FUNCTIONAL MODEL OF BENIGN PAROXYSMAL POSITIONAL VERTIGO USING AN ISOLATED FROG SEMICIRCULAR CANAL

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Abstract—Bull frogs posterior semicircular canals (psc) were used to simulate the condition of benign paroxysmal positional vertigo (BPPV). The psc was isolated in frog Ringer's solution, and the saccular otoconia were used as a responsible material to stimulate the cupula. When the otoconia were placed on the cupular surface to mimic the condition of cupulolithiasis, the psc ampullary nerve action potentials instantaneously changed according to the direction of the gravity produced by otoconia. When the otoconia were dropped into the canal to mimic the condition of moving otoconia in the canal, the action potentials changed together with the otoconial flow after a latent period. Both cupulolithiasis and moving otoconia are possibly valid mechanisms of BPPV, since they effectively stimulate the cupula. However, moving otoconia with a latent period would better explain clinical features of BPPV.

Keywords—mechanism; benign paroxysmal positional vertigo; otoconia.

Introduction

Benign paroxysmal positional vertigo (BPPV) is one of the common vestibular disorders. However, its mechanism is still controversial. Schuknecht's cupulolithiasis (1) is well known as one of the possible mechanisms. Recently, Epley proposed a concept of canalolithiasis, since several clinical points contradict the mechanism of cupulolithiasis (2). He and other workers claimed that free material inside the posterior semicircular canal (psc) exerts a drag effect on the endolymph, thus provoking nystagmus (2,3). However, how the free material, possibly the otoconia, actually moves in the canal and elicits neural excitation has not been observed. This study was designed to demonstrate how the otoconia in the psc behave and stimulate sensory cells using isolated frog psc.

Materials and Method

Twenty-one bull frogs (Rana catesbeiana) were used. The psc were isolated together with their nerves in frog Ringer’s solution. Details of this procedure were previously reported (4). The membranous wall of the sacculus was opened, and the otoconia were picked up with fine forceps. These otoconia were put into the opening of psc to simulate the condition of BPPV.

The psc ampullary nerve was sucked into a glass suction electrode to record ampullary nerve compound action potentials (CAP). The CAP were recorded in various positions of the psc. First, the psc was placed with the cupula-to-crista axis in the horizontal plane and with the utricular side opening upward. This was designated as canal-down position. When the psc was placed upside down, in other words, with the canal side up, this was designated as canal-up position. When the psc was placed...
with the cupula—crista axis along the gravity line, this was designated as the neutral position (Figure 1). The psc positions were changed with the approximate speed of the positioning nystagmus test.

In the first experiment (Experiment I), CAP was recorded without otoconia loading in 3 positions. This served as a control. In the second experiment (Experiment II), the sac­cular otoconia were placed on the cupular surface from the utricular side opening, and then the CAP were recorded in the same 3 positions (Figure 2). This served as a model of cupulolithiasis or so-called “heavy cupula”. Lastly (Experiment III), the otoconia were gently dropped into the canal from the canal side opening and the CAP were recorded while the otoconia were moving in either the canal or the utricular direction. This is a model of canalolithiasis. In order to let the otoconia move a long distance, the otoconia were first allowed to accumulate near the crista and the psc was quickly turned canal-down, thus producing ampullofugal movement of the otoconia (Figure 3-left). Secondly, the otoconia were allowed to accumulate at the far end of the canal, and then the specimen was turned canal-up, thus producing ampullopetal movement (Figure 3-right).

**Results**

**Experiment I. CAP Due to 3 Positions without Otoconial Loading (2 frogs)**

The spike amounts did not significantly change among the 3 positions.

**Experiment II. Otoconial Loading on the Cupular Surface (11 frogs)**

When removed from the sacculus, the otoconia had not dispersed as particles but could be picked up as a cluster. As soon as the otoconia were placed on the cupular surface of the utricular side, the discharge increased remarkably. Then the specimen was placed in a neutral position to allow the discharge to return to the spontaneous level. In the neutral position, the spike counts were the same as
Figure 3. A schema of the canalolithiasis model (Experiment III). In the canal-down position, the otoconia near the crista slide down along the canal (left). In the canal-up position, the otoconia in the far end of the canal slide down toward the crista. The shaded area is the cupula and the dotted mass is the otoconia.

those of the control. As soon as the psc was placed in canal-down position, remarkable CAP were evoked (Figure 4). The discharge was long sustained. The average and standard deviation of the decremental time constant was $16.8 \pm 4.9$ s. The rise time was $2.1 \pm 1.1$ s on average. When the psc was placed canal-up, the discharge was markedly inhibited (Figure 4). Again, this inhibitory effect was long acting. Moreover, particles of the otoconia remained on the cupular surface and were not easily detached by gravity force.

