Vergence neural pathways: A systematic narrative literature review.

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Abstract

Aim: To review the literature on vergence neural pathways and associated disorders.

Methods: A review of previous published literature through to March 2016 was conducted after a search of a variety of databases including Scopus, Web of Knowledge and PubMed. Search terms included ‘ocular motility following cerebral haemorrhage’ and ‘convergence spasm’.

Results: Intracranial pathologies which affect entire neural functioning were found to cause convergence insufficiencies and reduced fusional vergence. This includes conditions such as Parkinson’s disease and mild traumatic brain injury. In contrast, pathologies with a more localised intracranial lesion cause more specific vergence disorders such as convergence spasm and convergence paralysis. With regard to divergence disorders, there is debate as to the potential presence of a ‘divergence centre’ within the brainstem.

Conclusion: Convergence disorders have a higher prevalence in comparison to divergence anomalies within the reported literature. Conditions such as Parkinson’s disease, progressive supranuclear palsy and traumatic brain injury reduces neural functioning including the ability for a ‘normal’ convergence movement. In contrast, lesions with specific sites within the vergence neural pathway cause specific conditions leading to vergence disorders such as convergence spasm and convergence paralysis. Detailed information on the divergence pathway is lacking and warrants further research.

Keywords: Vergence, Neural pathways, Degeneration, Convergence, Divergence, Review

Introduction

The vergence eye movement system is unique as it is the only visual response causing the eyes to move in a disconjugate manner[1]. It plays a significant role in depth perception and the refixation of eye movements. By working with the saccadic system, both eyes can adapt and change fixation symmetrically and rapidly. Bifoveal fixation and stereopsis require accurate alignment of the visual axis to refixate from one distance to another, thus facilitating depth perception and localisation within space. This is dependent on an accurate working vergence system making it a vital component of extraocular movement in everyday life.[2-4]

Vergence eye movements can be segregated into two descriptive subcategories: convergence and divergence. Convergence is the inward disconjugate movement of the eyes whereas divergence is the ability for the eyes to move outwards in an opposite direction[1]. Stimuli for vergence includes retinal blur and target displacement.[5] Degenerative conditions and acquired brain injury due to trauma or ischaemia can cause vergence impairment. Symptoms of diplopia, asthenopic symptoms and reduced depth perception may subsequently be reported.[3] The purpose of this review is to consider the vergence neural pathways and their associated oculomotor disorders as a narrative synthesis of the related literature.

Methods

Search strategy

A systematic search strategy was used to search the following key electronic databases: MEDLINE (1948 to March 2016), SCOPUS (1823 to March 2016), AMED (1985 to March 2016), CINAHL (1937 to March 2016) and PsycINFO (1887 to March 2016). Citation tracking was performed using Web of Science Cited Reference Search for all included studies, and reference lists of included articles were searched. Search terms included a variety of MESH terms and alternatives in relation to Vergence, Neural pathways, Degeneration, Convergence, Divergence.

Inclusion and exclusion criteria

Articles related to vergence neural pathways were included along with literature that discussed the anatomy, physiology and pathophysiology of vergence from experimental research in animal and network models, and human studies. Studies in languages other than English were excluded.

Selection of studies

The titles and abstracts identified from the search were screened using the pre-stated inclusion criteria. The full papers of any studies considered potentially relevant were then considered and the selection criteria applied.

Neural control of vergence eye movements

Vergence eye movements include disconjugate inward movements of both eyes (convergence) and outward movements (divergence). Vergence consists of two phases: the initiation (transient) phase followed by the completion (sustained) phase.[1] Vergence responds to certain stimuli including disparity between images on the retina, retinal blur (an unfocused image), proximity of objects, the change in size of an image and monocular clues to stimulate a fusional response.[1] Cortical processing of such stimuli involves neural connections between the occipital lobe and the parietal lobe and frontal eye fields.[6] Evidence that an area located anteriorly to the saccade and smooth pursuit zone in the frontal eye fields is linked with depth perception which suggests this area could be involved with the initiation of vergence eye movement.[7-8] Moreover, some reports suggests the parietal lobe is associated with vergence-saccade systems, giving evidence this lobe is involved with changes with fixation distance, localisation and processing retinal blur.[9] Two key areas of the occipital lobe are: the primary visual cortex (V1) and the secondary visual cortex (V2). Studies report that cortical response to retinal disparity, retinal blur and depth perception lies within V1.[3, 10] Wong[1] continued this further outlining three types of disparity neurons within V1 that process the stimuli whilst other neurons tune for far fixation or near fixation. Area V2 has been implicated in the initiation of vergence movements.[3]

Cortical neural signals subsequently travel from the visual cortex to the supraocular motor area of the midbrain via the basal ganglia and thalamus. The brainstem houses the nuclei responsible for the initiation of extraocular eye movement.

Weist[11] and Tai et al[12] presented case studies demonstrating loss of control and deficiency of vergence secondary to thalamic haemorrhages. This suggests that vergence neural fibres could be associated with the thalamus. The fibres either travel close to or within the structure on its journey from the cerebral cortex to the supraocular motor area of the midbrain.

