Modern Otology and Neurotology

Kimitaka Kaga

Vertigo and Balance Disorders in Children

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Preface

Historically, one of the great physicians was André-Thomas, a pediatric neurologist who described how to observe postural response including labyrinthine righting reflexes. In otology and neurotology, there is increasing opportunity to see congenitally deaf infants with cochlear implants complicating vestibular loss. In deaf infants and children with loss of semicircular canal function, central vestibular compensation during their development and growth can accelerate balance function and locomotion.

In order to evaluate vestibular ocular response, the earth vertical axis damped rotational chair test is easily performed on these patients. Infants with absent or poor per-rotatory nystagmus were chosen to study. Development of gross motor, balance, and locomotive function was seriously delayed in each infant during the first 2 or 3 years of life. Thereafter, all infants could achieve most landmarks of gross motor development, such as head control, independent standing, walking, and running until school age. However, balance functions even at the age of entrance into elementary school (6 years of age) were variously impaired in all children. The better ones could swim under water, but the more affected children could not maintain static balance with their eyes closed. Although fine motor skills were normally achieved in all children, their gross motor development due to central vestibular compensation could depend on the integration of other sensory inputs such as those from visual, somatosensory, and proprioceptive senses, and on the maturation of motor control systems in the cerebellum, basal ganglia, and motor cortex. These results reveal that muscle tones of the neck and extremities are controlled by signals from the semicircular canals and otolith organs rather than from the brain in early infancy. Central vestibular compensation could play an important role in accelerating developmental motor functions of infant and children in spite of congenital loss of vestibular organs.

I thank Ms. Kayoko Sekiguchi and Ms. Masako Nakamura for their unlimited contribution in publishing this book.

Meguro-ku, Japan — Kimitaka Kaga

Contents

Chapter 1
Introduction: History

Abstract In 1824, Flourens in France demonstrated experimentally that destruction of the semicircular canal in pigeons caused nystagmus and abnormal posture, proving for the first time that the semicircular canal was a balance organ. Neuro-developmental study of balance disorders in infants and children initially started with observation of postural reflexes in infants and children by Magnus in Germany in the early twentieth century and followed clinically by André-Thomas from France in the middle of the twentieth century. Pediatric neurology was developed for a mere 50 years.

Keywords André-Thomas • Balance disorder • Labyrinthine righting reflex • Magnus • Pediatric neurology • Postural reflex • Semicircular canal

1.1 Pioneers of Postural Reflex Studies

Neuro-developmental study of balance disorders in infants and children initially started with observation of postural reflexes in infants and children. The pioneers in research date back to "Körperstellung" by Magnus [1] in Germany in the early twentieth century, followed by the clinical approach of "Equilibrium et Equilibration" by André-Thomas [2] from France in the middle of the twentieth century. While neurology has a history of nearly 200 years, neurology in infants/children has been studied for a mere 50 years. Quantitative evaluation of labyrinth function in children has rarely been used for diagnosis, even in overseas countries, and dissemination of the knowledge is much overdue.

The starting point for vertigo, or abnormal balance function, in children would be to understand myelination and maturation of the peripheral balance apparatus and central nervous system, integration processes of each function, and learning and acquisition of gross and fine motor skills at each age. Functional disorders are either congenital or acquired, but appropriate objective tests should be performed to make

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an accurate diagnosis because neurological signs of abnormal balance function are similar in children with peripheral abnormalities and those with central nervous system abnormalities. Diagnosis without objective testing is difficult because young children rarely obey instructions.

Given that the central nervous system is still developing in children with balance disorders, their systems are highly plastic, and rehabilitation including balance function training is very effective. It is therefore desirable to direct treatment in a favorable direction by planning treatment and evaluating the results with a rehabilitation specialist.

1.2 History of Vestibular Function and Postural Reflex Research

The vestibular semicircular canals were considered to be one of the auditory organs until the beginning of the nineteenth century. The semicircular canals were thought to be involved in perception of the sound source by turning the head, that is, an auditory perception apparatus for sound orientation. In 1824, Flourens [3] in France demonstrated experimentally that destruction of the semicircular canal in pigeons caused nystagmus and abnormal posture, proving for the first time that the semicircular canal was a balance organ. Many experiments with pigeons followed, and in 1892 Ewald [4] clarified the compensation process of postural change in pigeons with destroyed labyrinths (Fig. 1.1). The posture caused by labyrinth destruction and its compensation process differ between birds and mammals. The detailed study of labyrinth destruction in rabbits (Fig. 1.2) and the relationship between head presentation and the tonic labyrinthine reflex in cats by Magnus [1] of Germany in 1924 (Fig. 1.3) was the beginning of the research that led to the current study environment.

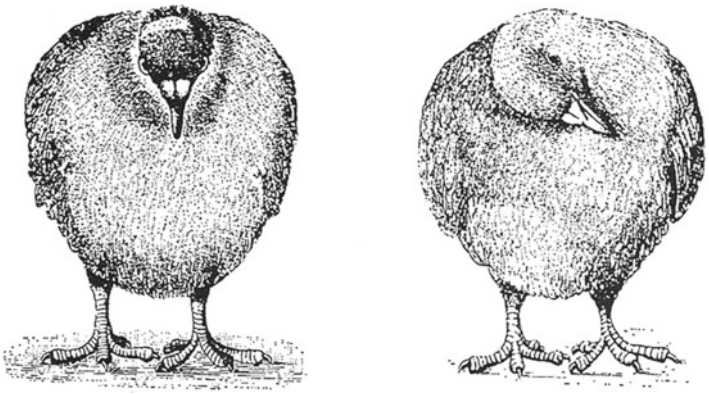

Fig. 1.1 Right labyrinth destruction and change in heal position of a pigeon, by Ewald (1892) [4]. A change due to loss of the tonic labyrinthine reflex is shown on the right

Fig. 1.2 Head position of a rabbit following bilateral labyrinth destruction, by Magnus (1924) [1]. The head remained lower due to loss of the tonic labyrinthine reflex

Magnus also showed that the tonic neck reflex (Fig. 1.4) observed in healthy children is present in adults as well (Fig. 1.5). In 1944 and 1952, André-Thomas of France found that the presence of the tonic neck reflex and labyrinthine righting reflex was useful for diagnosing neurological disorders in children (Fig. 1.6) [5, 6]. André-Thomas developed this research further and in 1963 described the characteristics of the development and postural changes of newborns [6], which became the basis of their application in pediatric neurology. In the research of semicircular canals and posture, on the other hand, Cohen and Suzuki [7] applied electronic stimulation individually to each ampullary nerve of the semicircular canal of a cat and three-dimensionally clarified changes in nystagmus, head movement, and posture, thus elevating the research to a modern level (Fig. 1.7). [8] demonstrated that righting reflex in a monkey is elicited by eyes covered, bilateral labyrinthine destruction, and both eyes covered and bilateral labyrinthine destruction [8] (Fig. 1.8). In Fig. 1.9, changes of head and neck righting reflex in a girl of severe deafness and vestibular loss with eyes open or eyes covered are shown.

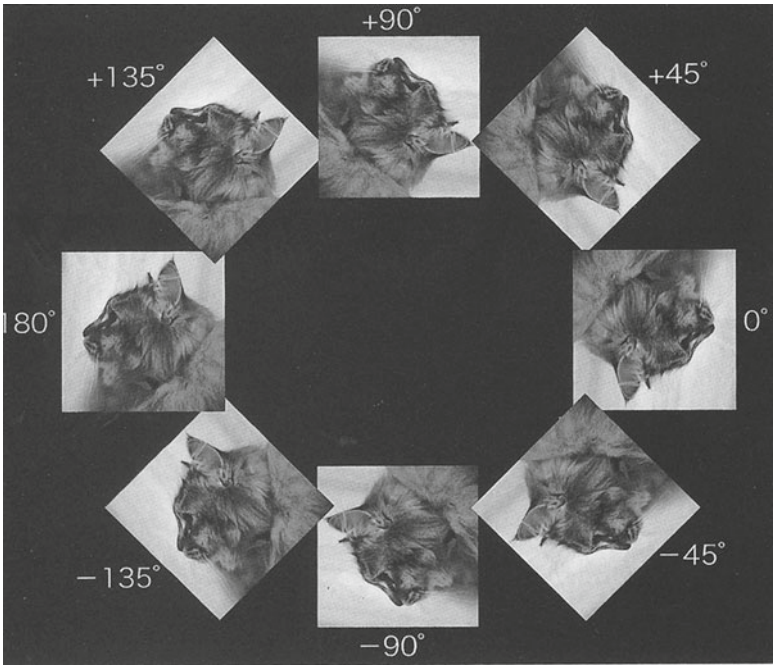

Fig. 1.3 Relationship between changes in head position and tonic labyrinthine reflex of cats, by Magnus (1924) [1]. Tonus of the protractor muscle is maximized in the supine position and becomes minimal in the prone position

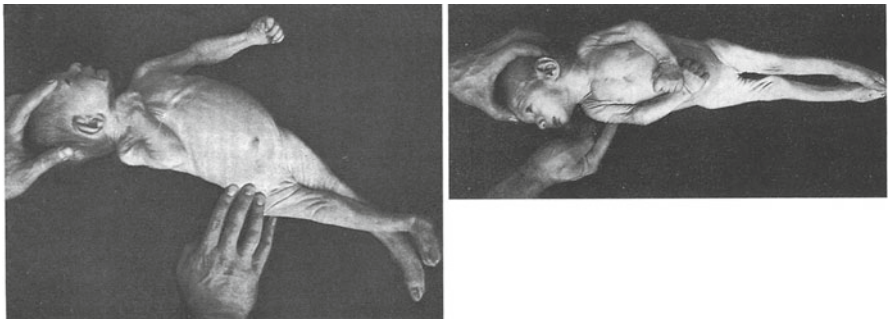

Fig. 1.4 Asymmetric tonic neck reflex of a newborn, by Magnus (1924) [1]. Tension is increased on the side where the nose is directed, which produces a right-left difference

Publications from Japan include "Clinical Pediatric Neurology" [9] by Norimitsu Yoshikura, a pediatric neurologist who studied under André-Thomas, "Diagnosis in Pediatric Neurology" [10] by Yoshimasa Sakamoto, and "Statokinetic Reflexes in Equilibrium and Movement" [11] by Tadashi Fukuda, a neuro-otologist from Gifu

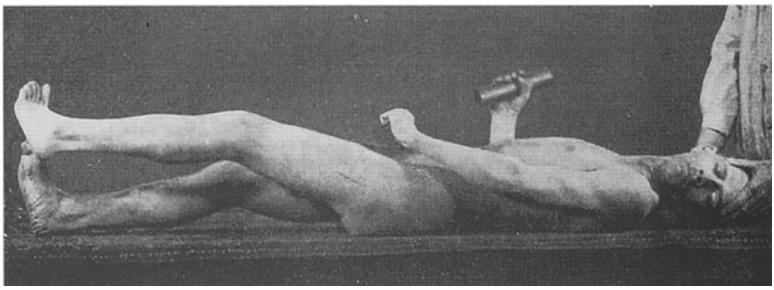

Fig. 1.5 Asymmetric tonic neck reflex observed in adults, by Magnus (1924) [1]. The head is twisted so that the nose is turned to the left when holding a heavy object in the right hand

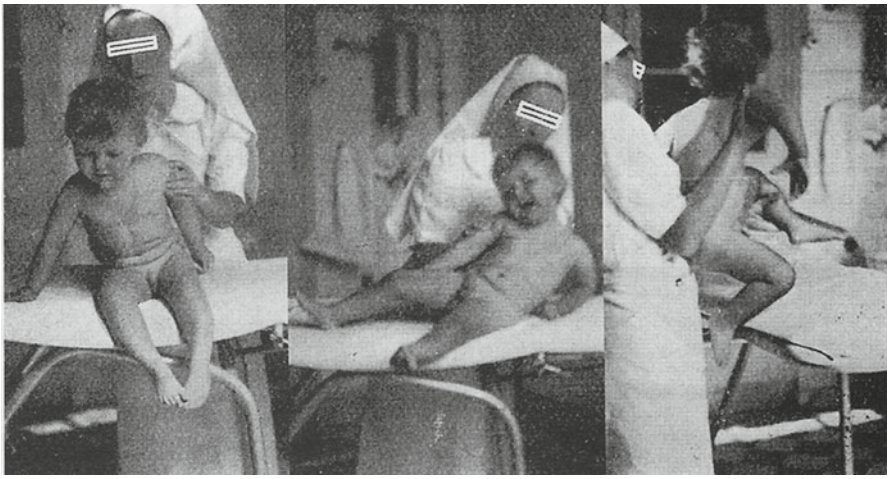

Fig. 1.6 Labyrinthine righting reflex of a child with polio, by André-Thomas (1944) [2]

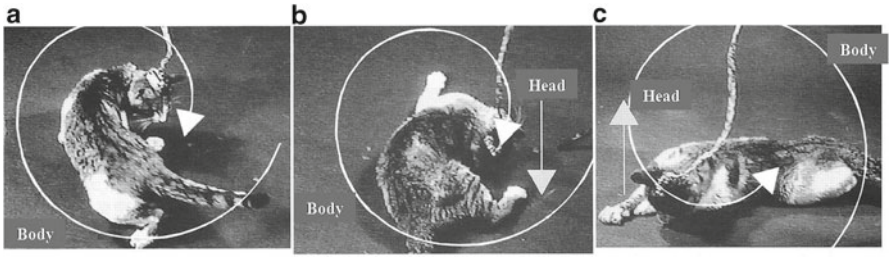

Fig. 1.7 A series of head and body movements elicited by electronic stimulation of ampullary nerve of the semicircular canal of a cat, by Cohen and Suzuki (1963) [7]. (**a**) Stimulation of the left lateral semicircular canal nerve. (**b**) Stimulation of the left anterior semicircular canal nerve. (**c**) Stimulation of the right posterior semicircular canal nerve

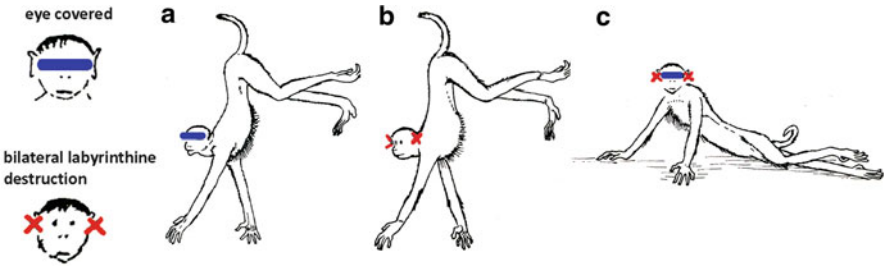

Fig. 1.8 Influence of eyes covered and/or bilateral labyrinthine destruction on righting reflex in a monkey, by Twitchell (1965) [8]. (**a**) Eyes covered (visual deprivation): normal righting reflex by vestibular organs. (**b**) Bilateral labyrinthine destruction (vestibular deprivation): normal righting reflex by vision. (**c**) Eyes covered and bilateral labyrinthine destruction: normal neck righting reflex by somatosensory sensation of body

University. The research on the labyrinthine postural reflex has been applied clinically to evaluate brain disorders without an abnormality of labyrinth function because limb reflexes are affected. Such clinical application of the postural reflex led to evaluation of postural reflexes in patients with cerebral palsy and was also used to evaluate the effect of training, such as the Vojta or Bobath methods, which are well known in rehabilitation. Sensory integration training was conceived based on this trend. Ayres (1972) of the USA [12] developed training in which labyrinth stimulation is applied for improvement of motor function or learning disability in handicapped children, and it is used also for training in patients with autism. The Japanese Academy of Sensory Integration was founded mainly by physical therapists and occupational therapists to promote sensory integration training. Ornitz of the USA considered that vestibular function is impaired in children with autism and recommended balance training [12]. Basic research of the righting reflex as the labyrinthine reflex and clinical research into application in diagnosis of neurosurgical disease and rehabilitation are ongoing in fields totally removed from the neuro-otology area.

Kaga et al. reported for the first time in 1981 quantitative research on the effect of early detection of a congenital vestibular function disorder on the development of balance and motor function [13]. Children with severe congenital deafness were evaluated by the one-direction damped rotational chair test, and compared with healthy children, holding up of the head and commencement of independent ambulation were reported to be considerably delayed in children showing no response in rotatory nystagmus. The discovery of the auditory brainstem response (ABR) by Jewett in 1970 and progress in its clinical application prompted this research [12].

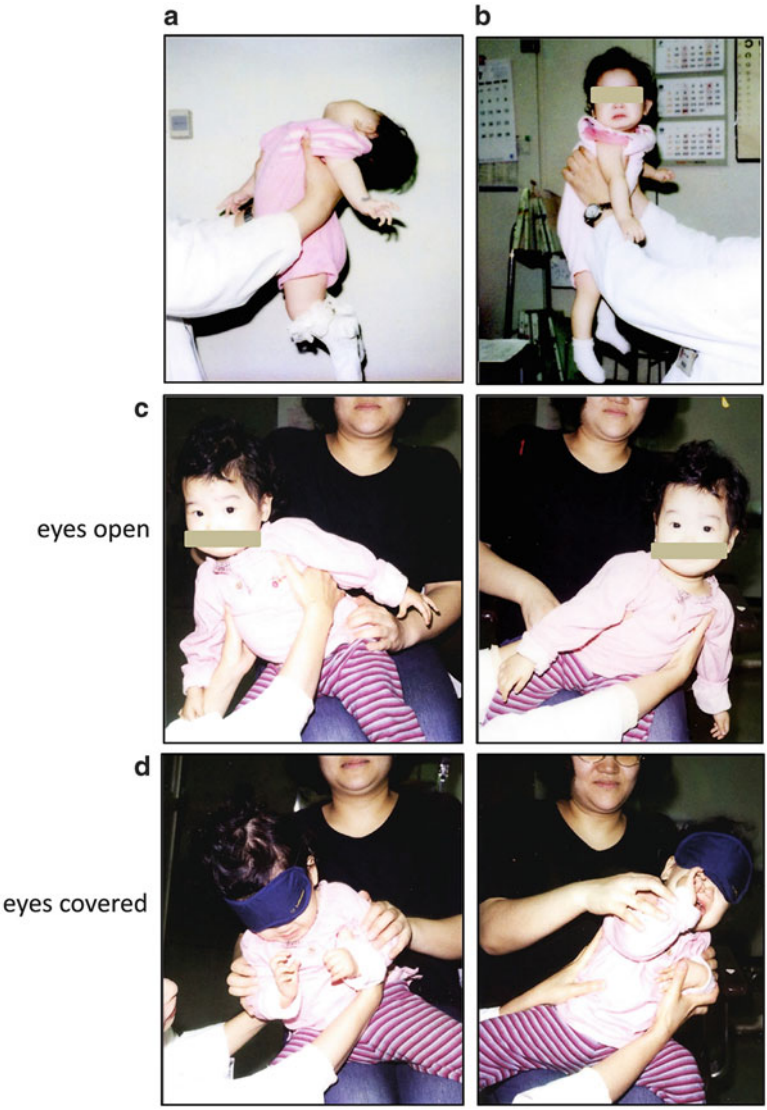

Fig. 1.9 Head and neck righting reflex in a girl of severe deafness and vestibular loss with eyes open and eyes covered [12]. (**a**) Head lagging and no head control at the age of 4 months. (**b**) Head control is achieved at the age of 14 months. (**c**) Head and neck righting reflex is well achieved at the age of 2 years with eyes open. (**d**) Head and neck righting reflex is lost with eyes covered

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Chapter 2
The Basis of Vertigo and Balance Disorders in Children

Abstract Embyrologically the vestibular semicircular canals and their sensory cells develop and are completed at relatively early stage of the fetus compared with the auditory organ.

Myelination in the human brain starts around gestation month 4. The vestibulospinal tract and vestibular eye movement system belong to older strains in the order of phylogenesis, and both myelination and development start early. The role of the labyrinthine sense in controlling posture is classified into maintenance of muscle tone and the righting reflex in newborns and infants. Unilateral and bilateral destruction of the labyrinth changes muscle tone and the righting reflex.

Keywords Damped rotational chair test • Labyrinthine destruction • Muscle tone • Postural change • Myelination • Primitive reflex • Righting reflex • Semicircular canal

2.1 Anatomical Development of the Vestibular Organ and Vestibular Nervous System

The relationship between maturation of the nervous system and development has been explained since Flechsig mainly as progression of myelination of the nervous system and Yakovlev as the age of its completion.

2.1.1 Development of Vestibular Semicircular Canals and Myelination of the Vestibular Nervous System

Embryologically the vestibular semicircular canals and their sensory cells develop and are completed at a relatively early stage of the fetus compared with the auditory organ (Fig. 2.1). The otocyst separates from the neural crest around gestation week 4,

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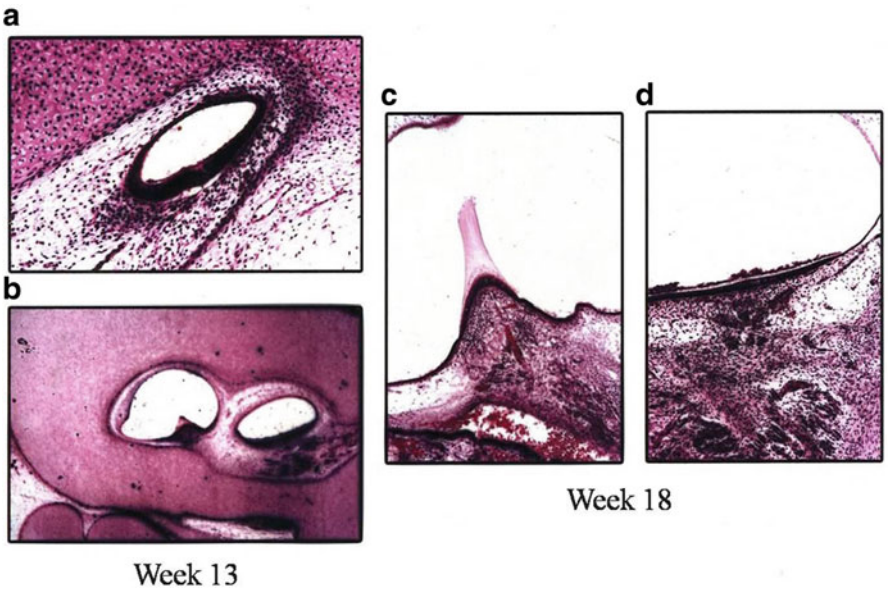

Fig. 2.1 Changes in structure and development of the semicircular canal and the otolithic organ. In gestation week 13, (**a**) cochlear duct and the organ of Corti are not at all formed; (**b**) semicircular canal ampulla and the otolithic organ are formed and differentiation of sensory cells has started to differentiate. In week 18, (**c**) cupula and sensory cells of the semicircular canal and the ampulla, as well as (**d**) otolith and sensory cells of the otolithic organ, are differentiated [1]

the endolymphatic duct develops around gestation week 5, the semicircular canals form around gestation week 6, and the vestibular area differentiates into the utricle/saccule around gestation week 7. The membranous labyrinth develops into nearly the shape and size of the adult around gestation week 12, and the inner ear is already complete at approximately gestation week 24. In other words, the vestibular semicircular canals of a newborn have been morphologically completed by this time [1].

Scarpa's ganglion is located in the vestibular nerve inside the internal auditory canal. This ganglion markedly increases its size with progression of gestation. Its size at week 39 is fourfold of that at week 13 (Fig. 2.2) [2].

