomas involved the anterior limb of the internal capsule and occasionally the head of the caudate nucleus, because the haematoma extended anterolaterally. Often the haematomas ruptured into the anterior horn of the lateral ventricle. Patients were examined clinically and found to have acute

confusion and memory impairment but were generally alert. No eye movement or pupillary abnormalities were documented and clinical outcome was found to be excellent.[19]

### Inferolateral territory

A study by Bogousslavsky *et al.*[22] that reported on 40 patients found the most frequent type of thalamic infarct (45%; 18/40 cases) was inferolateral. Vertical gaze palsies were not reported in any of these patients and the only ocular abnormality noted was hypermetric saccades.

### Global involvement

The global type of haematoma found to occupy the majority of the thalamic mass often extends into the internal capsule and putamen that are located adjacently.[19] The most common feature of this type of haematoma was an upgaze palsy in 15 of 31 patients (48%).[9] However, in some patients downgaze palsy or a combination of up- and downgaze palsy was found. Another clinical feature noted was 'peering at the nose'. This is described as a tonic deviation in which both eyes are depressed and adducted.[9] The mechanism for this clinical finding appears to be unknown, but it has featured in patients with ischemic infarcts in the regions of the posterior circulation, lateral pontine tegmentum and in thalamic haemorrhages. Choi *et al.*[9] reported 4 patients with this characteristic and all patients in this study had midbrain involvement. Peering at the nose does not occur in other brainstem lesions that exclude the thalamus.

Pseudo-abducens palsy is described by Caplan[45] as 'a failure of ocular abduction which is not due to dysfunction of the sixth nerve'. Two patients in a report by Pullicino *et al.*[10] had predominantly thalamic infarcts with associated upgaze and pseudo-abducens palsies. These signs resolved together at the same pace. The authors suggest a probable involvement of the riMLF/INC area of the midbrain and propose that the inhibitory descending pathways for convergence travelling through the thalamus are disrupted.

### Saccadic abnormalities

Several studies have investigated the function of the neurons and the nuclei of the thalamus and their role regarding saccades.[8,13,14,16,46–50] The mediodorsal nuclei are a large collection considered to be one of the main nuclei groups of the thalamus. Communications occur with other cortical areas as well as amongst other thalamic nuclei. Therefore several authors have attempted to investigate their role in saccadic activity.

As previously mentioned the mediodorsal nuclei link with the paralaminar nuclei within the thalamus structure but links are also thought to exist with the superior colliculus. This connection is an important relay in relation to saccadic activity.[14–16,39] In particular Sommer and Wurtz[13] indicate that the corollary discharge signals provide information regarding impending saccades and are carried on projections travelling from the superior colliculus to the frontal eye fields via the mediodorsal nuclei. Dysmetria and asymmetry of saccades can occur

when a lesion in the human thalamus disrupts corollary discharge signals.[46] In relation to vertical saccadic movement, downward movement is likely to be more affected than upward movement. Furthermore only minor abnormalities involving smooth pursuit and vestibulo-ocular reflexes occur if bilateral ischemia of the dorsomedial area of the thalamus, with lesions involving the riMLF, is present.[37]

The work of Sommer and Wurtz is in concurrence with that of Tanibuchi and Goldman-Rakic[16] who found that the mediodorsal nuclei were activated prior to saccadic activity. The authors further compared the paralaminar nuclei of the thalamus with mediodorsal nuclei in monkeys and found similar properties, i.e. both nuclei were activated specifically for memory-guided saccades. However, the paralaminar nuclei activity was recorded during or after saccadic activity.

Tehovnik *et al.*[51] suggested that within the human thalamus the pathway is located more laterally, possibly involving the ventrolateral nucleus, than is the case in monkeys. Results from patients with lateral ventrolateral nucleus lesions of the thalamus show similar features as those in monkeys with mediodorsal lesions, i.e. partial deficits of saccades.[46] Thus the mediodorsal nucleus in monkeys and the ventrolateral nucleus in humans may have similar roles. However, the similarities between monkey mediodorsal nuclei reports and human ventrolateral nuclei reports are based on small numbers of patients (5 of 13 cases). Thus a larger study would be needed to confirm that lesions to the lateral ventrolateral nucleus lead to corollary discharge information disruption in humans, resulting in saccadic defects. Sommer and Wurtz[14] and Bellebaum *et al.*[46] further explain that the lesions in their subjects may not have affected all aspects of the relay neurons, thus resulting in a partial deficit.