Evidence of vergence signals have been found within the mesencephalic reticular formation, around the oculomotor nucleus and the abducens nucleus.[6, 13-15] Research undertaken to find pure vergence signals was conducted by Mays.[13] The findings showed the firing rate was linearly proportional to the vergence angle and the cells were found to be placed approximately 2mm from the medial recti motorneurons. The findings were further supported in a subsequent study concluding that cells with a pure vergence signal were only found in the midbrain. Mays and Porter[14] identified a pulse-step action similar to that of saccades. They also proposed the possibility of vergence neurons within the abducens nucleus having found increased activity in two cell types during pure convergent movements.[14] However the majority of cells showed combined versional and vergence signals.[14]

Types of vergence neurons within the mesencephalic reticular formation can be subdivided into tonic cells (involved with vergence angle), burst cells (involved with vergence velocity) and tonic-burst cells (control both vergence angle and velocity). They are also known as near-response cells.[1]These pre-motor neurons are mainly involved with convergence, with a fewer number of divergence cells reported. Subtypes synapse with medial recti subnuclei; this has been proven through antidromic activation.[16-17] Further findings showed firing rate to be directly proportional to vergence angle and

velocity.[1, 13-14] With limited evidence of pure vergence signals being released from the abducens nucleus, divergence could be caused by inhibition or decrease of convergent firing rate.[14] In Cullen and Van Horn's[15] review, the authors found an increase of firing rate of the near-response cells which lead to convergence. Divergence followed a decrease of activity of these cells. These cells were unresponsive during vergence-saccade eye movements. This supports the theory proposed by Mays and Porter[14] regarding pure vergence neurons. Cullen and Van Horn[15] reviewed the neural activity of fast versus slow vergence movement. Evidence has shown fast vergence integrates with conjugate activity while slow vergence does not. Pure vergence signals can therefore be responsible for the smooth vergence that is tested currently whereas vergence-saccades are the fast form of vergence used for depth perception and refixation within space.

One particular structure within the pons has raised questions about further neural components involved in the vergence pathway. The nucleus reticularis tegmenti pontis (NRTP) has been studied by Gamlin and Clarke.[18] This structure was found to have an effect on vergence angle and had an increased firing rate for both near and far responses. Additional connections were found between this structure and the cerebellum.

Evidence for cerebellar connections involved with vergence neural activity has been sought. Two specific nuclei in the cerebellum were shown to have neural connections to the supraocular motor area and mesencephalic reticular formation in the midbrain[19] Two key structures were the interposed and fastigial nuclei. Interestingly neurons from the cerebellum were found to decussate before synapsing in the midbrain. However fibres

travelling from the midbrain to the cerebellum remained ipsilateral. Its highly specific arrangement would be at a greater risk of dysfunction. The fastigial nucleus specifically synapses close to the Edinger-Westphal nucleus, raising the question whether this structure could be more involved with the near-response mechanism. Vergence eye movements are integrally linked with accommodation and pupil constriction functions with interconnections between midbrain neurons that project to the Edinger-Westphal nucleus and oculomotor nuclei. The Edinger-Westphal nuclei supply preganglionic parasympathetic fibres that result in pupil constriction, lens accommodation and convergence.[20]

Furthermore, the Edinger-Westphal nucleus receives neural input from the superior colliculi and the pretectal region in the midbrain. Afferent nerve signals of the pupillary light pathway arrive at the pretectal region whilst corticotectal fibres from the visual cortex synapse in the superior colliculi in the pupillary near reflex. Information then travels with the oculomotor nerve to eventually synapse in the ciliary ganglion. A small percentage of fibres synapse in the sphincter muscle of the iris to initiate pupil constriction. Pupil constriction, through the reduced pupil aperture, provides an increased depth of focus which further enables clarity of vision at near fixation. The other percentages of fibres synapse with the ciliary muscle to initiate lens accommodation.[21] In patients with light-near dissociation, a lesion is often located near the pretectal area of the midbrain. This accounts for weak pupillary light reflex with normal pupillary accommodation.[22] In comparison to the fastigial nuclei being involved with convergence, the area of the interposed nuclei showed more activity during divergence and distance fixation.[23]

Connections between the NRTPand the deep cerebellar nuclei were studied by Gamlin.[6] Vergence cells found in the pontine structure connected to the cerebellar nuclei with afferent connections to the frontal eye fields. The NRTPhad more activity at near response commands, supporting the theory it could be connected to the cerebellar fastigial nuclei. However it showed decreased response to far distance fixation whereby interposed nuclei had more activity on testing. Research in this area is limited and therefore further study is warranted to fully understand the relationship between vergence movement, the cerebellar nuclei, the area of the midbrain and the pons. Following signal exchange between these structures, there is an eventual synapse either in the medial recti sub-nucleus or abducens nuclei for convergence and divergence respectively to initiate movement of the horizontal extraocular muscles.

Convergence disorders

The efferent vergence pathway starts at the visual cortex and has connections with the lateral parietal cortex and the frontal eye fields.[8-9] Acquired brain injury is a generic term used to describe disruption of the neuronal and vascular processes that occur within the brain. Disruption of the connections between the areas associated with vergence is shown to decrease the ability for fusion and the ability to converge the eyes to 'normal' values.[24-26]

Ciuffreda et al[24] conducted a retrospective analysis on 300 participants with an oculomotor disturbance following acquired brain injury. Convergence insufficiency was the most common vergence abnormality. They reported traumatic brain injury can cause diffuse axonal damage which in turn could cause vergence neural fibre disruptions. A global coup-contrecoup injury can cause multiple axonal damage rendering the

accommodative and vergence neural pathway more susceptible to impairment. This is due to its highly complex and numerous stages of motor innervation. Ciuffreda et al[24] concluded that individuals who suffered a stroke had a higher frequency of strabismus and cranial nerve palsies secondary to more localised lesions and less vergence disorders.

