The Relationship between Saccades and Locomotion

Anshul Srivastava,1 Omar F. Ahmad,1 Christopher Pham Pacia,2 Mark Hallett,1 Codrin Lungu3

1Human Motor Control Section, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, MD, USA
2Department of Biomedical Engineering, Washington University in St. Louis, Saint Louis, MO, USA
3Division of Clinical Research, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, MD, USA

ABSTRACT

Human locomotion involves a complex interplay among multiple brain regions and depends on constant feedback from the visual system. We summarize here the current understanding of the relationship among fixations, saccades, and gait as observed in studies sampling eye movements during locomotion, through a review of the literature and a synthesis of the relevant knowledge on the topic. A significant overlap in locomotor and saccadic neural circuitry exists that may support this relationship. Several animal studies have identified potential integration nodes between these overlapping circuitries. Behavioral studies that explored the relationship of saccadic and gait-related impairments in normal conditions and in various disease states are also discussed. Eye movements and locomotion share many underlying neural circuits, and further studies can leverage this interplay for diagnostic and therapeutic purposes.

Key Words
Gait; posture; saccade; fixation; locomotion; deep brain stimulation.
INTRODUCTION

Visual information from the environment is gathered through quick eye movements, which consist of a series of saccades and fixations. Saccades align the fovea with an object of interest.1 Once an object is foveated, it is held stationary during a fixation, allowing time for the visual information to be collected.1 Efficient locomotion is dependent upon visual information that is gathered by these quick eye movements. Understanding the relationship among fixations, saccades and locomotion may provide insight into how these seemingly parallel and potentially integrated systems work together.

When studied independently, saccadic and locomotor parameters (Table 1) can be measured precisely. It is difficult to reach the same level of precision when measuring both parameters simultaneously. To get around this, most studies in the literature have correlated saccadic eye movement or gait-related parameters2,3 with a given disease state or functional impairment.

In this review, we explore the literature for correlations made between saccades and locomotion. We present the neural circuitry of saccadic and gait-related circuitry and the similarities between them. We highlight brain regions that have been found in animal studies that potentially integrate these two networks. Lastly, we review neurodegenerative diseases that manifest saccadic and gait-related impairments.

NEURAL COMPONENTS OF SACCADES, FIXATIONS AND LOCOMOTION

Fixation, saccades and locomotion are served by specific areas and networks of the brain. It is particularly interesting to compare the neural components of saccades and locomotion because there are many overlapping brain areas, suggesting a potential integrated neural network between them.

The most relevant areas that support neural integration between saccades and locomotion would likely be at the level of the brainstem and the cerebellum (Figure 1). Afferent inputs between these two parallel networks differ greatly, in that spinal cord pathways provide the majority of sensory information for locomotion, while the geniculate and extrageniculate pathways are important for saccades. On the other hand, modulating structures such as the cerebral cortex, basal ganglia and thalamus are common to all sensorimotor networks and are non-specific to locomotion and saccades. Saccades and locomotion are primitive functions, are well-developed in lower species4,5 and are more likely to be preserved in primitive integrating brain areas, such as the brainstem and cerebellum, more specifically, the mesopontine tegmentum and the cerebellar vermis.

| Table 1. Eye movement/fixation parameters and gait/balance parameters |
|--------------------|------------------------------------------------------------------|
| **Saccadic/fixation parameters**^2 | **Gait/balance parameters**^2 |
| Fixation duration | Distance between initial ground contact of one foot and initial ground contact of the opposite foot. |
| Saccadic duration | Time in seconds between initial ground contact of one foot and initial ground contact of the opposite foot. |
| Saccadic latency | Lateral distance between the centers of the heels when both feet are on the ground (i.e., double stance). |
| Saccadic amplitude | Distance between initial ground contact of one foot and initial ground contact of the opposite foot, constituting the distance of one gait cycle. |
| Saccadic peak velocity | Time between initial ground contact of one foot and initial ground contact of the same foot, constituting the time of one gait cycle. |
| Saccadic intrusions | Horizontal movement of the center of gravity while standing still. |
| Saccadic gain | Remaining 40% of the gait cycle, when the foot no longer is in contact with the ground, spanning from initial swing phase to initial contact. |
| Main sequence | Steps per minute. |
| **Step length** | Initial 60% of the gait cycle, when the foot is in contact with the ground, spanning from initial contact to terminal double stance. |

^2 Eye movement/fixation parameters and gait/balance parameters are measured in millimeters, milliseconds, seconds, millimeters/second, and degrees, respectively.
The PPN contains cholinergic, glutaminergic and GABAergic neurons; the cholinergic neurons are those closely associated with locomotion.15 PPN cholinergic neurons are also associated with rapid eye movements in sleep.15 The PPN directly innervates the motor neurons involved in eye movements and receives direct projections from the frontal and supplementary eye fields in the cortex.16-20 Neuronal recordings of the PPN in primates have shown different firing patterns during fixations and saccades.21,22

The PPN receives input from the cerebral cortex and has reciprocal connections with components of the basal ganglia, namely, the substantia nigra [both the substantia nigra pars reticulata (SNr) and the substantia nigra pars compacta (SNC)], globus pallidus and subthalamic nucleus (STN).23-28
explored. The PPRF receives input from the frontal eye fields (FEF) through the contralateral SC and contains burst neurons that generate horizontal saccades.

**Pontomesencephalic reticular formation**

Reticulospinal neurons in the pontomesencephalic reticular formation are involved in controlling and maintaining head movements and in generating the quick phase of vestibular and optokinetic head nystagmus toward the same side. Omnidirectional pause neurons (OPNs) are inhibitory interneurons in the pontomesencephalic reticular formation that are thought to stabilize fixations and saccades in the horizontal, vertical and oblique directions. OPNs are tonically active during fixations and are silent (i.e., “paused”) during saccades. Dysfunction in OPNs is thought to result in fixational instability, with reports of macrosaccadic oscillations, saccadic dysmetria, ocular flutter, and opsoclonus. The pontomesencephalic reticular formation is also involved in transmitting locomotor signals to central pattern generators in the spinal cord and in controlling balance, locomotion and posture.

**Cerebellar vermis**

The cerebellum is involved in both locomotion and saccades. The fastigial nucleus (FN) of the cerebellum receives input from the vermis, which in turn receives input from the SC through the nucleus reticularis tegmenti pontis. Brainstem saccade generators are driven by the FN and the vermis. Studies of transcranial magnetic stimulation directed toward the cerebellar vermis have demonstrated that this area coordinates saccades ipsilateral to the side of stimulation. Neuronal discharge in the FN, also known as the cerebellar locomotor region, is linked to coding of proximal movement during locomotion. The FN is thought to act as a pacemaker during locomotion and projects to the pontomedullary reticular formation in the brainstem.

**Thalamus**

The thalamus serves as the major relay between cortical and subcortical saccadic generators. The internal medullary lamina, a myelinated area that divides the thalamus into the anterior, medial and lateral masses, contains nuclei that relay information among multiple areas that control saccades, namely, the frontal and parietal eye fields, SC, PPRF, striatum, cerebellum and the lateral geniculate nuclei.

The lateral geniculate nuclei and pulvinar are two thalamic nuclei in the ventrolateral area that specifically process visual input. The lateral geniculate nucleus projects information from the retina to the VC. Connections between the SC and the lateral geniculate nucleus contribute to saccades that are involved in foveating objects of interest with a high degree of resolution (e.g., facial recognition). The pulvinar has connections between the SC and visual cortices and is involved in visuospatial attention to areas in the visual field. The pulvinar is an important relay for generating saccades toward visual targets or reflexive saccades toward or away from stimuli, and this nucleus influences visually guided behavior, including locomotion. It has been speculated that visual and motor information may be integrated in the pulvinar, allowing a distinction between changes in the visual environment caused by external sources versus self-generated visual motion (caused by eye movements or locomotion).

