**Physiology.** — "*Concerning Vestibular Eye-reflexes.* II. *The Genesis of cold-water nystagmus in rabbits*". By Dr. A. DE KLEYN and Dr. W. STORM VAN LEEUWEN. (Communicated by Prof. R. MAGNUS).

(Communicated at the meeting of January 31, 1920).

For an explanation of cold-water nystagmus we may have recourse to two theories. BARANY's theory is founded on the assumption of a stream of endolymph in one or more semicircular canals, brought about by local cooling of the labyrinthwall. This will cause also the endolymph, present there, to cool down and to flow off to the lowermost part of the semicircular canal. The ensuing lymph stream stimulates the sensory epithelium of the ampulla. In case the head of the animal is in a position in which the ampulla lies higher than the cooled part of the semicircular canal, the stream will be ampullofugal; if the reverse be the case an ampullopetal stream will result. The nystagmus elicited by each stream is of an opposite character.

BARTELS holds that by douching of the meatus with cold water the labyrinth would be eliminated, so that the nystagmus provoked would be like the spontaneous nystagmus after unilateral extirpation of the labyrinth. A warm water flow would be like stimulation of the N. vestibularis on the same side.

In a previous paper, issued from this institute, we have *disproved* BARTELS's *theory* [1]).

Moreover, it has already been contended by many other researchers. It was first of all pointed out that, if BARTELS's conception were correct, a cold-water nystagmus could not possibly be elicited from the unimpaired ear after unilateral extirpation of the labyrinth. HOFER [2]) has phrased it so well: "dieses tatsächliche Auftreten eines rotatorischen Nystagmus nach der operierten Seite wäre nach BARTELS'

1) A. DE KLEIJN and W. STORM VAN LEEUWEN. Ueber vestibuläre Augenreflexe I. Ueber die Entstehungsursache des kalorischen Nystagmus, nach Versuchen an Katzen und Kaninchen, Graefe's Arch. 5 Bd. 94 316, 1917.

A. DE KLEIJN and W. STORM VAN LEEUWEN. Over vestibulaire oogreflexen I Mededeeling. Kon. Acad. van Wetensch., Amsterdam. Wis- en Nat. Afd. Versl. Deel XXVI, 381, 1917.

2) J. HOFER. Untersuchungen über den calorischen Kaltwassernystagmus. Monatschr. f. Ohrenheilk. (1912) S. 1313.

Theorie, wie er ja selbst zugesteht, total unmöglich, weil eben das operierte Labyrinth fehlt und also nicht überwiegen kann über das gesunde, welches durch die kalte Ausspülung gelähmt werden soll; es sollte also nach BARTELS in so einem Fall gar kein Nystagmus auftreten, was aber den klinischen Tatsachen vollständig widerspricht" (S. 1317 und 1318). This argument, however, is not valid. BECHTEREW's [1]) wellknown experiments have shown us that when we extirpate a labyrinth and remove the other after some days, a nystagmus will occur again in the direction [2]) of the labyrinth that was removed first. So, if the cold-water-nystagmus were resulting from extirpation of the labyrinth on the douched side, we might also expect, some days after unilateral *extirpation, on douching the unimpaired ear, a nystagmus towards the extirpated side.* Indeed, BARTELS [3]) himself has suggested this interpretation. Another argument put forward by BARTELS [4]) against BARANY's theory, we *do not quite* understand. In a rabbit, with one octavus cut through, a cold-water or a warm water flow into the meatus of the unimpaired ear could provoke a nystagmus only towards the *unimpaired ear. This finding* of BARTELS's is not explained by BARANY's *theory nor even by that* of BARTELS. Neither were we ever confronted with this case in a prolonged series of experiments [5]). It is difficult to say what may have led to BARTELS's abnormal experience. *It would be better perhaps in similar experiments* to perform an extirpation of the labyrinth than a section of the octavus, since the latter operation may be attended with lesions of the central nerve-system.