A later study directed by Syzmanowicz et al[25] also found convergence insufficiency to occur frequently following traumatic brain injury. In comparison to the study by Ciuffreda et al[27], subjects and controls had dynamic and static aspects of vergence assessed for comparison alongside near point of convergence measurements. On dynamic testing, peak velocity was significantly lower in mild traumatic brain injury subjects ($p<0.100$). This could indicate the motor control of vergence being largely impaired. Results of the static testing were insignificant.

Visual disturbances was assessed by Capó-Aponte et al[28] in 20 war veterans diagnosed with mild traumatic brain injury and assessed on average 30.5 days following their incident. Similar to previous research[27], near point of convergence, near latent phoria and vergence fusional reserves were assessed. Scoring of symptoms in mild traumatic brain injury was significantly higher than the control group with a higher frequency and incidence of symptoms (i.e. asthenopia, fatigue and visual stress) secondary to convergence insufficiency in the subject group.

Evidence has shown convergence disorders related to lesions of the thalamus. Areas of the thalamus involved with the visual system are the lateral geniculate body, the thalamic reticular nucleus and the pulvinar thalamus. Lesions around the pulvinar nuclei have been shown to be related to convergence disorders.[29] This can raise question with

regard to its role within the visual system and vergence. Saalman and Kastner[30] reviewed the literature for thalamic involvement with visual perception. The pulvinar thalamus is considered a higher order thalamic nucleus due to its involvement with the input and output loops connected to the cortex. Pulvinar thalamic lesions have been reported to cause defects in coding spatial information and cause problems with visually guided behaviour. If neural components that control a vergence-saccade are affected then visually guided behaviour will also be poor. Furthermore the defect is commonly on the contralateral side of the lesion.[31] Lesions on the contralateral side may give evidence of decussation of fibres as they interact with the thalamus. This is supported by case studies with lesions in the thalamus causing disorders seen clinically on the contralateral side.[11-12]

Impaired convergence has been noted in up to 40% of patients following a thalamic stroke.[32] Kumral et al[33] evaluated the comparison between the localization and associated clinical features of thalamic haemorrhages. They found convergence disorders can be caused by involvement of the intralaminar and dorsomedial nucleus of the thalamus; however lesions in the upper midbrain were also present. Convergence spasm has been reported in 1-30% of cases following haemorrhage or infarction in the thalamic region.[11-12,33-35] As lesions often extend further than the thalamus, it is difficult to judge whether disruption at the level of midbrain or at the thalamus results in the disorder. Figure 1 demonstrates the thalamic nuclei reported to cause convergence disorders secondary to thalamic haemorrhage or lesions.

Evidence of thalamic infarctions causing convergence paralysis have also been reported. Linder et al[29] discussed a case of unilateral thalamic haemorrhage causing the

convergence paralysis whilst Kumral et al[33] reported cases of bilateral infarctions causing convergence paralysis alongside upgaze palsies. Bilateral infarction encompasses a larger area of the thalamus which increases the risk of other associated structures and neural pathways being damaged.

Dorsal midbrain syndrome also known as Parinaud's syndrome, pretectal syndrome and Sylvian aqueduct syndrome has diagnostic ocular clinical features including vertical gaze palsy, convergence retraction nystagmus, light-near dissociation and lid retraction (Collier's sign).[3] Convergence paralysis and convergence spasm has also been noted in the literature.[3] The aetiology of dorsal midbrain syndrome will involve a lesion in the pretectal area and of the posterior commissure.[3] Convergence retraction nystagmus was initially thought to be a saccadic anomaly. However research undertaken by Rambold et al[36] has provided evidence towards it being a vergence dysfunction. Findings showed the inward movement of convergence retraction nystagmus fell into the main neural sequence of convergent eye movements and not with the horizontal saccadic movements.[37] An additional study was undertaken by the same author, in which the neural patterns elicited during convergence retraction nystagmus were found to be very similar to neural signals in vergence-saccade eye movements.[35]

A variety of disorders have been reported to disrupt the function of vergence around the area of the oculomotor nuclei and mesencephalic reticular formation. These range from degenerative disorders to vascular lesions and encephalitis.[3] Parkinson's disease particularly causes neuronal loss within the substantia nigra which reduces the production of the neurotransmitter dopamine.[38] Repka et al[39] studied the severity of Parkinson's disease and its effects on ocular motility. They found patients who had the

condition the longest and/or were most severely affected had the smallest convergence fusional range and weakest near point of convergence.

Early stage disease may have normal near point of convergence and slightly reduced positive fusional range.[40] Lepore[41] suggested the vergence pathway has extra-striatal involvement. Thus, disruption to vergence neural signals may be caused by extra-striatal defects in Parkinson's disease. They found 33% of subjects had convergence insufficiency but did not state the length of time participants had suffered Parkinson's disease.