The ventrolateral nucleus (VL) receives all major saccade-generating afferents in the brainstem and cerebellum and projects to the frontal eye field and the supplementary eye field. Similar to the pulvinar, the VL is closely involved in visually guided saccades. The VL is also a major afferent to the primary motor cortex, and it is not surprising that this region is important for locomotion. The thalamic reticular nucleus is a thin capsule of inhibitory GABAergic neurons that surrounds the dorsolateral thalamus and functions to modulate thalamocortical and corticothalamic signals for a multitude of functions. In terms of saccadic and locomotor networks, this region functions as an inhibitory modulator. The thalamic reticular nucleus sends reciprocal inhibitory signals to the lateral geniculate nucleus in response to saccade-related visual perturbations to maintain a stable image. Recordings have revealed phasic bursts of activity in reticular neurons within the receptive field of distal limbs during walking tasks that are thought to fine tune ongoing locomotor activity.

**Basal ganglia**

The basal ganglia refers mainly to the caudate and the putamen, which consist of the striatum, globus pallidus, substantia nigra and STN. The nigrostriat-
tal pathway modulates the striatum, affecting all motor output, and is not specific to saccadic or locomotor control, though its influence over these functions is considerable. The STN receives inputs from the cortex via the striatum and the globus pallidus externa (GPe) through the indirect pathway and direct connections from the cortex through the hyperdirect pathway. The STN receives inputs from the brainstem, thalamus and cortex. Efferents from the STN travel mainly to the GPi and SNr. There is evidence that patients with Parkinson disease (PD) who receive deep brain stimulation (DBS) of the STN experience a significant improvement in both saccadic performance and locomotion compared to patients that receive other DBS targets, such as the globus pallidus interna (GPI). GPi DBS has been shown to improve locomotion, but there is less evidence supporting an improvement in saccadic performance, though one study found improvement in antisaccades.

ANIMAL STUDIES EXPLORING THE INTEGRATION BETWEEN EYE MOVEMENT AND LOCOMOTOR CIRCUITRY

Thus far, we have identified brain areas that are common to both saccades and gait in humans. Animal studies have provided much of the direct evidence for the integration of networks controlling saccades and gait.

Semi-intact experiments in lampreys undergoing electrical stimulation of the optic tectum have demonstrated a stimulus-dependent coordination of eye movements with steering and goal-directed behavior. Saitoh et al. showed that, with increasing stimulation of the lateral optic tectum, there is a stepwise recruitment of eye movements, followed by a coordinated lateral bending of the body, and then by coordinated locomotor movements. Stimulating other areas, such as the caudomediale tectum, elicits different behaviors, such as struggling behavior, characterized by undulating body movements with antiphasic eye movements. These experiments have lent support for the role of the optic tectum (SC in primates) as a stepwise integrating interface for patterned visuomotor and locomotor behavior.

The coordination between eye movements and spinal locomotor patterns is also preserved and adaptable at different stages of development. Uckerman et al. demonstrated how the Xenopus laevis (XL) frog adapts visuomotor control to maintain image stabilization when swimming as it transitions from a tadpole to an adult frog. In the tadpole, propulsion is achieved with undulating tail movements, requiring conjugate left-right eye rotations to maintain a stable binocular image. In the frog, forward acceleration is achieved with rhythmic bilateral leg kicking that requires nonconjugate, convergent-divergent, eye movements. In fixed-head preparations, a strict 1:1 relationship was found between eye movements and spontaneous fictive swimming movements. Vestibular and visual input were controlled for by transecting the optic nerves and ablating the vestibular end organs. In tadpoles, the eyes rotate laterally, countering each lateral tail movement, while in frogs, the eyes converge or diverge in phase with the kick cycle. This experiment provided evidence for multimodal integration between spinal central pattern generators and eye movements during locomotion in XL. More importantly, the ability of visuomotor and locomotor networks to change in a coordinated fashion at different stages of development in XL suggested that they are integrated. This adaptability is probably evolutionarily preserved in other forms of locomotion, such as quadrupedal and bipedal ambulation. The OPN, as mentioned earlier, coordinates horizontal, vertical and oblique fixations and saccades. It is possible that the omnidirectional stabilizing capability of these interneurons provides a mechanism for the adaptability of reflexive saccades to different locomotive head perturbations across species.

Schwarz et al. performed microelectrode recordings of nondopaminergic SNr neurons in cats as they received different sensory stimuli, such as mechanical skin stimulation, passive and active limb movement, and visual and vestibular stimuli. Neurons within the receptive field of each limb showed regular discharge patterns that were in phase with the step cycle during locomotion. Avoiding or navigating around an obstacle had the greatest effect on neuronal firing rates. Objects moving within the contralateral visual field modulated the firing rates of a small population of neurons related to saccades. Similar findings of saccades and neuronal discharge in the SNr have been found in monkeys. The authors concluded that the SNr functions as an output...
station that processes convergent multimodal sensory input (e.g., joint position, limb movement, direction and amplitude of saccades) and fine tunes spinal motor output to adequately address changing environments.

The PPN has also been suggested to serve as a multimodal integrative interface. Suppression of spontaneous locomotion and rhythmic eye movements was observed with stimulation of the ventral PPN in anesthetized and acutely decerebrated cats. Saccade-related and locomotion-related neuronal activity has been reported in Purkinje cells in the cerebellar vermis in various studies using microstimulation and optogenetic techniques in non-human primates and other mammals.

The SC and PPRF have been shown in rhesus monkeys to influence coordinated head-eye movements, an important component of steering during locomotion.

Saleem et al. showed that, in order for mice to accurately gauge their speed when navigating their environment, visual speed, derived from optic input, and running speed, derived from proprioceptive input, are integrated and encoded with weighted sums within the neurons of the V1 area of the occipital cortex. While this does not pertain to eye movements per se, it at least provides more evidence linking visual sampling (which requires adequate saccades and fixations) and locomotion.

While numerous studies have suggested a multimodal integration between saccades and locomotion, the challenge of establishing a neural basis for this interaction, especially in humans, is hindered by the technical limitations related to studying the circuitry of eye movements during the act of walking. Therefore, the level at which these circuits interact with each other in real time and how activating or inactivating various nodes within one neural circuit may affect the functions of the other are not yet known.

BEHAVIORAL STUDIES IN HEALTHY INDIVIDUALS
EXPLORING THE RELATIONSHIP AMONG SACCADES, FIXATIONS AND LOCOMOTION

During ambulation, the limbs, body, head and eyes move in a coordinated manner. Saccadic eye movements allow the fovea to maintain fixations on relevant objects in the environment in a dynamic manner to allow guidance of locomotion. Any problems in this fixation-saccade strategy may lead to visual and gait impairments.

The visuomotor and locomotor systems influence each other via a continuous feedback loop, though the exact network is not well delineated. Several studies have focused on gaze fixations and saccadic eye movements during stepping to describe how eye movements influence gait parameters. In one study, visual information gathered during the latter half of the preceding step was shown to influence the step length of the following step. It has also been suggested that, while walking on uneven ground or terrain, visual information from two steps is required to direct foot placement.

Marigold and Patla found that, when walking on a varying terrain, participants visually fixated on areas of the ground where they eventually stepped. Additionally, fixations were frequently guided to the transition zones between the varying surfaces (e.g., solid to compliant, rocky to slippery, tilted to irregular, etc). Hollands and Marple-Horvat studied the eye movements of healthy participants who were made to walk in different conditions that varied in terms of the amount visual information available to the participants as they stepped onto stepping stones. The time interval between saccadic onset and footlift was similar in all conditions, but the interval between saccadic onset and footfall onto the stepping target differed significantly depending on the amount of visual information present. Patla and Vickers found that healthy participants fixated on footfall targets that were an average of two steps ahead. Elderly participants with a history of falls tended not to look two steps ahead but instead fixated more on the imminent footfall target. This finding may be the result of impaired central processing of visually guided information in that group, as suggested in another study, in which elderly participants with a high risk of falling had longer latencies from saccadic initiation to footlift than elderly individuals with a low risk of falling.

Saccades were also studied in individuals during turning maneuvers. These studies supported a “topdown” model, in which saccadic initiation precedes, and possibly influences, turning of the head, trunk and legs. Imai et al. observed that when participants were asked to move in a straight line and
Saccades and Locomotion

Srivastava A, et al.

www.e-jmd.org

99

turn 90 degrees, a saccade was made in the direction of the turn. A similar observation was made by Hollands et al., in which healthy participants made saccades in order to position their gaze in line with the endpoint of the required travel path.