Another cogent argument against the theory of BARTELS, put forward also by BARTELS himself, is that experimenters succeeded, by provoking a caloric nystagmus with various *positions of the head in space,* in obtaining now a nystagmus towards the non-douched ear, now again towards the douched one. This, indeed, is the main argument that turns up repeatedly in the literature. Still, it cannot be adduced against BARTELS's theory without also considering that, when examining

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1) W. BECHTEREW. Ergebnisse der Durchschneidung des N. acusticus nebst Erörterung der Bedeutung der semizirkulären Kanäle für das Körpergleichgewicht. Pflüg. Arch. Bd. 30. (1883) S. 312.

2) In speaking about a nystagmus in a certain direction we always mean a nyst. with the quick component in that direction.

3) M. BARTELS. Ueber die vom Ohrapparat ausgelösten Augenbewegungen (Ophtalmostatik). Klin. Monatsbl. f. Augenh. Jhrg. 50. (1912) S. 200.

4) Discussion Verh. d. Otol. Gesellsch. Frankfurt. (1911) S. 214.

5) See F. QUIX. Ein Fall von translabyrintharisch operiertem Tumor acusticus. Verh. d. Otol. Gesellsch. Hannover (1912) S. 252

the caloric nystagmus, with various positions of the head in space, tonic reflexes of the eye-muscles may occur: the so-called compensatory eye-positions, which alter the position of the eye in the orbita. Therefore, it must be ascertained beforehand whether or no the spontaneous nystagmus occurring after unilateral extirpation of the labyrinth, alters its direction with different positions of the head in space.

Such experiments have been carried out, for aught we know, only by KUBO [1]). They will be briefly discussed here: KUBO severed one octavus. He does not tell us how he did it, nor whether he tried to ascertain by a subsequent control section if the process was successful. It would seem from the protocols that this is highly doubtful. Six of the experiments are reported in detail, of which a short description follows here:

Experiment 1, 4, and 5 will not receive consideration, because in them the nystagmus was not examined with different positions of the head.

Experiment 2.

In this experiment a nystagmus appeared with the quick component towards the operated side, after section of the right octavus had been performed. The nystagmus consequent on unilateral extirpation of the labyrinth, however, turns towards the unimpaired ear. KUBO adds only: "Diese Bewegungen bleiben unverändert, wenn man die Körperlage des Tieres ändert."

Experiment 3.

Left acusticus cut through. Subsequent vertical nystagmus-movements. After a couple of hours perfectly horizontal nystagmus with the quick component on the operated side towards the nose. Just as with the vertical nystagmus this direction is the same for any position of the animal. A flow of cold water into the right meatus is of no influence. After the semi-circular canal of the right ear has been laid bare, the experimenter states: "Nach Einspritzen von kaltem Wasser ändert sich die Richtung und es tritt eine rückweise Bewegung nach der Nase hin auf der operierten (linken) Seite auf."

This, however, was also the existing direction and opposite to the one we can look for in the case of cold-water nystagmus from the right ear. The vertical nystagmus also points to an imperfect section.

Experiment 6.

Section of left acusticus. First vertical, afterwards horizontal nystagmus (on the left with the quick component towards the nose.)

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[1]) KUBO INO. Ueber die vom N. acusticus ausgelösten Augenbewegungen (besonders bei thermalen Reizungen.) Pflüg. Arch. 114. (1906) S. 143. 167.

On the right a cold-water flow: Reversion of the nystagmus. In ventral position right eye with quick component towards the nose. In other position same direction. Here, then, in caloric examination no influence on the direction of the nystagmus through change of the position of the head in space. This, no doubt, is anomalous. Compensatory eye-positions are no longer distinct. This again indicates the deficiency of the experiment. Repeated application of cold water in the right ear yields on the right a nystagmus with the quick component towards that ear. This nystagmus is not affected by the position of the head in space.

The appearance of a nystagmus towards the douched ear on cold-water flow is the reverse of what is normally observed, and also the reverse of what was seen after the first washing. The imperfection of the experiment is also seen in the absence of any influence of the position of the head in space.