2.1.2 Development of the Vestibular/Motor Nervous System

Myelination in humans starts around gestation month 4, but full-fledged development starts after birth and continues through infancy into puberty. However, myelination does not progress at the same time, and myelination is completed early or later depending on the strain, following a certain order. The rule applies here, in

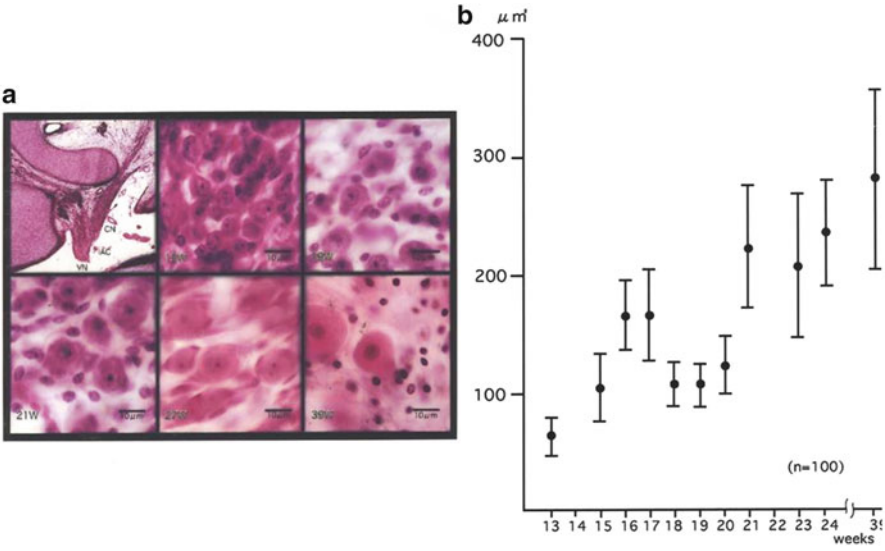

Fig. 2.2 Developmental changes in vestibular nerve cells. (**a**) The somatic area of the Scarpa's ganglion is shown to increase with progression of gestation week. (**b**) The area of the vestibular ganglion of a newborn is fourfold of that at gestation week 13 [2]

principle, that developmentally older strains are completed sooner also in individual development. Flechsig [3] concluded that the fascicle becomes completely functional after completion of myelination. In fact, function and myelination are closely related, and myelination tends to be completed sooner in strains with an earlier start of function. The vestibulospinal tract and vestibular eye movement system belong to older strains in the order of phylogenesis, and both myelination and development start early [4].

Yakovlev et al. [5] reported in their study of myelination that the duration required for completion of the myelin sheath differs, as each fiber bundle starts developing a myelin sheath at a different time. Each fiber bundle follows a predetermined cycle of myelination, which is called the "myelogenetic cycle" (Fig. 2.3). For instance, myelination of motor nerves has a short cycle (between gestation months 5 and 10), whereas myelination of the sensory nerves starts later and takes longer to complete (between gestation month 6 and 4 years of age). Myelination of the vestibular nerves is short cycled and occurs between gestation months 5 and 9, and each nerve of the eye movement system is myelinated at the same period. In other words, myelination of the conducting pathway of the vestibular system inside the brainstem starts during the prenatal period and is completed by birth. On the other hand, the duration of the cycle of brainstem reticular formation, which is closely related to the vestibular system, is longer (1 month to 10 years of age), and that of the cerebellar system starts at 8 months and is completed at 3 years of age.

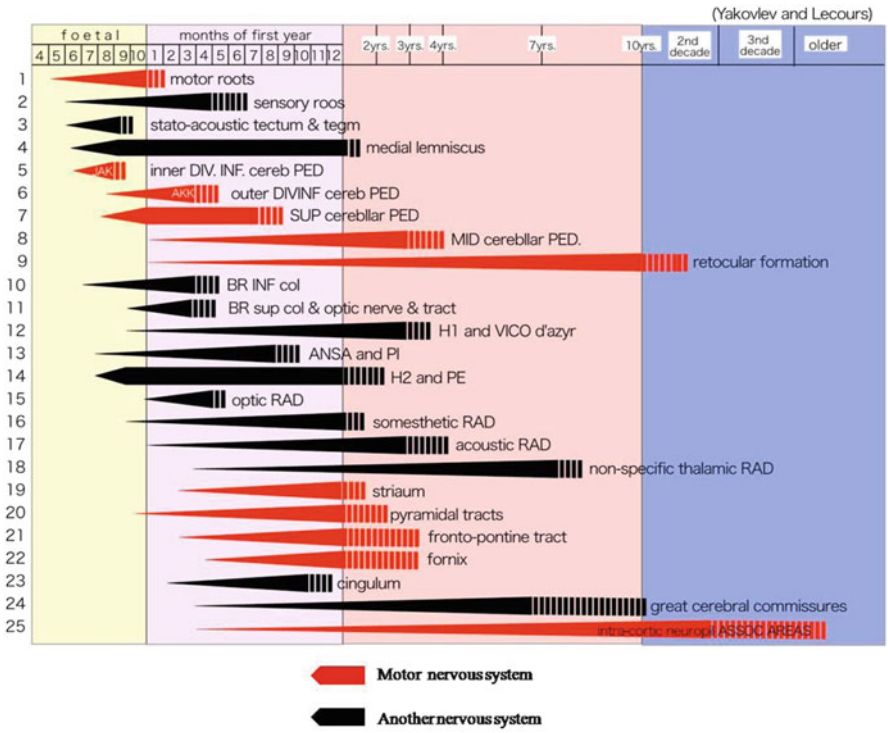

Fig. 2.3 The myelination cycle [5]. The width and length of graphs show the progression of stainability of myelinated nerve fibers and the intensity of concentration. *Dark shaded* portions at the far right indicate the age when myelination has been completed, by comparing specimens of fetuses, newborns, and adults

2.2 Motor Development of Healthy Infants and Children

2.2.1 Newborns and Infants

The primitive reflex is the motor function during this period, which disappears over the course of subsequent development. The timings of onset and disappearance of typical reflexes are shown in Fig. 2.4. A disorder of motor development is suspected when the primitive reflex is delayed or not induced at the usual timing. The primitive reflex disappears with maturation of the superordinate center of the brain, or progression of so-called corticalization [4].

2.2.2 Childhood

Milestones of motor development from the pediatric textbook in Japan are summarized as follows [6]: (1) holding up the head, 3–4 months of age; (2) sitting up, 7 months;

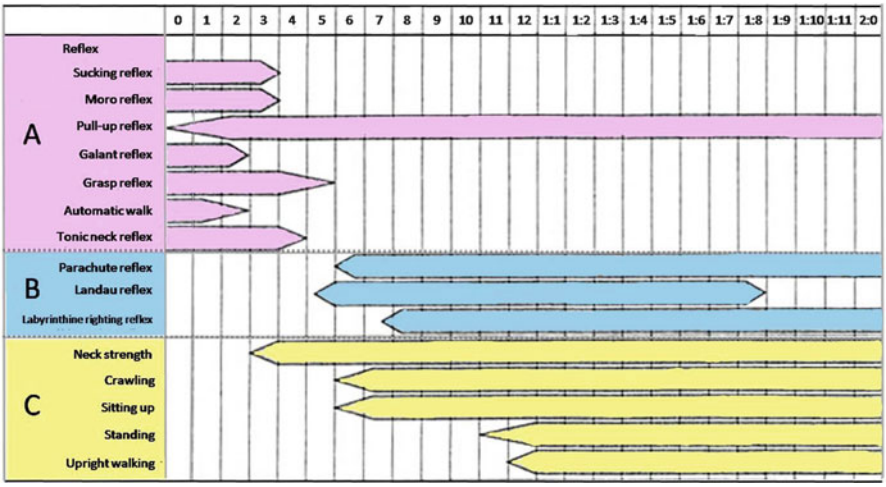

Fig. 2.4 Indices of motor development [1]. (**a**) Timings of onset and disappearance of primitive reflex. (**b**) Timings of onset of postural reflex. (**c**) Timings of acquisition of each gross motor item

(3) pulling up to standing, 9 months; (4) walking by holding on to things, 11 months; (5) standing up, 12 months; and (6) unassisted walking, 13–14 months on average. These milestones are called gross motor development, whereas development of grasping or holding is called fine motor development. Whether or not movement, such as holding a block or a pencil and shifting an object grabbed by one hand to the other hand, and the duration of holding an object appear at appropriate ages should be examined.

Development of gross or fine motor skills is likely influenced by intelligence or emotion in childhood, so a comprehensive evaluation should be made. Gesell [7] classified behavioral development in children into motor characteristics, adjustment, language, social, and self areas, while the Tsumori- Inage's questionnaire of psychomotor development often used in Japan is classified into motor, exploration, manipulation, social, eating/elimination, life habits, and comprehension/language areas [8]. The latter is useful for approximate evaluation because the ratio of chronological age and developmental age is expressed as the development index. Similar methods include the analytic test for development in infancy and childhood by Denver development scale [9].

2.3 Development of the Righting Reflex and Examination Methods

The role of the labyrinthine sense in controlling posture is classified into (1) maintenance of muscle tone (to the antigravity muscles, in particular); and (2) the righting reflex. Eviator et al. [10] classified the postural reflex mediated by the labyrinthine sense into the following four groups according to age and maturation level of the central nervous system.

2.3.1 Group I: 0–4 Months

The pyramidal tract and the medial lemniscus are not myelinated. The posture response is primitive and controlled at the brainstem level.

The tonic neck reflex is the most characteristic in this group. Neck movement induces impulses from the semicircular canals, but impulses are produced also by deep sensation stimulation via the cervical spine and muscles. Normal responses are generated by a combination of these:

- Neck righting (Fig. 2.5a): When the face is turned to one side, the righting reflex of the body occurs to the same direction.
- Asymmetric tonic neck reflex (ATNR) (Fig. 2.5b): When the face is turned to one side and the chest is held to prevent the neck reflex, the leg on the side to which the face is turned extends and the leg on the opposite side flexes.
- Symmetric tonic neck reflex (STNR): Tilting the head back while placing a hand under the chest causes the arms to extend and the legs to bend.
- Moro reflex (Fig. 2.5c): Dropping the subject's head backward by 30° while supporting the head and the back with both hands causes the arms to extend and spread out (abduction).

Vertical acceleration and the doll's eye phenomenon are mainly caused by the vestibular reflex.

- Vertical acceleration (Fig. 2.5d): When the examiner sits and suspends the child with his or her hands under its axillae, the arms are extended and the fingers spread. It is caused by stimulation to the utricle and saccule of the otolithic organ.
- Doll's eye phenomenon (Fig. 2.5e): Tilting the subject's head forward by 30° and rotating the body cause the eyes and the head to displace in opposite directions. This phenomenon usually lasts 2–6 weeks in healthy newborns and up to 3 months in premature infants.

2.3.2 Group II: 4–6 Months

This is a period between Group I and Group III in terms of pediatric neurology, and interindividual differences are notable. Electronystagmography (ENG) recording for damped rotational chair tests and caloric tests would be performed.

2.3.3 Group III: 6–48 Months

Cortical neuron synapses as well as myelination of the pyramidal tract and the medial lemniscus progress markedly. Vision/deep sensation and labyrinthine stimulation are integrated at the red nucleus level to cause the so-called righting reflex.

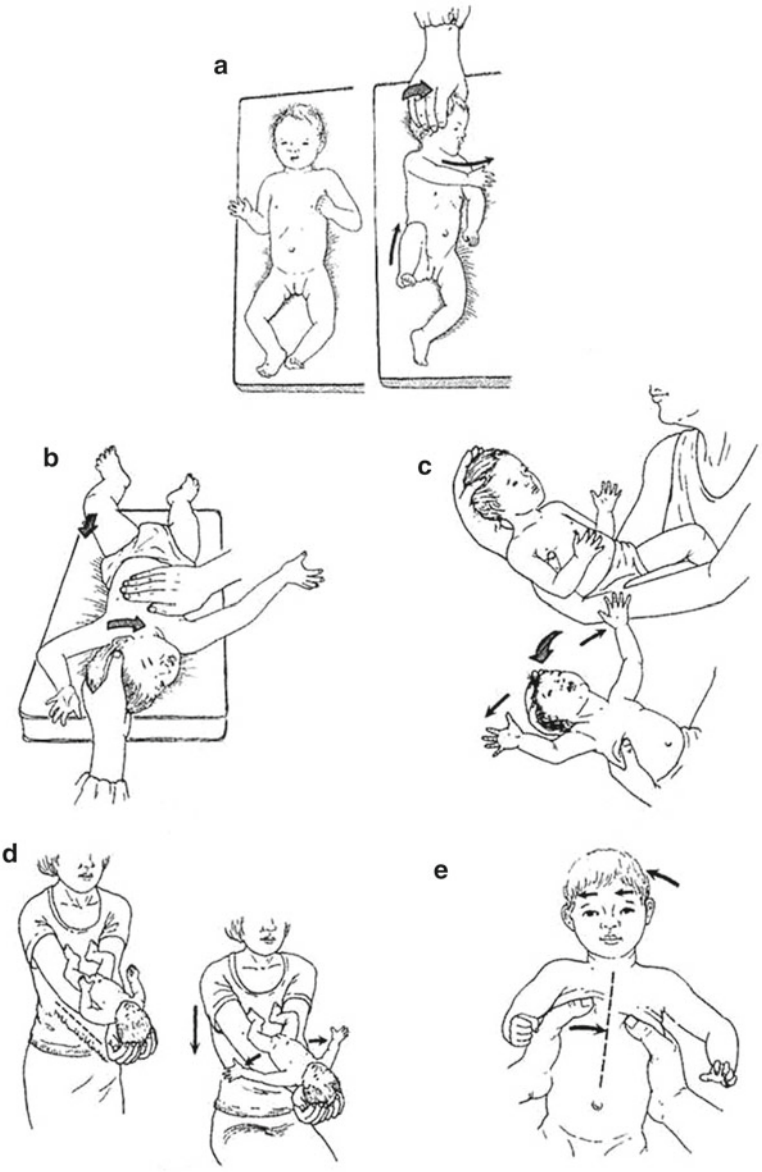

Fig. 2.5 Primitive reflexes of infants 0–4 months of age in Group I (see Table 2.1) [1]

- Head righting reflex (Fig. 2.6a–c): Shifting the body position in all of the tests causes righting of the head to make the mouth-eye line vertical.
- Buttress reflex (Fig. 2.6d): When the examiner places the infant in the sitting position and displaces the center of gravity with a gentle push on one shoulder, the head is righted and the contralateral hand is extended. It signifies maintaining the balance of a sitting position.

Table 2.1 Development of the labyrinthine reflex according to age

Group I: 0–4 months (Fig. 2.5)	Primitive reflexes (vestibular and proprioceptive afferents)
	Neck righting (a)
	Asymmetric tonic neck (b)
	Symmetric tonic neck
	Moro (c)
	Vestibular tests
	Vertical acceleration (d)
	Doll's eye phenomenon (e)
Group III: 6–48 months (Fig. 2.6)	Vestibular righting responses (patient blindfolded)
	Head over body righting >24 months
	Head righting
	Prone (a)
	Supine (b)
	Sideways (c)
	Buttress (d) >24 months
	Hopping (e) >24 months
	Parachute (f)

- Hopping reaction (Fig. 2.6e): Tested in infants who can stand up. When the examiner holds the child and shifts the body horizontally, forward, or backward, the head is righted and the child walks a few steps.
- Parachute reaction (Fig. 2.6f): When the child is suspended horizontally about the waist, facedown, the arms are extended/abducted and the fingers spread.

2.3.4 Group IV: 4 Years of Age to Adults

An adult equilibrium test may be performed for healthy children 4 years of age or older.

- Pulling the arm of a child in a sitting position (Fig. 2.7a) causes head righting and extension of the contralateral arm. A similar reaction is observed also in the kneeling position (Fig. 2.7b) and when on all fours (Fig. 2.7c).

The whole-body posture reaction may be induced also in a supine position using an inclined board (Fig. 2.7d, e). Slanting an inclined board by 45° causes head righting and extension/abduction of the arms and legs.

2.4 Role of Labyrinthine Muscle Tone

The effect of labyrinthine muscle tone is not obvious in humans. An adult with a bilateral labyrinthine disorder may present with a notable balance abnormality with eyes closed, but reduced muscle tone is not observed. However, in children under 1 year old, muscle tone is so reduced that the head becomes temporarily unsteady in the acute phase. In an adult patient with a unilateral labyrinthine disorder,

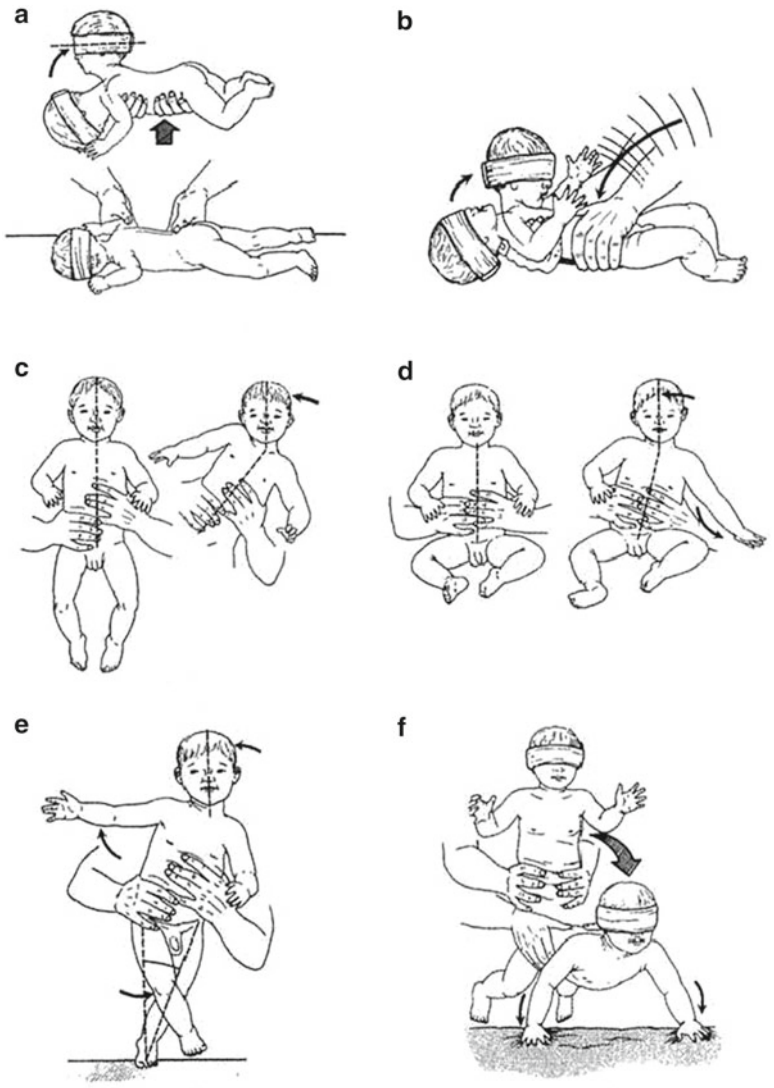

Fig. 2.6 Postural reflexes in children 6–48 months of age in Group III (see Table 2.1) [1]

displacement on the disabled side caused by a stepping test or a pointing test barely demonstrates its effect. The role of the labyrinth on muscle tone may therefore be ignored, but it is more notable in other vertebrate animals.

The labyrinthine muscle tone plays a greater role in infants because muscle control by a higher tonus is immature due to insufficient myelination of the cerebellum and the cerebrum. Labyrinth destruction in birds, fish, and small animals with a small cerebrum is known to cause abnormal posture or abnormal behavior due to loss of labyrinthine tone.

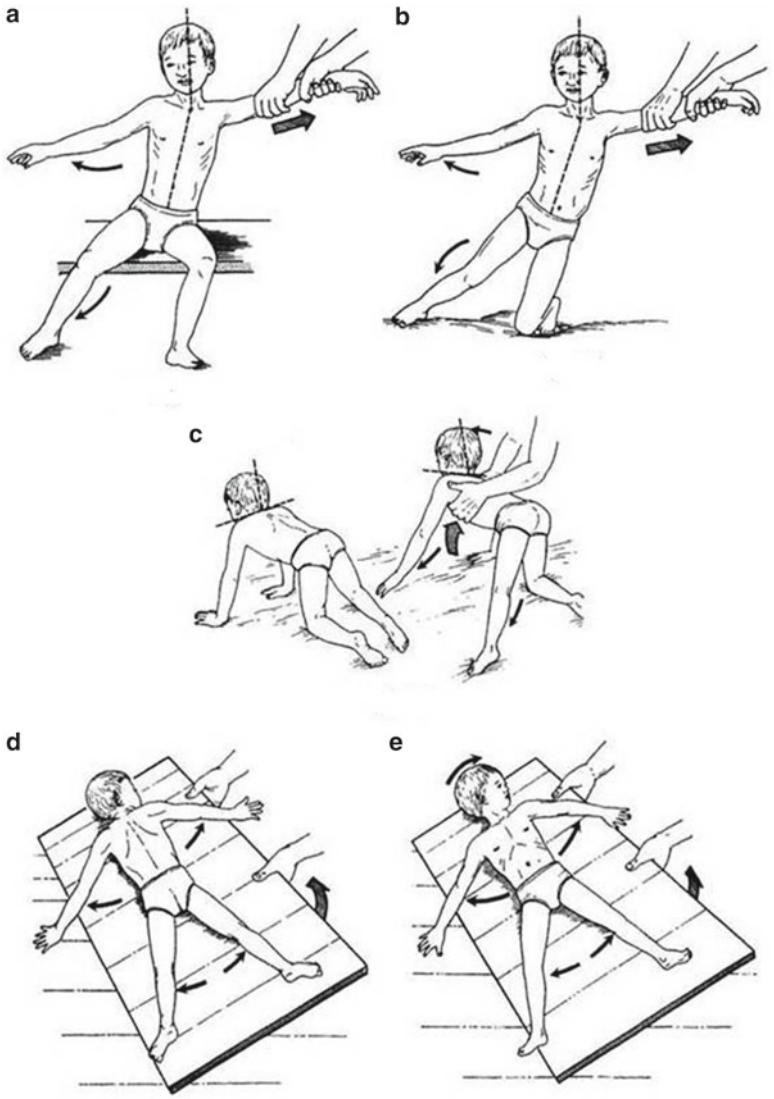

Fig. 2.7 Labyrinthine righting reflexes in children 4 years of age to adults in Group IV [1]

2.4.1 Unilateral Labyrinth Destruction of Pigeons, Frogs, and Cats and Changes in Muscle Tone

Unilateral labyrinth destruction causes:

- Tilting of the head to the affected side in pigeons (see Fig. 1.1), although flying is still possible
- A forced posture to the affected side in frogs and a spinning movement when immersed in water

- Tilting of the head to unaffected side in cats as well as walking in circles with affected side facing the center

The mechanism for these effects is thought to be as follows: unilateral labyrinthine destruction results in reactions only from the remaining labyrinth; stronger dominant tension is applied to contralateral side and stronger muscle contraction occurs on the unaffected side, tilting the head to the affected side, resulting in a forced posture with limbs of the damaged side bent (adduction) and on the affected side, abducted. Ocular displacement also occurs, with the eyes turned to the damaged side. Although compensation following unilateral destruction improves the condition, improvement is delayed and insufficient in lower animals because of the limited number of commissural fibers of the right and left vestibular nucleus and limited development of motor cortex.

2.4.2 Bilateral Labyrinth Destruction and Changes in Muscle Tone

Following bilateral labyrinth destruction, pigeons cannot fly because of the loss of labyrinthine muscle tone. Gait motion is decreased in cats. Fish can still swim despite bilateral labyrinth destruction because the lateral-line organs along the side of the body control the lateral reflex, which plays a role in maintaining posture. Primates such as monkeys suffer only disequilibrium. However, severe disequilibrium appears when an animal is blindfolded to block the influence of vision.

2.5 Labyrinthine Sense Disorder and Neurological Signs

Of the abnormal signs of dyskinesia associated with neurological diseases observed in newborns and infants up to 1 year of age, the following should be watched the most carefully: (1) abnormal posture; (2) increased or decreased muscle tone; (3) abnormal postural reflex; and (4) dyskinesia. Development of gross and/or fine motor control and an abnormal righting reflex should be monitored carefully in children 1 year of age or older. In normal infants, acquisition age of gross motor developmental milestones was reported by Ministry of Health, Labour and Welfare of Japan. The 90 percentile of acquisition age is compared in normal infants (Fig. 2.8).