Anxiety can influence the interplay between gait and saccades. It has been suggested that early gaze transfer due to anxiety over impending obstacles is correlated with stepping inaccuracies. Investigators observed the visual and stepping behavior of an 87-year-old female when she was directed to walk along a stepping path before and after an obstacle. At the beginning of the experiment, she fixated on the stepping path before the obstacle. After falling twice, she stopped fixating on the stepping path, and instead fixated on the obstacle itself. In a similar study, elderly participants with a high risk of falling were more likely to transfer their gaze early from a stepping target along a path to an impending obstacle. One study indirectly showed a relationship between saccades and gait during an episode of anxiety/fear, in which participants with a fear of heights made more vertical than horizontal saccades when walking on a fire escape 20 meters above ground compared to the saccades of the controls. The amygdala plays an important role in anxiety and has been found to be involved in saliency coding when scanning a visual scene. States of increased anxiety may disrupt fixations and saccades through this pathway.

The relationship between saccades and gait was observed in healthy participants as they moved along a pathway with irregularly placed stepping stones, both with and without an alcohol dose. Gait impairments were observed in terms of increased step cycle durations and missed footfall targets. In terms of saccadic impairments, a large proportion of the saccades of the successive stepping stones were inaccurate and were accompanied by corrective saccades. Alcohol has been shown to cause saccadic dysmetria. The combination of impaired saccadic control and stepping accuracy implicates the cerebellum [See Supplementary Table 1 (in the online only Data Supplement) for summary of the studies of this section].

SACCADES AND GAIT IN NEURODEGENERATIVE DISEASES

While saccadic and gait abnormalities have been studied separately in various neurodegenerative disorders (Table 2), simultaneous recordings of eye movements and gait in these disorders have rarely been reported.

PD is well known as having both saccadic and gait abnormalities. In PD, both saccades and step length can be hypometric. Side-to-side asymmetry, in terms of step length and saccadic amplitude, is often seen in PD. Nemanich and Earhart reported that, in PD, freezing of gait is associated with increased saccadic latency and variability. The researchers found that PD patients with freezing of gait were slower in initiating pro- and antisaccades. Saccadic velocity and gain variability were also increased in PD with freezing of gait. Performance of antisaccades was impaired in PD patients with freezing of gait compared to patients without freezing.

| Disorder          | Saccadic abnormalities                                                                 | Gait abnormalities                                                                 |
|-------------------|---------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|
| Essential tremor  | Slow saccades and increased square-wave jerks                                        | Tandem gait difficulty                                                              |
| PD                | Hypometric saccades and prolonged saccadic latency                                     | Freezing of gait, falls, turning impairment, and decreased stride length             |
| PSP               | Fixational saccades that are abnormally large. Square wave jerks more frequent, larger, and markedly more horizontal | Hypokinetic gait characteristics: decreased velocity and step length, Interstep variability and asymmetry during gait. Slower cadence. Freezing of gait and frequent falls |
| Huntington disease| Slow saccades                                                                          | Gait characteristic variation in each walk, with mean decreases in velocity, stride length, and cadence. Decreased gait velocity, Disordered regulation of footstep timing; reduced stride length |
| Cerebellar ataxia | Square-wave jerks, saccadic dysmetria, and reduced saccadic velocity                   | Decreased step length, stride length, and gait speed                                |

PD: Parkinson disease, PSP: progressive supranuclear palsy
other study, saccadic frequency was found to increase in both patients with PD and their age-matched controls when approaching a turn, but the PD patients made fewer preparatory saccades than the controls before the turn.\textsuperscript{178,179} During the turn, the PD patients made more saccades, and the saccadic velocity was slower than that of the controls.\textsuperscript{180}

The likely neural components affecting both saccades and locomotion in PD include the STN, the SNr, and the MLR/MFR.\textsuperscript{175} In PD, degeneration of dopaminergic neurons in the SNc affects the direct and indirect pathways, resulting in bradykinetic movements that affect locomotion and saccades. More specifically, there is increased excitation of the STN, causing an increased inhibitory effect of the GPi and SNr through the indirect pathway. As mentioned earlier in the current review, DBS of the STN affects both saccadic and locomotor performance when compared to DBS of the GPi.\textsuperscript{191-197} In terms of eye movements, the effect on these pathways in PD results in increased excitation of the SNr, which leads to abnormal saccade generation in the SC. There is also increased excitation of the PPN, which, as mentioned previously, has projections that are related to saccades and locomotion. In a recent imaging study, PPN alterations were suggested to be related to both saccadic and postural impairments in patients with PD.\textsuperscript{181} It was observed that functional connectivity involving the PPN and FEF correlated with antisaccadic latencies in healthy participants but not in PD patients with postural instability. Additionally, saccadic impairment correlated with gait initiation impairment in patients.

Additional examples of neurological disorders with abnormal saccades and postural instability other than PD\textsuperscript{182,183} include progressive supranuclear palsy,\textsuperscript{184} cerebellar ataxia,\textsuperscript{185} essential tremor,\textsuperscript{186} and Huntington disease.\textsuperscript{187,188} Some studies have reported that abnormalities in saccadic eye movements are correlated with body sway, even in healthy individuals.\textsuperscript{189,190,191} These findings of these studies reflect an integration between postural dynamics and eye movements.

Patients with cerebellar ataxia have ataxic gait and dysmetric saccades. Dysmetric saccades consist of hypometric or hypermetric initial saccades, followed by a corrective saccade. TMS studies have implicated the ipsilateral cerebellar vermis in saccadic dysmetria.\textsuperscript{68} Studies of visual fixation in patients with cerebellar ataxia have discovered the presence of dysmetric saccades. During locomotor tasks with visually guided stepping, both dysmetric saccades and ataxic gait were detected.\textsuperscript{191,192} Other studies have found correlations between efficient footfalls and oculomotor function\textsuperscript{127,129,130} in healthy subjects.

Studies of saccadic performance in patients with gait impairment could provide insight into how eye movements affect motor abnormalities such as freezing of gait, imbalance, turning difficulties and falls. Beyond that, saccadic eye movement training as a gait rehabilitation strategy could be an important therapeutic option. Some studies have reported saccadic eye movement training as a strategy for alleviating gait abnormalities in terms of improvement in

Table 3. Eye movement training and gait

| Authors | Year | Participants | Method | Main findings |
|---------|------|--------------|--------|--------------|
| Zampieri and Di Fabio\textsuperscript{193} | 2008 | 19 moderately affected progressive supranuclear pals patients | Balance training and eye movement exercises | Improvements in stance time and walking speed in the treatment group |
| Eye movement training: eye movement practice on the computer screen with randomly appearing arrows on the screen |
| Crowdy et al\textsuperscript{194} | 2002 | 2 cerebellar patients | Foot placement (stepping task) | Improvements in oculomotor and locomotor performance following eye-movement rehearsal |
| Eye movement training: rehearsal of saccades for footfall targets in a stationary standing condition |
| Kang and Yu\textsuperscript{195} | 2016 | 14 stroke patients | Foot placement (stepping task) | Improvements in walking speed, step length and cadence |
| Eye movement training: visual scanning of the picture cards, fixating gaze on a moving baton |
stance time and accuracy in stepping in patients (Table 3).193-195

CONCLUSIONS AND FUTURE DIRECTIONS

Eye movements and locomotion share common neural substrates and potentially have interlinked neural circuitry. The mesopontine tegmentum and cerebellar vermi are the most likely areas to have specific neural connections between these parallel networks. Physiological studies in animals and behavioral studies in healthy individuals have supported the hypothesis that these connections are preserved and adaptable across species. Many neurodegenerative disorders demonstrate coexisting eye movement and gait abnormalities. Correlations have been made in these disease states, further providing evidence of interlinked neural circuitry. As the technology of mobile eye-tracking improves, future studies exploring eye movement abnormalities in real time with simultaneous gait recording will further elucidate the interplay between these two networks. In addition, such studies may potentially serve to develop new diagnostic or disease severity markers.