In our first communication it has been shown that in cats the spontaneous nystagmus after unilateral extirpation of the labyrinth, with different positions of the head in space, varies in nature and frequency, but not in direction. In our investigation of the cold-water nystagmus in normal animals and in animals after unilateral extirpation of the labyrinth, on the contrary, a considerable difference in the direction of the nystagmus with different positions of the head in space, has been demonstrated. It also appeared from subsequent experiments with rabbits that with them the case was fundamentally the same. Slight variations in the direction of the spontaneous nystagmus after unilateral extirpation of the labyrinth, however, do manifest themselves here, when the position of the head is varied, in consequence of the compensatory eye-positions, to be discussed later on, whereby the place of insertion of the eye-muscles in the orbita is altered. In the first communication evidence was also adduced to show that BARTELS's conception of the origin of the caloric nystagmus cannot be correct.

In the present investigation we purpose to ascertain whether additional data can be collected to support the theory of BÁRÁNY, who ascribes the caloric nystagmus to endolymph-streams. There are plenty of indications in the literature; to our knowledge an extensive experimental investigation has not been performed as yet.

Doubtless, the first question that arises is, whether douching of the meatus with cold-, resp. warm-water through the tympanum will engender such cooling down, resp. warming of the labyrinth-wall that endolymph streams are possible.

The result of a similar investigation carried on[1]) together with Prof. MAGNUS, was published in GRAEFE's Archiv., and led to the following conclusion:

"Bei Katzen, bei denen die Sympathicusbahnen zum Auge durch das Mittelohr verlaufen, tritt bei Ausspritzen des äusseren Gehörganges mit kaltem Wasser eine Sympathicuslähmung am Auge auf, die sich vor allem im Vortreten der Nickhaut äussert. Sie beruht auf einer Kälteparese der genannten Bahnen. Dadurch ist der Beweis geliefert dass beim Auslösen des kalorischen Nystagmus mit kaltem Wasser die Wand des Mittelohres über dem Labyrinth sich nachweisbar abkühlt."

We now pass on to report the results of our new experiments on the cold-water nystagmus in rabbits.

Our reason for selecting rabbits, while our previous experiments were chiefly carried out with cats, is the following:

First, in rabbits we seldom meet with rotatory nystagmus, of which the direction is always difficult to indicate. It is encountered in cats. The principal reason, however, is that in our experimentation we made use of an inquiry into the compensatory eye-positions, which have been carefully determined for the rabbit in conjunction with V. D. HOEVE[2]), but are difficult of determination for the cat.

## *Technique of our method.*

A rabbit was suspended on an operation-board, and the head fixed firmly in a Czermak-clamp. Now in order to be able to bring the animal in any given position in space, the following contrivance was made (Fig. 1). The operation-board p-q-r-s is fixed to a wooden frame P-Q-R-S in such a way that the board p-q-r-s can rotate on the axis U-T, while the frame P-Q-R-S is again fixed to a second frame A-B-C-D, so that both P-Q-R-S and p-q-r-s can rotate on the axis V-W. A protractor is attached to P-Q-R-S, as well as to A-B-C-D, so that the degree of the rotation can be noted exactly in every direction. Now when the animal has been tied to the board in ventral position, a rotation on the axis V-W causes the animal to rotate on its bi-temporal axis. When moving the board round the axis U-T the animal turns on its occipito-caudal axis. When finally

[1]) A. DE KLEIJN und R. MAGNUS. Sympathicuslähmung durch Abkühlung des Mittelohres beim Ausspritzen des Gehörganges der Katze mit kaltem Wasser. Graefe's Archiv Bd. 96. (1918) S. 368.