In patients with congenital vestibular impairment or loss:

1. Control of the head is delayed, particularly in posture, and the head flops backward when an infant is placed in a sitting position (head lag).
2. Lowered muscle tone is notable and a so-called “floppy” status often appears.
3. Abnormality in postural reflex, delay in the Landau reflex and parachute reflex, and loss of the labyrinthine righting reflex are pronounced. However, delay in these reflexes is mostly recovered by improvement of muscle tone by a non-labyrinthine motor route and functions of vision, and tough and deep sensation.

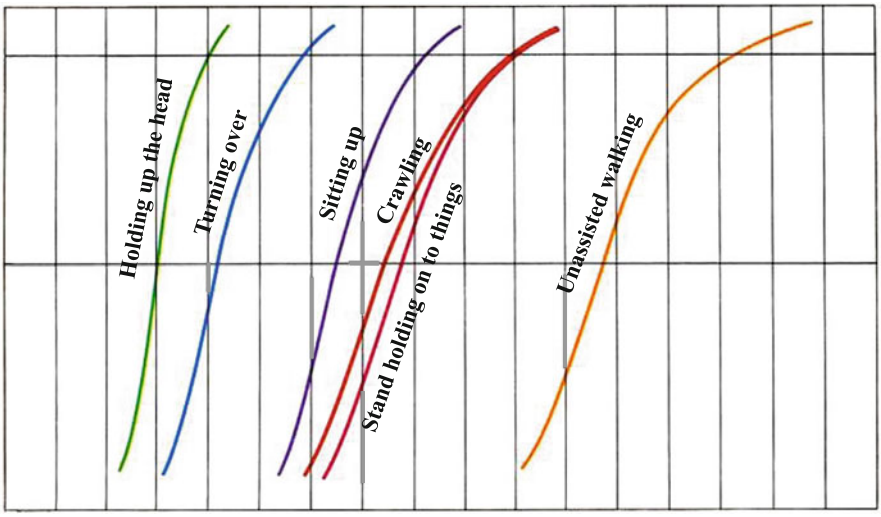

Fig. 2.8 Ninety percentile of acquisition age of gross motor developmental milestones in normal infants of Japan (from a report of Ministry Health, Labour and Welfare, 2010)

4. Dyskinesia does not appear. However, development of gross motor control, such as head steadiness, sitting position, standing up by holding on to things, and unassisted walking, is delayed.

2.6 Development of the Vestibulo-Ocular Reflex and Examination Methods

Caloric tests are conducted for adult patients with vestibulo-ocular reflex, and damped rotational chair tests are not preferred because of strong stimulation of the inner ear. However, children often do not cooperate with caloric tests and damped rotational chair tests are required.

2.6.1 Damped Rotational Chair Tests

Damped rotational chair tests consist of threshold one-direction rotation and various subthreshold rotation methods [11]. One-direction rotation is usually selected for infants and children (Fig. 2.9). A rotatory chair is rotated either manually, using a spring, or electrically, while ENG is recording, analyzing nystagmus during and after rotation.

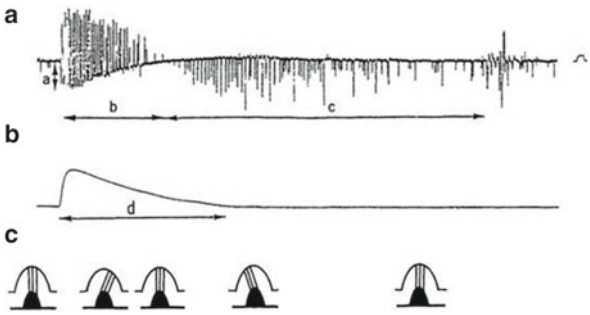

Fig. 2.9 ENG recordings of one-direction damped rotational chair test [1]

Of the per-rotatory and post-rotatory nystagmus elements in Bárány's rotational test, the frequency, duration, and latency of nystagmus are less varied, whereas the total amplitude of nystagmus and maximum velocity of the slow nystagmus phase are more varied. Per-rotatory nystagmus is less varied than post-rotatory nystagmus.

A similar tendency is observed also with the one-direction rotation damping method, and the frequency of nystagmus and duration of per-rotatory nystagmus are useful as practical parameters. However, post-rotatory nystagmus is difficult to judge due to the presence of artifact associated with body movement [12, 13].

2.6.1.1 Development of the Vestibulo-Ocular Reflex in Infants and Children

With respect to the two elements, per-rotatory frequency of nystagmus and duration of nystagmus induced by one-direction rotation damping stimuli [14], changes in the mean values with left and right rotation of six subjects in each group are shown in Figs. 2.10 and 2.11. The frequency of nystagmus increased with growth; newborns and infants 1 month of age had few episodes of nystagmus, which increased twofold in 1-year-old infants, threefold in 4-year-old children, and fourfold in adults. The duration of nystagmus increased to nearly threefold in 1-year-olds and fourfold in 6-year-old children, but decreased to 2.5-fold in adults. Such a pattern is observed also with Bárány rotation.

2.6.1.2 Precautions for Damped Rotational Chair Tests

1. Newborns and infants spend more time sleeping than awake. Make sure that the newborn/infant is fully awake before testing.
2. Adjust the fixation device so that the head is tilted 30° forward.
3. Correct weight for a rotation device so that predetermined load is applied irrespective of the weight of the subject.
4. When nystagmus is not recorded, confirm by gross observation whether it is caused by eye deviation or no response.
5. The laboratory should be kept dark to eliminate the influence of vision.

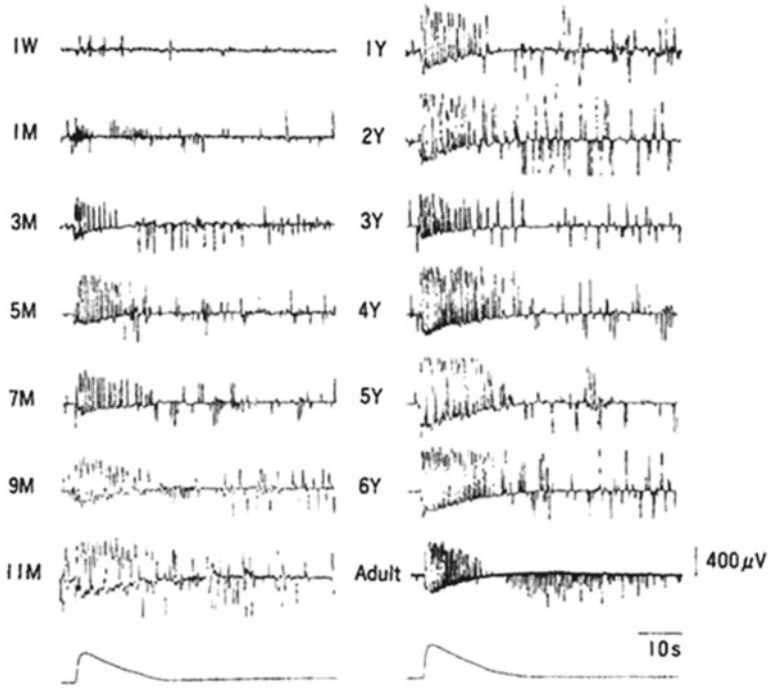

Fig. 2.10 ENG recordings of one-direction damped rotational chair tests classified by age [1]

2.6.2 Caloric Nystagmus Test

This test may be conducted in infants and children 4 months of age or older, but they are often uncooperative, e.g., crying and fussing, making accurate observations impossible. Testing is usually possible in children at least 2 years of age (Fig. 2.12). Increases in the frequency of nystagmus and the velocity of the nystagmus-damping phase with growth were identified from caloric nystagmus testing [14].

2.7 Examination of Total Locus Length by Stabilograph

Total locus length (accumulated shift distance length) can be recorded and analyzed when children reach 4 years of age or older (Fig. 2.13). Body sway is considered equivalent to gravity sway in this test, which analyzes factors such as total locus length, area, actual value, power spectrum, and velocity. As far as Romberg's coefficient and Mann's coefficient are concerned, the younger the child, the greater the body sway, although the sway is almost comparable to adults when a child reaches 7 years of age. Figure 2.14 shows changes in total locus length and actual body sway values in healthy children by age [15].

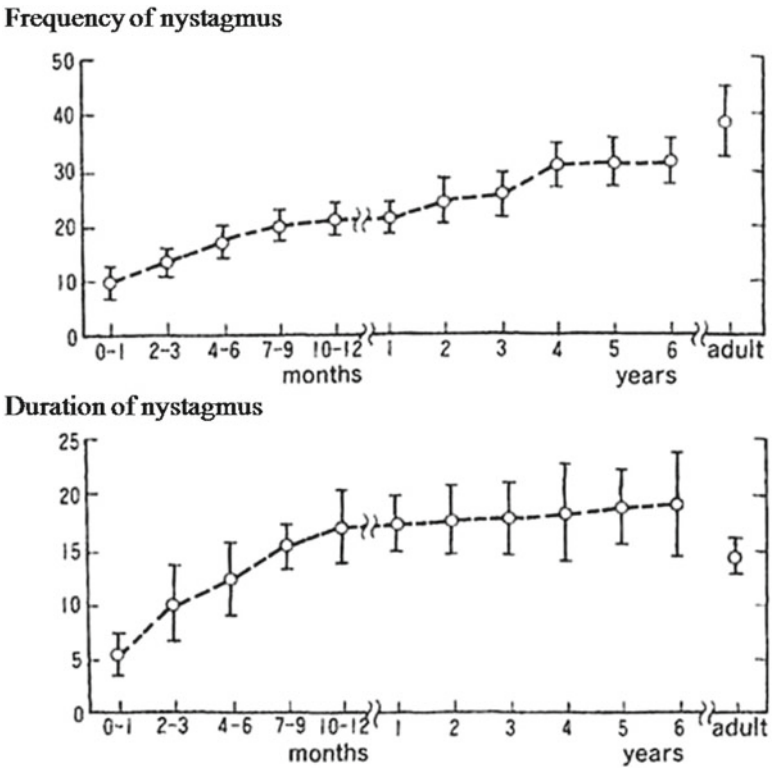

Fig. 2.11 Frequency of per-rotatory nystagmus during a one-direction damped rotational chair test (*top*) and changes in duration of nystagmus (*bottom*) by age [1]

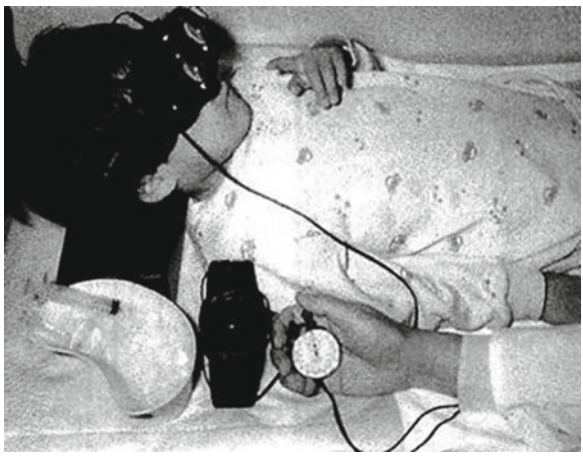

Fig. 2.12 Caloric nystagmus reaction [1]. Ice water infused into the external auditory canal

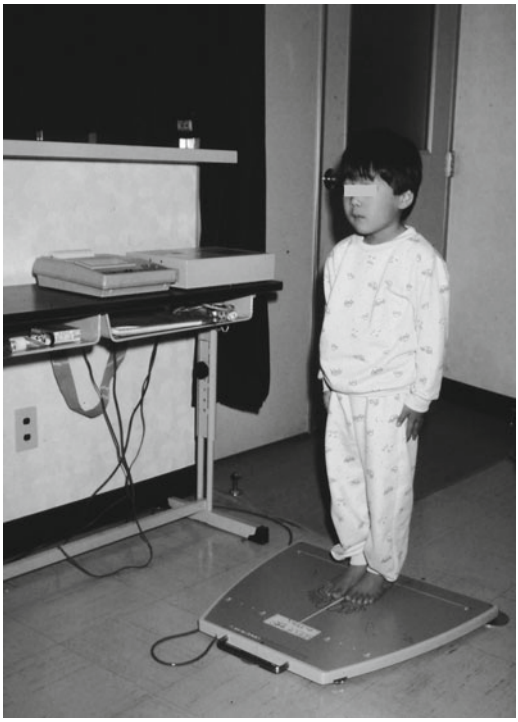

Fig. 2.13 Examination by stabilometry [1]

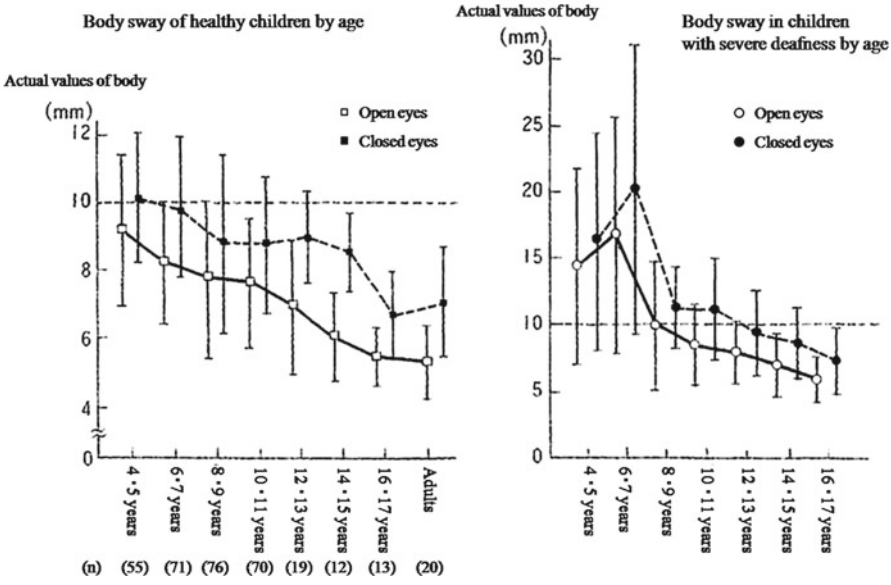

Fig. 2.14 Changes in Romberg posture by stabilometry in healthy children and children with severe deafness by age [1]

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Chapter 3
Disequilibrium: Abnormal Posture Control

Abstract In congenital disorders of the inner ear and cerebellar hypoplasia, muscle tone is considerably reduced in patients during the early phase of these diseases, and a persisting floppy phase and considerable delays in head and neck stability and the timing of first walking are seen in such babies.

Patients with congenital disorders of the inner ear are often misdiagnosed as cerebral palsy development because the symptoms are similar in the early stage.

In acquired disorders of the inner ear, such as meningitis, balance function and motor development could degenerate due to sudden onset of labyrinthine disorder in a normally delivered new born. The symptoms may be too severe to be mistaken a serious brain disorder. Visual disturbances have a considerable impact on the development of motor function. Children with congenital blindness start walking around 2 years of age, a delay of approximately 1 year.

Moreover, various congenital brain diseases such as cerebellar and cerebellar anomaly or meningitis cause serious delay in motor development.

Keywords Acquired inner ear disorder • Benign paroxysmal torticollis • Cerebellar hypoplasia • Congenital • Congenital blindness • Congenital oculomotor apraxia

3.1 Pathophysiology of Postural Control

A patient with a balance disorder or disequilibrium has difficulty controlling posture at standstill or during exercise, although a pyramidal tract lesion or extrapyramidal disorder is not observed. The lesion of the disorder is the semicircular canals or the otolith of the inner ear, in other words, the labyrinth or the cerebellum. The condition may be congenital or acquired.

Many diseases presenting congenital motor abnormalities are caused by abnormal muscle tone associated with a disorder of the extrapyramidal system, such as paralysis or athetoid cerebral palsy caused by a pyramidal tract lesion as observed in patients with spastic cerebral palsy. Diseases without paralysis will be explained

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below. Congenital disorders of the inner ear and cerebellar hypoplasia are examples. Muscle tone is considerably reduced in patients during the early phase of these diseases, and a persisting floppy phase and considerable delays in head and neck stability and the timing of first walking are seen in such babies. Patients with the above disease are often misdiagnosed in pediatric or orthopedic departments as cerebral palsy or severe delay in psychomotor development because the symptoms are similar in the early stages. Accurate diagnosis can be made now, thanks to progress in imaging diagnostics using CT and MRI of the inner ear and cerebellum, as well as damped rotational chair tests of the semicircular canals, but it remains a problem that knowledge of these diseases has not been sufficiently disseminated.

Damped rotational chair tests are performed for diagnosis of labyrinthine disorders in infants and small children in particular, because caloric tests for the vestibulo-ocular reflex are useless when a child cries and closes their eyes. Per-rotational nystagmus is used for evaluation in children because post-rotational nystagmus is not likely to develop [1, 2].

3.2 Congenital Disequilibrium

3.2.1 Balance Disorder due to Congenital Bilateral Loss of Labyrinthine Function

Damped rotational chair tests are used for evaluation of semicircular canal function. Furthermore, vestibular-evoked myogenic potential (VEMP) is recorded. It is the newest test for balance function used for evaluation of otolithic function [3] (Fig. 3.1).

A balance disorder is often observed as a complication in children with severe congenital sensorineural hearing loss, but it has been known to resolve by adulthood, although the mechanism was not verified. The impact of labyrinthine disorder on motor development during infancy/childhood was identified by Rapin [4] through her retrospective interviews of students of a school for the deaf. Rapin, a famous American pediatric neurologist, reported in 1974 that head and neck stability, walking by holding on to things, and independent ambulation were delayed in some children with congenital labyrinthine disorder in her retrospective study. The author reported, using a 16-mm film at a Bárány Society meeting held in New York in 1980, that follow-up of the development of balance and motor activities in children showed there was a reduced response to a damped rotational chair test among children with severe congenital hearing loss diagnosed by ABR and that the more impaired the labyrinthine function was, the more pronounced the delay in achieving head and neck stability, walking by holding on to things, and independent ambulation was (Fig. 3.2) [5, 6]. Although they initially move by shuffling and are called a “shuffling baby,” motor and balance functions are acquired by compensation, which occurs over the course of growth (Figs. 3.2 and 3.3). Dr Rapin sent me

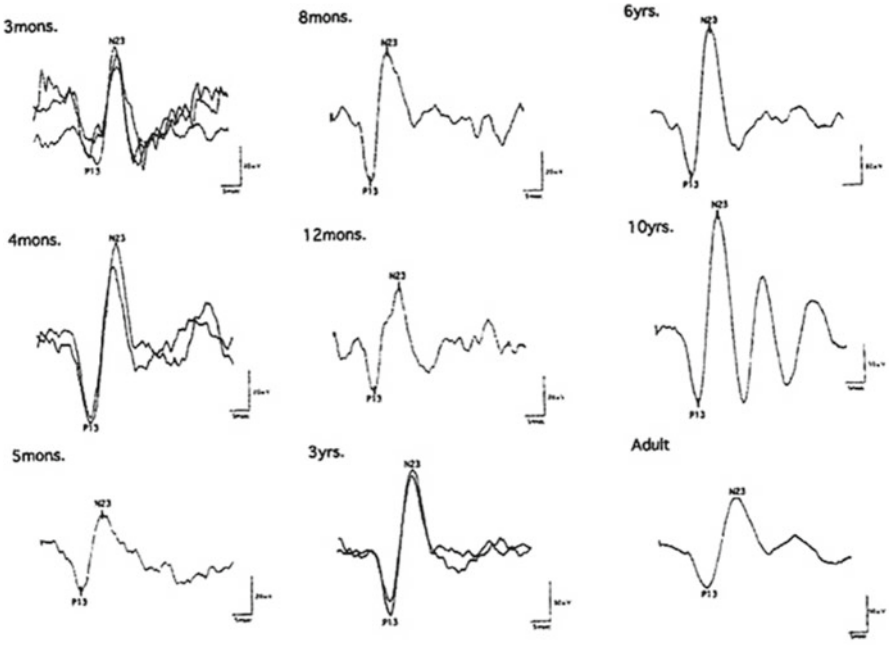

Fig. 3.1 Vestibular-evoked myogenic potential (VEMP) in infants. VEMP in infants is characterized by earlier latency and smaller amplitude than adults (*right bottom*). This is because of shorter neuromuscular circuits of the otolith, inferior vestibular nerve, vestibular nucleus, vestibulospinal tract, and cleidomastoid muscle, as well as weaker muscle tone [3]

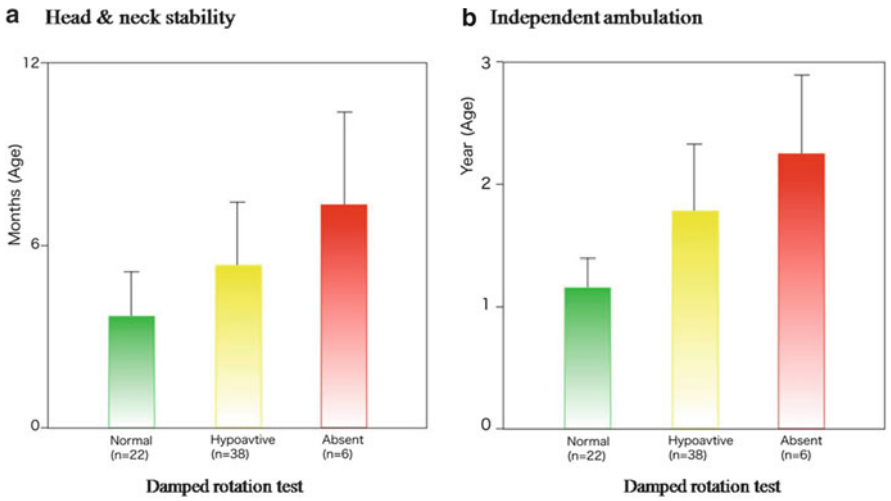

Fig. 3.2 Impaired congenital vestibular function and delay in head and neck stability and independent ambulation. (**a**) Head and neck stability is achieved at a mean of 3.5 months of age in healthy children, 5.5 months of age in children with impaired vestibular function (hypoactive), and 8 months of age in children with severe hypoactivity (absent). (**b**) Independent ambulation is achieved at 13 months of age in healthy children and 18 months of age in hypoactive children and is remarkably delayed at 24 months of age in severely hypoactive children [5, 6]

Fig. 3.3 A case of congenital disorder of bilateral vestibular semicircular canals. Development of balance from infancy to adolescence [6]. (**a**) Cannot walk unless assisted at 12 months of age (*left*). Can walk when one arm is held at 1 year and 8 months of age (*middle*), and balance is kept while running but cannot stop at age 2 years and 1 month (*right*). (**b**) Cannot walk on a balance beam at 1 year and 8 months of age (*left*), can walk when one hand is held at 2 years and 5 months of age (*middle*), and can stand up at 3 years and 2 months (*right*). (**c**) Can walk on a balance beam blindfolded at 6 years of age. Jumping on one foot is possible, although standing on one foot is difficult. (**d**) Walking and even skateboarding are possible in the ninth grade (15 years of age)

a letter before my presentation at the Bárány Society meeting, indicating that she was very interested in my study, which would confirm her theory (Fig. 3.4). In our report, 34, 57, and 9 % of children with severe congenital hearing loss showed normal function, reduced function, and no response, respectively, in a damped rotational chair test. The more severe the reduced labyrinthine function, the more delayed the timing of achieving head and neck stability, standing up, and independent ambulation. However, sitting up and walking by holding on to things are not delayed as much. In other words, the function with support is less delayed. In a letter that we received after completion of Bárány Society meeting, Rapin thanked me for having proved her theory, and our friendship has continued for the 25 years since. Although many of the diseases causing hearing loss have not been elucidated, a notable delay in the development of balance function is often observed in patients with cytomegalovirus infection and an inner ear anomaly. Findings shown by brain CT and CT of the temporal bone is the characteristic abnormality of the former and the latter, respectively (Fig. 3.5).