Supplementary Materials

The online-only Data Supplement is available with this article at https://doi.org/10.14802/jmd.18018.

Conflicts of Interest

The authors have no financial conflicts of interest.

REFERENCES

1. Purves D, Augustine GJ, Fitzpatrick D, Hall WC, LaMantia AS, McNamara JO, et al. Eye movements and sensory motor integration. In: Purves D, Augustine GJ, Fitzpatrick D, Hall WC, LaMantia AS, McNamara JO, et al. editors. Neuroscience. 3rd ed. Sunderland, MA: Sinauer Associates, Inc., 2004;453–467.
2. Holmqvist K, Nyström M, Andersson R, Dewhurst R, Jarodzka H, van de Weijer J. Eye Tracking: A Comprehensive Guide to Methods and Measures. 1st ed. Oxford: Oxford University Press, 2011;537.
3. Hollman JH, McDade EM, Petersen RC. Normative spatio-temporal gait parameters in older adults. Gait Posture 2011;34:111-118.
4. Harcourt-Smith WE, Aiello LC. Fossils, feet and the evolution of human bipedal locomotion. J Anat 2004;204:403-416.
5. Walls GL. The evolutionary history of eye movements. Vision Res 1962;2:69-80.
6. Rycklo D, Dubuc R. The multifunctional mesencephalic locomotor region. Curr Pharm Des 2013;19:4448-4470.
7. Graf WM, Ugolini G. The central mesencephalic reticular formation: its role in space-time coordinated saccadic eye movements. J Physiol 2006;570:433–434.
8. Waitzman DM, Silakov VL, Cohen B. Central mesencephalic reticular formation (cMRF) neurons discharging before and during eye movements. J Neurophysiol 1996;75:1546–1572.
9. Perkins E, May PJ, Warren S. Feed-forward and feedback projections of midbrain reticular formation neurons in the cat. Front Neuroanat 2014;7:55.
10. Skinner RD, Kinjo N, Henderson V, Garcia-Rill E. Locomotor projections from the pedunculopontine nucleus to the spinal cord. Neuroreport 1990;1:183-186.
11. Garcia-Rill E, Skinner RD, Fitzgerald JA. Activity in the mesencephalic locomotor region during locomotion. Exp Neurol 1983;82:609-622.
12. Garcia-Rill E, Houser CR, Skinner RD, Smith W, Woodward DJ. Locomotion-inducing sites in the vicinity of the pedunculopontine nucleus. Brain Res Bull 1987;18:731-738.
13. Sherman D, Fuller PM, Marcus J, Yu J, Zhang P, Chamberlin NL, et al. Anatomical location of the mesencephalic locomotor region and its possible role in locomotion, posture, cataplexy, and parkinsonism. Front Neuro 2015;6:140.
14. Takakusaki K, Saitoh K, Harada H, Okumura T, Sakamoto T. Evidence for a role of basal ganglia in the regulation of rapid eye movement sleep by electrical and chemical stimulation for the pedunculopontine tegmental nucleus and the substantia nigra pars reticulata in decerebrate cats. Neuroscience 2004;124:207-220.
15. Garcia-Rill E, Hyde J, Kezunovic N, Urbano FJ, Petersen E. The physiology of the pedunculopontine nucleus: implications for deep brain stimulation. J Neural Transm (Vienna) 2015;122:225-235.
16. Cohen B, Waitzman DM, Büttnier-Ennever JA, Matsuo V. Horizontal saccades and the central mesencephalic reticular formation. Prog Brain Res 1986;64:243-256.
17. Huerta MF, Krubitzer LA, Kaas JH. Frontal eye field as defined by intracortical microstimulation in squirrel monkeys, owl monkeys, and macaque monkeys: I. Subcortical connections. J Comp Neurol 1986;253:415-439.
18. Stanton GB, Goldberg ME, Bruce CJ. Frontal eye field efferents in the macaque monkey: I. Subcortical pathways and topography of striatal and thalamic terminal fields. J Comp Neurol 1988;271:473-492.
19. Huerta MF, Kaas JH. Supplementary eye field as defined by intracortical microstimulation: connections in macaques. J Comp Neurol 1990;293:299-330.
20. Shook BL, Schlag-Rey M, Schlag J. Primate supplementary eye field: I. Comparative aspects of mesencephalic and pontine connections. J Comp Neurol 1990;301:618-642.
21. Okada K, Kobayashi Y. Fization saccade-related activity of pedunculopontine tegmental nucleus neurons in behaving monkeys. Eur J Neurosci 2014;40:2641-2651.
22. Okada K, Kobayashi Y. Rhythmic firing of pedunculopontine tegmental nucleus neurons in monkeys during eye movement task. PLoS One 2015;10:e0128147.
23. Lavoie B, Parent A. Pedunculopontine nucleus in the squirrel monkey: projections to the basal ganglia as revealed by anterograde tract-tracing methods. J Comp Neurol 1994;344:210-231.
24. Matsunura M, Nambu A, Yamaji Y, Watanabe K, Inai H, Inase M, et al. Organization of somatic motor inputs from the frontal lobe to the pedunculopontine tegmental nucleus in the macaque monkey. Neuroscience 2000;98:97-110.
25. Martinez-Gonzalez C, Bolam JP, Mena-Segovia J. Topo-
graphical organization of the pedunculopontine nucleus. Front Neuroanat 2011;5:22.
26. Martinez-Gonzalez C, van Andel J, Belam JP, Mena-Segovia J. Divergent motor projections from the pedunculopontine nucleus are differentially regulated in Parkinsonism. Brain Struct Funct 2014;219:1451-1462.
27. Lau B, Welter ML, Belaid H, Fernandez Vidal S, Bardinet E, Grabli D, et al. The integrative role of the pedunculopontine nucleus in human gait. Brain 2015;138:1284-1296.
28. Strumpf H, Noesselt T, Schoenfeld MA, Voges J, Panther P, Kaufmann J, et al. Deep brain stimulation of the pedunculopontine tegmental nucleus (PPN) influences visual contrast sensitivity in human observers. PLoS One 2016;11:e0155206.
29. Perry VH, Cowey A. Retinal ganglion cells that project to the superior colliculus and pretectum in the macaque monkey. Neuroscience 1984;12:1125-1137.
30. Harting JK, Glendingen KK, Diamond IT, Hall WC. Evolution of the primate visual system: anterograde degeneration studies of the tecto-pulvinar system. Am J Phys Anthropol 1973;38:383-392.
31. Fries W. Cortical projections to the superior colliculus in the macaque monkey: a retrograde study using horseradish peroxidase. J Comp Neurol 1984;230:55-76.
32. Lock TM, Baizer JS, Bender DB. Distribution of corticotectal cells in macaque. Exp Brain Res 2003;151:455-470.
33. Iizawa Y, Sugiyuchi Y, Shinoda Y. Neural organization from the superior colliculus to motoneurons in the horizontal oculomotor system of the cat. J Neurophysiol 1999;81:2597-2611.
34. Munoz DP, Guitton D. Control of orienting gaze shifts by pontomesencephalic reticular formation neurons in horizontal head movements: an integrative study. Brain Res 1987;422:389-397.
35. Munoz DP, Wurtz RH. Fixation cells in monkey superior colliculus. I. Characteristics of cell discharge. J Neurophysiol 1993;70:559-575.
36. Munoz DP, Wurtz RH. Fixation cells in monkey superior colliculus. II. Reversible activation and deactivation. J Neurophysiol 1993;70:576-589.
37. May PJ. The mammalian superior colliculus: laminar structure and connections. Prog Brain Res 2006;142:331-378.
38. Leichnetz GR, Gonzalo-Ruiz A, DeSalles AA, Hayes RL. The origin of brainstem afferents of the paramedian pontine reticular formation in the cat. Brain Res 1987;422:389-397.
39. Sparks DL. The brainstem control of saccadic eye movements. Nat Rev Neurosci 2002;3:952-964.
40. Cohen B, Komatsu-Suzuki A. Eye movements induced by stimulation of the pontine reticular formation: evidence for integration in oculomotor pathways. Exp Neurol 1972;36:101-117.
41. Scudder CA, Kaneko CS, Fuchs AF. The brainstem burst generator for saccadic eye movements: a modern synthesis. Exp Brain Res 2002;142:439-462.
42. Suzuki SS, Siegel JM, Wu MF. Role of pontomedullary reticular formation neurons in horizontal head movements: an ibotenic acid lesion study in the cat. Brain Res 1989;484:78-93.
43. Optican LM. The role of omnipause neurons: why glycine? Prog Brain Res 2008;171:115-121.
44. Averbuch-Heller L, Kori AA, Rottach KG, Dell'osso LF, Remmelr BF, Leigh RJ. Dysfunction of pontine omnipause neurons causes impaired fixation: macrosaccadic oscillations with a unilateral pontine lesion. Neuro-ophthalmology (Aeolus Press) 1996;16:99-106.
45. Thurtell MJ, Tomsk RL, Leigh RJ. Disorders of saccades. Curr Neurol Neurosci Rep 2007;7:407-416.
46. Sakai ST, Davidson AG, Buford JA. Reticulospinal neurons in the pontomedullary reticular formation of the monkey (Macaca fascicularis). Neuroscience 2009;163:1158-1170.
47. Scheepens B, Stapley P, Drew T. Neurons in the pontomedullary reticular formation signal posture and movement both as an integrated behavior and independently. J Neurophysiol 2008;100:2235-2253.
48. Stapley PJ, Drew T. The pontomedullary reticular formation contributes to the compensatory postural responses observed following removal of the support surface in the standing cat. J Neurophysiol 2009;101:1334-1350.
49. He YC, Wu GH, Li D, Tang B, Li B, Ding Y, et al. Histamine promotes rat motor performances by activation of H(2) receptors in the cerebellar fastigial nucleus. Behav Brain Res 2012;228:44-52.
50. Chambers WW, Sprague JM. Functional localization in the cerebellum. I. Organization in longitudinal cortico-nuclear zones and their contribution to the control of posture, both extrapyramidal and pyramidal. J Comp Neurol 1955;103:105-129.
51. Chambers WW, Sprague JM. Functional localization in the cerebellum. II. Somatotopic organization in cortex and nuclei. AMA Arch Neurol Psychiatry 1955;4:653-680.
52. Sprague JM, Chambers WW. Regulation of posture in intact and decerebrate cat. I. Cerebellum, reticular formation, vestibular nuclei. J Neurophysiol 1953;16:451-463.
53. Thach WT, Goodkin HP, Keating JG. The cerebellum and the adaptive coordination of movement. Annu Rev Neurosci 1992;15:403-442.
54. Dichgans J, Diener HC. Clinical evidence for functional compartmentalization of the cerebellum. In: Bloedel JR, Dichgans J, Precht W, editors. Cerebellar Functions. Berlin Heidelberg: Springer-Verlag, 1984;126-147.
55. Zhang XY, Wang JF, Zhu JN. Cerebellar fastigial nucleus: from anatomic construction to physiological functions. Cerebellum Ataxias 2016;3:9.
56. Joshi AC, Das VE. Muscimol inactivation of caudal fastigial nucleus and posterior interposed nucleus in monkeys with strabismus. J Neurophysiol 2013;110:1882-1891.
57. Kleine JF, Guan Y, Buttner U. Saccade-related neurons in the primate fastigial nucleus: what do they encode? J Neurophysiol 2003;90:3137-3154.
58. Helmchen C, Straube A, Buttner U. Saccade-related activity in the fastigial oculomotor region of the macaque monkey during spontaneous eye movements in light and darkness. Exp Brain Res 1994;84:474-482.
59. Fuchs AF, Robinson FR, Straube A. Role of the caudal fastigial nucleus in saccade generation. J Neurological discharge pattern. J Neurophysiol 1993;70:1723-1740.
60. Robinson FR, Straube A, Fuchs AF. Role of the caudal fastigial nucleus in saccade generation. II. Effects of muscimol inactivation. J Neurophysiol 1993;70:1741-1758.
61. Ohtsuka K, Noda H. Saccadic burst neurons in the oculomotor region of the fastigial nucleus of macaque monkeys. J Neurophysiol 1991;65:4791-4806.
62. Nelken I, Mc Alpine D, Gross C, Moschovakis J, Li J, Wang Y, et al. The adaptive coordination of movement. Annu Rev Neurosci 1992;15:403-442.
63. Dichgans J, Diener HC. Clinical evidence for functional compartmentalization of the cerebellum. In: Bloedel JR, Dichgans J, Precht W, editors. Cerebellar Functions. Berlin Heidelberg: Springer-Verlag, 1984;126-147.
64. Sprague JM, Chambers WW. Regulation of posture in intact and decerebrate cat. I. Cerebellum, reticular formation, vestibular nuclei. J Neurophysiol 1953;16:451-463.
65. Thach WT, Goodkin HP, Keating JG. The cerebellum and the adaptive coordination of movement. Annu Rev Neurosci 1992;15:403-442.
66. Helmchen C, Straube A, Buttner U. Saccade-related activity in the fastigial oculomotor region of the macaque monkey during spontaneous eye movements in light and darkness. Exp Brain Res 1994;84:474-482.
67. Fuchs AF, Robinson FR, Straube A. Role of the caudal fastigial nucleus in saccade generation. I. Neuronal discharge pattern. J Neurophysiol 1993;70:1723-1740.
68. Robinson FR, Straube A, Fuchs AF. Role of the caudal fastigial nucleus in saccade generation. II. Effects of muscimol inactivation. J Neurophysiol 1993;70:1741-1758.
69. Ohtsuka K, Noda H. Saccadic burst neurons in the oculomotor region of the fastigial nucleus of macaque monkeys. J Neurophysiol 1991;65:4791-4806.
70. Nelken I, Mc Alpine D, Gross C, Moschovakis J, Li J, Wang Y, et al. The adaptive coordination of movement. Annu Rev Neurosci 1992;15:403-442.
64. Thier P, Dicke PW, Haas R, Thielert CD, Catz N. The role of the oculomotor vermis in the control of saccadic eye movements. Ann N Y Acad Sci 2002;978:50-62.