Kitthaweesin et al[42] measured vergence amplitudes and vergence peak velocities in patients with progressive supranuclear palsy (PSP) compared to healthy controls. Both amplitude and peak velocity were reduced in PSP patients. Vergence movements smaller than 4 degrees were equal to control subjects; movements any higher had a slower response. The study only looked at jump vergence and not smooth vergence movements raising the question whether reaction time could be the cause for the slower response. PSP patients have been shown to have significantly reduced visual reaction times in comparison to Parkinson's disease patients and controls.[43]

Evidence suggests the superior colliculi also play a role in the vergence neural pathway. Two case reports present patients who were diagnosed with convergence paralysis following infarction in the rostral superior colliculi.[44-45] Both patients had full adduction of either eye, however convergence was absent. Van Horn et al[4] further studied the role of the rostral superior colliculi. The results found vergence can be evoked by microstimulation of these neurons. A small selection of neurons involved with reorientation from distance and near fixation were found within this area.[4] Additional

evidence also identified combined pathways of vergence and smooth pursuit movements in the rostral superior colliculi.[4]

Following the research directed by Gamlin and Clarke[18] and Gamlin[6] on the involvement of the NRTPin vergence, further studies have considered pontine lesions and their effect on vergence eye movements.

Two types of vergence were specifically tested: fast versus slow movement. The most common finding following these studies was the increasing association of the NRTPin slow movements. Furthermore there is recent evidence of NRTPinvolvement in the smooth pursuit neural pathway.[46] This suggests the NRTPis involved in the smooth and disconjugate movements of the eyes. Possible neural connections between the rostral superior colliculus and the NRTPmay be disrupted by pontine lesions.

Rambold et al[47] presented two findings of patients who underwent magnetic resonance imaging (MRI) with pontine lesions in which slow and fast vergence movements were affected. They proposed the NRTPimpacted the slow vergence movement and fast vergence movements are related to other pontine nuclei. Further studies indicate a more specific function of the NRTP with divergence.

One of the first studies analysing the anatomical relation between the cerebellum and vergence eye movements was conducted by Westheimer and Blair[48] on macaque monkeys. Results had shown that following removal of the cerebellum, subjects were left with the inability to converge. Subsequently subjects had trouble maintaining the converged position. This evidence suggests possible cerebellar connections involved with the vergence neural pathway. Other oculomotor defects included reduced smooth

pursuit movement and the inability to maintain fixation for prolonged periods. With this in mind, the convergence defect following the cerebellectomy could either be a combination of vergence and gaze-holding fault or due to the inability to maintain fixation alone. Further support has been in favour of cerebellar involvement in vergence. Gamlin and Clarke[18] reported neural connections between the NRTPand the cerebellum. Figure 2 diagrammatically illustrates the sites of the lesions with possible involvement of the convergence pathway within the brainstem and cerebellum.

Further evidence of cerebellar involvement lies with a case reported by Ohtsuka et al.[44] Convergence paralysis was diagnosed in a patient following a haemorrhage in the cerebellum. The lesion included both the right cerebellar peduncle and hemisphere. Complete absence of convergence was noted, particularly fusional vergence in comparison to accommodative vergence. Sander et al[49] studied vergence in patients with or without lesions in the cerebellar vermis. Divergence was only found to be reduced in slow and sinusoidal vergence eye movements. Step vergence was found to be unaffected. Referring back to the review undertaken by Gamlin[6], the fastigial and posterior interposed nuclei located either within or close to the vermis were implicated in having an effect on types of vergence pathways. Further research into their relation is required.

Divergence disorders

It has been proposed that divergence defects are due to impairment of the relaxation process for convergence.[50] However, lesions in the NRTPand cerebellum causing divergence abnormalites could support the theory of a separate divergence neural pathway or ‘divergence centre’. Divergence paralysis was reported in two patients with

lesions in the paramedian and left inferior portion of the pontine tegmentum.[51] However, distinction between the role of each structure cannot be made.

The paucity of cohort studies on these clinical entities renders a reliance on reported case studies of divergence paralysis following lesions in the thalamus, midbrain and pons.[51-55] Further research has reported activity within the midbrain tegmentum during divergence eye movement.[13] In contrast, Lepore [55] found no localised pathology which accounted for divergence paralysis but reported a variety of more diffuse aetiologies which caused divergence paresis such as Wernicke's encephalopathy and Parkinson's disease.

As indicated in figure 3, there are a variety of possible anatomical sites within and around the brainstem related to divergence disorders. Further prospective research is required to determine whether there is a divergence centre causing abnormalities in divergence.

Conclusions

Vergence disorders can be caused by a variety of conditions, more commonly traumatic brain injury, acquired brain injury of the brainstem and ischemic defects. Review of the literature has outlined the neural anatomy which, when affected, gives rise to different vergence disorders. Disruptions within the cerebral cortex caused by traumatic brain injury and, less commonly stroke, cause convergence insufficiency more than the vergence abnormalities of convergence spasm or paralysis. Convergence insufficiency in those with traumatic brain injury may be due to diffuse axonal damage. Traumatic

brain injury can also cause loss of positive fusional vergence which could account for associated convergence insufficiency. Thalamic haemorrhage also commonly causes vergence defects: both convergence spasm and convergence paralysis. Theories include damage to convergence inhibitory fibres passing either close or within the thalamus resulting in vergence disorders. However characteristics of convergence spasm and paralysis are very different and the possible presence of these inhibitory fibres has yet to be confirmed. Fibres which control both entities may travel together close to the thalamus. The theory of decussation of fibres around the thalamus has been repeatedly discussed which would explain contralateral lesions to the affected eye. Improved understanding of vergence mechanisms will add to the knowledge base for vergence-saccade defects and related anatomy. Degenerative conditions involving the midbrain are found to cause convergence insufficiency and decreased fusional vergence ability, similar to that of traumatic brain injury. Divergence abnormalites occur significantly less in comparison to convergence abnormalities.