The neurological characteristics of congenital disequilibrium are:

1. Weaker head stability and support of the trunk by the legs due to reduced labyrinthine muscle tone, i.e., bad balance, in children under 1 year of age
2. Difficulty in independent ambulation due to impaired labyrinthine reflex and likely retroflexion of the head in children between 1 and 2 years of age (Fig. 3.6)
3. A tendency to fall when highly balanced function is required such as walking on "futon, sand, or snow" in children between 3 and 5 years of age [7]

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Dear Colleagues:

In reviewing the program of the forthcoming conference on Vestibular and Occular Motor Physiology at the New York Academy of Sciences in New York in September, I note that you are presenting a paper that interests me particularly, "Influence of Labyrinthine Hypoactivity on Gross Motor Development of Infants". Unfortunately, I shall be out of town on that day otherwise I could come to hear you. As you may know, I have found that a proportion, but not all, children with labyrinthine hypoactivity sit late and walk late. (see enclosed reprint) My study was unfortunately a retroactive one. Since I am teaching that vestibular impairment is one of the causes for late achievement of motor milestones and possibly for hypotonia in early life, I am anxious to know whether your study, which no doubt is prospective and more detailed than was possible in mine, confirms my results.

I would be very grateful if when you are in New York you might send me a copy of your manuscript. I apologize again for being unable to come and listen to you and wish you a pleasant trip in the United States.

Sincerely yours,

Isabelle Rapin, M.D.
Professor
Neurology and Pediatrics (Neurology)

IR/hm
encl.

Fig. 3.4 A letter from Dr. Rapin, professor of Neurology and Pediatrics, Albert Einstein University in the USA (1980). Dr. Rapin wrote that she would be anxious to know whether my study, presented at the Bárány Society meeting in New York, would confirm her theory that "labyrinthine disorder is a cause of delayed motor development" [4]

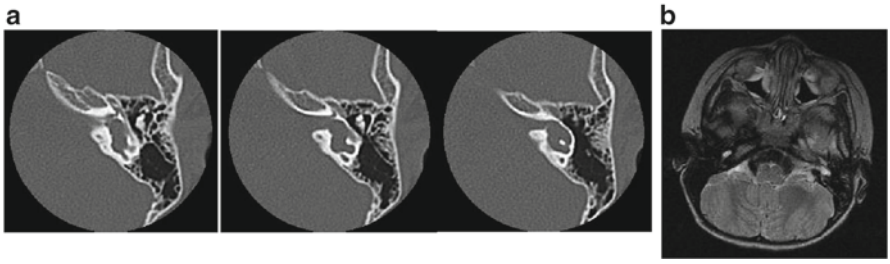

Fig. 3.5 CT and MRI of a patient with common cavity, anomaly of both inner ears (7 years of age). (**a**) CT and (**b**) MRI [7]. Severe hearing loss and balance disorder are present. Holding up the head: 5 years old. Unassisted walking: 19 months. A bag-like formation of the cochlea and vestibular semicircular canals

However, delay in fine motor control of the arms is not observed at first, and the balance abnormality improves with growth/development even with a decrease or loss of the labyrinthine reflex. Most children achieve normal motor function by the time they start elementary school, and they can enjoy most exercises by the time they start junior high or high school (Fig. 3.7). The mechanism of compensation

Fig. 3.6 Opisthotonus-like bridging posture in a patient with congenital bilateral vestibular function disorder (2 years of age) [7]

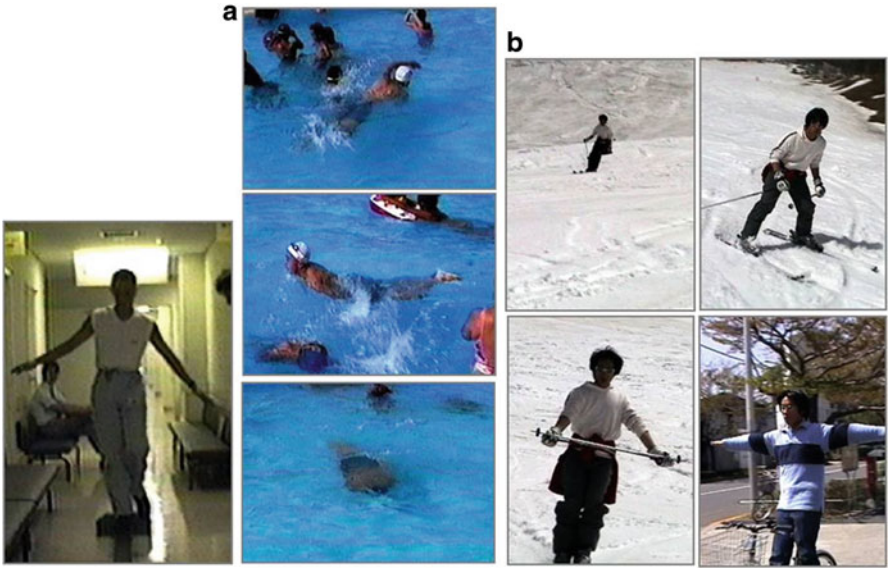

Fig. 3.7 Development of balance and motor function achieved during high-school years in two patients with congenital bilateral dysfunction of vestibular semicircular canals. (**a**) A child with an inner ear anomaly (Mondini type) can walk skillfully on a balance beam and swim submerged in water. (**b**) Head and neck stability and walking were delayed in this patient, but he grew up to be a good skier and to even ride a bicycle without holding on to the handlebars [7.8]

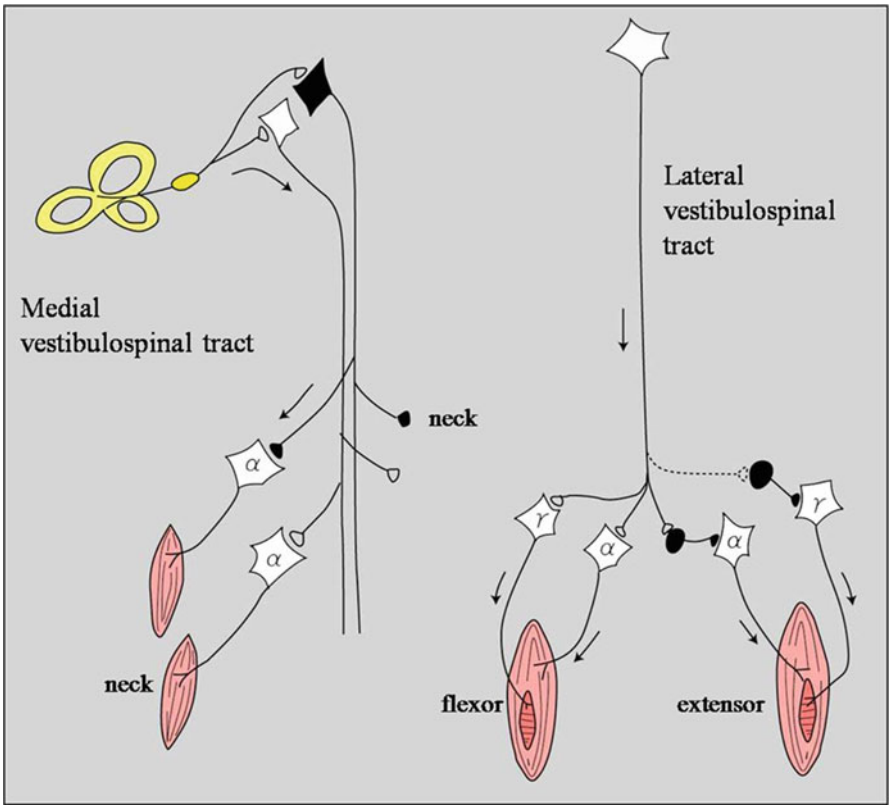

Fig. 3.8 Vestibulospinal tract [8]. *Left*: Neck muscles are controlled starting with the vestibular semicircular canals via the vestibular nucleus to the inner vestibulospinal tract. Delayed head and neck stability in a child with hearing loss is considered attributable to dysfunction of this neural circuit. *Right*: The flexor is reached from the vestibular semicircular canals, via the vestibular nucleus, external vestibulospinal tract, and connector neurons α, γ, whereas the extensor is reached via the suppression neurons and the connector neurons α, γ. Delayed walking in a child with hearing loss is considered attributable to dysfunction of this neural circuit

through development is shown in Fig. 3.8; the vestibulospinal tract uses the vestibular semicircular canals as a sensor, but the labyrinthine muscle tone required for the neck and leg muscles is not achieved during the early phase of development because of dysfunction caused by impairment of sensors. With growth, however, central tone is achieved by the cerebellum, basal ganglia, and cerebrum [7, 8] (Table 3.1).

Children with a congenital balance disorder rarely experience vision abnormalities during exercise (such as the jumbling phenomenon or blurred vision that is observed in adult patients with bilateral labyrinth loss), difficulty walking in the

Table 3.1 Acquisition age of head control and independent walk in deaf children with impaired vestibular function

Damped rotational chair test	Head control	Independent walks
Normal response	3–4 months	12–13 months
Poor response	4–6 months	1.5–2 years
No response	6–7 months	2–2.5 years

Fig. 3.9 Schema showing sketches of an inner ear abnormality based on CT of the temporal bone. The vestibule is bag-shaped with an absence of semicircular canals. The cochlea formed as merely one and a half turns. The *shaded areas* indicate no formation [9]

dark, or positive Romberg sign with eyes closed, and near drowning due to loss of orientation in water while swimming. The function of mechanism compensating for this has been attracting attention. The Mondini type is the typical anomaly of the inner ear characterized by a bag-shaped otolith and absence of the semicircular canals. Balance/motor development is delayed in patients with such an inner ear abnormality as observed in children with severe congenital hearing loss. Although the vestibulo-ocular reflex may not respond to a caloric test, nystagmus may be induced by damped rotational chair tests, indicating that the otolith responds to rotation [7].

Inner ear abnormalities are often found using high-resolution CT in children with congenital hearing loss. One of the typical inner ear abnormalities is a bag-shaped otolith and absence of semicircular canals (Fig. 3.9). Balance/motor development is delayed in patients with such inner ear abnormality as observed in children with severe congenital hearing loss. Although vestibulo-ocular reflex may not respond to a caloric test, nystagmus is often induced by damped rotational chair tests (Fig. 3.10), indicating that the otolith may respond to rotation [9]. Patients with an inner ear abnormality also have a high frequency of complications of anomalies of the eyes, heart, or mouth. It suggests the likelihood of the occurrence of a developmental abnormality in these organs during the prenatal period because the timing of completion of the semicircular canals is close to that of these organs (Fig. 3.11) [10].

Development of balance/motor development is further delayed in patients with multiple disorders. Complication by mental retardation or sequelae of meningitis/encephalitis is considered to delay the compensatory effect and the learning of motor functions [11, 12].

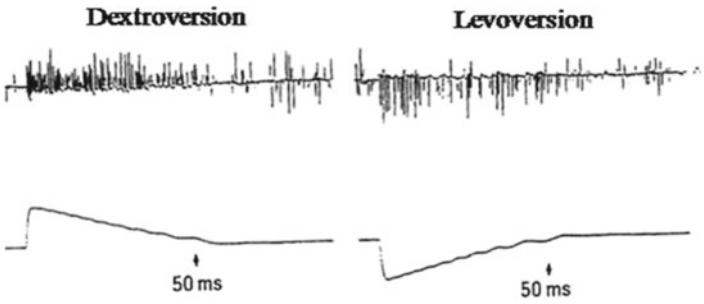

Fig. 3.10 Results of damped rotational chair tests in the patient from Fig. 3.9. Per-rotatory nystagmus was induced by both *right* and *left rotation*. Caloric nystagmus reaction is absent [9]

Typical of such cases is cytomegalovirus infection during the prenatal period. The incidence of complication of labyrinthine disorder with nuclear jaundice, athetoid cerebral palsy due to neonatal hyperbilirubinemia, is high in patients with cerebral palsy. It is also observed in the spastic type due to neonatal asphyxia and considerably delays motor development [1].

Patients with labyrinthine disorder are often misdiagnosed as cerebral palsy, delayed psychomotor development, muscular disease, or cerebellar disorder by a pediatrician or an orthopedician because of symptoms such as hearing loss induced by a cochlear disorder, delay in language development associated with it, and/or delay in motor development induced by vestibular semicircular canal disorder, so due attention is required when making a diagnosis.

Misdiagnosis is preventable by performing ABR and damped rotational chair tests. However, a complication of labyrinthine disorder is more common in patients with cerebral palsy, and the frequency is higher in the athetosis type than the spastic type. Labyrinthine disorder is likely overlooked in such a case because of the presence of cerebral palsy.

3.3 Acquired Abnormality of Balance Function and Motor Development

Balance function and motor development could degenerate due to the sudden onset of labyrinthine disorder in a normally delivered newborn, although there was no problem with motor development in the early stages. The symptoms may be too severe to be mistaken for a serious brain disorder. However, balance function is regained through compensation by the central nervous system and relearning, even though the disorder may continue up to a certain age. After certain age, children merely present a temporary balance abnormality without degradation of symptoms. What will that age be?

AGE (days)	LENGTH (mm)	STAGE Streeter	EYE	EAR	FACE	HEART
19	1	IX				Merging mesoblast anterior to prechordal plate
24	2	X early somites	Optic evagination 	Otic placode 	Mandible Hyoid arches	Single heart tube Propulsion 
30	4	XII 21–29 somites	Optic cup 	Otic in vagination 	Fusion, mand. arches 	Ventric. outpouching Gelatinous reticulum 
34	7	XIV	Lens invagination 	Otic vesicle 	Otfactory placodes 	Auric. outpouching Septum primum 
38	11	XVI	Lens detached Pigmented retina 	Endolymphic sac Ext. auditory meatus Tubotympanic recess 	Nasal swellings 	Fusion mid. A-V canal Muscular vent. sept. 
44	17	XVIII	Lens fibers Migration of retinal cells Hyaloid vessels 		Choana, Prim. palate 	Aorta Pulmonary artery Valves Membrane ventricular septum
52	23	XX	Corneal body Mesoderm No lumen in optic stalk			Septum secundum 
55	28	XXII	Eyelids	Spiral cochlear duct Tragus		

Fig. 3.11 Development of the eyes, ears, face, and heart. Helpful for understanding inner ear anomalies and anomaly complications [10]. Adapted from Jones KL, [Smith's recognizable patterns of human malformation. W.B. Saunders Philadelphia 1988]

3.3.1 *Effect of Bilateral Loss of Labyrinthine Function in Newborns and Infants*

Eviator et al. [13] investigated newborns treated with aminoglycoside for sepsis and observed that abnormalities shown by equilibrium tests, such as the caloric test, coincided with a notable delay in neck/head stability, which indicates a contribution of labyrinthine function to neck/head stability. The effect of gentamicin sulfate is more pronounced than that of kanamycin sulfate. The authors also noted the impact of the acquired labyrinthine disorder on balance function during infancy, which is similar to that of congenital labyrinthine disorder.

3.3.2 *Effect of Bilateral Loss of Labyrinthine Function in Childhood*

In many cases, the effect of meningitis or encephalitis on the labyrinth is the cause of bilateral loss of labyrinthine function. Ototoxicity attributable to antibiotic administration may be another cause. Disequilibrium in the acute and subacute phase is likely misunderstood as central or cerebellar ataxia due to a balance abnormality and lowered muscle tone. However, differential diagnosis is possible because of the decrease or loss of caloric nystagmus, presence of ataxia in the legs but not in the arms, and absence of abnormal cerebellar eye movement. Neurological signs are difficult to understand as elements in patients with encephalitis because of the overall deterioration of cerebral function, so differentiation is often difficult.

When bilateral loss of labyrinthine function occurs for the first time at around 1 year of age, motor functions acquired so far, such as neck/head stability, sitting up, standing up, and walking, are lost for several months, and mothers lament that their child “went into regression.” However, regaining the functions will be possible within 1 and 4 months, unless abnormality of cerebral function is present (Fig. 3.12). The time to regain function would increase twofold or more in a child with concomitant mental disabilities because of the delay in motor learning.

Temporary balance disorders in children of 2 years of age or older are immediately compensated. This shows that the central control of posture from the cerebellar and cerebral levels is dominant and replaces the labyrinthine function after 2 years of age.

Aminoglycosides have an ototoxic effect. They have been used cautiously in recent years, but an intraspinal injection of gentamicin sulfate may be required as a lifesaving treatment in meningitis. Adverse reactions of hearing loss and disequilibrium may occur, so it is advisable to perform ABR and damped rotational chair tests prior to administration to enable comparison of results after treatment.

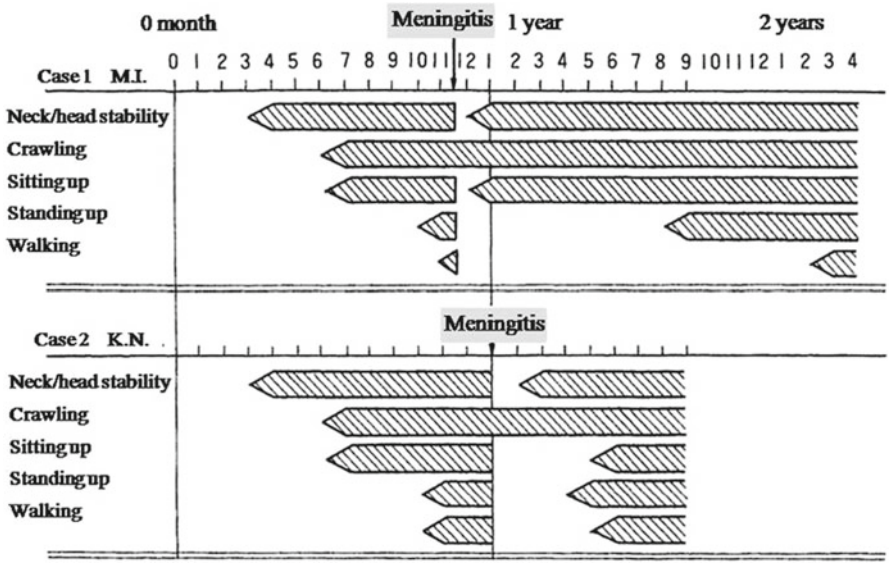

Fig. 3.12 Processes of loss and reacquisition of motor function in two patients with acquired disequilibrium [11]

3.4 Bilateral Loss of Labyrinthine Function After School Age

Ototoxic drugs, such as gentamicin sulfate and amikacin sulfate, or meningitis induces bilateral loss of labyrinthine function in adults. The symptoms include the jumbling phenomenon, or blurred vision caused by disturbed gaze function due to loss of the vestibulo-ocular reflex, and disequilibrium in the dark. Patients with congenital labyrinthine disorder present neither of these symptoms. The age when the symptoms become permanent is not known in cases of acquired disorder. In my experience with a 12-year-old patient with bilateral loss of labyrinthine function due to meningitis, the jumbling phenomenon disappeared and the Romberg phenomenon also became negative after a few months. Brain plasticity, sensory compensation, and motor learning must have been immediately triggered.

3.5 Unilateral Labyrinthine Disorder

Unilateral hearing loss and disequilibrium frequently occur in the acute phase of mumps in children. Vertigo/disequilibrium may also develop via intrusion of a temporal bone fracture into the labyrinth due to head trauma or labyrinthine concussion following a labyrinth contusion. The symptoms develop only in the acute phase and are immediately compensated. The rate of compensation is rapid as long as one of the labyrinths remains functional.

3.6 Complications of Visual and Labyrinthine Disorders and Development of Balance

3.6.1 Delay in Motor Function due to Visual Disturbance Alone

Congenital visual disturbances have a considerable impact on the development of motor function. Children's development is promoted by receiving and reacting to external stimuli and information. It is easily conceivable that restriction of visual information, the most important route for obtaining information, would greatly hinder development. Senda [14] of the National Institute of Special Education in Japan reported in "Restriction of behavior due to visual disturbance and subsequent reactions" that a child with congenital blindness starts walking around 2 years of age, a delay of approximately 1 year.

Myelination of the visual cortex starts at birth and is complete at around 5 months of age. The myelination cycle is completed quite early compared with myelination of the auditory cortex, which is complete at the age of 2 years. Visual cortex control should therefore be possible during infancy when it functions normally.

3.6.2 Vision and the Cerebellum

Ito [8] pointed out that "the vestibulo-ocular reflex functions to maintain the stability of the visual field. Blurred vision due to poor reflex to the target cannot be immediately feedback to the vestibular nucleus because such a route does not exist. The vestibulo-ocular reflex therefore has the structure of a forward control system, which is one of the so-called open loop control systems," and proposed the following floccular theory with the discovery of the climbing fiber pathway and mossy fiber pathway projected from the inferior olivary nucleus to the flocculus of the cerebellum.

1. The flocculus is inserted to the tri-neuron arc of the vestibulo-ocular reflex as a bypass, thereby contributing to motor characteristics of the vestibulo-ocular reflex.
2. The flocculus rapidly corrects a movement of the vestibulo-ocular reflex after receiving visual signals to stabilize the retinal image.
3. Repeated corrections above gradually change inner parameters inside the flocculus and improve the motor characteristics of the vestibulo-ocular reflex by learning.

The neural circuit of vision, inferior olivary nucleus, and cerebellar flocculus thus have an impact on balance function. That even a healthy person has difficulty in maintaining balance when walking blindfolded is the most decisive evidence. This theory, however, is not applicable to the central compensation effect after development of congenital disorder of the vestibular semicircular canal system and learning.

3.6.3 Visual Space Perception and Behavior of Children with Severe Amblyopia

Senda [14] reported on actual locomotor function in children with severe amblyopia. "Baby 'N' was born in the tenth month of pregnancy, weighing 3,620 g, to parents with visual disturbances. He presented with severe congenital cataracts. Neck/head stability was achieved at 3 months, sitting up at 6 months, rolling over at 8 months, standing up by holding onto something at 9 months, walking by holding on to something at 11 months, crawling at 12 months, and *walking at 16 months.* The right eye and the left eye were operated at age 2 years 8 months and 3 years 4 months, respectively." "Baby 'Y' who had prematurity retinopathy and mild right paralysis started crawling at 2 years 6 months, and *walking at 3 years 2 months of age.* Visual acuity was 0.04 in both eyes at 4 years of age." Children born with impaired vision (congenital amblyopia) are not aware that they cannot see well. Besides, they cannot communicate it to others. They are therefore often misunderstood because others do not understand their behavior (meaning), such as a shuffling walk due to the inability to perceive steps because of their difficulty judging distance and shaking of the head to ease nystagmus.

3.6.4 Influence of Blindness on Congenital Vestibular Failure

Vision plays a very important role in stabilizing gaze and maintaining balance of the body. Patients with low vision or blindness, in addition to vestibular failure, have great difficulty in acquiring central vestibular compensation and both in darkness and in the light.

Bilateral vestibular dysfunction could be manifested as the loss of postural control and the delay of development in gross motor function. Meantime, the motor developments in the congenitally blind children are delayed due to the difficulties in space perception. However, there are hardly any report about the vestibular function and motor development of the children who are congenitally deaf and blind. The development assessments of four children with congenitally severe deaf and severe blind are described. One patient was with congenital rubella syndrome, one was the with CHARGE syndrome, one was with anophthalmia and with congenitally deafness of unknown origin, and one was an extremely immature and extremely low birth weight infant. All cases were accompanied with very severe hearing loss and with very severe visual impairment (Table 3.2). Only case 2 had inner ear anomaly.

The vestibular function was examined by the damped rotational chair test. The development of gross motor function was checked on the acquirement age in the items such as head control, sitting, standing, and walking.

The gross motor developments of all cases were severely delayed. All cases could not stand up and walk by oneself until at least 2 years and 4 months of age.