65. Kojima Y, Soetedjo R, Fuchs AF. Effect of inactivation and disinhibition of the oculomotor vermis on saccade adaptation. Brain Res 2011;1401:30-39.

66. Giorli RA, Gregory KM, Suzuki DA, Blanks RH, Lui F, Betelak KF. Cortical and subcortical afferents to the nucleus reticularis tegmenti pontis and basal pontine nuclei in the macaque monkey. Vis Neurosci 2001;18:725-740.

67. Matsuzaki R, Kyuhou S. Pontine neurons which relay projections from the superior colliculus to the posterior vermis of the cerebellum in the cat: distribution and visual properties. Neurosci Lett 1997;236:99-102.

68. Hashimoto M, Ohtsuka K. Transcranial magnetic stimulation over the posterior cerebellum during visually guided saccades in man. Brain 1993;118:1185-1193.

69. Ilg W, Giese MA, Gizewski ER, Schoch B, Timmann D. The influence of focal cerebellar lesions on the control and adaptation of gait. Brain 2008;131:2913-2927.

70. Zoergal A, la Fougère C, Lorend S, Rominger A, Xiong G, Deutschenbaur L, et al. Functional disturbance of the locomotor network in progressive supranuclear palsy. Neurology 2013;80:634-641.

71. Schlag J, Schlag-Rey M. Role of the central thalamus in gaze control. Prog Brain Res 1986;64:191-201.

72. Watanabe Y, Funahashi S. Neuronal activity throughout the primate midiodorsal nucleus of the thalamus during oculomotor delay-responses. II. Activity encoding visual versus motor signal. J Neurophysiol 2004;92:1756-1769.

73. Kunimatsu J, Tanaka M. Roles of the primate motor thalamus in the generation of antisaccades. J Neurosci 2010;30:5108-5117.