References

1. Wong A. *Eye Movement Disorders.* 6th ed. New York: Oxford University Press, 2008
2. Coubard OA. Saccade and vergence eye movements: a review of motor and premotor commands. *Eur J Neurosci* 2013;**38:**3384-3397
3. Leigh R, Zee D. *The Neurology of Eye Movements.* 4th ed. New York: Oxford University Press, 2006

4. Van Horn MR, Waitzman DM, Cullen KE. Vergence Neurons Identified in the Rostral Superior Colliculus Code Smooth Eye Movements in 3D Space.*J Neurosci* 2013; 33:7274-7284.

5. Glaser JS. Eye Movement Characteristics and Recording Techniques. In: *Neuro-ophthalmology* 1999. Philadelphia: Lippincott Williams & Wilkins:337.

6. Gamlin P. Neural Mechanisms for the Control of Vergence Eye Movements.*Ann N Y Acad Sci* 2002;956:264-272.

7. Gamlin PD, Yoon K. An area for vergence eye movement in primate frontal cortex.Nature 2000; 407**:**1003.

8. Akao T, Kurkin SA, Fukushima J, Fukushima K. Visual and vergence eye movement-related responces of pursuit neurons in the caudal frontal eye fields to motion-in-depth stimuli. *Exp Brain Res* 2005*;*164**:**92-108.

9. Alkan Y, Biswal BB, Alvarez TL. Differentiation between Vergence and Saccadic Functional Activity within the Human Frontal Eye Fields and Midbrain Revealed through fMRI. *PLoS ONE* 2011;6:1-14.

10. Richter HO, Costello P, Sponheim SR, Lee JT, Pardo JV. Functional neuroanatomy of the human near/far response to blur cues: eye-lens accommodative/vergence to point targets varying in depth. *Eur J Neurosci* 2004;20: 2722-2732.

11. Weist G, Mallek R, Baumgartne C. Selective loss of vergence control secondary to bilateral paramedian thalamic infarction. *Neurology* 2000;53:1997-1999.

12. Tai Y, Tang S, Jeng J. Spontaneous thalamic haemorrhage causing convergence excess. *Neuology* 2013*;*81:e23-4.

13. Mays LE. Neural control of vergence eye movements: Convergence and Divergence neurons in the midbrain.*J Neurophysio* 1984; 51:1091-1108.

14. Mays L, Porter J. Neurol Control of Vergence Eye Movements: Activity of Abducens and Oculomotor Neurons. *J Neurophysio* 1984; 52:743-761.

15. Cullen K, Van Horn M. The Neural Control of Fast vs Slow Vergence Eye Movements. *Eur J Neurosci* 2011; 33:2147-2154.

16. Zhang Y, Gamlin PD, Mays LE. Antidromatic identification of midbrain near responce cells projecting to the oculmotor nucleus. *Exp Brain Res* 1991;84**:**525-528.

17. Zhang Y, Mays LE, Gamlin PD. Characteristics of near responce cells projecting to the oculomotor nucleus. *J Neurophysio* 1992; 67:944-960.

18. Gamlin PD, Clarke RJ. Single-unit acitivity in the primate nucleus reticularis tegmenti pontis related to vergence and ocular accommodation. *J Neurophysio* 1995; **73**:2115-2119.

19. May PJ, Porter JD, Gamlin PD. Interconnections between the primate cerebellum and midbrain near-response regions. *J Comp Neurol* 1992; 315:98-116.

20. Kaufman PL, Levin LA, Alm A. *Adler's Physiology of the Eye.* Elsevier Health Sciences, 2011

21. Patestas M, Gartner LP. *A Textbook of Neuroanatomy*, 2nd edn. Hoboken, New Jersey: Wiley Blackwell, 2015

22. Shams PN, Bremmer FD, Smith ST, Plant GT,Matthews TD. Unilateral Light-Near Dissociation in Lesions of the Rostral Midbrain. *Arch Ophthalmol* 2010;128:1486-1489.

23. Gamlin P, Yoon K, Zhang H. The Role of Cerebro-ponto-cerebellar Pathways in the Control of Vergence Eye Movements. *Eye* 1996;10:167-171.

24. Ciuffreda KJ, Kapoor N, Rutner D, Suchoff IB, Han ME, Craig S. Occurrence of oculomotor dysfunctions in acquired brain injury: A retrospective analysis. *Optometry* 2007; 78**:** 155-61.

25. Master CL, Scheiman M, Gallaway M, Goodman A, Robinson RL, Master SR, Grady MF. Vision Diagnoses Are Common After Concussion in Adolescents. *Clin Pediatr (Phila) 2016;* 55 (suppl 3): 260-7

26. Pearce KL, Sufrinko A, Lau BC. Near Point of Convergence After a Sport-Related Concussion: Measurement Reliability and Relationship to Neurocognitive Impairment and Symptoms. *Am J Sports Med 2015;*43:3055-3061

27. Szymanowicz D, Ciuffreda KJ, Thiagarajan P, Ludlam DP, Green W,Kapoor N. Vergence in mild traumatic brain injury: A pilot study. *JRRD* 2012;49:1083-1100.

28. Capó-Aponte JE, Urosevich TG, Temme LA, Tarbett AK,Sanghera NK. Visual Dysfunctions and Symptoms During the Subacute Stage of Blast-Induced Mild Traumatic Brain Injury. *Mil Med* 2012;177:804-813.