Table 3.2 The motor developments of deaf-blindness cases were compared with these of normal, poor vestibular function, and blind children. All deaf-blindness cases could not stand up and walk until 2 years and 4 months of age

Cases	Remarks	Head control	Sitting	Standing by oneself	Walking by oneself
Normal body		3.5	8	10	12
Poor vestibular function		8	14	13	21
Blind					24
Deaf-blind case No. 1	Congenital nubella	6	44	>55[a]	>55[a]
Deaf-blind case No. 2	CHARGE	7	12	>28[a]	>28[a]
Deaf-blind case No. 3	Anophthalmia	6		>28[a]	>28[a]
Deaf-blind case No. 4	Low birth weight	12	>33[a]	>33[a]	>33[a]

[a]Not yet until (months old)

Fig. 3.13 Case 3 is a 2-year-old boy with opisthotonus-like persistent retroflexion of the head with congenital anophthalmia and deafness. It was not possible to perform the caloric test. In this case, VEMP revealed that saccular function was well preserved. It is possible that semicircular canal function was lost because of long-lasting opisthotonus-like head retroflexion. Central compensation was not good because he could not maintain body balance and did not walk (from Structure of Vertigo, Kanehara Shuppan, Tokyo, Kaga (2006))

Opisthotonus-like retroflexion of the head had persisted longer in all (Figs. 3.13 and 3.14).

The gross motor development in children with severe congenital deaf-blindness was found to be delayed further than that in the cases with congenital hearing impairment alone.

In these cases, vision is shown to play a very important role in acquiring central vestibular compensation in congenitally deaf infants with vestibular failure.

Careful treatment and planning for rehabilitation with cochlear implant are needed in the children with congenital deaf-blindness.

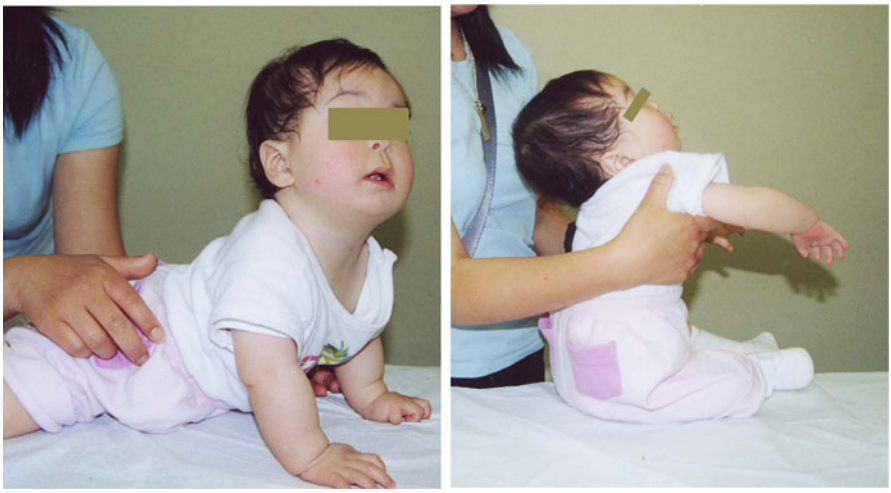

Fig. 3.14 Case 4 is a 2-year-old girl with congenital blindness and deafness with loss of vestibular function which was revealed by the caloric test, the damped rotational chair test, and VEMP. In this case, long-lasting opisthotonus-like head retroflexion continued, and delayed motor development was marked with slow central vestibular compensation [14]

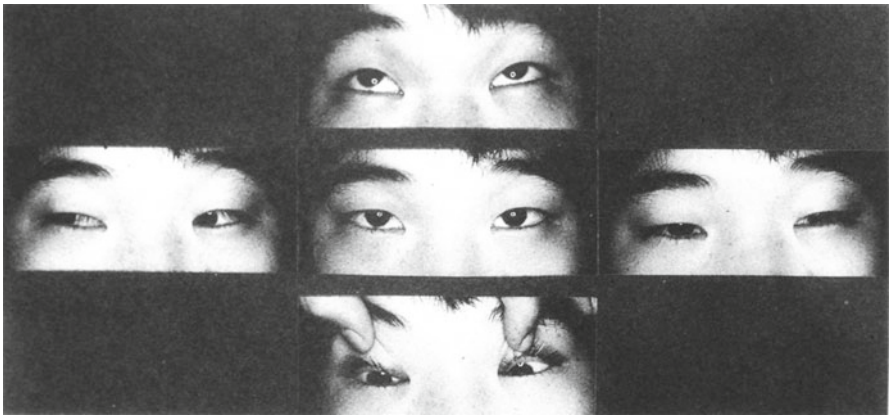

Fig. 3.15 Abnormal eye position due to pons glioma. Ocular dyskinesia of the *left* and *right* eyes is observed while gazing left [15]

3.7 Brain Tumor of the Posterior Cranial Fossa

Children who have been growing up healthy may suddenly start tripping, followed by an abnormal eye position such as abducent nerve paralysis (Fig. 3.15), which are the signs of a brain tumor of the pons or the cerebellum. Recordings of the ABR will show waves I to VII in normal children, whereas an abnormality is easily diagnosed

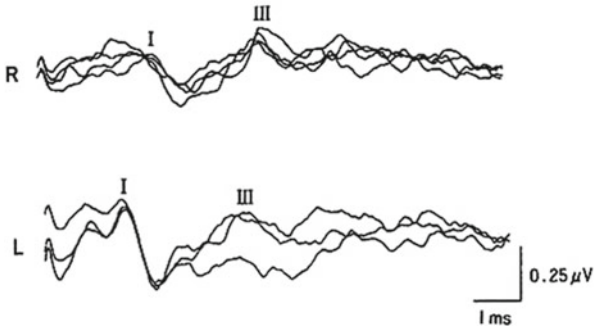

Fig. 3.16 ABR of the patient from Fig. 3.15. Only waves I, II, and III appear on both the *right* and *left* [15]

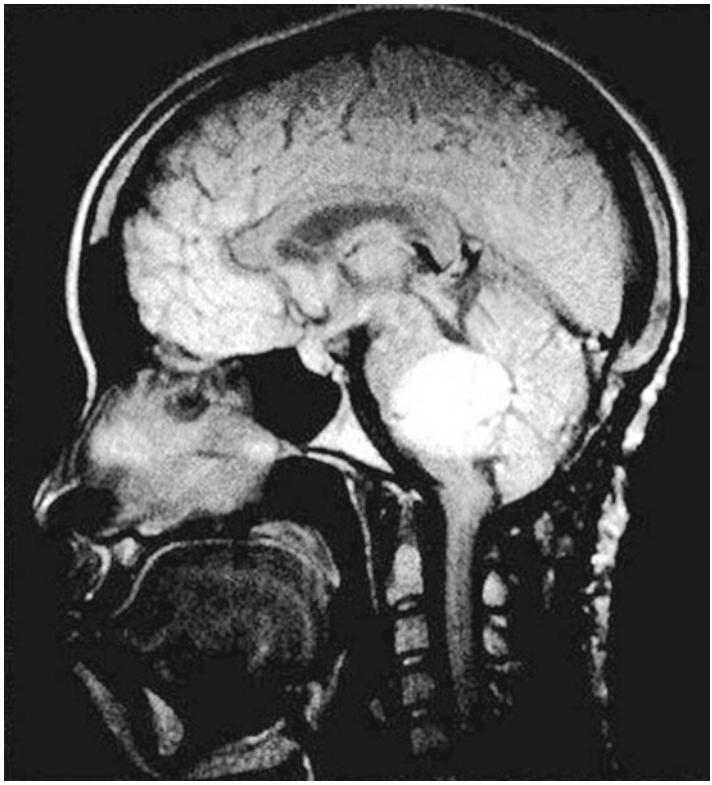

Fig. 3.17 MRI of the patient from Fig. 3.15. The tumor shadow is visible over the entire pons [15]

because only wave I or II, or I to III are visible (Fig. 3.16) [15] in addition to ABR will clearly show a tumor shadow and a definite diagnosis can be made (Fig. 3.17). A deviation only to the side receiving ice water is often observed in a caloric nystagmus test. However, patients experience rotatory vertigo, which suggests dissociation of vertigo sensation and eye movement (Fig. 3.18).

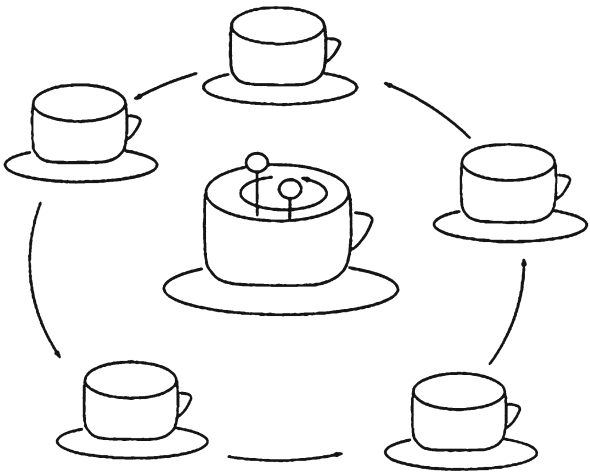

Fig. 3.18 Experience of vertigo of a patient with organic dizziness. Although fast-phase nystagmus is not induced by the caloric nystagmus test in a patient with a brainstem tumor, the patient experiencing ocular displacement complained of vertigo. The patient drew the experience of vertigo [15]

3.8 Cerebellar Disorders

When infants and children tend to stumble or fall down during walking due to a balance abnormality even though they have no labyrinthine disorder, it is often due to acquired disease of the brainstem or the cerebellum as a result of a tumor or infection. Tumors of the brainstem are diagnosed based on abnormal waveforms by ABR and tumor imaging using MRI. Tumor tissues are classified pathologically often into glioma and medulloblastoma. Infections include cerebellitis/cerebellar abscess as otogenic intracranial complications due to bacterial infection and acute cerebellar ataxia with a favorable prognosis suspected of viral infection [16]. Cerebellar hemorrhage induced by head trauma and a cerebellar tumor are also included. The cerebellum controls locomotor activity and motor learning functions, and the compensation processes for cerebellar symptoms following a permanent disorder should be understood from the perceptive of cerebro-cellebellar interactions and integration of sensations.

3.9 Brain Anomaly: Cerebellar Hypoplasia

Congenital disequilibrium is observed in children with severe balance disorders alone, although they do not present a labyrinthine disorder or mental retardation. However, a cerebellar anomaly is often shown upon the availability of CT and MRI, in particular, for imaging diagnosis.

Development of the cerebellum starts in gestation month 3 with the emergence of the vermis, nodulus, and flocculus, which make up the paleocerebellum, which controls equilibrium at the unconscious level. Development of the cerebellar hemisphere, or neocerebellum, starts at the end of gestation month 3, and it interacts functionally with the cerebral cortex, which develops in relation to development of the neocerebellum. Maturation of the paleocerebellum is completed before birth,

but the neocerebellum continues gradual development [17, 18]. The layers of the cerebellar cortex develop at the vermis at 4 months of age and continue to develop in the cerebellar hemisphere. Cerebellar anomalies are classified into three types:

3.9.1 Hypoplasia or Defect of the Cerebellar Vermis/ Hemispheres

This anomaly is often observed in children with poor balance, although they do not present a labyrinthine disorder. The MRI findings include (1) separation of the left and right hemispheres; (2) wide communication between the fourth ventricle and the cistern; and (3) hypoplasia of the cerebellar hemisphere (Fig. 3.19). Neurological symptoms include clumsiness and poor handwriting (Fig. 3.20), slow actions, and difficulty maintaining balance. They appear to be mild symptoms but in fact pose a serious problem at school because a patient cannot keep up with other students in study. It is not known how much growth-related improvement is expected in the symptoms of congenital cerebellar disorder.

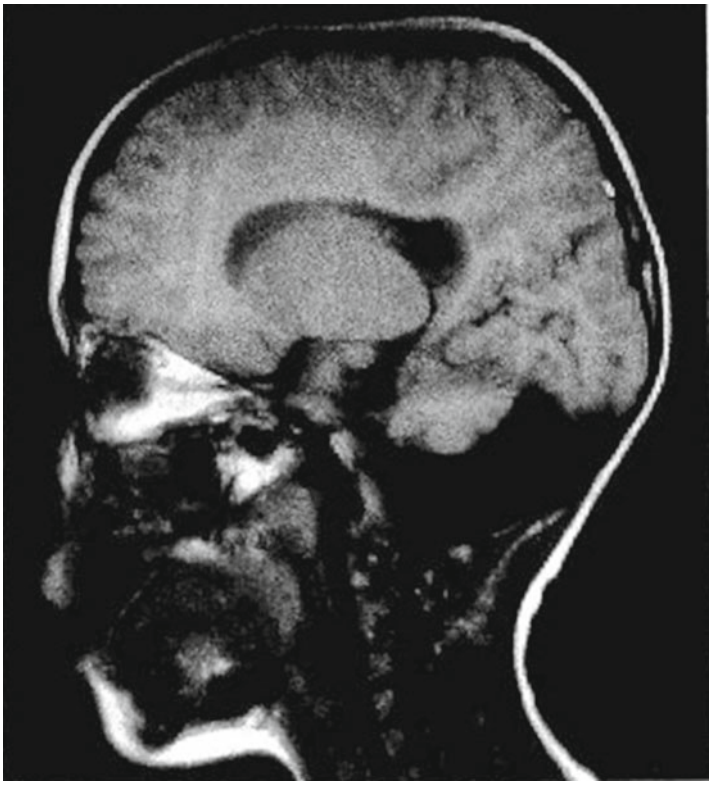

Fig. 3.19 MRI showing a cerebellar anomaly in a 7-year-old child. Hypoplasia of the cerebellar hemisphere can be seen

Fig. 3.20 Vertical handwriting of the patient in Fig. 3.19. The outline of each character is not smooth. The writing is very clumsy

3.9.2 Arnold-Chiari Malformation

This is a disease of the magnovertebral junction. The symptoms develop during growth because of a congenital anomaly of the bone system. Diagnosis is often made because a patient performs poorly in physical education. Chiari II is the most common type, in which the cerebellum protrudes downward through the foramen magnum, intrudes into the cervical vertebrae, and compresses the pons and the medulla oblongata. Diagnosis became possible by sagittal section of the head and neck using MRI (Fig. 3.21). Symptoms include cerebellar disequilibrium, as well as neurological symptoms such as left and right gaze nystagmus, downbeat nystagmus (Fig. 3.22) (of the cerebellum/medulla oblongata), and disequilibrium. The systemic course should be observed carefully in patients because the symptoms may induce spina bifida, hydrocephalus, stiff neck, wheezing, and respiratory/swallowing disorder.

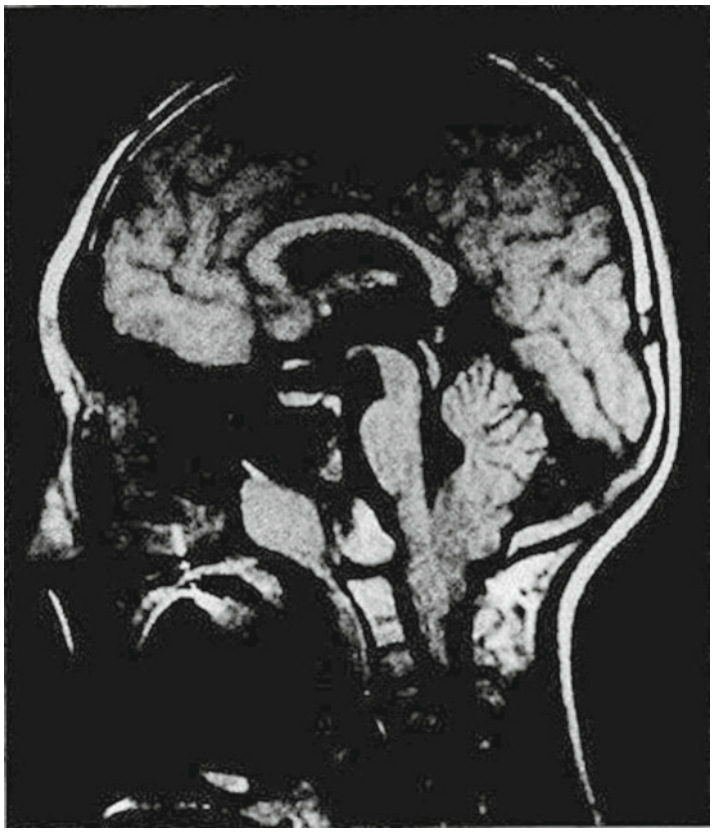

Fig. 3.21 MRI of a 15-year-old girl with Arnold-Chiari II type. The cerebellar tonsil is invaginated into the foramen magnum

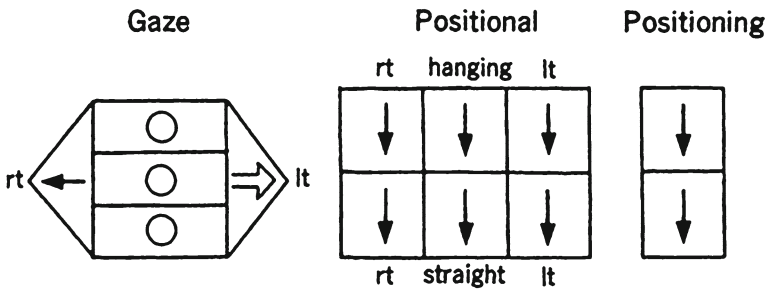

Fig. 3.22 Gaze nystagmus and positional and positioning downbeat nystagmus of the patient in Fig. 3.21

3.9.3 Dandy-Walker Syndrome

Symptoms of Dandy-Walker syndrome include cystic enlargement of the fourth ventricle, defect of the cerebellar vermis, separation of the left and right hemispheres, occlusion of Magendie's foramen and Luschka's foramen, hydrocephalus, and elevation of the cerebellar tentorium.

Neurological abnormalities are often mild but motor development is delayed because of nystagmus and disequilibrium.

Cerebellar ataxia is the most common motor ataxia observed in children, which causes the development disorder of the above syndrome. Hypotony alone is notable during infancy due to disorders of equilibrium and coordination, and cerebellar ataxia may be overlooked. Cerebellar ataxia is classified into two types depending on the site of the lesion (symptoms develop on the same side as the lesion). One is called medial cerebellar syndrome associated with truncal ataxia. A patient cannot keep balance, stands with legs apart, and sways considerably although hypotony and limb ataxia are not notable. It is caused by a medial cerebellar disorder, or disorder of the vermis. The other is called lateral cerebellar syndrome associated with limb ataxia and pronounced hypotony. Symptoms include asynergy, asthenia, dysmetry, and intension tremor. It is caused by a disorder of the cerebellar hemispheres or the brachium conjunctivum cerebelli [19].

3.10 Congenital Oculomotor Apraxia [20]

Some children gaze at an object by obviously moving their head in its direction (Fig. 3.23) or merely casting a sideways glance. They have complications of disequilibrium and cerebellar symptoms and a sideways glance is different from that of minimal brain dysfunction. The gaze of a healthy person at an object is called eye-head coordination, which does not look unnatural because the eyes move first, followed by the head. Cogan reported this neural symptom for the first time in 1952 and named it congenital oculomotor apraxia. He stated "the movement for voluntarily moving the eyes to the left and right is missing. Random eye movement is preserved. When gazing or fixing the eyes on an object, the head is moved too far and overshoots the target. When the head is rotated, the eyes remain deviated to the side opposite the rotation." This is clearly shown by recording the head-eye coordination movement (Fig. 3.24). This congenital disease is caused by a disorder of horizontal eye movement, and the abnormality is observed in visual stimulation tests such as gaze, eye tracking, and optokinetics.

Patients with ataxia telangiectasia, or Louis-Bar syndrome, develop similar symptoms. Slow spinocerebellar degeneration either develops during childhood or is already present at birth.

Symptoms of this syndrome are induced by a disorder in the rapid phase of the vestibulo-ocular reflex, although the slow phase is preserved. The rapid phase is

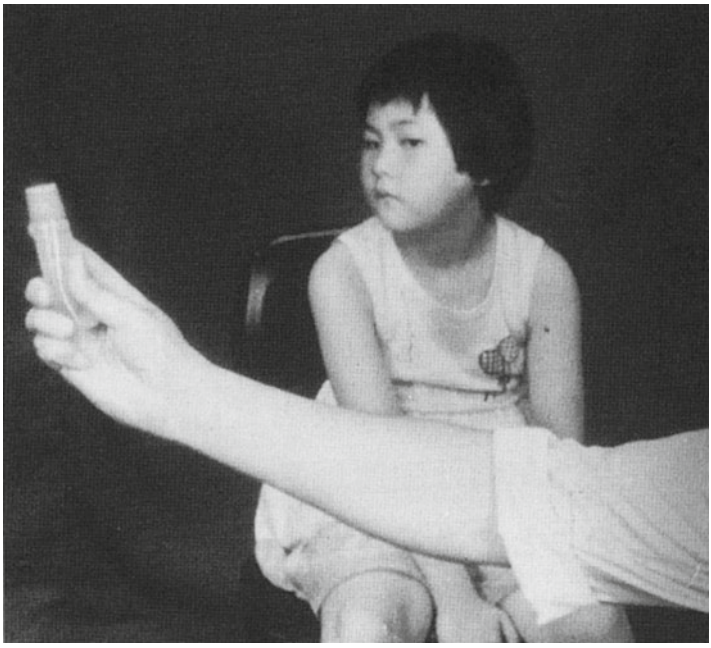

Fig. 3.23 Sideways glance due to congenital oculomotor apraxia [20]

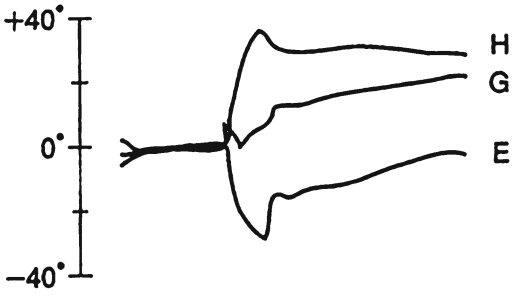

Fig. 3.24 Head-eye coordination movement in a patient with oculomotor apraxia [20]. E, eyeball movement and position; H, head movement and position; and G = H + E (gaze). It is understood that, first, the head turns in the direction of the target and the eyes move in the opposite direction before turning towards the target. As a result, gaze is initially impaired

related to the neuron circuit of the parapontine reticular formation (PPRF) at the pons, so a disorder should be detected at least in the pons and the cerebellum. "Apraxia" is a condition in which instructed voluntary movement is not executed normally, although a patient does not present a motor disorder, such as paralysis and

ataxia, perception or mental disorder. It is a higher nerve dysfunction of the cerebral level. This syndrome, however, is a disorder below the brainstem level and is not named appropriately. I asked Cogan about this issue when we met, and he admitted that "the mechanism of the eye movement system was not clarified around 1952 when the report was made public."

3.11 Benign Paroxysmal Torticollis

3.11.1 Definition of Benign Paroxysmal Torticollis

Otitic torticollis is a common disease in the otorhinolaryngology field, but true torticollis is rarely encountered. When deafness is present in one ear, a patient with otitic torticollis tries to hear by turning the unaffected ear towards the sound, so the head appears inclined. The head returns to the normal position when a patient is not trying to hear. Torticollis is one of the common pediatric diseases.

Torticollis with vertigo discussed below is called benign paroxysmal torticollis (BPT) in infancy, a concept proposed for the first time in 1969 by Snyder [21]. One such case was reported in Japan [22]. However, no other case has been reported other than our neuro-otological report of a case presenting vertigo/disequilibrium, which was presented at the meeting of Japan Society for Equilibrium Research in 1996.

Torticollis occurs periodically in patients with BPT, but the symptom disappears after 6 years of age. It is likely to develop in girls under 1 year of age and upon waking up in the morning. Depression, irritability, vomiting, unstable ambulation, and motor ataxia develop in nearly half of the patients, and some patients also present abnormal posture, ocular anomaly, and headache (Table 3.3).

Two cases we experienced are described below [23].

