Superior canal dehiscence syndrome is a newly recognized syndrome characterized by vertigo and nystagmus induced by sound (Tullio phenomenon) or changes of middle ear (Hennebert sign) or intracranial pressure. We report on a patient with bilateral superior canal dehiscence syndrome who presented with unusual manifestations including pulse-synchronous vertical pendular nystagmus and Valsalva-induced, up and counterclockwise-beating jerk nystagmus. These unusual symptoms may be a clue to a better understanding of the pathophysiology of superior canal dehiscence syndrome. Abnormal communication between the inner ears and the intracranial space may explain the vertical pendular and pulse-synchronous nystagmus, modulated by increased intracranial pressure.

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Case Report
The patient was a 50-year-old woman with a history of bipolar affective disorder that was well stabilized for 7 years by medication with lithium. She presented with vertical oscillopsia of 1 year’s duration. Oscillopsia first occurred while the patient was driving in the Alps, and symptoms since then have been permanent. She had no complaint of vertigo, tinnitus, or instability.

Neurological and ophthalmological examinations were normal except for the presence of eye movement disorders. She had spontaneous conjugate eye movement disordered form in the primary position of gaze. Examination also disclosed gaze-evoked nystagmus in the lateral gaze and saccadic horizontal smooth pursuit. The patient self-reported that oscillopsia was heart pulse synchronous. Indeed, clinical examination showed that eye oscillations in the primary position of gaze were phase related to her pulse, even with the increased pulse rate following physical exercise. The primary-position pendular nystagmus did not change with hyperventilation, change in head position, or the horizontal or vertical head-shaking test. The head-thrust maneuver in the horizontal plane and the planes of vertical canals indicated symmetrical normal vestibulo-ocular reflex. Our patient also noted that symptoms increased with physical activity. The Valsalva maneuver against the closed glottis induced a jerk-form up and counterclockwise-beating nystagmus. The blood level of lithium was in the therapeutic range. An audiogram indicated normal pure-tone threshold and speech discrimination scores bilaterally. The patient had hypersensitivity to bone-conducted sounds and a normal Weber test. The tympanogram test was normal. Pressure changes in the middle ear did not induce vertigo, oscillopsia, or nystagmus.

Results of brain magnetic resonance imaging and magnetic resonance angiography were normal. A computed tomography scan of the temporal bone with 0.5mm slice thickness was performed. The scan disclosed a bilateral dehiscence of the bony roof of the superior semicircular canals (Fig 1).

Subjects and Methods
Eye movements were recorded with three-dimensional infrared video oculography (50Hz sampling; Torsio VNG Ulmer; Synapsys, Marseille, France). The patient wore a mask, with a camera fixed in front of the right eye. The horizontal, vertical, and torsional positions of the eye were processed on line using contrast image detection of the iris. The description of torsional eye movements follows the standard nomenclature. Therefore, we have used terms with respect to the patient’s point of view. For example, clockwise means torsion of the superior pole of the eye to the patient’s clockwise direction. Normative data (mean ± 2 standard deviations) were obtained from 40 normal subjects (20 men, 20 women; mean age, 55 years old; range, 24–89 years old).
Results
Spontaneous vertical eye oscillations in the primary position of gaze had a peak velocity of 4 degrees/sec, mean amplitude of 5 degrees, and a frequency of 1.4Hz (Fig 2A). This vertical oscillation was accompanied by a torsional oscillation, having 1.5 degrees of maximal amplitude and 1 degree/sec of maximal velocity. This nystagmus was not influenced by hyperventilation, the horizontal or vertical head-shaking test, tragus compression, or changes in head position. The nystagmus was not diminished by visual fixation. It was associated with gaze-evoked nystagmus in the horizontal plane. However, horizontal pendular vestibulo-ocular reflex (VOR; 0.25Hz, 60-degree/sec peak velocity) showed normal gain (67%) and a left-directional preponderance (20%) compared with normative data (mean VOR gain: 15 to 75%, directional preponderance: 10 to 14%). VOR was abnormal (up to 53%}

Fig 1. Computed tomography scan of left (left)- and right (right)-zoomed temporal bone with 0.5mm slice thickness, in the coronal (A) and axial (B) planes and in a plane aligned with the superior semicircular canal (C). Bilateral dehiscence of the superior semicircular canal is shown by white arrows.
decrease of gain) during visual fixation. A bithermal calor-ic test using 30-second irrigation of each eye with 60ml of cold (23°C) or warm (44°C) water was normal and symmetrical.

The Valsalva maneuver against the closed glottis induced a jerk-form up and counterclockwise-beating nystagmus, with a peak slow-phase velocity of 18 degrees/sec and 4 degrees/sec for vertical and torsional components, respectively (see Fig 2B). The end of the maneuver was followed by immediate down and clockwise-beating nystagmus. Jugular compression led to the same, although less intense, up and counterclockwise-beating nystagmus.

Three-dimensional ocular movements were also recorded after presentation of pure tones from 500 to 4,000Hz (every 500Hz), at intensities ranging from 50 to 100dB (every 10dB) in both ears alternatively. This result did not indicate the Tullio phenomenon.

In addition, conventional electrooculography (EOG) was used for simultaneous recording of the electrocar-diogram (EKG). EOG electrodes were placed on the upper and lower part of the right eye to record vertical eye movement only. EKG and EOG had the same frequency and a fixed relationship (Fig 3). The downwardmost eye position occurred approximately at the P wave of the EKG.

Discussion
Although this patient presented with unusual signs, the occurrence of pulse-related vertical oscillations strongly suggests the influence of bone canal dehiscence bilaterally.