29. Lindner K, Hitzenberger P, Drlicek M, Grisold W. Dissociated unilateral convergence paralysis in a patient with thalamotectal haemorrhage. *J Neurol Neurosurg* Psychiatry 1992;55:731-733.

30. Saalman Y, Kastner S. Cognitive and Perceptual Functions of the Visual Thalamus. *Neuron* 2011;**71:**209-223.

31. Wilke M, Turchi J, Smith K, Mishkin M, Leopold DA. Pulvinar Inactivation disrupts Selection of Movement Plans. *J Neurosci* 2010;30:8650-8659.

32. Rowe FJ,VIS Group. Ocular motility consequences of thalamic infarcts. Trans. 33rd European Strabismological association. Belgrade, Serbia 2009:59-62

33. Kumral E, Kocaer T, Ertubey N, Kumral K. Thalamic Hemorrhage. A prospective study of 100 patients. *Stroke* 1995;26:964-970.

34. Barraquer-Bordas L, Escartin A, Ruscalleda J. Thalamic hemorrhage: a study of 23 patients with diagnosis by computed tomography. *Stroke* 1981;12:524-527.

35. Hertle R, Bienfang D. Oculographic Analysis of Acute Esotropia Secondary to a Thalamic Hemorrhage. *J Clin Neuroophthalmol* 1990;;10:21-26.

36. Dickson D. Parkinson's Disease and Parkinsonism: Neuropathology. *Cold Spring Harb Perspect Med* 2012;2:15.

37. Hardiman O, Doherty CP. *Neurodegenerative disorders [electronic book]: a clinical guide.* London; New York: Springer, 2011.

38. Lepore F. Parkinson's Disease and Diplopia. *Neuro-ophthalmol* 2006;30:37-40.

39. Repka M, Claro M, Loupe D, Reich S. Ocular Motility in Parkinson's disease. *J Pediatr Ophthalmol Strabismus* 1996; 33:144-147.

40. Biousse V, Skibell BC. Watts RL, Loupe DN, Drews-Botsch C, Newman NJ. Ophthalmologic features of Parkinson's disease. *Neurology* 2004;62:177-180.

41. Kitthaweesin K, Riley D, Leigh R. Vergence Disorders in Progressive Supranuclear Palsy. *Ann N T Acad Sci* 2002;956:504-507.

42. Molinuevo J, Valls-Solé J, Valldeoriola F. The effect of transcranial magnetic stimulation on reaction time in progressive supranuclear palsy. *Clin Neurophysiol* 2000;111:2008-2013.

43. Ohtsuka K, Maeda S, Oguri N. Accommodation and convergence palsy caused by lesions in the bilateral rostral superior colliculus. *Am J Ophthalmol* 2002;133425-427.

44. Ogasawara K, Kato C, Mori T, Tamura K. Impairment of convergence due to a lesion in the rostral part of the superior colliculus. *Neuro-ophthalmol* 2003;28:7-11.

45. Mustari MJ, Ono S, Das VE. Signal Processing and Distribution in Cortical-Brainstem Pathways for Smooth Pursuit Eye Movements. *Ann N Y Acad Sci* 2009;1164:147-154.

46. Rambold H, Sander T, Neumann G, Helmchen C. Palsy of "fast" and "slow" vergence by pontine lesions. *Neurology* 2005;64:338-340.

47. Tsuda H, Shikawa H, Koga N. Magnetic resonance imaging findings in divergence paralysis. *Neuro-ophthalmol* 2006;30:59-62.

48. Westheimer G, Blair SM. Oculomotor defects in cerebellectomized monkeys. *Investig Ophthalmol* 1973;12:618-621.

49. Sander T, Sprenger A, Neurmann G, Machner B, Gottschalk S, Rambold H et al. Vergence deficits in patients with cerebellar lesions. *Brain* 2009;132:103-115.

50. Bender MB, Savitsky N. Paralysis of divergence. *Arch Ophthalmol* 1940;23:1046-1051.

51. Lee SA, Sunwoo IN, Kim KW. Divergence paralysis due to a small hematoma in the tegmentum of the brainstem. *Yonsei Med J* 1987;28:326-328.

52. Fujioka T, Kurihara T, Kinoshita M. Divergence paralysis due to a lesion of the lateral tegmentum of the midbrain caused by a thalamic haemorrhage. *Rinsho Shinkeigaku* 1992;32:767-770.

53. Tsuda H, Kamata K, Tanaka K, Kishida S. Magnetic resonance Imaging Finding in Divergence Paralysis. *Neuro-Ophthalmol* 2012;36:52-53.

54. Tsuda H, Shinozaki Y, Tanaka K, Ohashi K. Divergence paralysis caused by acute midbrain infarction. *Intern Med* 2012;51:3169-3171.

55. Lepore FE. Divergence paresis: A nonlocalising cause of diplopia. *J Neuroophthalmol* 1999;19:242-245.

Figure 1 Schematic diagram of the areas in the thalamus causing convergence disorders secondary to thalamic haemorrhage or lesions in the pulvinar nuclei.