Case 1

Patient: A girl aged 1 year and 4 months at the time of initial examination
Chief complaint: Periodic torticollis and disequilibrium (Fig. 3.25)
Family history: None
Medical history: Head/neck steadiness at 3 months, independent ambulation at 12 months
Current illness: Normal development up to 1 year and 3 months of age. Attacks of torticollis and disequilibrium have recurred since then, and the patient was examined at Saitama Children's Medical Center
Test findings: Normal righting reflex during non-attack state. Normal reaction to caloric test. ABR was normal and no abnormality was detected by CT of the brain. EEG showed no epilepsy waves
Course: The frequency of attacks was once a month while the patient was 2 years of age, 2–3 times a year between 3 and 4 years of age, and once a year between 5 and 9 years of age

Table 3.3 Main symptoms of Benign Paroxysmal Torticollis (BPT)

	Case 1	Case 2
Age of onset	−	+
Girl under 1 year of age	+	+
Time of onset (upon waking up in the morning)	−	−
Depression	+	−
Vomiting	−	−
Unstable ambulation	+	+
Abnormal posture	+	+
Ocular anomaly	−	+
Headache	−	−

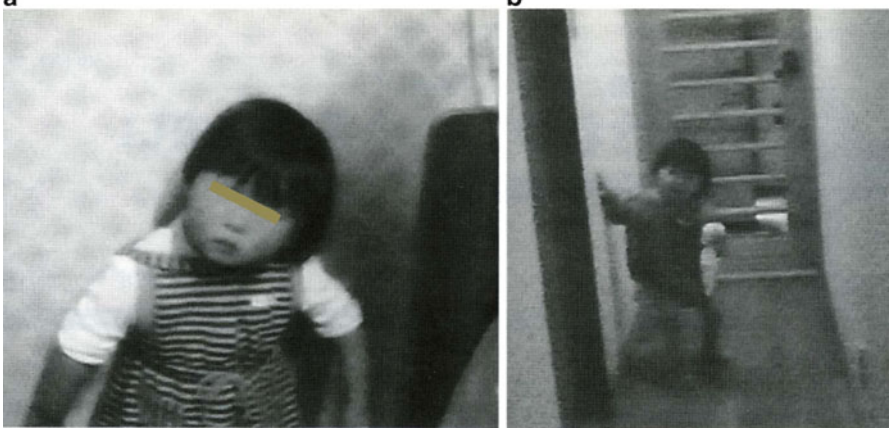

Fig. 3.25 Pictures of case 1 captured from a video filmed during an attack [23]. She inclined her head to the left (**a**) and kept her balance by touching the wall (**b**) because of a balance disorder

Conditions during attack in case 1:
Torticollis, vertigo, and disequilibrium developed accompanied by nausea. Attacks last about 1 h. Nausea persisted after the conclusion of the attack. The patient now recalls that the view looked slanted

Case 2

Patient: A girl aged 2 years at the time of initial examination
Chief complaint: Periodic torticollis, disequilibrium, and right ocular displacement (Fig. 3.26)

Family history: None
Medical history: Head/neck steadiness at 4 months, independent ambulation at 1 year and 3 months. Otitis media with effusion
Current illness: She developed right torticollis and ocular displacement around 6 months of age. A nearby doctor referred her to Saitama Children's Medical Center for close examination

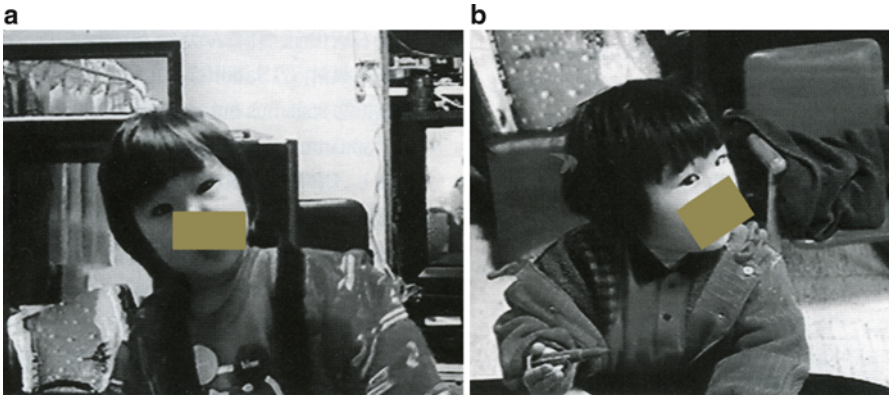

Fig. 3.26 Pictures of case 2 captured from a video filmed during an attack [23]. She inclined her head to the right (**a**) and right ocular displacement occurred (**b**)

Test findings: Normal righting reflex during non-attack state. Gaze nystagmus was present. Normal reaction to caloric test. ABR was normal. MRI of the brain showed hyperplasia of the left cerebellar hemisphere. EEG showed no epilepsy waves
Course: Attacks developed almost every month when she was 2 years of age, but the frequency decreased when she turned 3 years old but developed when she was tired or sleepy. She experienced one attack at 4 years of age, and so far no attacks at 5 years of age
Conditions during attack in case 2:
Right torticollis, bilateral ocular displacement to the right, and disequilibrium. Not associated with nausea or vomiting

BPT differs from epilepsy in that consciousness is clear during an attack. In BPT, it is thought that "a mechanism similar to neck reflex is possibly involved because patients appear to take a posture similar to nonsymmetric tonic neck reflex and the symptoms spontaneously improved or disappeared when torticollis attacks recurred." BPT should be differentiated from the following diseases: posterior cranial fossa tumor in particular; spinal cord tumor; dislocation or calcification of the cervical spine; epilepsy; drug toxicity; Sandifer syndrome; abnormal amino acid metabolism; and spasmus nutans [22]. Of these, spasmus nutans is characterized by the three symptoms of nystagmus, salaam attacks, and torticollis, and like BPT persists between several months to several years after onset during infancy [24, 25]. However, no patient with spasmus nutans develops torticollis alone among the three symptoms, and symptoms do not recur with a certain cycle, although some patients experience recurrence.

Snyder [21] reported the pathology and physiology of BPT for the first time and presumed the disease to be peripheral vestibular dysfunction based on the four symptoms (ocular symptoms during the torticollis attack, vertigo and ataxia, negative to caloric test, and hearing disorder) and also because the condition in 4 of 12 patients later turned into BPT. Sanner et al. [26] later observed a patient presenting

Fig. 3.27 Course of a cat following destruction of one inner ear (*left*) [23]. The head is inclined to the left, the side of destruction. Nystagmus is to the right during the rapid phase and left during the slow phase. (**a**) Day 1 after destruction of the left inner ear. (**b**) Day 2 after destruction of the left inner ear. (**c**) Day 7 after destruction of the left inner ear

cerebellar ataxia and intention tremor and assumed the condition to be a cerebellar or cerebellar-vestibular abnormality. Deonna et al. [27] consider it to be central vestibular disorder. However, cerebellar attacks have not been confirmed to date.

What is the mechanism of onset of BPT? Assuming that it is a temporary disorder of the inner/vestibular disorder, as with Meniere's disease or vestibular neuronitis, the head should be inclined to the slow-phase side of nystagmus. Why does BPT occur only in children and not in adults? What mechanism improves symptoms in line with growth? It is similar to the head inclination to the slow-phase side of paretic nystagmus, or the destroyed side, that follows labyrinth destruction in cats (Fig. 3.27). Torticollis in BPT patients is associated with nystagmus during attacks and causes disequilibrium while consciousness is clear, so a recurrent transient disorder of the vestibule or semicircular canals is strongly suspected, as assumed by Snyder. Transient episodes of the cerebellum and vestibular nucleus cannot be excluded, but it is not likely because patients do not present clouding of consciousness. During a caloric test using ice water in adults, the head is inclined to the side where ice water is injected during the slow phase of nystagmus, and it is also considered a type of mechanical torticollis. BPT is therefore assumed to be a sudden and periodic disease of the vestibule or the semicircular canals, which occurs at the site of torticollis. It is not known, however, whether the site is the semicircular canals, vestibular nerve, vestibular nucleus, cerebellum, or cerebrum.

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Chapter 4
Vertigo in Children

Abstract Vertigo can be diagnosed in children of 4–5 years of age when they complain of subjective feeling of rotation.

Typical diseases causing vertigo such as orthostatic dysregulation and school refusal should not be ignored in infants and children.

Keywords Antral vertigo • Jaw arthrosis • Labyrinthine vertigo • Orthostatic regulation • School refusal

4.1 Perception of Vertigo

Vertigo in children may be classified into "vertigo" complaints from the patients themselves and "abnormal balance" due to disequilibrium. "Vertigo" is an abnormality of perception, whereas abnormal balance is a problem with motor control. Many patients, of course, experience these symptoms simultaneously.

The difficulty in diagnosing children is attributable to the vagueness of the complaints. Adults may often be diagnosed merely by systematic and thorough questioning. Childhood spans a wide range starting with newborns and then infants and children, school children, and adolescents. A child may be too young to complain, may not be able to articulate the complaint, if any, or may be too nervous to complain even when he/she grows up to almost adulthood. Diagnosing children is difficult in many cases, and knowledge of, and experience with, issues specific to children is required to make a definite diagnosis. Vertigo will be explained below according to abnormalities of perception and abnormalities of balance control.

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4.2 "Vertigo" as Abnormal Perception

Children seldom develop labyrinthine vertigo, such as Meniere's disease, vestibular neuronitis, benign paroxysmal positional vertigo, which adults often experience, or medullary or cerebellar disorders such as Wallenberg syndrome and malignant positional vertigo. However, it is interesting that vertigo is explained as "the head spin as if during a Cup & Saucer ride in an amusement park," and, in my experience, a 4-year-old girl was the youngest child who accurately complained of vertigo.

4.2.1 Vertigo Due To Inner Ear Disorders

Vertigo can be diagnosed in children of 4 or 5 years of age when they complain of a "subjective feeling of rotation." Typical diseases causing vertigo are vestibular neuronitis, inner ear concussion following head trauma, and loss of unilateral labyrinth function due to epidemic parotitis. The onset of direction-fixed horizontal rotatory nystagmus in the acute phase makes a child feel that his/her surroundings are rotating. Figure 4.1a is a drawing of the experience and the child accurately expressed it as "a dog looked like many." She meant to express the "waggling" feeling during an episode of vertigo. Labyrinthine vertigo tends to improve sooner in children than in adults.

4.2.2 Central Vertigo

Children may complain of "vertigo" during the acute phase of cerebellar infections, such as meningitis, cerebellitis, and acute cerebellar ataxia, and nystagmus may be observed.

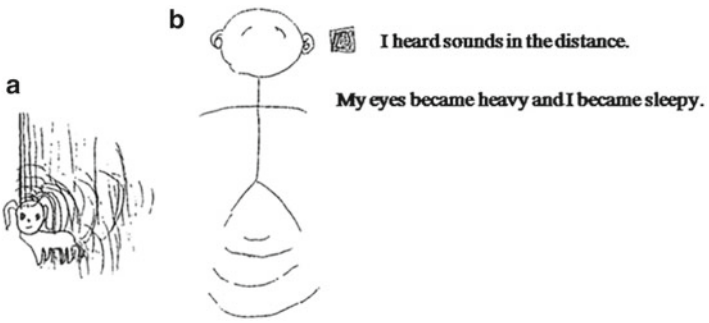

Fig. 4.1 Illustration of the experience of vertigo. (**a**) Experience of vertigo illustrated by a girl in an early elementary grade. (**b**) Experience of postural hypotension episode drawn by a fourth-grade girl

In a patient with brainstem glioma, a disease frequently observed in children, diplopia is a more common complaint than “feeling of vertigo” due to abducent nerve paralysis (explained below).

4.2.3 Orthostatic Dysregulation

The most common cause of “vertigo” in children is orthostatic dysregulation (OD), which is more common in girls. So-called cerebral anemia is often caused by OD. Figure 4.1b shows a fourth grader’s drawing of the experience of OD. She explained that her eyes became heavy and she became sleepy, and the voice of the schoolmaster sounded distant while listening to his speech in the school yard.

“Vertigo” due to OD may be considered psychogenic, but few patients are authentically psychogenic.

4.2.4 Jaw Arthrosis

Jaw arthorosis is a concept proposed by the pediatric dentistry and oral surgery fields and is now handled as one of the causes of unidentified complaints in children. The incidence of jaw arthrosis is reported to be high in pediatric patients with unidentified complaints such as vertigo, tinnitus, and migraine, although no abnormality is found in the ear or the cerebral nerve. In other words, the above symptoms occur due to an imbalance of the head and spine, which is caused by occlusal disharmony of the upper and the lower jaws.

4.2.5 Psychogenic: School Refusal

Psychogenic vertigo often occurs in boys in middle or senior grades of elementary school. They refuse to go to school saying that they cannot study at school because of vertigo. Although no abnormality is found upon examination, vertigo occurs sporadically and makes them skip school abruptly or over the longer term. They are then lazy at home without studying, which causes a vicious cycle where they are behind at school, and hate to go back to school.

Psychotherapy often reveals a hidden cause of this symptom, such as physical punishment inflicted by a teacher or bullying of friends. Children rarely talk about what is on their minds over the course of only a couple of interviews, so considerations should be made to encourage them to return to school while patiently continuing the interviews. Small incidents between friends or with parents, which pass unnoticed by adults, may induce psychological conflict and cause vertigo as a physical reaction and further result in school or study refusal.

4.3 Cochlear Implantation and Vestibular Problems

The electrode of cochlear implant is inserted in to the scala tympani from round window or cochleostomy. Because cochlea and vestibular end organ is connected in the labyrinth, vestibular problems are easy to occur. However, the unlike preoperative prediction occurrence of vestibular problems is limited [1].

4.3.1 Vestibular Nystagmus After Cochlear Implantation in Adults

In our ENG studies, 1 day after cochlear implantation, most of patients revealed that only weak slow phase of nystagmus with 2–3° to the operated side or the opposite side appears but disappears within 10 days (Fig. 4.2). However, exceptional patients manifest severe vertigo and show large paretic nystagmus which disappear within 1 month, probably because of severe influence of the electrode insertion which induces similar effect of inner ear destruction (Fig. 4.3).

4.3.2 Head Tilt to the Side of Cochlear Implantation

Infants with cochlear implantation manifest head tilt to the operated side and balance dysfunction but disappear within 1 week (Fig. 4.4). In the cat experiment, the electrical stimulation of the left horizontal semicircular canal nerve induces the head to the right (Fig. 4.5a); the unilateral labyrinthine destruction causes the head tilt to the destructed side because of loss of tonus from the destructed side (Fig. 4.5b). This similar effect is considered to occur only to the infant patients but not adult patients.

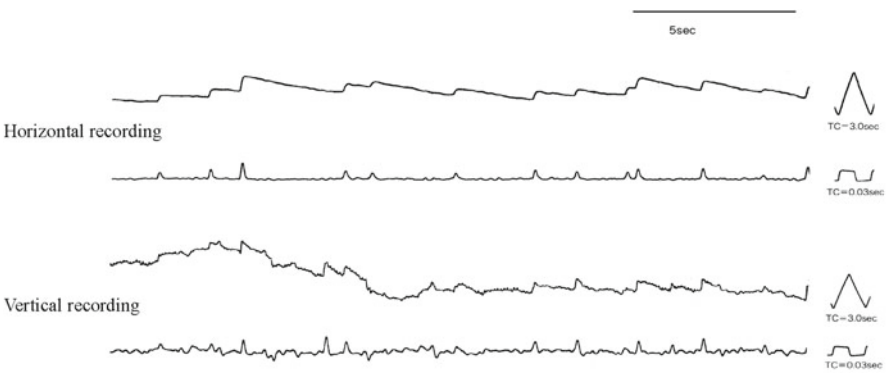

Fig. 4.2 Spontaneous nystagmus on ENG recording 1 day after cochlear implantation

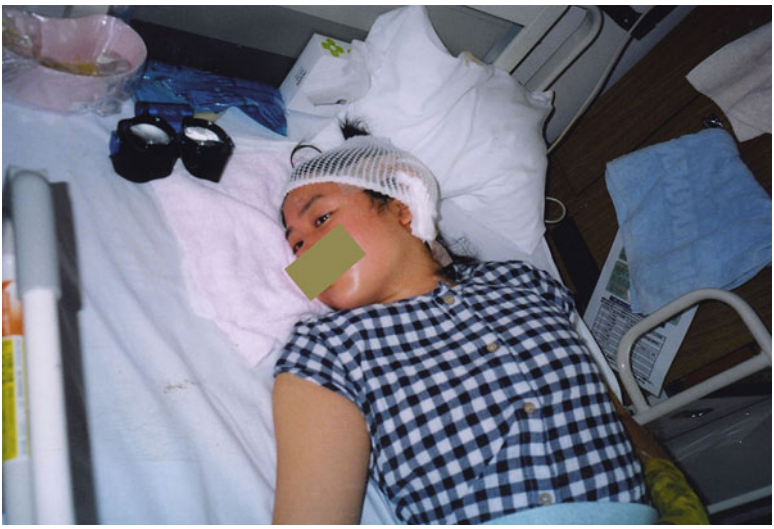

Fig. 4.3 After cochlear implantation, an 18-year-old girl lies down to the *left* suffering vertigo

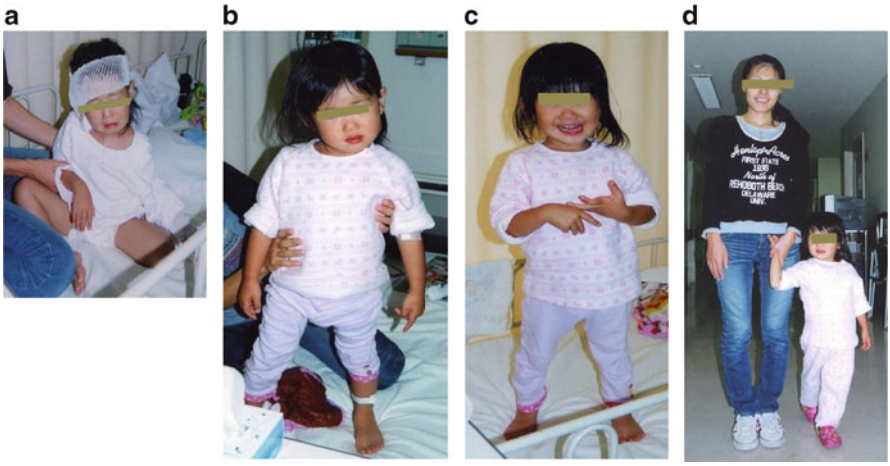

Fig. 4.4 A 3-year-old girl manifest the head tilt to the *right* which is the operated side. (**a**) Day 2 (**b**) Day 4 (**c**) Day 6 (**d**) Day 7

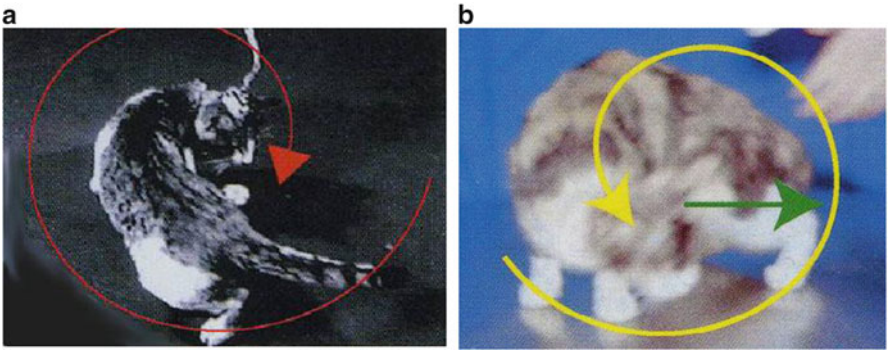

Fig. 4.5 In the cat experiment, (**a**) electrical stimulation of the *left horizontal semicircular canal* nerve induces the head to the *right* and (**b**) the *left labyrinthine destruction* induces the head to the *left*

4.3.3 Cochlear Implants and VEMP

We attempted to clarify the diagnostic value of VEMPs in cochlear implantation patients [2]. The click-evoked myogenic potentials of 12 children who underwent cochlear implantation surgery were investigated. The latency and amplitude of the VEMP responses were measured. Before surgery, 6 of the 12 children showed normal VEMPs, one showed a decrease in the amplitude of VEMPs and five showed no VEMP response. After surgery, with the cochlear implant device off, one child showed a decreased VEMP and 11 showed no VEMPs. With the cochlear implant device on, four children showed VEMPs and eight did not. The sacculi of most children with cochlear implants can easily be damaged, as shown by the absence of VEMPs in response to click stimuli [3]. Also, in most of the children, the vestibular nerve was seemingly stimulated by the cochlear implant (Fig. 4.6). Electrical stimulation at the comfortable level can stimulate the cochlear nerve (Fig. 4.7); however, this stimulation did not spread to the vestibular nerve in our children. In some children with Mondini dysplasia or vestibulocochlear nerve abnormality, the vestibular nerve was stimulated when the cochlear implant device was on, because of a VEMP response to electrical stimulation [4].

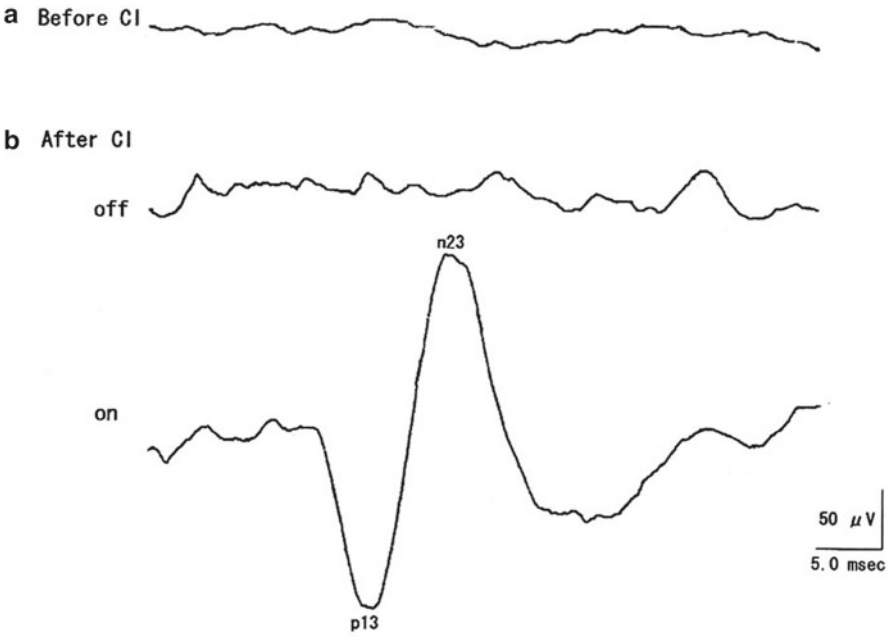

Fig. 4.6 In a case, absence of VEMP before and after CI and appearance of VEMP response on cochlear implant device activation [2, 4]

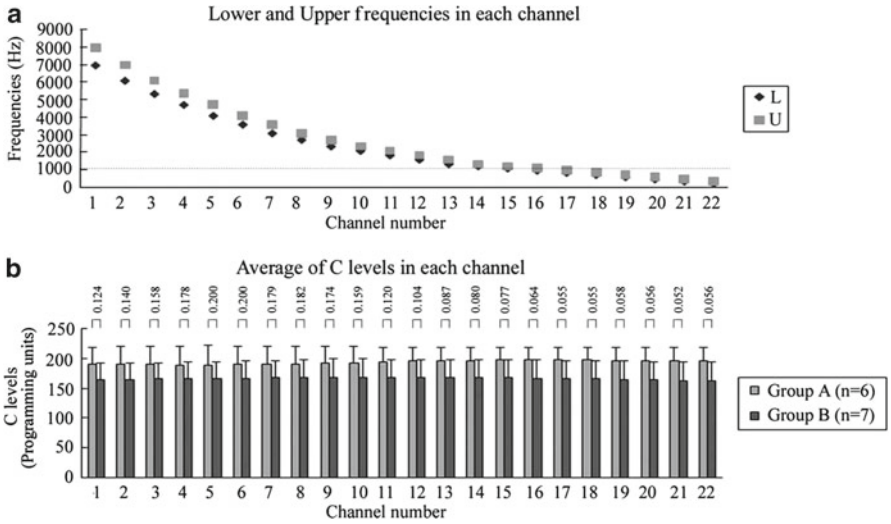

Fig. 4.7 Average of C levels in each channel in groups A ($n=6$) and B ($n=7$). (**a**) Lower and upper frequencies in channel; *L* lower frequency, *U* upper frequency. (**b**) Average of C levels in each channel in groups A ($n=6$) and B ($n=7$) [5]

4.3.4 VEMP Evoked by Multichannel Cochlear Implant: Influence of C Levels

In order to investigate the correlation between VEMPs and C level of each channel, we studied 24 children who underwent cochlear implantation. VEMPs were recorded from the operated ears with the cochlear implant switched "off" or "on." To investigate the correlation between VEMPs and C level, we selected 13 patients with Nucleus 24 (SPrint) and divided them into groups A (normal VEMPs) and B (absence of VEMPs). In these children, all the 22 electrodes were active and were mapped in the same frequency range for each channel. Twenty children (83 %) showed no VEMPs with the cochlear implant "off." Among them, ten elicited VEMPs with the CI "on," but the other ten did not. In all channels, the mean C levels of cochlear implant were higher in group A than in group B. The *p* values in channels 1–12 were >0.10, in channels 13–16 were 0.06–0.09, and in channels 17–22 were 0.05–0.06, which were lower but not statistically significant [5].