[2]) J. V. D. HOEVE und A. DE KLEIJN. Tonische Labyrinthreflexe auf die Augen. Pflüg. Arch. Bd. 169. (1917) S. 241.

the board p-q-r-s is first revolved 90° about U-T, so that the animal is in lateral position, and when in this position the board is turned

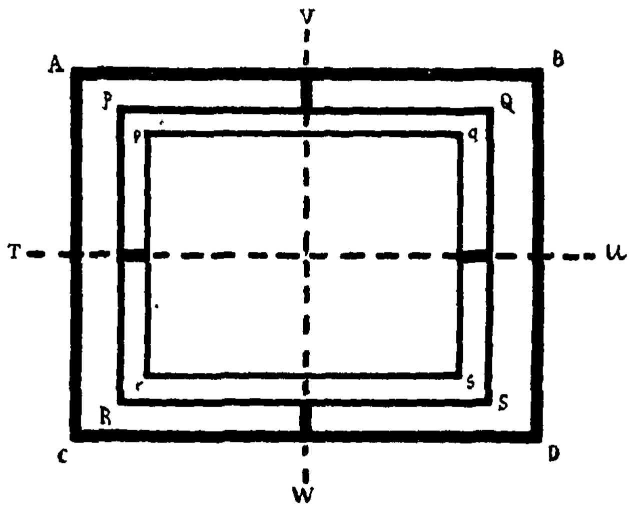


Fig. 1.

about the axis V-W, the animal will revolve about its dorso-ventral axis. A combination of rotations round the axes U-T and V-W enables us to bring the animal in any given position in space. In all of them the direction of the nystagmus consequent on a cold-water flow could be determined. In the following expositions the rotations in the different directions are described:

*Rotation I.*

Animal in ventral position, mouth-fissure horizontal. Rotation of the animal on its bi-temporal axis. Direction of rotation · head down, tail up.

*Rotation II.*

Animal in ventral position, mouthfissure horizontal. Rotation of the animal on its occipito-caudal axis. Direction of rotation: douched ear downwards.

*Rotation III.*

Animal in lateral position with irrigated ear downwards, mouth-fissure vertical. Direction of rotation: head down, tail up.

In these experiments the direction of the nystagmus consequent on a cold-water irrigation, was determined 37 times for every rotation of 360°. The first determination was always made at the normal position of that rotation; so e. g. at rotation I: the animal in ventral position, mouth-fissure horizontal. After this, while the ear was constantly being douched, the animal was moved every time 10° in the given direction and the direction of the nystagmus was noted. At the 37th determination the animal had come round again to its original position. Then the last determination served for a control-estimation. A short interval after every rotation of 10° was required before each reading, to preclude the possibility of a nystagmus, resp. deviation brought about by the *rotation* itself.

The irrigation of the *right* meatus took place from a height of 1,5 m., the cold-water used was of a temperature of ± 12° C. For every position in space, after it had continued for some time, the direction of the nystagmus was *valued* and the direction of the *rapid* component was marked down. (Figs 2, 3, and 4 not corrected).

This method does not yield perfectly reliable data; for a correct determination of the direction one might resort to cinematographic photos from which to decide on the direction. However, this was impracticable for a large number of determinations. Still, from what follows here we may infer that our method of valuation of the direction of the nystagmus yielded useful results.

In figs. 2—4

→ = Direction of the quick component of the nyst. towards the nose
← = „ „ „ „ „ „ „ towards the temporal
↑ = „ „ „ „ „ „ „ upwards relative to the *orbita*
↓ = „ „ „ „ „ „ „ downwards.

Fig. 2—4 (not corrected) gives the mean of 5 experiments.

Now, however, the question rises: what influence is exerted on the nystagmus by the above-mentioned tonic eye-reflexes, occurring in the eye-muscles (compensatory eye-positions) with different positions of the head in space. On p. 246 of V. D. HOEVE's research, mentioned above, a curve is given of the rotatory movements.

With the aid of this curve the directions of the caloric nystagmus found, were now corrected as follows

We assume that douching with cold water, with the head in normal position, engenders an absolutely horizontal nystagmus with the quick component towards the nose. Now, when the position of the head changes from the normal into another position in space, so that a rotatory movement of the eyes ensues, e.g. of 45° with the upper cornea-pole towards the temporal, the insertion-points of the eye-muscles, notably of the Mm. internus and externus, will also be changed by this rotatory movement, and the same contractions and relaxations of these two eye-muscles, which caused with the normal position an horizontal nystagmus, will bring about a nystagmus of quite a different direction, viz. about 45° anteriorly upwards.