74. Roth MM, Dahmen JC, Muir DR, Imhof F, Martini FJ, Hofer SB. Thalamic nuclei convey diverse contextual information to layer 1 of visual cortex. Nat Neurosci 2016;19:299-307.

75. Robinson DL, McClurkin JW. The visual superior colliculus and pulvinar. Rev Oculomot Res 1989;3:337-360.

76. Tanaka M, Kunimatsu J. Contribution of the central thalamus to the generation of voluntary saccades. Eur J Neurosci 2011;33:2046-2057.

77. Kronenbueger M, Gonzalez EG, Liu LD, Moro E, Steinbach MJ, Lozano AM, et al. Involvement of the human ventrolateral thalamus in the control of visually guided saccades. Brain Stimul 2010;3:226-229.

78. Armstrong DM, Drew T. Discharges of pyramidal tract and other motor cortical neurones during locomotion in the cat. J Physiol 1984;404:471-495.

79. Drew T. Motor cortical activity during voluntary gait modifications in the cat. I. Cells related to the forelimbs. J Neurophysiol 1993;70:179-199.

80. Pinsaut D. The thalamic reticular nucleus: structure, function and concept. Brain Res Brain Res Rev 2004;46:1-31.

81. Wurtz RH, McAlonan K, Cavanaugh J, Berman RA. Thalamic pathways for active vision. Trends Cogn Sci 2011;15:177-184.

82. Marlinski V, Belousovera IN. Burst firing of neurons in the thalamic reticular nucleus during locomotion. J Neurophysiol 2014;112:181-192.

83. Watanabe M, Munoz DP. Probing basal ganglia functions by saccade eye movements. Eur J Neurosci 2011;33:2070-2090.

84. Watanabe M, Munoz DP. Saccade reaction times are influenced by caudate microstimulation following and prior to visual stimulus appearance. J Cogn Neurosci 2011;23:1794-1807.

85. Ding L, Gold JI. Separate, causal roles of the caudate in saccadic choice and execution in a perceptual decision task. Neuron 2012;75:865-874.

86. Phillips JN, Everling S. Neural activity in the macaque putamen associated with saccades and behavioral outcome. PLoS One 2012;7:e51596.

87. Kravitz AV, Freeze BS, Parker PR, Kay K, Thwin MT, Deisseroth K, et al. Regulation of parkinsonian motor behaviours by optogenetic control of basal ganglia circuitry. Nature 2010;466:622-626.

88. Jahanshahi M, Obeso I, Rothwell JC, Obeso JA. A frontostriato-subthalamic-pallidal network for goal-directed and habitual inhibition. Nat Rev Neurosci 2015;16:719-732.

89. Van Der Kooy D, Hattori T. Single subthalamic nucleus neurons project to both the globus pallidus and substantia nigra in rat. J Comp Neurol 1980;192:751-768.

90. Canteras NS, Shammah-Lagnado SJ, Silva BA, Ricardo JA. Afferent connections of the subthalamic nucleus: a combined retrograde and anterograde horseradish peroxidase study in the rat. Brain Res 1990;513:43-59.

91. Kita T, Kita H. The subthalamic nucleus is one of multiple innervation sites for long-range corticofugal axons: a single-axon tracing study in the rat. J Neurosci 2012;32:5990-5999.

92. Nilson MH, Patel M, Ruhncona S, Magnusson M, Fransson PA. Subthalamic deep brain stimulation improves smooth pursuit and saccade performance in patients with Parkinson's disease. J Neuroeng Rehabil 2013;10:33.

93. Lohnes CA, Earlhart GM. Effect of subthalamic deep brain stimulation on turning kinematics and related saccadic eye movements in Parkinson disease. Exp Neurol 2012;236:389-394.

94. Ferrarin M, Carpinella I, Rabuffetti M, Rizzione M, Lopiano L, Crenna P. Unilateral and bilateral subthalamic nucleus stimulation in Parkinson's disease: effects on EMG signals of lower limb muscles during walking. IEEE Trans Neural Syst Rehabil Eng 2007;15:182-189.

95. Chang JY, Shi LH, Luo F, Woodward DJ. High frequency stimulation of the subthalamic nucleus improves treadmill locomotion in unilateral 6-hydroxydopamine lesioned rats. Brain Res 2003;983:174-184.

96. Pöster-Nerger M, Volkman J. Deep brain stimulation for gait and postural symptoms in Parkinson's disease. Mov Disord 2013;28:1609-1615.

97. Fridley J, Adams G, Sun P, York M, Atassi F, Lai E, et al. Effect of subthalamic nucleus or globus pallidus interna stimulation on oculomotor function in patients with Parkinson's disease. Stereotact Funct Neurosurg 2013;91:113-121.

98. Antoniades CA, Rebello P, Kennard C, Aziz TZ, Green AL, FitzGerald JJ. Pallidal deep brain stimulation improves higher control of the oculomotor system in Parkinson's disease. J Neurosci 2015;35:13043-13052.

99. Saitoh K, Ménard A, Grillner S. Tectal control of locomotion, steering, and eye movements in lamprey. J Neurophysiol 2007;97:3093-3108.

100. von Uckermann G, Lambert FM, Combes D, Straka H, Deutschenbaur L, et al. Functional disturbance of the locomotor system and other motor cortical neurones during locomotion in the cat. J Physiol 1984;404:471-495.

101. Saitoh K, Ménard A, Grillner S. Tectal control of locomotion, steering, and eye movements in lamprey. J Neurophysiol 2007;97:3093-3108.