In our study VEMPs evoked by cochlear implant, could be related to the comfortable level (C level), particularly in the channels that are closer to the apical turn of the cochlea.

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Chapter 5
Rehabilitation of Children with Disequilibrium

Abstract Training of balance function is crucial for eliminating sport in children. In children with labyrinthine disorders, integrated training consisting of vision, somatic sensation, and joint sensation could facilitate progress of delayed motor development. In children of congenital and acquired vestibular loss central vestibular compensation is stimulated by visual or proprioceptive sensory and motor integration in the cerebellum and cerebrum.

Keywords Central vestibular compensation • Labyrinthine disorders • Rehabilitation • Sensory integration • Vestibular loss

5.1 Mechanism of Compensation and Adaptation in Disequilibrium

Of the three types of vestibular reflex—vestibulo-ocular reflex, vestibulospinal reflex, and vestibulo-vegetative reflex—dysfunction of the vestibulo-ocular reflex and vestibulospinal reflex causes considerable delay in locomotor activities as well as reduced labyrinthine function in children. The spinal reflex has two functions: one is a conduction pathway of the righting reflex of the head, limbs, and trunk; and the other is a conduction pathway of labyrinthine muscle tone. A disorder of the peripheral vestibulo-semicircular canals therefore delays acquisition of reflex movements for keeping balance, such as rolling over and standing up. Tonic stimuli that convey labyrinthine tone from the vestibulo-semicircular canals and otolith to the muscles of the neck, limbs, and trunk play a substantial role in newborns and infants. One of the causes of delayed acquisition of locomotor activities in patients with a labyrinthine disorder is a floppy state due to lowered labyrinthine muscle tone. However, locomotor activities are acquired eventually, although the delay ranges between several months and 1 year. Recovery is not likely when the vestibulo-semicircular canals are disturbed congenitally or after birth, and the effect of spinal

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reflexes other than the reflex of the vestibulo-semicircular canals, as well as compensation, adaptation, and learning of other sensory systems, plays a significant role in acquisition of motor skills.

Locomotor activities are achieved by complexes of various reflexes and the vestibulospinal reflex is merely one of them. Other spinal routes involved in the higher control of reflexes include the corticospinal tract (pyramidal tract), rubrospinal tract, tectospinal tract, and reticulospinal tract. The vestibular nucleus, on the other hand, has suppressive binding from the cerebellum. The vestibulospinal routes consist of the outer and inner vestibulospinal routes. The former, which starts at the lateral vestibular nucleus and reaches the lumbosacral spinal cord of the same side, is a descending route similar to the pyramidal tract and the rubrospinal tract for conveying instructions from the higher centers, such as the cerebellum and the medulla oblongata, to the spine. The inner vestibulospinal route starts at the medial vestibular nucleus and inferior vestibular nucleus, descends along the spinal midline, and directly conducts suppressive or excitation synapse binding with motor neurons in the cervical and thoracic spinal cords. The descending route is a pathway of the vestibulospinal reflex for holding the head in a constant position by adjusting the muscle tone of the neck and the back in response to the position and movement of the head. It is a portion of the reflex route itself, rather than a descending route that dominates reflexes.

The vestibulospinal route and vestibulo-ocular motor system develop early in terms of phylogenetic order, and myelination and development of function also start early. In other words, myelination starts in the prenatal period and both are completed before birth. However, myelination of vision, deep sensation, and reticular formation of the brainstem, basal ganglia, cerebellum, and cerebrum have not been formed prior to birth, and they are completed at different times after birth [1].

The spinal routes dominated by the higher centers develop later than the vestibulospinal reflex. Its tonic input into the muscles of the neck, limbs, and trunk is extremely advanced. Disequilibrium due to a disorder of the congenital peripheral sensory organs means reduced spinal reflex function, so acquisition of locomotor activity is delayed more when a patient is younger. Tonic input to the spinal cord and muscles from the cerebellum, red nucleus, cerebral cortex, and subcortical nucleus increases with growth, so a delay in motor activity can eventually be recovered. Eviator et al. [2] explained that vision, deep sensation, and balance stimulation are integrated at the red nucleus between 6 and 48 months after birth, when various righting reflexes develop following rapid progression of synapses of cortical neurons and myelination of the pyramidal tract and medial lemniscal route.

As explained above, direct and indirect inputs are sent from the higher center to the vestibular nucleus, and inputs promoting reflexes are sent at the same time from other spinal routes to the neck, limbs, and trunk, even when the vestibular labyrinthine organs are congenitally impaired. Maturation of these neural routes enables smooth execution of actions and movements even if labyrinthine organ function is impaired.

Table 5.1 shows the development locomotor functions of children with spastic paraplegia types of cerebral palsy and athetoid type of cerebral palsy. All activities

Table 5.1 Comparison of age of acquiring locomotor activities between healthy children, deaf children, and children with cerebral palsy

		Deaf children		Children with cerebral palsy	
	Healthy children	Normal vestibular function (four patients)	Lowered vestibular function (four patients)	Spastic paraplegia	Athetoid palsy
Neck/head steadiness	4 months	3.5 months	8.8 months	6 months	1 year, 4 months
Rolling over	6 months	5.3 months	8.5 months	1 year, 2 months	1 year, 6 months
Lying on stomach	8 months	7.3 months	11.6 months	1 year, 2 months	2 years, 9 months
Sitting up	10 months	9.5 months	1 year, 2 months	1 year, 6 months	3 years, 6 months
Crawling	10 months	8.3 months	1 year, 0.3 months	2 years, 7 months	4 years, 11 months
Standing while holding on to things	8 months	8.1 months	1 year, 3.4 months	2 years, 6 months	5 years, 6 months
Walking while holding on to things	12 months	9.5 months	1 year, 3.5 months	3 years, 7 months	6 years, 7 months
Standing up	1 year, 2 months	10.4 months	1 year, 6.3 months	4 years, 5 months	5 years, 2 months
Independent ambulation	1 year, 3 months	11.5 months	1 year, 9 months	4 years, 10 months	6 years, 3 months

were delayed twofold or more, and the functions were more easily gained in patients with a peripheral disorder. Children with severe deafness did not show the caloric nystagmus reaction, but hardly any difference was observed in static equilibrium tests, such as the Romberg test, compared with healthy children [3]. Standing on one foot with eyes closed is more difficult. Use of the righting reflex test above is recommended for detecting a latent labyrinthine disorder.

5.2 Labyrinthine Disorder and Actual Rehabilitation

The balance control of athletes on a balance beam, which requires high balance function, and in sports requiring rigorous training, such as the still rings and vaulting in gymnastics, jumps and turns in skiing, and figure skating, is amazing. Will such sports be possible for a person with a labyrinthine disorder? The author previously treated a ninth-grade girl with loss of equilibrium due to a labyrinthine anomaly caused by thalidomide and asked her which sports she was best at. She replied

that she was good at most sports, except for difficult ones requiring special training such as logrolling. She was capable of playing sports by integration of vision, somatic sense, and joint sense as well as high-level function of the cerebellum and the cerebrum, such as motor learning ability, memory, and judgment. A patient with a congenital labyrinthine disorder can play most sports, but a person with an acquired disorder cannot. For instance, a person previously good at swimming is known to have nearly drowned after bilateral loss of labyrinthine function because balance cannot be maintained, especially during diving.

Training of equilibrium function has been attracting attention lately, not only for healthy children, but also for children with a labyrinthine disorder, children with a learning disability without a labyrinthine disorder, and children with a psychosomatic disorder complicated by a motor disorder. However, such training has not been established in all of the medical fields, and theological and methodological solutions are required for various issues.

5.2.1 Training of Equilibrium Function in Healthy Children

Training of balance function is crucial for eliminating sport injuries in children. Delays in the development of balance function, however, are a concern in children living in urban areas today because they spend fewer hours playing sports because of time studying at school and also at "cram" schools. Their environment, such as a school yard covered with concrete and fewer vacant fields, deprives them of opportunities to train for balance function. Various methods were devised to address this issue. Motohashi et al. [4] divided third graders into a group given training of equilibrium function using a unicycle for 1 year and a group without training and compared the groups using a standing-on-one-foot test as an index. Significantly longer standing time was reported for the first group, indicating that training with a unicycle was effective. Various training methods, such as using an old car tire and a wooden horse, have also been reported.

5.2.2 Training of Equilibrium Function in Children with a Labyrinthine Disorder

Children with a labyrinthine disorder are classified into a floppy period with poor muscle tone up to 1 or 2 years of age (Stage I); a period with unstable balance up to 3 or 4 years of age, although ambulation is possible (Stage II); and a subsequent period for acquiring higher motor activity (Stage III). Integrated training consisting of vision, somatic sensation, and joint sensation is given for each stage. Training methods similar to the Vojta and Bobath methods, which are intended for children with cerebral palsy, are employed for Stage I. Useful training for Stage II includes

standing up by holding onto something, standing up, walking, and swimming, whereas a balance board, balance beam, bicycle riding, skating, skiing, and trampolining are useful during Stage III.

5.2.3 *Sensory Integration Training by Vestibular Stimulation in Children with a Learning Disability*

Learning disabilities are neuropsychological disorders of understanding or using spoken or written language, although children present neither mental retardation, emotional/physical disorders, nor abnormal EEG or CT findings. This theory was proposed in the USA for children with a specific delay in one of the language elements such as hearing, thinking, speaking, reading, writing, spelling, and calculating. Similar symptoms are observed in adults with aphasia. It would be easier to call them children with academic problems. The incidence of dyslexia is particularly high and problematic in the USA and Israel, whereas it is low in Japan and China. Thus, the possibility of an influence of the differences in letters and sentence structures between Western countries using the alphabet and countries such as Japan and China using kanji is attracting attention.

A concept of systemizing sensory integration training mainly for children with a learning disability and patients with vestibular dysfunction was proposed by Ayres [5], a professor of University of Southern California. The test items include intersensory integration, laterality of the cerebrum, cognition of visual space, hearing, language, and posture response. Rotational nystagmus by the Bárány method is also used as a vital index of quantitative testing. Of the five to six syndromes of learning disability, the main syndrome is called "vestibular-bilateral integrative dysfunction. Typical characteristics are excessively suppressed rotational nystagmus and symptoms induced by underdevelopment of integration of the cerebral hemispheres, including disturbed posture reaction, eye movement, bilateral physical integration, and mild to moderate speech and visual field recognition." Ayres considered that "dysfunction at the brainstem level mainly of the vestibular system influences the development of higher brain function" and regarded children with a learning disorder as having a typical sensation integration disorder, although many researchers disagree with this view.

The purpose of sensory integration training is to enhance the structural function of the brain by adjusting the input of the vestibular sense, tactile sense, and proprioceptive sense through a whole-body purposive behavior and to achieve a state where the adaptive reaction to the environment coordinates with the processing of the sensory input [6].

The basic concept of sensory integration therapy is a hypothesis. The facilitation effect of evaluation and training of the vestibulo-ocular reflex, proposed in neurotology, is the axis of the hypothesis and is attracting attention. However, more than a few aspects are difficult to understand. For instance, concepts such as

vestibulo-ocular split and vestibulo-proprioceptive dissociation have not been handled in the neurotology field. Considerable differences lie between these two fields but vestibular neurologists have started to investigate the theory and methods of rehabilitation for patients with vertigo and disequilibrium. Sensory integration training is not yet established theoretically and methodologically and is fraught with challenges.

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Chapter 6
Inner Ear Anomalies and Vestibular-Evoked Myogenic Potentials (VEMP)

Abstract Inner ear malformations represent a major inner ear disorder in approximately 20 % of children with congenital sensorineural hearing loss. They are usually characterized by profound hearing loss, and their development delays gross motor functions such as head control or independent walking, because such functions are related to abnormal inner ear structures. However, it is not easy to unequivocally determine whether vestibular sensory cells of semicircular canals and otolith organs or primary vestibular afferent neurons are present in patients with inner ear malformations, particularly common cavity deformity. In an embryological study, it has been found that, in the human fetal developmental stage, the vestibular system develops earlier than the cochlear system. Thus, it is speculated that sensory cells of vestibular end organs and vestibular afferent neurons may be present in patient with inner ear malformations, which is similar to early-stage inner ear development.

In our study, we reported that VEMPs could be elicited with cochlear implant switched on and suggested that the electrical stimulation of a cochlear implant may directly stimulate the inferior vestibular nerve. If VEMPs are evoked with the cochlear implant switched on, it suggests that some of the inferior vestibular neurons are present. In contrast, if VEMPs are absent with the cochlear implant switched on, it suggests that the inferior vestibular neurons may be absent.

Keywords Cochlear implant • Inner ear anomaly • Saccules • Vestibular myogenic potential

6.1 VEMP in Patients with Inner Ear Anomalies

In non-mammals the saccule has been found to be sensitive not only to inner acceleration but also to auditory stimuli, e.g., in fish [1]. Since Tullio [2] described this phenomenon more than 80 years ago, it has been known that the vestibular system of pigeons was sensitive to sound over low frequency. Bleeker and De Vries [3]

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showed that electrical responses induced by auditory stimulation can be obtained from the vestibular system of pigeons. Other vestibular end organs have also been found to be sensitive to loud auditory stimuli, particularly following fenestration of the semicircular canal (SCC), e.g., in pigeons [4]. Vestibular sensitivity to sound has been reported in mammals (in deaf mice, Mikaelian [5]; in squirrel monkeys, Young et al. [6], in guinea pigs, Cazals et al. [7], in cats, McCue and Guinian [8]). However, questions concerning this sensitivity of the mammalian vestibular end organs have not been satisfactorily answered. Some studies have found auditory sensitivity in all five vestibular end organs (Young et al. [6]). However, others report auditory sensitivity in the saccule only (Cazals et al. [7]; MaCue and Guinian [9]).

Evidence of this kind has led to suggestions that the human vestibular system can function in hearing for the perception of low-frequency or bone-conducted sounds. In this regard, Bocca and Perani [10] reported that in some profoundly hearing impaired subjects, bone conduction thresholds were surprisingly better than the corresponding air conduction thresholds up to 500 Hz. This striking discrepancy between air and bone conduction thresholds in the lower frequencies is generally present in cases where vestibular excitability is within normal limits. Sheykholeslami et al. [11] revealed that bone-conducted VEMP has a well-defined frequency sensitivity range at stimulus frequencies of 100–800 Hz with maximum response amplitude at stimulus frequencies between 200 and 400 Hz. If the vestibular system is sensitive to low-frequency sound stimulation, then use of the vestibular system would be a serious alternative for the cochlear implant, especially because of the grater dynamic range of the vestibular signal [12].

Recent evidence suggests that the saccule retains an ability to trigger acoustic reflexes of certain muscles in man, the VEMP (Colebatch et al. [13]). However, this hypothesis of an otolithic origin of the VEMP in human has not been firmly validated electrophysiologically and anatomically. We studied to determine the origin of VEMPs and the contribution of vestibular sound sensitivity to human perception.

The seven patients' result (audiogram, tympanometry, neurological and radiological findings) are tabulated and summarized in Table 6.1. Audiometrically, four patients had hearing levels off the audiogram scale, two had moderate hearing losses, and one had a severe hearing loss. Some of the patients (five out of seven) reported a sound sensation at frequencies up to 1,000 and 1,500 Hz for bone and air conduction, respectively.

Standard measure of tympanic mobility (Tympanometry) revealed normal patterns in all patients. Neurological and motor system evaluations were normal in all patients, except patient no. 2. The Romberg, Mann, and stepping tests were abnormal with eyes closed.

Caloric responses following strong stimulation with 20 cc ice water were absent in all patients. Spontaneous nystagmus was found only in patient no. 2.

CT revealed two patients with cystic cochlea, three with shortened cochlea, and two with completely absent cochlea. Horizontal SCCs were cystic in two patients and absent in five. Posterior SCCs were normal in two patients, cystic in two, and

Table 6.1 Summary of clinical, audiological, and neurological findings in patients with inner ear anomalies

	Case no.						
	1	2	3	4	5	6	7
Age	21	30	5	18	21	11	5
Gender	Male	Female	Male	Male	Male	Male	Male
Audiogram: degree of loss	Os	Os	Os	Os	Mod	Sev	Mod
Tympanometry	Nor	Nor	Nor	Nor	Nor	Nor	Nor
VEMPs	Nor	Nor	Nor	Nor	Nor	Nor	Nor
Neurological examination							
Motor	Nor	Abn	Nor	Nor	Nor	Nor	Nor
Gait	Abn	Abn	Abn	Abn	Abn	Abn	Abn
Nystagmus	None	Hn	None	None	None	none	none
CT scan							
Cochlea	1.5 turn	Abs	Abs	1.5 turn	1 turn	Cys	Cys
HSCC	Abs	Abs	Abs	Abs	Abs	Cys	Cys
PSCC	Abs	Nor	Abs	Abs	Nor	Cys	Cys
SSCC	Abs	Nor	Cys	Abs	Nor	Cys	Cys
Vestibule	Nor	Nor	Nor	Nor	Cys	Nor	Nor

Os off the audiogram scale, *Mod* moderate, *Sev* severe, *VEMP* vestibular-evoked myogenic potentials, *Cys* cystic, *Nor* normal, *Abn* abnormal, *Hn* horizontal nystagmus, *HSCC* horizontal semicircular canal, *PSCC* posterior semicircular canal, *SSCC* superior semicircular canal, *abs* absent [11]

absent in three patients. Superior SCCs were cystic in three patients, normal in two patients, and absent in two patients. The vestibules were normal in six patients and cystic in one patient.

All of these patients with significant pathologies of the SCCs and cochlea showed short-latency VEMP responses to 95 dB nHL air-conducted clicks and short tone bursts (STBs) presented during tonic neck flexor activation. The VEMP response to air-conducted stimuli was biphasic and consisted of a p13 and an n23 peak. Mean latency measurements of the click- and the STB-evoked VEMP response were 13 and 15 ms for p13 and 22 and 25 ms for n23. The mean amplitude was 112 ± 40 μV for click-evoked and 154 ± 57 μV for STB-evoked potentials. Figure 6.1 represents the data obtained from case 1 (a 21-year-old male) with normal vestibule but shortened cochlea and no SCC.

The human vestibular end organs has preserved an ancestral sound sensitivity, and it has been suggested that a reflex could originate from this property underlying cervical muscle micro-contractions secondary to strong acoustic stimulation. Previous studies have established that an early component of loud sound-evoked myogenic potentials from the sternocleidomastoid muscle originate in the vestibule. This is based on findings that the response can still be obtained from patients with complete loss of cochlear and vestibular (semicircular canal) function. It is confirmed, in a more direct way, a saccular acoustic response persists in the human ear. It is concluded that vestibular response to sound might be used to assist in the auditory rehabilitation of children with deafness.

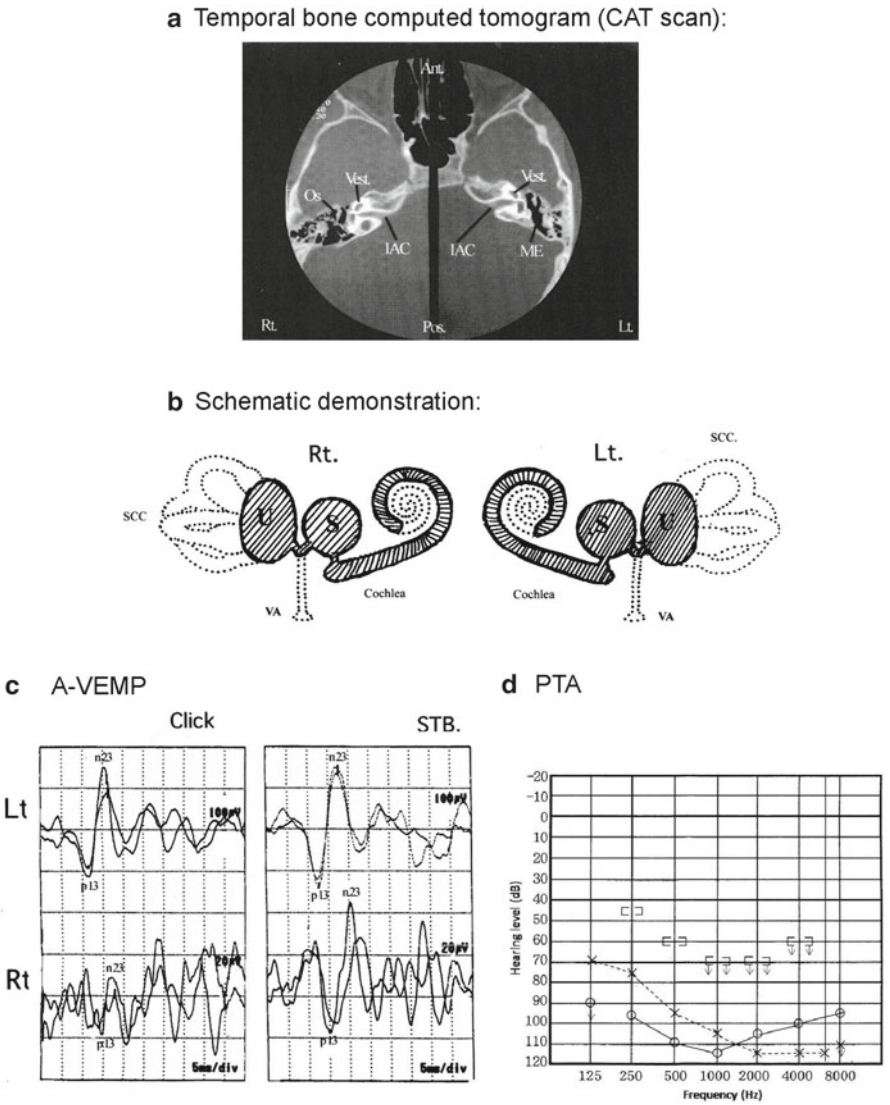

Fig. 6.1 (**a**) Computed tomograms of a temporal bone in a 21-year-old patient (patient no. 1) showing inner ear anomalies. *Ant.* anterior, *Post.* posterior, *Vest.* vestibule, *IAC* internal auditory canal, *ME* middle ear, *Os* middle ear ossicles, *Rt.* right ear, *Lt.* left ear. (**b**) Schematic demonstration of the cochleovestibular apparatus for the same patient. *Shaded areas* indicate existing structures. *S* saccule, *U* utricle, *VA* vestibular aqueduct, *SCC* semicircular canal. (**c**) Air-conducted VEMP (A-VEMP) recorded from the same patient with bilateral inner ear anomalies. *Lt* indicates electromyographic responses of the left SCM muscle to left ear stimulation, and *Rt* indicates responses of the right SCM to right ear stimulation. Peak positive (p13) and negative (n23) VEMPs were recorded from each ipsilateral SCM to unilaterally presented loud sound. *STB* short tone bursts. (**d**) Shows the pure-tone audiogram (PTA) of the same patient. *Open circle* = right air conduction hearing level, *cross* = left air conduction hearing level, *opening bracket* = right bone conduction hearing level, *closing bracket* = left bone conduction level [11]

6.2 VEMP of Children with Inner Ear Malformation Before and After Cochlear Implantation

Inner ear malformations represent a major inner ear disorder in approximately 20 % of children with congenital sensorineural hearing loss [14]. They are usually characterized by profound hearing loss, and their development delays gross motor functions such as head control or independent walking, because such functions are related to abnormal inner ear structures [15]. However, it is not easy to unequivocally determine whether vestibular sensory cells of semicircular canals and otolith organs or primary vestibular afferent neurons are present in patients with inner ear malformations, particularly common cavity deformity. In an embryological study, it has been found that, in the human fetal developmental stage, the vestibular system develops earlier than the cochlear system [16]. Thus, it is speculated that sensory cells of vestibular end organs and vestibular afferent neurons may be present in patient with inner ear malformations, which is similar to early-stage inner ear development.