So for instance if an horizontal nystagmus appears at the normal

*Rotation I (no correction).*

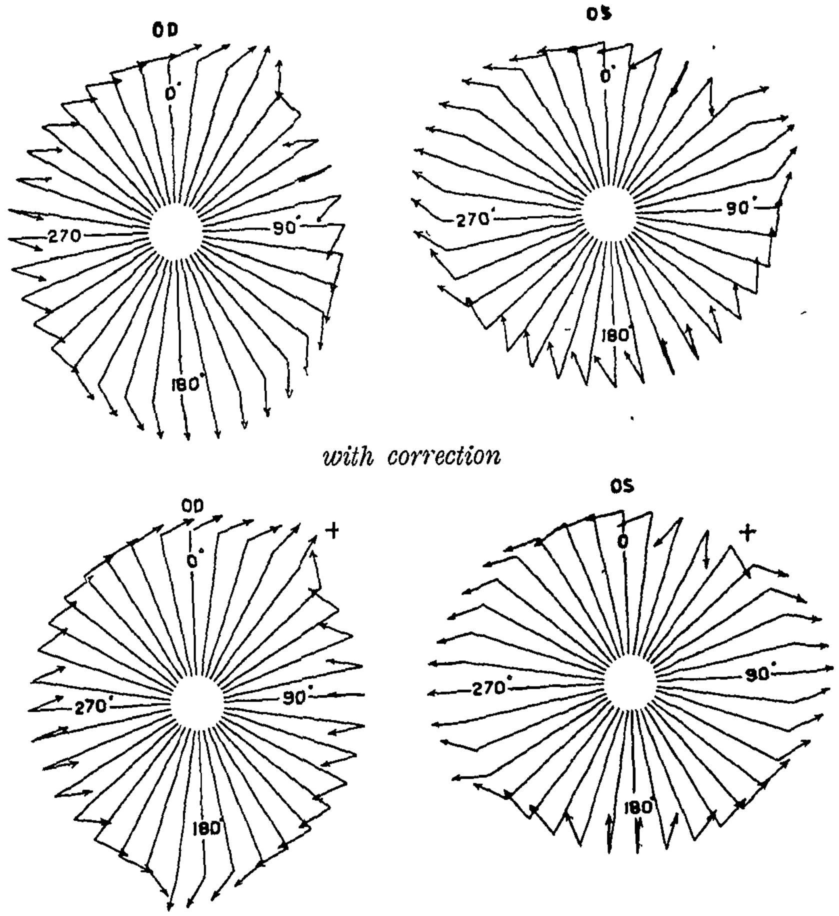


**Fig. 2.**

*Rotation II (no correction).*

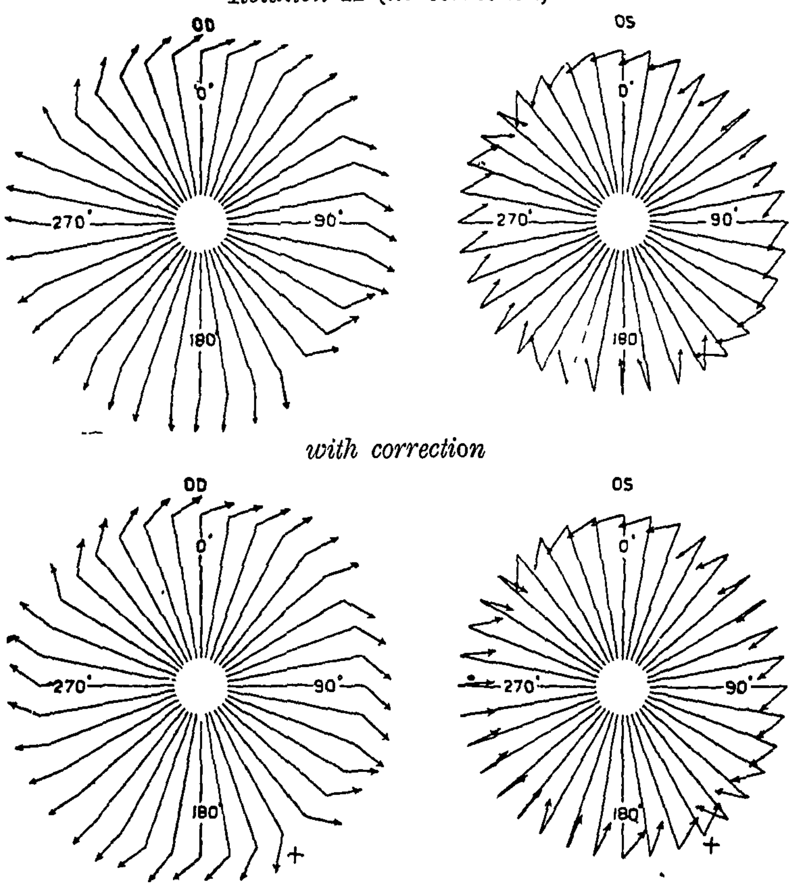


**Fig. 3.**

position and at another position of the head in space, with a rotatory

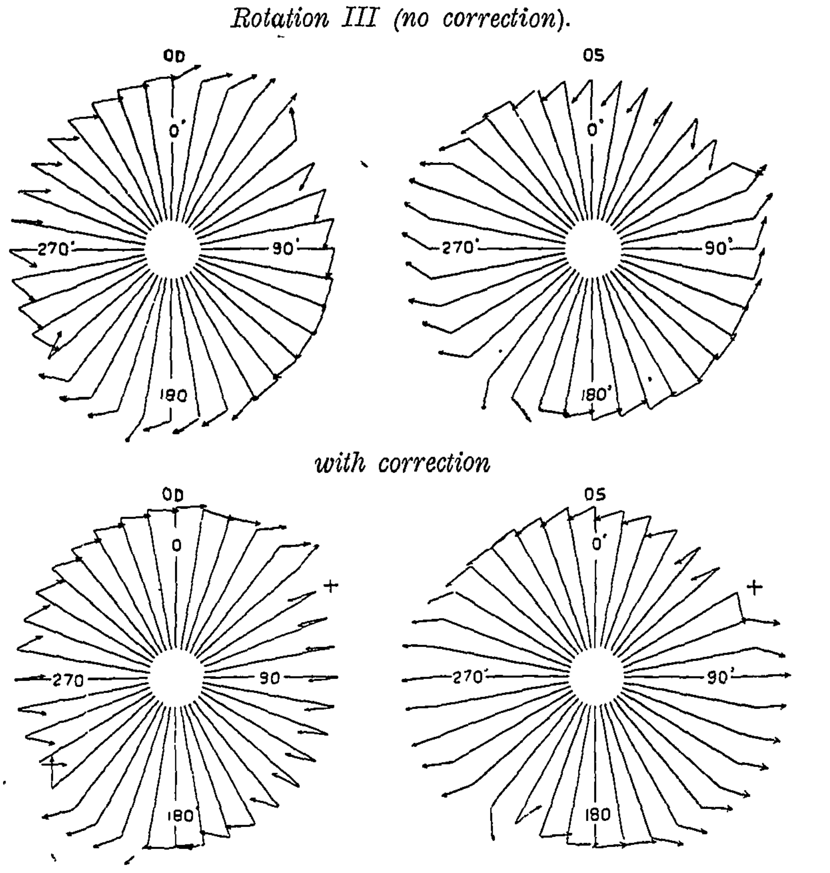


Fig. 4.

movement of 45° with the upper cornea-pole towards the temporal, a nystagmus of 75° anteriorly upwards, the correction is 75°—45°=30°.

*The corrected direction, therefore, is that direction of the nystagmus that would be found, if the eyes were only under the influence of the labyrinth-stimulant consequent on the douching, and if there were no compensatory eye-positions.*

Figs 2—4 illustrate our results before and after correction.

## RESULTS.

As stated above, it had already been detected by BÁRÁNY, HOFER, and others that the direction of the nystagmus in man varies with different position of the head in space. This result was borne out by our experience.