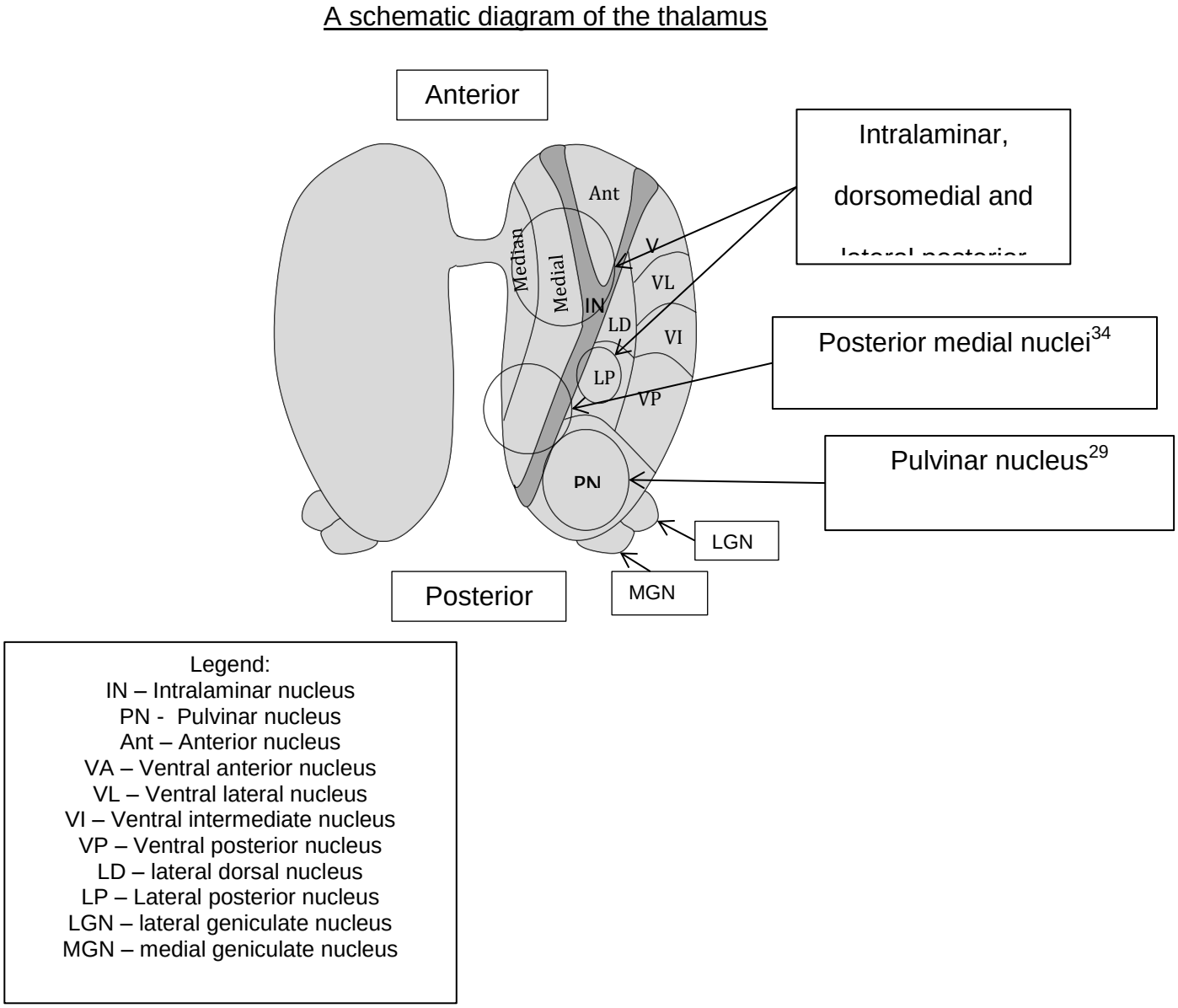


Figure 2 Schematic diagrams showing the brainstem and cerebellum. Areas highlighted indicate the area of a lesion identified to have an involvement with the convergence pathway.