102. Srivastava A, et al. Saccades and Locomotion www.e-jmd.org
of monkey substantia nigra pars reticulata. I. Relation of visual and auditory responses to saccades. J Neurophysiol 1983;49:1230-1253.
103. Winn P. Experimental studies of pedunculopontine functions: are they motor, sensory or integrative? Parkinsonism Relat Disord 2008;14 Suppl 2:S194-S198.
104. Ohtsuka K, Edamura M, Kawahara K, Aoki M. The properties of goal-directed eye movements evoked by microstimulation of the cerebellar vermis in the cat. Neurosci Lett 1987;76:173-178.
105. Godschalk M, Van der Burg J, Van Duin B, De Zeeuw CI. Topography of saccadic eye movements evoked by microstimulation in rabbit cerebellar vermis. J Physiol 1994;480:147-153.
106. El-Shamayleh Y, Kojima Y, Soetedjo R, Horwitz GD. Selective optogenetic control of Purkinje cells in monkey cerebellum. Neuron 2017;95:51-62.e4.
107. Sauerbrei BA, Lubenov EV, Siapas AG. Structured variability in Purkinje cell activity during locomotion. Neuro 2015;87:840-852.
108. Hoogland TM, De Gruijl JR, Witter L, Canto CB, De Zeeuw CI. Role of synchronous activation of cerebellar Purkinje cell ensembles in multi-joint movement control. Curr Biol 2015;25:1157-1165.
109. Andersson G, Armstrong DM. Complex spikes in Purkinje cells in the lateral vermis (b zone) of the cat cerebellum during locomotion. J Physiol 1987;385:107-134.
110. Gandhi NJ, Barton EJ, Sparks DL. Coordination of eye and head components of movements evoked by stimulation of the paramedian pontine reticular formation. Exp Brain Res 2008;189:35-47.
111. Gandhi NJ, Katnani HA. Motor functions of the superior colliculus. Annu Rev Neurosci 2011;34:205-231.
112. Grasso R, Prévost P, Ivanenko YP, Berthoz A. Eye-head coordination for the steering of locomotion in humans: an anticipatory synergy. Neurosci Lett 1998:253:115-118.
113. Saleem AB, Ayaz A, Jeffery KJ, Harris KD, Carandini M. Integration of visual motion and locomotion in mouse visual cortex. Nat Neurosci 2013;16:1864-1869.
114. Inai T, Moore ST, Raphan T, Cohen B. Interaction of the body, head, and eyes during walking and turning. Exp Brain Res 2001;136:1-18.
115. Wilkie RM, Wann JP. Judgments of path, not heading, guide locomotion. J Exp Psychol Hum Percept Perform 2006;32:88-96.
116. Rietdyk S, Rhea CK. Control of adaptive locomotion: effect of visual obstruction and visual cues in the environment. Exp Brain Res 2006;169:272-278.
117. Vitório R, Lirani-Silva E, Barbieri FA, Raile V, Stella F, Gobbi LT. Influence of visual feedback sampling on obstacle crossing behavior in people with Parkinson’s disease. Gait Posture 2013;38:330-334.
118. Stuart S, Alcock L, Galna B, Lord S, Rochester L. The measurement of visual sampling during real-world activities in Parkinson’s disease and healthy controls: a structured literature review. J Neurosci Methods 2014;222:175-188.
119. Land MF, Lee DN. Where we look when we steer. Nature 1994;369:742-744.
120. Land MF. Motion and vision: why animals move their eyes. J Comp Physiol A 1999;185:341-352.
121. Land MF. Eye movements of vertebrates and their relation to eye form and function. J Comp Physiol A Neuroethol Sens Neural Behav Physiol 1995:195-214.
122. Patla AE, Tomescu SS, Greig M, Novak A. Gaze fixation patterns during goal-directed locomotion while navigating around obstacles and a new route-selection model. In: van Gompel RPG, Fischer MH, Murray WS, Hill RL, editors. Eye Movements: A Window on Mind and Brain. 1st ed. Amsterdam: Elsevier; 2007:677-696.
123. Higuchi T. Visuomotor control of human adaptive locomotion: understanding the anticipatory nature. Front Psychol 2013;4:277.
124. Rivers TJ, Sirota MG, Guttenagl AJ, Ogordnikov DA, Shah NA, Belozerova IN. Gaze shifts and fixations dominate gaze behavior of walking cats. Neuroscience 2014;275:477-499.
125. Foulsham T. Eye movements and their functions in everyday tasks. Eye (Lond) 2015;29:196-199.
126. Matthys JS, Barton SL, Fajen BR. The biomechanics of walking shape the use of visual information during locomotion over complex terrain. J Vis 2015;15:10.
127. Matthys JS, Fajen BR. Visual control of foot placement when walking over complex terrain. J Exp Psychol Hum Percept Perform 2014;40:106-115.
128. Marigold DS, Patla AE. Gaze fixation patterns for navigating complex ground terrain. Neuroscience 2007;144:302-313.
129. Hollands MA, Marple-Horvat DE. Coordination of eye and leg movements during visually guided stepping. J Mot Behav 2001;33:205-216.
130. Patla AE, Vickers JN. How far ahead do we look when required to step on specific locations in the travel path during locomotion? Exp Brain Res 2003;148:133-138.
131. Yamada M, Higuchi T, Mori S, Uemura K, Nagai K, Aoyama T, et al. Maladaptive turning and gaze behavior induces impaired stepping on multiple footfall targets during gait in older individuals who are at high risk of falling. Arch Gerontol Geriatr 2012;54:e102-e108.
132. Greany JF, Di Fabio RP. Saccade to stepping delays in elders at high risk for falling. Aging Clin Exp Res 2008;20:428-433.
133. Hollands MA, Patla AE, Vickers JN. "Look where you’re going!": gaze behaviour associated with maintaining and changing the direction of locomotion. Exp Brain Res 2002;143:221-230.
134. Young WR, Hollands MA. Newly acquired fear of falling leads to altered eye movement patterns and reduced stepping safety: a case study. PLoS One 2012;7:e49765.
135. Young WR, Wing AM, Hollands MA. Influences of state anxiety on gaze behavior and stepping accuracy in older adults during adaptive locomotion. J Gerontol B Psychol Sci Soc Sci 2012;67:43-51.
136. Kugler G, Huppert D, Eck M, Schneider B, Brandt T. Visual exploration during locomotion limited by fear of heights. PLoS One 2014;9:e105906.
137. Gonzalez Andino SL, Grave de Peralta Menendez R. Coding of saliency by ensemble bursting in the amygdala of primates. Front Behav Neurosci 2012;6:179-185.
138. Crowley KA, Marple-Horvat DE. Alcohol affects eye movements essential for visually guided stepping. Alcohol Clin Exp Res 2004;28:402-407.
139. Jantti V, Lang AH, Keskinen I, Lehtinen I, Palkkanen A. Acute effects of intravenously given alcohol on saccadic eye movements and subjective evaluations of intoxication. Psychopharmacology (Berl) 1983;79:251-255.
140. Gitchel GT, Weitzel PA, Baron MS. Slowed saccades and increased square wave jerks in essential tremor. Tremor Other Hyperkinet Mov (N Y) 2013;3:tre-03-178-4116-2.
141. Singer C, Sanchez-Ramos I, Weiner WJ. Gait abnormality in essential tremor. Mov Disord 1994;9:193-196.
Saccades and Locomotion
Srivastava A, et al.

142. Hubble JP, Busenbark KL, Pahwa R, Lyons K, Koller WC. Clinical expression of essential tremor: effects of gender and age. Mov Disord 1997;12:969-972.

143. Stolze H, Petersen G, Raethjen J, Wenzelburger R, Deuschl G. The gait disorder of advanced essential tremor. Brain 2001;124:2278-2286.

144. Lim ES, Seo MW, Woo SR, Jeong SY, Jeong SK. Relationship between essential tremor and cerebellar dysfunction according to age. J Clin Neuro 2005;1:76-80.

145. Kronenburger M, Konczak J, Ziegler W, Buderath P, Frank B, Coenen VA, et al. Motor and balance gait impairment in essential tremor. Cerebellum 2009;8:389-398.

146. Fasano A, Herzog J, Raethjen J, Rose FE, Muthuraman M, Volkman M, et al. Gait ataxia in essential tremor is differentially modulated by thalamic stimulation. Brain 2010;133:3635-3648.

147. Rao AK, Gillman A, Louis ED. Quantitative gait analysis in essential tremor reveals impairments that are maintained into advanced age. Gait Posture 2011;34:63-70.

148. Hoskovcová M, Ulmanová O, Sprdlík O, Sieger T, Nováková J, Jech R, et al. Disorders of balance and gait in essential tremor are associated with midline tremor and age. Cerebellum 2013;12:27-34.

149. Rao AK, Louis ED. Timing control of gait: a study of essential tremor patients vs. age-matched controls. Cerebellum Ataxias 2016;3:5.

150. MacAskill MR, Anderson TJ. Eye movements in neurodegenerative diseases. Curr Opin Neurol 2016;29:61-68.

151. Srivastava A, Sharma R, Sood SK, Shukla G, Goyal V, Behari M. Saccadic eye movements in Parkinson's disease. Indian J Ophthalmol 2014;62:538-544.

152. Bloom BR, Hausdorff JM, Visser JE, Giladi N. Falls and freezing of gait in Parkinson's disease: a review of two interconnected, episodic phenomena. Mov Disord 2004;19:871-884.

153. Swehlík M, Zwick EB, Steinwender G, Linhart WE, Stegemöller EL, Hack N, et al. The disturbance of gaze in progressive supranuclear palsy: implications for pathogenesis. Front Neurol 2010;1:147.

154. Hatanaka N, Sato K, Hishikawa N, Takemoto M, Ohta Y, Yamashita T, et al. Comparative gait analysis in patients with Parkinson's disease off dopaminergic therapy. Arch Phys Med Rehabil 2009;90:1880-1886.

155. Otero-Millán J, Serra A, Leigh RJ, Troncoso XG, Macknik SL, Martinez-Conde S. Distinctive features of saccadic intrusions and microsaccades in progressive supranuclear palsy. J Neurosci 2011;31:4379-4387.

156. Chen AL, Riley DE, King SA, Joshi AC, Serra A, Liao K, et al. The disturbance of gaze in progressive supranuclear palsy: implications for pathogenesis. Front Neurol 2010;1:147.

157. Stolze H, Klebe S, Petersen G, Raethjen J, Wenzelburger R, Witt K, et al. Typical features of cerebellar ataxic gait. Eur Neurol 2016;75:282-289.

158. Anano S, Skinner JW, Lee HK, Siegenmüller EL, Hack N, Akbar U, et al. Discriminating features of gait performance in progressive supranuclear palsy. Parkinsonism Relat Disord 2015;21:888-893.