Experiment III. Otoconial Loading in the Canal Lumen (8 frogs)

As soon as the otoconia were dropped into the canal lumen, they reached the lowest part of the canal in accordance with the gravitational force. It was observed that the otoconia always slid down along the canal wall as a clustered mass and never fell down as free particles (Figure 5). At the canal down position, when the otoconia moved (or slid) toward the canal side, the spikes increased after a latency of 1 or 2 seconds (Figure 6). There was a tendency such that the slower the moving speed of the otoconia, the longer the latency. The averaged time constant was $10.3 \pm 1.9$ s, which is shorter than that of Experiment II. The averaged rise time was $5.3 \pm 1.0$ s, which is longer than that of Experiment II. When the otoconia moved toward the utricu-

lar side (canal-down position), the discharge was inhibited after the same latency.

Discussion

The mechanism of BPPV has long been discussed, but still remains controversial (1–3,5). Epley (2) and Brandt and colleagues (3) pointed out that Schuknecht’s cupulolithiasis contradicts several clinical features of BPPV, and claimed that canalolithiasis can explain most of the clinical pictures. Yet, in either case, how the otoconia physiologically stimulate the cupula has not been demonstrated.

Isolated frog semicircular canal is functionally viable for hours in Ringer’s solution. Its membranous labyrinth is thick and resists mechanical rupture. Furthermore, the physiology and function of the cupula have been studied in detail. For these reasons, bull frog psc was selected as a model of BPPV.

The exact nature and origin of the cupular deposit and of the floating substance have not been determined (1,7,8). These substances quite possibly have their origins in detached or degenerated otoconia (1–3). In the present study, the saccular otoconia were chosen as a responsible material, since they are abundant in the sacculus and can be easily removed.

As shown in Experiment II, changing of the psc position instantaneously affects the neural discharge. Obviously the pattern of discharge changes, and is excitatory or inhibitory
Figure 4. Spike density histograms of the ampullary nerve compound action potentials induced by loading the otoconia on the cupula (Experiment II). In the canal-down position, the action potentials increased (upper trace). In the canal-up position, the spontaneous discharge was inhibited (lower trace). Note that these responses were the least adaptive.

Figure 5. Dissection microscopic view of canalolithiasis model. The white mass of the otoconia (asterisk) is in the canal. A: ampulla, N: nerve.

in accordance with the gravitational force on the cupula. When the otoconia impinged upon the cupula to move toward the canal side, the response was excitatory, and vice versa. This is comparable to responses due to conventional mechanical endolymphatic flow. The finding that there was little latency reflects a direct pressure effect to the cupula and is characteristic of "heavy cupula". As Epley (2) and Harvey and colleagues (9) postulated, the response was well sustained. The authors reported that there are receptors with different time constants that allow a semicircular canal to respond to various kinds of acceleration (6). In the present experiment, the receptors with long time constants selectively fired in response to gravitational stimulus. The time constant value of the present study was larger than that of our previous study using mechanical depression as a stimulus (6), possibly because of the sustained nature of gravitational acceleration.

In Experiment III, characteristic movement of the otoconia was observed. The otoconia never moved or floated as dispersed free particles, as is often depicted in the literature (2,3). They invariably moved as a compact mass and slid along the canal wall. This is due to the weight of the otoconia, which are composed mainly of calcium carbonate.
When the otoconia moved inside the canal, the neural discharge changed according to the direction of the otoconial movement. There was also a latent period before discharge change took place. This is possibly because the otoconia drag the surrounding endolymph in the same direction due to frictional force. The long rise time possibly indicates a slow buildup of acceleration of the otoconial motion. The presence of a latent period and the short duration of the discharge fit better with clinical pictures of BPPV. Epley (2) proposed a piston-type effect of the otoconia, which compresses the cupula due to Pascal’s principle. This type of mechanism would be possible if an otoconial mass is large enough to obstruct the canal lumen.

The present experiments demonstrated that both cupulolithiasis and canalolithiasis effectively stimulate the cupula and thus potentially evoke nystagmus. Classic features of BPPV could be explained more favorably by the mechanism of canalolithiasis. However, cupulolithiasis still remains valid as another part of the mechanism, since the authors observed that the otoconial mass slid down along the canal and eventually hit the cupula base, thus leaving dispersed otoconia on the cupular surface. Canalolithiasis concurrent with cupulolithiasis, or cupulolithiasis alone, may account for atypical BPPV with persistent symptoms or less fatiguability.

REFERENCES