Characteristic clinical presentation of the superior canal dehiscence syndrome consists mostly of vertigo, oscillopsia, nystagmus, and/or disequilibrium resulting specifically from sound (ie, the Tullio phenomenon), changes in middle ear pressure (ie, the Hennebert sign), and/or changes in intracranial pressure. 1-4 In previous reports of superior canal dehiscence syndrome,
eye movement recording indicated vertical and torsional jerk nystagmus or slow phase induced by pressure changes or sound, aligned with the plane of the affected superior canal.\textsuperscript{5,7} We report in this article the first case of spontaneous vertical pendular nystagmus due to this affection. One recent publication reports the case of a patient presenting with vertical oscillopsia during locomotion due to bilateral superior canal dehiscence syndrome.\textsuperscript{7} However, this patient did not disclose spontaneous eye oscillation or nystagmus. Our patient also showed jerk vertical and torsional nystagmus during changes in intracranial pressure. We could not demonstrate the Tullio phenomenon sensitivity to sound neither to pressure changes in the middle ear. This nystagmus was mostly vertical and aligned with a plane between both superior semicircular canals. Furthermore, spontaneous vertical nystagmus was pulse synchronous. Horizontal pulse-synchronous eye oscillation has already been described in perilymph fistula.\textsuperscript{8} Pulse-synchronous tinnitus has already been described in cases of superior canal dehiscence.\textsuperscript{4} A recent publication reports on the presence of subtle rotatory nystagmus synchronous with heartbeat in two cases of unilateral superior canal dehiscence syndrome.\textsuperscript{3}

The pulse-synchronous eye oscillations and sensitivity to the Valsalva (against the glottis) maneuver suggest a transfer of intracranial pressure to structures involved in eye movement control. Intracranial pressure is known to be pulse related, a result of transfer of blood pressure changes. The spontaneous pulse-related nystagmus in our patient might therefore be explained by transmission of intracranial pulsations to the dehiscent superior canals. Indeed, the dehiscence of bone overlying the superior canal creates a third mobile window that allows the canal to be responsive to changes in intracranial pressure.\textsuperscript{7} In this case, permanent intracranial pulsation results in pulsed flow of the endolymph, pulse-related deflection of the ampulla, and pulse-related nystagmus.\textsuperscript{1,9} On the other hand, increased intracranial pressure, such as that obtained during the Valsalva maneuver against the glottis, induces ampullopetal deflection and jerk-form nystagmus. Air pressure change due to the altitude in the mountains might have made dehiscence symptomatic in this patient.

The prominent vertical direction of the nystagmus in our patient is also unusual. Vertical nystagmus is usually suggestive of involvement of central oculomotor pathways.\textsuperscript{10} However, rare cases of bilateral involvement of the vertical canal (either both superior or both posterior) can result in vertical nystagmus since both torsional aspects of eye movement are in opposite directions.\textsuperscript{10} We suggest that vertical eye oscillation such as that observed in our patient is strongly suggestive of bilateral involvement of superior canal bone dehiscence. Furthermore, the fact that the nystagmus has a clockwise slow-phase component during the Valsalva maneuver indicates an asymmetrical involvement of both inner ears. Indeed, the Valsalva maneuver induces

![Fig 3. Combined recording of vertical eye position (electrooculography [EOG], in red) and electrocardiogram (EKG, in blue). Note that EKG and EOG have the same frequency and a fixed relationship. The downwardmost eye position occurred approximately at the P wave of the EKG.](image)
ampullopetal deflection and inhibition of the superior canal.\textsuperscript{1,9} Clockwise direction of the slow phase indicates predominant inhibition of the right superior canal that might be more affected than the left one.

The permanent oscillopsia in our patient might be explained by abnormal visual inhibition of VOR, which in association with gaze-evoked nystagmus and the abnormal clinical aspect of smooth pursuit might be linked to cerebellar lithium toxicity. Indeed, these different cerebellar oculomotor symptoms are known to occur with lithium therapy even within the range of that drug’s therapeutic blood level.\textsuperscript{11}

In conclusion, this article adds important data to the clinical description and pathophysiological understanding of superior canal dehiscence syndrome. Vertical oscillopsia and pulse-synchronous nystagmus may be observed in bilateral symptomatic forms as a result of an abnormal communication between the inner ear and intracranial space.

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References

We report a cytochrome c oxidase (COX)–deficient patient, clinically affected with Leigh-like disease, with a homozygous mutation in the \textit{COX10} start codon. Two-dimensional gel electrophoresis showed a decrease of fully assembled COX without the accumulation of partially assembled COX subcomplexes. Western blot analysis with antibodies directed to COX subunits I, II, and IV showed a decrease of these subunits in this patient compared with control. Overexpression of the COX10 protein in the patient's fibroblasts proved that the detected mutation was indeed the disease cause.

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Human cytochrome \( c \) oxidase (COX) consists of 13 subunits; three of these are encoded by the mitochondrial DNA. Because of the bigenomic origin of the complex, isolated COX deficiencies can be caused by mutations in either the mitochondrial or the nuclear genome. In contrast to complexes I, II, and III, no mutations have yet been described in any nuclear-encoded structural subunit of COX.\textsuperscript{1–3} However, six genes involved in COX biogenesis have been linked to COX deficiency in humans (\textit{SURF1}, \textit{SCO1} and \textit{SCO2}, \textit{COX10}, \textit{COX15}, and \textit{LRPPRC}).\textsuperscript{4–13} The COX10 and COX15 proteins play a role in the mitochondrial heme biosynthetic pathway. COX10 catalyzes the conversion of protoheme to heme O. COX15 exerts its role in the next step, in which heme O is converted to heme A, an essential group for the functioning of complex IV.\textsuperscript{10} To date, three patients harboring mutations in COX10

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