159. Lasker AG, Zee DS. Ocular motor abnormalities in Huntington's disease. Vision Res 1997;37:3639-3645.

160. Golding CV, Danchavijitr C, Hodgson TL, Tabrizi SJ, Kennard C. Identification of an oculomotor biomarker of preclinical Huntington disease. Neurology 2006;67:485-487.

161. Hicks SL, Robert MP, Golding CV, Tabrizi SJ, Kennard C. Oculomotor deficits indicate the progression of Huntington's disease. Prog Brain Res 2008;171:555-558.

162. Patel SS, Jankovic J, Hood AJ, Jeter CB, Sereno AB. Reflexive and volitional saccades: biomarkers of Huntington disease severity and progression. J Neurol Sci 2012;313:35-41.

163. Pletsch A, Hoffman A, Armstrong I, Pari G, Munoz DP. Saccadic impairments in Huntington's disease. Exp Brain Res 2008;186:457-469.

164. Winograd-Gurvich CT, Georgiou-Karistianis N, Evans A, Millist L, Bradshaw JL, Churchyard A, et al. Hypometric primary saccades and increased variability in visually-guided saccades in Huntington's disease. Neuropsychologia 2003;41:1683-1692.

165. Koller WC, Trimple J. The gait abnormality of Huntington's disease. Neurology 1985;35:1450-1454.

166. Rao AK, Muratori L, Louis ED, Moskowitz CB, Marder KS. Spectrum of gait impairments in presymptomatic and symptomatic Huntington's disease. Mov Disord 2008;23:1100-1107.

167. Thaut MH, Millner R, Lange HW, Hutt CP, Hoemberg V. Velocity modulation and rhythmic synchronization of gait in Huntington's disease. Mov Disord 1999;14:808-819.

168. Bilney B, Morris ME, Churchyard A, Chiu E, Georgiou-Karistianis N. Evidence for a disorder of locomotor timing in Huntington's disease. Mov Disord 2005;20:51-57.

169. Thamsarasab P, Thammongkolchai T, Rucker JC, Frucht SJ. The diagnostic value of saccades in movement disorder patients: a practical guide and review. J Clin Mov Disord 2015;2:14.

170. Christova P, Anderson JH, Gomez CM. Impaired eye movements in presymptomatic spinocerebellar ataxia type 6. Arch Neurol 2008;65:530-536.

171. Federighi P, Cevenini G, Dotti MT, Rosini F, Pretigiani E, Federico A, et al. Differences in saccade dynamics between spinocerebellar ataxia 2 and late-onset cerebellar ataxias. Brain 2011;134:879-891.

172. Stolze H, Klebe S, Petersen G, Raethjen J, Wenzelburger R, Witt K, et al. Typical features of cerebellar ataxic gait. J Neurol Neurosurg Psychiatry 2002;73:310-312.

173. Buckley E, Mazzà C, McNeill A. A systematic review of the gait characteristics associated with cerebellar ataxia. Gait Posture 2018;60:154-163.

174. Palliyath S, Hallett M, Thomas SL, Lebedowska MK. Gait in patients with cerebellar ataxia. Mov Disord 1998;13:958-964.

175. Boonstra TA, van der Kooij H, Munneke M, Bloom BR. Gait disorders and balance disturbances in Parkinson's disease: clinical update and pathophysiology. Curr Opin Neurol 2008;21:461-471.

176. Nemanich ST, Earhart GM. Freezing of gait is associated with increased saccade latency and variability in Parkinson's disease. Mov Disord 1998;13:966-969.

177. Chen AL, Riley DE, King SA, Joshi AC, Serra A, Liao K, et al. The disturbance of gaze in progressive supranuclear palsy: implications for pathogenesis. Front Neurol 2010;1:147.

178. Walton CC, O'Callaghan C, Hall JM, Gilat M, Mowzoonski I, Naimsmith SL, et al. Antisaccade errors reveal cognitive control deficits in Parkinson's disease with freezing of gait. J Neurol Neurosurg Psychiatry 2003;41:1683-1692.
lated to turning performance in Parkinson disease. J Parkinsons Dis 2011;1:109-118.

181. Ewenczyk C,Mesmoudi S, Gallea C, Welter ML, Gaymard B, Demain A, et al. Antisaccades in Parkinson disease: a new marker of postural control. Neurology 2017; 88:853-861.

182. Mancini M,Carlson-Kuhta P,Zampieri C, Nutt JG, Chiari L, Horak FB. Postural sway as a marker of progression in Parkinson’s disease: a pilot longitudinal study. Gait Postlure 2012;36:471-476.

183. Stylianou AP,McVey MA, Lyons KE, Pahwa R, Luchies CW. Postural sway in patients with mild to moderate Parkinson’s disease. Int J Neurosci 2011;121:614-621.

184. Takamatsu Y, Matsuda N, Alba I. Body sway during static standing in patients with progressive supranuclear palsy. J Neurol Sci 2017;381:836.

185. Umemura K, Ishizaki H, Matsuoka I, Hoshino T, Nozue M. Analysis of body sway in patients with cerebellar lesions. Acta Otolaryngol Suppl 1989;468:253-261.

186. Arkadir D, Louis ED. The balance and gait disorder of essential tremor: what does this mean for patients? Ther Adv Neurol Disord 2013;6:229-236.

187. Panzera R,Salomonczyk D, Pirogovsky E, Simmons R, Goldstein J, Coreyn-Bloom J, et al. Postural deficits in Huntington’s disease when performing motor skills involved in daily living. Gait Posture 2011;33:457-461.

188. Grimbergen YAM,Knol MJ, Bloem BR, Kremer BPH, Roos RAC, Munneke M. Falls and gait disturbances in Huntington’s disease. Mov Disord 2008;23:970-976.

189. Legrand A,Mazars KD, Lazzareschi J, Lemoine C,Olivier I, Barra J, et al. Differing effects of prosaccades and antisaccades on postural stability. Exp Brain Res 2013;227:397-405.

190. Rodrigues ST,Aguirar SA, Polaistri PF, Godoi D, Morea R, BareLA JA. Effects of saccadic eye movements on postural control stabilization. Motriz: Revista de Educação Fisica 2013;19:614-619.

191. Crowdy KA,Hollands MA, Ferguson IT, Marple-Horvat DE. Evidence for interactive locomotor and oculomotor deficits in cerebellar patients during visually guided stepping. Exp Brain Res 2000;135:437-454.

192. Marple-Horvat DE,Crowdy KA. Direct visualisation of gaze and hypometric saccades in cerebellar patients during visually guided stepping. Gait Posture 2005;21:39-47.

193. Zampieri C, Di Fabio RP. Balance and eye movement training to improve gait in people with progressive supranuclear palsy: quasi-randomized clinical trial. Phys Ther 2008;88:1460-1473.

194. Crowdy KA,Kaur-Mann D, Cooper HL, Mansfield AG, Offord JL, Marple-Horvat DE. Rehearsal by eye movement improves visuomotor performance in cerebellar patients. Exp Brain Res 2002;146:244-247.

195. Kang KY,Yu KH. The effects of eye movement training on gait function in patients with stroke. J Phys Ther Sci 2016;28:1816-1818.

196. Hollands MA, Marple-Horvat DE, Henkees S, Rowan AK. Human eye movements during visually guided stepping. J Mot Behav 1995;27:155-163.

197. Stuart S, Galna B, Delicato LS, Lord S, Rochester L. Direct and indirect effects of attention and visual function on gait impairment in Parkinson’s disease: influence of task and turning. Eur J Neurosci 2017;46:1703-1716.

198. Paquette C, Fung J. Old age affects gaze and postural coordination. Gait Postlure 2011;33:227-232.

199. Di Fabio RP,Greany JF, Zampieri C. Saccade-stepping interactions revise the motor plan for obstacle avoidance. J Mot Behav 2003;35:383-397.

200. Di Fabio RP, Zampieri C, Greany JF. Aging and saccade-stepping interactions in humans. Neurosci Lett 2003;339:179-182.