Leigh and Zee[12] noted that a shift in gaze can result in memory-guided saccades being abnormal, if the shift occurred in the memory period. This is particularly prevalent in central thalamic lesions. Evidence of this exists in reports that impairment of memory-guided saccades did occur with lesions to the central thalamus if gaze was shifted.[43] It is reported that in normal subjects accuracy remains constant during the memory-guided saccade, whether gaze is shifted or remains stable.[52]

Saccadic deficits are often noted on examination in patients with thalamic lesions, due to the thalamocortical tracts that traverse the thalamus being affected. More severe deficits occur if the internal capsule is also involved.

### Smooth pursuit abnormalities

It has been suggested that the internal feedback pathways run through the central thalamus. Tanaka[8] demonstrated in monkeys that the inactivation of the thalamus did reduce the eye velocity soon after initiation of the pursuit movement; however, the latency was not affected. This study further found that neurons of the ventrolateral thalamus display sustained activity during the pursuit movement, and activity was recorded prior to the movement taking place. Tanaka provided direct evidence that thalamic nuclei were involved in pursuit

movement, specifically the ventrolateral nuclei which were direction-specific, and activity was related to the speed of the object. Cui *et al.*[53] proposed that the caudate nucleus plays an essential role in smooth pursuits and that the basal ganglia and thalamus are linked together with a feedback loop.

## Conclusion

Bilateral thalamic lesions tend to produce more severe deficits than unilateral lesions.

The pathology that affects the thalamus tends to be of a vascular nature. There is some evidence that thalamic anomalies do exist in the paediatric population.

With regard to ocular abnormalities, unilateral infarcts mainly cause upgaze palsies. Bilateral infarcts were found to cause upgaze, downgaze or combined vertical palsies and abnormalities such as convergence paralysis, bilateral internuclear ophthalmoplegia and involvement of the III nerve nucleus with ptosis. Pseudo-abducens palsy is thought to be caused by the disruption of inhibitory descending pathways for convergence travelling through the thalamus. Only an autopsy would definitely prove or disprove the presence of brainstem involvement, as imaging may not always show the true extent of the lesion residing in the thalamus.

Saccadic and smooth pursuit defects may also be noted. Corollary discharge signals allow the superior colliculus to communicate with frontal eye fields and this pathway is connected with the mediodorsal nuclei of the thalamus. Therefore dysmetria and asymmetry that are greater in downward vertical saccadic movement occur. Smooth pursuit pathways have been shown to pass through the thalamus and lesions may cause pursuit deficits.

The literature that has been discussed in this review tends to focus on whether brainstem involvement causes the vertical gaze abnormalities or whether it is due to pathology affecting the thalamus structure alone. The literature favours the idea that the midbrain and thalamus vascular supply have a similar origin. In particular some individuals are seen to have vascular variations and this in itself increases the risk of the midbrain simultaneously being affected with the thalamus, thus causing gaze palsies. There is, however, evidence that thalamic pathology causes vertical gaze palsies with no apparent midbrain involvement.

There are several limitations to this literature report because it is difficult to draw conclusions with regard to the exact location of thalamic lesions causing specific clinical manifestations. There are reasons for this. Firstly, thalamic lesions in the general population are a relatively rare occurrence. Secondly, the studies undertaken have used a variety of investigative techniques and the majority of reports are based on small numbers of patients. Thirdly, whilst rate and completeness of recovery may differ with respect to location and severity, there are only a small number of patients in whom thalamic lesions actually lead to death. Literature regarding thalamic lesions is therefore rarely described anatomically using post-mortem investigation.

This literature review indicates that further research is needed. In particular larger studies are needed which incorporate neuro-centres throughout the United Kingdom and other countries. This would lead to larger numbers of patients being investigated and comparisons made in relation to location of lesion, clinical manifestations and aspects of recovery. Further investigation into the precise locations of lesions and structures that are affected is required, specifically in relation to the thalamic nuclei and tracts travelling through the thalamus. Also, it would be interesting to fully evaluate whether patients who suffer from vascular pathology in this region with potential midbrain involvement, have a vascular variant.

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