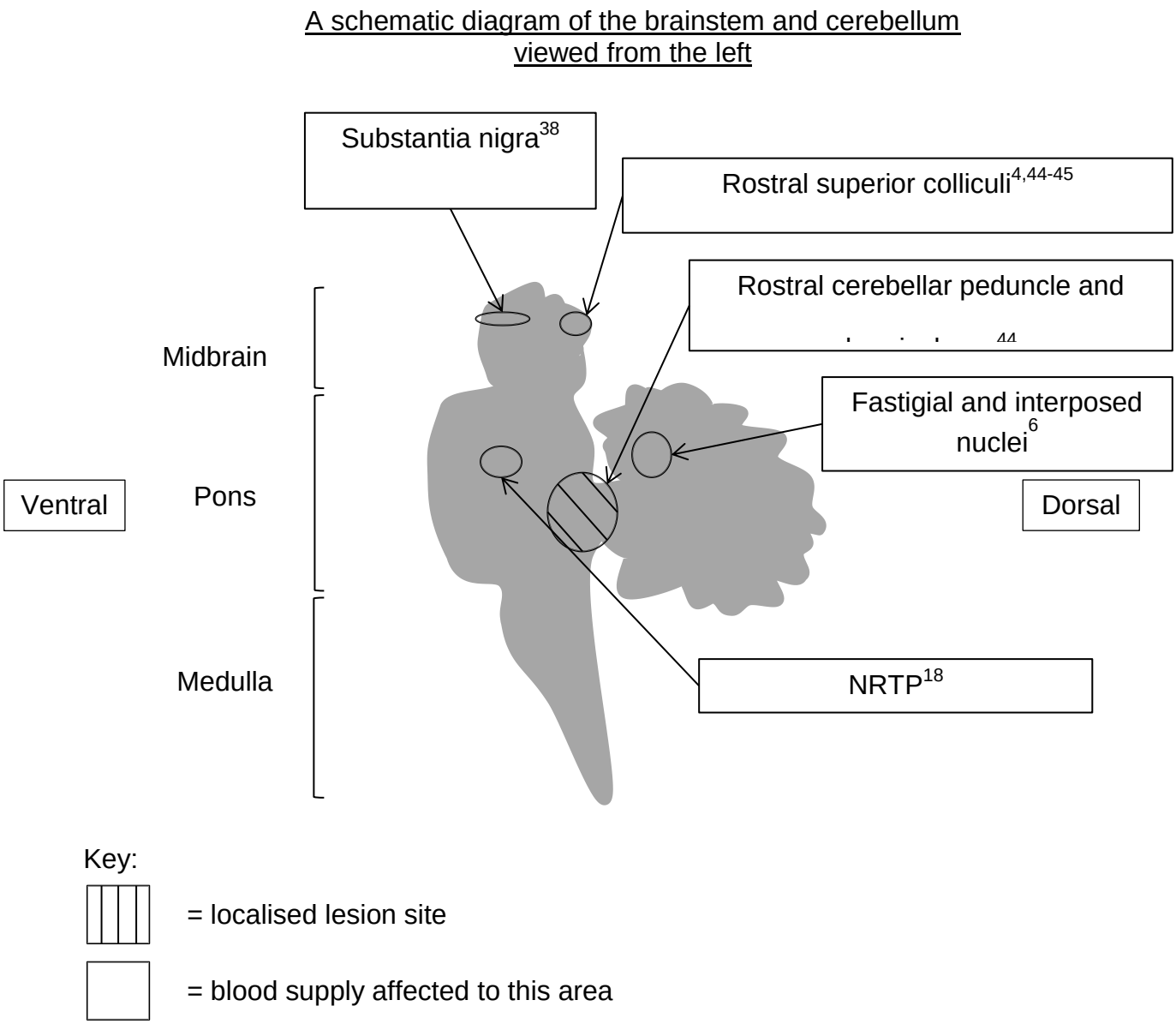
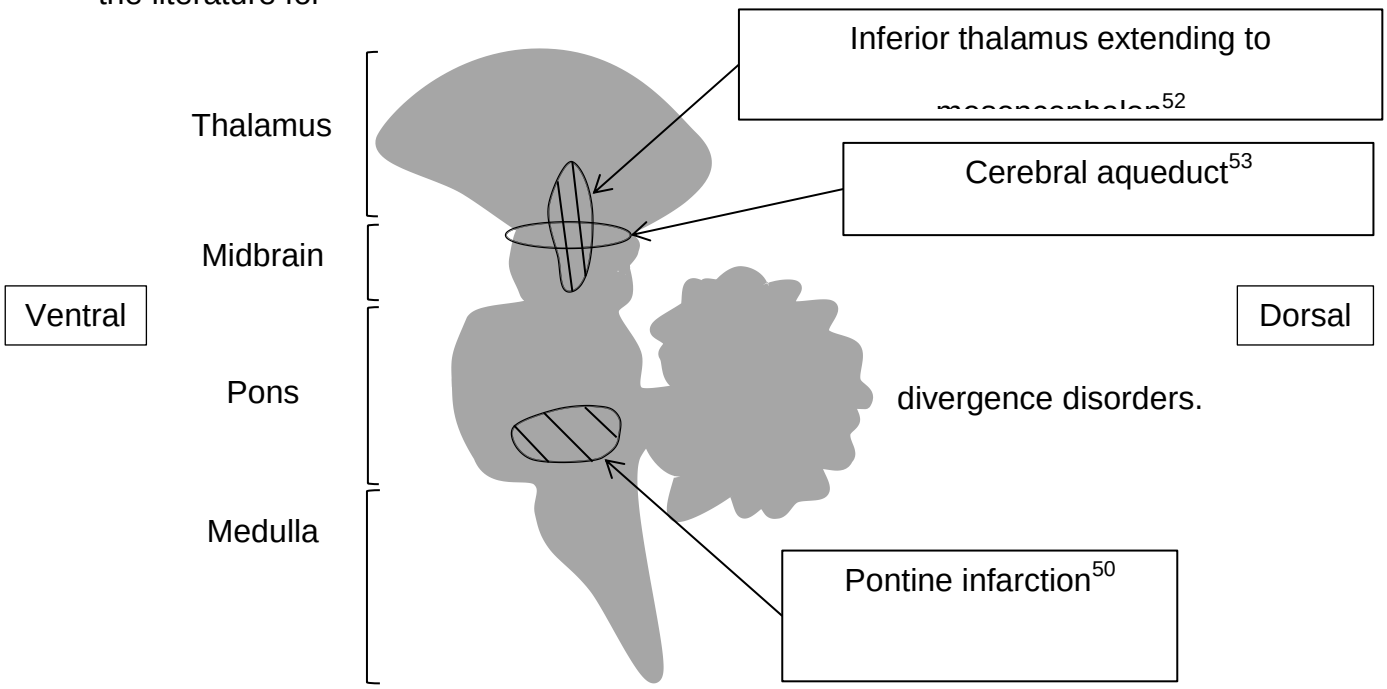


Figure 3 Schematic diagrams of the brainstem and thalamus. Locations identified represent the lesions noted in the literature for divergence disorders.



Thalamus and brainstem viewed from the right.