In our study, we reported that VEMPs could be elicited with cochlear implant switched on and suggested that the electrical stimulation of a cochlear implant may directly stimulate the inferior vestibular nerve [17, 18]. If VEMPs are evoked with the cochlear implant switched on, it suggests that some of the inferior vestibular neurons are present. In contrast, if VEMPs are absent with the cochlear implant switched on, it suggests that the inferior vestibular neurons may be absent.

Seven children with inner ear malformation who underwent cochlear implantation participated in this study (Table 6.2). The patients had common cavity deformity ($n=2$), incomplete partition type I ($n=2$), incomplete partition type II ($n=1$), or a narrow internal auditory canal. It was possible to record VEMPs before and after cochlear implantation in three patients and not before but after cochlear implantation in four patients. After surgery, VEMPs were recorded with the cochlear implant device switched both off and on. Before the cochlear implantation, two patients showed VEMPs and one patient showed no VEMPs, whereas in four patients no VEMPs could be recorded. All the patients showed VEMPs with the cochlear implant on (Figs. 6.2 and 6.3).

Table 6.2 Profiles of patients

Patient no.	Sex	Ear	Age at surgery (years)	Type of inner ear malformation	CI type	Speech processor	Strategy	Pulse width
1	M	L	5	Common cavity	24M	ESPrit 3G	ACE	25
2	M	R	5	IP-II LVAS	24M	Sprint	ACE	25
3	M	R	4	IP-I, narrow IAC	24R	Sprint	SPEAK	200
4	M	L	3	Common cavity	24M	Sprint	SPEAK	50
5	M	R	3	IP-I	22M	ESPrit 3G	SPEAK	0
6	M	R	4	IP-I	24M	Sprint	ACE	25
7	M	L	2	Narrow IAC	24M	Sprint	ACE	100

IP-I incomplete partition type I, *IP-II* incomplete partition type II, *IAC* internal auditory canal, *LVAS* large vestibular aqueduct syndrome, *CI* cochlear implantation

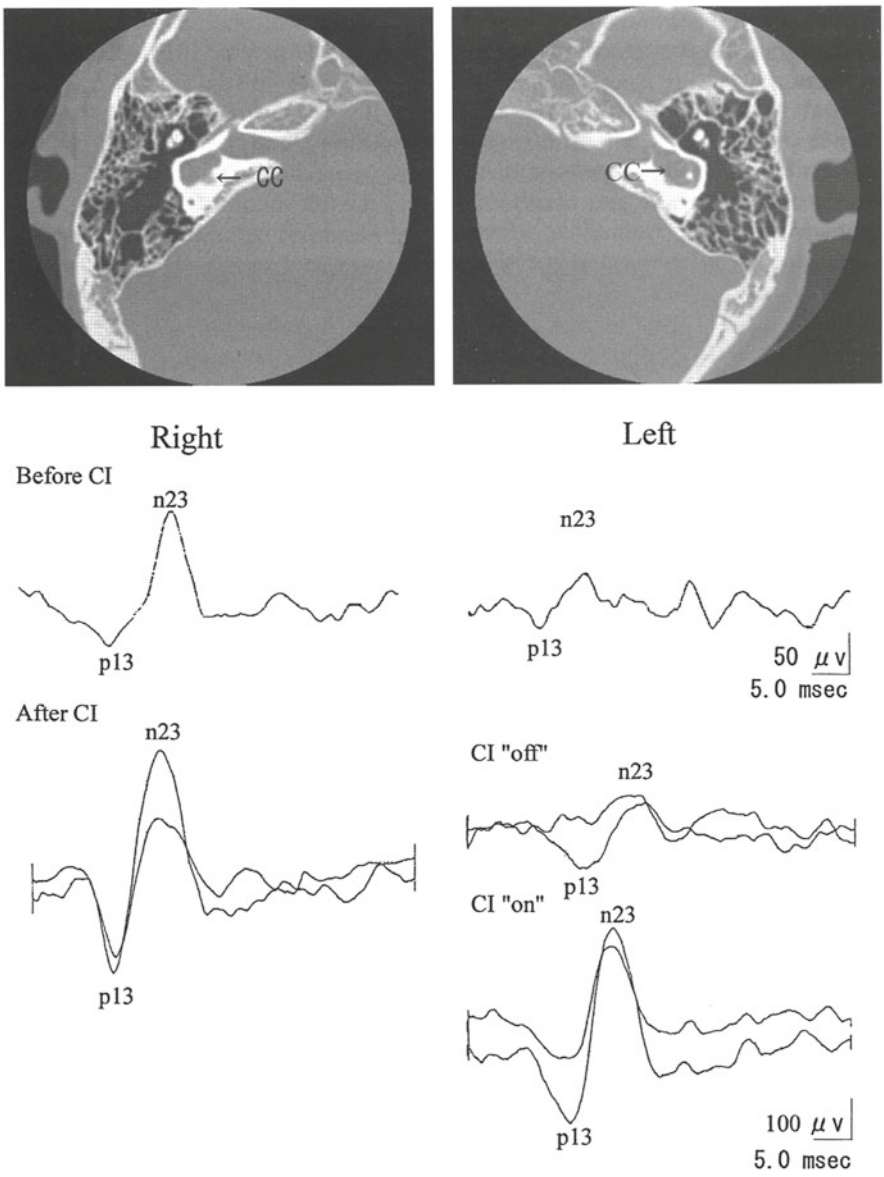

Fig. 6.2 Patient 1: a 7-year-old boy, common cavity deformity, left cochlear implantation (CI). CT scan demonstrated a deformity of the common cavity communicating with IAC. VEMPs were present in both ears before CI. VEMPs were present with the CI on [17, 18]

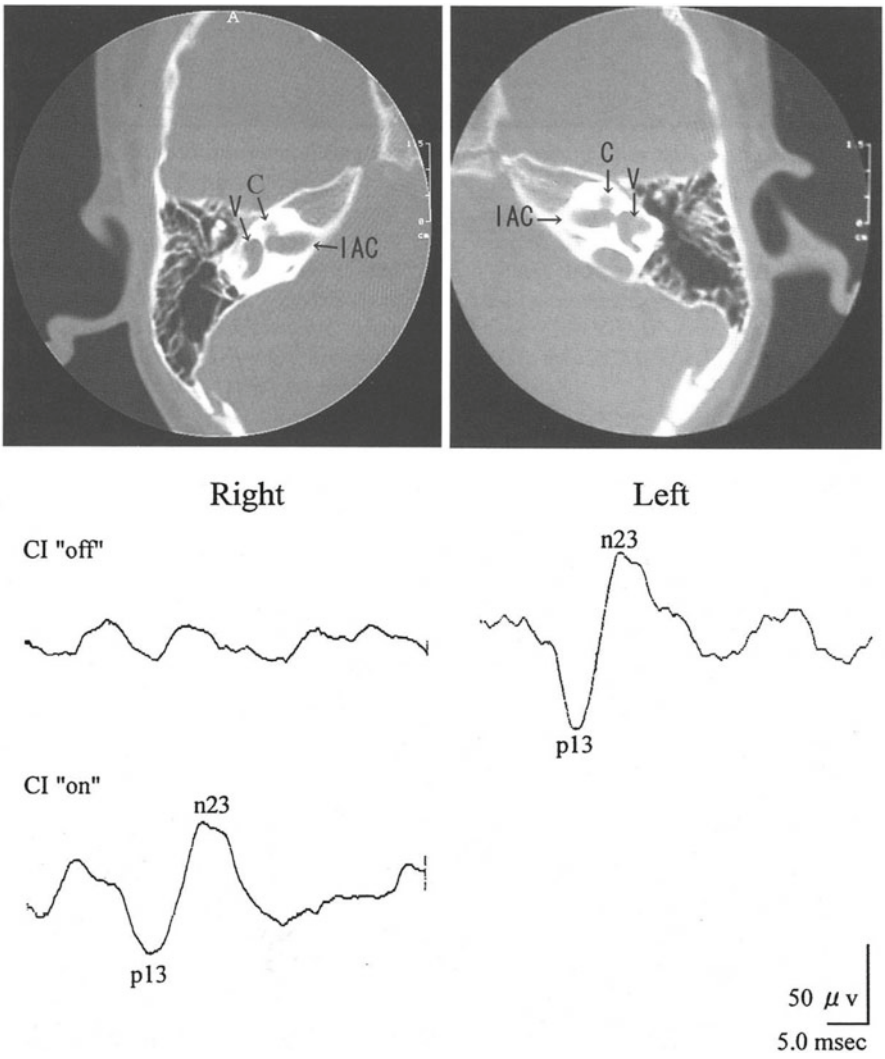

Fig. 6.3 Patient 5: an 8-year-old boy, IP-I deformity, *right CI*. CT scan demonstrated IP-I deformity. After CI, VEMPs were present with the CI on [17, 18]

In our study, two patients showed VEMPs before cochlear implantation and also showed VEMPs after cochlear implantation with the cochlear implantation on. This suggests that in these cases the sensory cells of both saccule and inferior vestibular neurons may be present. One patient showed no VEMPs before cochlear implantation, but showed VEMPs with the cochlear implantation on. This suggests that in this case the sensory cells of saccule may be absent, but the inferior vestibular neurons may be present. However, the possibility that these responses are of vestibular origin cannot be ruled out.

Table 6.3 Summary of results of VEMPs

		VEMP						
		Before CI			After CI			
Patient no.	Type of inner ear malformation	Age at recording (years)	Operated ear	Nonoperated ear	Age at recording (years)	CI off	CI on	Nonoperated ear
1	Common cavity	5	+	+	6	+	+	+
2	IP-II LVAS	5	+	+	5	−	+	No recording
3	IP-I, narrow IAC	5	−	−	5	−	+	−
4	Common cavity	No recording	No recording	*	6	−	+	+
5	IP-I	No recording	No recording	*	8	−	+	+
6	IP-I	No recording	No recording	*	7	−	+	−
7	Narrow IAC	No recording	No recording	*	5	−	+	−

* Significances of cochlear implantation to elicit VEMPs in inner ear malformation

Common cavity deformity has been reported to occur in 2 % of patients with congenital profound sensorineural hearing loss [19]. In this inner ear malformation, the cochlea and vestibules form a common cavity, usually lacking an internal architecture. This deformity is regarded as hypoplasia of the cochleovestibular nerve or complete aplasia of the cochleovestibular nerve [20]. In embryos of approximately 5 weeks or less, the saccule is demarcated from the remainder of the vesicle: it sends out a single ventral evagination, the primordium of the cochlear duct. Common cavity deformity most probably results from an arrest in otocyst development during the fourth gestational week [14]. In the human early development stage, neuroblasts of the cochlear ganglion separate from the otic epithelium at approximately the fourth gestational week. The cochleovestibular nerve (CVN) develops at approximately 9 weeks of gestation [21]. Sennaroglu et al. reported that a patient with a common cavity, who had a "common CVN" without branching into the cochlear and vestibular nerves, showed good benefit from cochlear implantation, but showed nystagmus after cochlear implantation [22]. This suggests that the cochlear and vestibular nerve fibers must be present in their CVN. However, the function of the inferior vestibular nerve remains unknown.

Our results show that among the patients with inner ear malformations, there were two patients with sensory cells of saccule and inferior vestibular neurons and at least five patients with inferior vestibular neurons only, but no patients without sensory cells and vestibular neurons, as determined on the basis of VEMPs (Table 6.3). The aim of this study was to investigate whether sensory cells of sacculus or inferior vestibular neurons or both are present in cochlear implant patients with inner ear malformations, particularly common cavity deformity, using VEMPs.

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Chapter 7
Gene Mutation in Congenital Deafness and Vestibular Failure

Abstract Since a correlation between the peripheral auditory and vestibular systems has been identified both anatomically and phylogenetically, a subgroup of children with congenital deafness may be associated with vestibular and balance impairments. The vestibular disturbance in these children gradually disappears as they grow up, probably because of a compensatory mechanism of the central nervous system.

Congenital vestibular failure is found in 10–20 % of infants with congenital deafness. Gene mutation which causes congenital deafness has been reported to be of various types such as *GJB2*, *PDS*, *Mitochondria 1555*, and *OTOF*.

Gene mutations of vestibular end organs are not well investigated.

Keywords Gene mutation of deafness • *GJB2* • *Mitochondria 1555* • *OTOF* • *PDS* • Vestibular failure

7.1 Gene Mutation of Vestibular Failure

Congenital vestibular failure is found in 10–20 % of infants with congenital deafness. Gene mutation which causes congenital deafness has been reported to be various types such as *GJB2*, *PDS*, *Mitochondria 1555*, and *OTOF*. Usami illustrates various types of gene mutation on the histology of the cochlea (Fig. 7.1) [1]. However, gene mutations of vestibular end organs are not well investigated.

7.2 *GJB2* Gene Mutation

Since a correlation between the peripheral auditory and vestibular systems has been identified both anatomically and phylogenetically, a subgroup of children with congenital deafness may be associated with vestibular and balance impairments [2]. The vestibular disturbance in these children gradually disappears as they grow up, probably because of a compensatory mechanism of the central nervous system.

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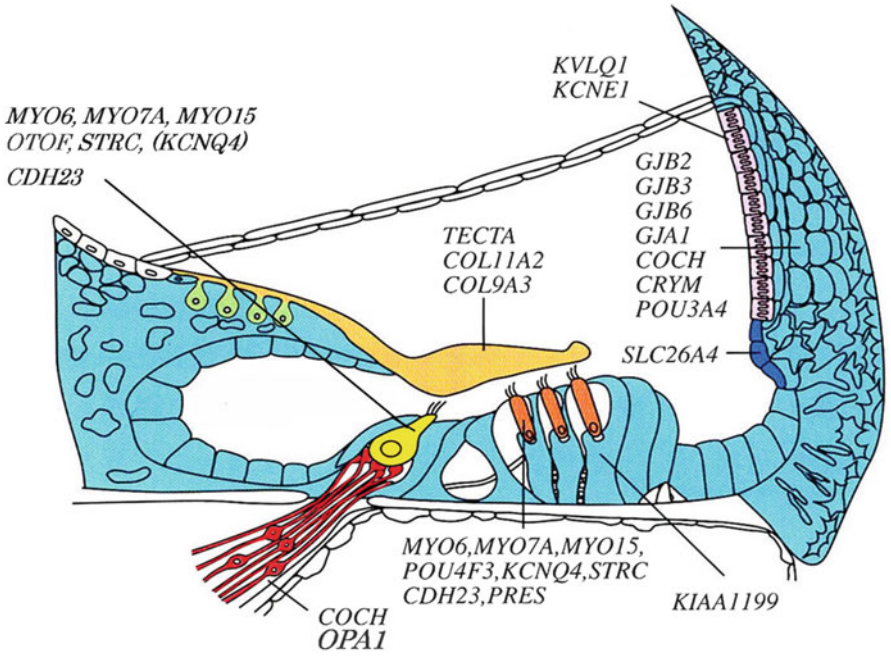

Fig. 7.1 Gene mutation in illustration of the cochlea [1]. Courtesy of S. Usami, Shinshu University, Matsumoto Japan

Mutation in the *GJB2* gene, which encodes Cx26 in the gap junction, is known to be a most common cause (up to 50 % of such cases). Gap junction channels enable the neighboring cells to exchange small signaling molecules. Immunohistochemical studies have revealed the Cx26 exists not only in the cochlear but also in the vestibular organs [3]. K^+ cycling involving gap junction protein Cx26 in the vestibular labyrinth, which is similar to that in the cochlea, is thought to play a fundamental role in the endolymph homeostasis and sensory transduction [4]. The percentage of vestibular dysfunction of the patients with congenital deafness related to *GJB2* mutation was statistically higher than in patients with CT unrelated *GJB2* mutation and in healthy controls [2].

GJB2 mutations are responsible not only for deafness but also for the occurrence of vestibular dysfunction. However, vestibular dysfunction tends to be unilateral and less severe in comparison with that of bilateral deafness.

7.3 *SLC26A4/PDS* Gene Mutation

Enlargement of the vestibular aqueduct (EVA) and its contents, the endolymphatic sac and duct, is the most common radiological malformation of the inner ear associated with sensorineural hearing loss. It may occur alone or in combination with an

incomplete partition of the apical turn of the cochlea as part of a complex of malformations known as a Mondini deformity. Hearing loss in ears with EVA is typically pre- or perilingual in onset, sensorineural or mixed, and fluctuating or progressive. EVA may be unilateral or bilateral; asymmetry of the hearing loss and the anatomical defect is common in bilateral cases [5].

In many patients with EVA, vertiginous attack occur repetitively with progressive hearing impairment like Meniere's disease. Particularly head trauma is a risk factor to induce these signs.

7.4 *Mitochondria* Gene Mutation

Sensorineural hearing loss is known to be frequently associated with mitochondrial diseases [6]. Deafness is observed in about half of the patients with the three main syndromes: Kearns-Sayre syndrome (KSS); myoclonus epilepsy associated with ragged-red muscle fibers; and mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes (MELAS). Hearing loss involves the cochlea in some mitochondrial diseases; in others, it accompanies central auditory abnormalities. The vestibular disorders are caused by central origins.

Several mitochondrial disorders have been attributed to deletion or mutations in the mitochondrial DNA (mtDNA) gene. An A-to-G transition mutation at nucleotide pair (np) 3243 has been documented in most patients with MELAS and in a few patients with KSS and progressive external ophthalmoplegia.

7.5 *OTOF* Gene Mutation in Auditory Neuropathy

Historically, in 1996, a new type of bilateral auditory nerve disease was reported by Dr. K. Kaga et al. and Dr. A. Starr et al. in different journals. Auditory nerve disease paper was published in the *Scandinavian Audiology* by Dr. Kaga [7] and auditory neuropathy paper was published in *Brain* by Dr. A. Starr [8]. These different terms are considered to be identical in pathophysiology.

The auditory nerve disease or auditory neuropathy is a disorder characterized by mild-to-moderate pure-tone hearing loss, poor speech discrimination, and absent ABR but normal cochlear outer hair cell function revealed by normal OAE and -SP of electrocochleography.

Auditory neuropathy (AN) is a hearing disorder characterized by normal outer hair cell function, as revealed by the presence of otoacoustic emissions (OAEs) or cochlear microphonics, and abnormal neural conduction of the auditory pathway, as revealed by the absence or severe abnormality of auditory brainstem responses (ABRs). Hearing disorders having the same characteristics have also been reported as auditory nerve disease in adult cases. Individuals with AN invariably have difficulties in understanding speech, and approximately 10 % of infants diagnosed with profound hearing loss have AN.

Auditory Neuropathy Spectrum Disorders (ANSD) are new classification which was proposed in 2008 by Colorado Children's Hospital Group and defined as normal otoacoustic emissions and absent ABRs in newborns [9]. In our long-term follow-up study, such OAEs and ABRs of ANSD are changed into three types. Type I is normal OAE and normal ABR (normal hearing). Type II is absent OAE and absent ABR (sensorineural hearing loss). Type III is normal OAE and absent ABR (typical auditory neuropathy). However, complications of vestibular problems in ANSD are not known so far.

About 50 % of subjects with congenital or early-onset AN have risk factors such as perinatal hypoxia, whereas the remaining 50 % of subjects are likely to have a genetic factor. To date, four loci responsible for non-syndromic AN have been mapped: DFNB9 caused by *OTOF* mutation and DFNB59 caused by *PJVK* mutation, both of which are responsible for autosomal recessive AN; AUNA1 caused by DIAPH3 mutation, which is responsible for autosomal dominant AN; and AUNX1, which is responsible for X-linked AN. Mutations in *OTOF*, which contains 50 exons and encodes short and long isoforms of otoferlin, are the most frequent mutations associated with AN with various frequencies depending on the population studied. Most *OTOF* genotypes have been associated with stable, severe-to-profound hearing loss with only a few exceptions. Studies of genetic backgrounds and clinical phenotypes in various populations will extend our knowledge of genotype-phenotype correlations and may help in the management and treatment of AN [10].

Etiology and clinical presentation of congenital or early-onset AN are heterogeneous, and their correlations are not well understood. In our study, genetic backgrounds and associated phenotypes of congenital or early-onset AN were investigated by systematically screening a cohort of 23 patients from unrelated Japanese families. Of the 23 patients, 13 (56.5 %) had biallelic mutations in *OTOF*, whereas little or no association was detected with GJB2 or *PJVK*, respectively. Nine different mutations of *OTOF* were detected, and seven of them were novel. p.R1939Q, which was previously reported in one family in the USA, was found in 13 of the 23 patients (56.5 %), and founder effect was determined for this mutation. p.R1939Q homozygotes and compound heterozygotes of p.R1939Q and truncating mutations or a putative splice site mutation presented with stable, and severe-to-profound hearing loss with a flat or gently sloping audiogram, whereas patients who had non-truncating mutations except for p.R1939Q presented with moderate hearing loss with a steeply sloping, gently sloping, or flat audiogram or temperature-sensitive AN. These results support the clinical significance of comprehensive mutation screening for AN [10].

7.6 Gene Mutation in Vestibular Labyrinth

Matsunaga T and Namba K illustrated gene mutation on the histology of the vestibular labyrinth (Fig. 7.2) [Matsunaga (2013) Personal communication].

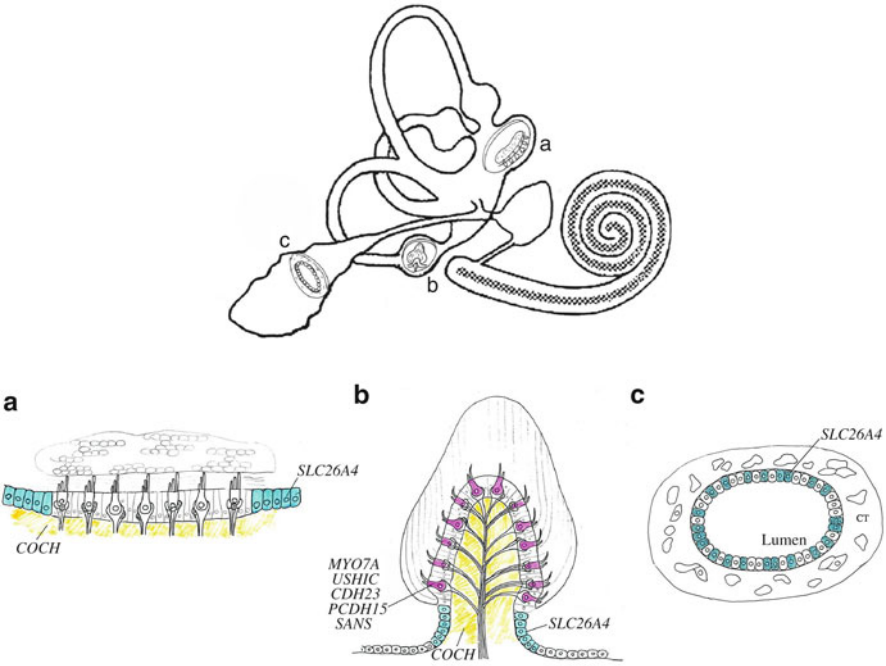

Fig. 7.2 Vestibular failure gene mutation in the illustration of vestibular labyrinth [Matsunaga and Namba (2013) Personal communication]. (**a**) Otolith organ. (**b**) Ampulla of semicircular canal. (**c**) Lumen of endolymphatic sac

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