When examining a rabbit, first in ventral position and subsequently with its head hanging downwards, we found a difference of 180° in the direction of the nystagmus.

At first we supposed that, when e.g. the nystagmus of the left eye on douching the left meatus was directed anteriorly upwards in ventral position, and posteriorly-downwards with the head down, there would be an intermediate position in which there would be no nystagmus at all. In other words, if the nystagmus in ventral position is owing to an ampullo-fugal stream in the horizontal semicircular canal, and the nystagmus with the head down to an ampullo-petal stream, there would be no difference in the level of ampulla and of that portion of the semicircular canal that is cooled down by the douche and the nystagmus would consequently not appear. This proved not to be the case. True, in this reasoning the possibility has been eliminated of an influence of the cold water on the lymph-streams in the vertical semi-circular canals.

Considering that, although also the vertical canals may come into play, the horizontal canals are on account of their anatomic location, most exposed to the influence of the cold water, it could be anticipated on the ground of BARANY's theory that in the transition from ampullo-fugal to ampullo-petal stream in the horizontal canals, there would exist a short zone in which, with a slight variation in the position of the head, a marked change in the direction of the nystagmus would manifest itself abruptly. The critical point at which neither ampullo-fugal, nor ampullo-petal streams occur in the horizontal canals, so that only streams in the vertical canals can exert an influence here, receives a full discussion below.

Now when looking at the corrected figures, which illustrate the mean result of our experiments with the several rotations, the following observations can be made:

*a. Rotation I. Douche of the right ear.*

*Observation right eye.* With the animal in ventral position the nystagmus is anteriorly upwards. At 20° (i.e. head 20° below the

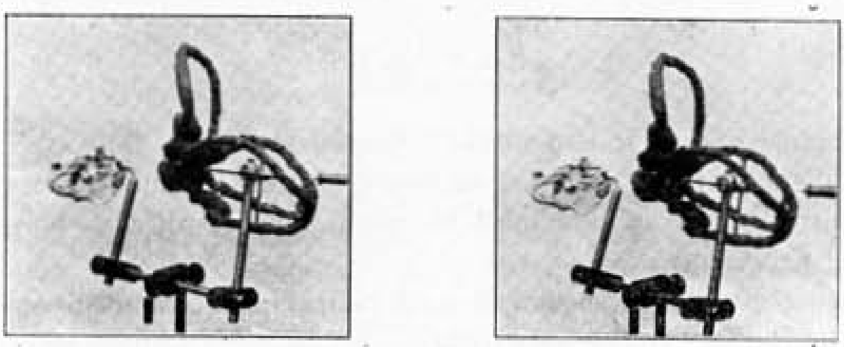

Fig. 5.

horizontal plane) the direction is still the same; at 30° a slight deviation begins; at 50° it is much more pronounced. At 80° the direction of the nystagmus deviates as much as 135° from the initial position and at 100° the change of direction of the nystagmus of 180° has been completed. Something like this occurs between the position of 170° and 270°.

*Observation left eye.* Fundamentally the same as right eye.

*b. Rotation II. Douche of right ear.*

*Observation left eye*: A sudden change in the direction of the nystagmus takes place here between 140° and 150°. While the nystagmus at 140° moves posteriorly-upwards, at 150° it is already anteriorly upwards. A similar marked change of direction is observed between 310° and 320°, the direction being respectively anteriorly downwards and downwards.

*Observation right eye*: Here it is less easy to say where the change of direction takes place. Presumably also between 140° and 150° and between 300° and 330°. That in this case the curve differs from all the others may be explained by the fact that the process of the experiments averagely represented by this curve, was very irregular in two out of five cases, which could not but be of great influence on the mean curve. There was no such irregularity with the left eye of these animals (which was examined on another day).

*c. Rotation III. Douche of the right ear.*

*Observation left eye.* Very great change of direction is found between 50° and 70° and a second change between 210° and 230°.

*Observation right eye.* Very great change between 40° and 60° and a second between 220° and 240°.

After the above facts had been ascertained, the critical point was

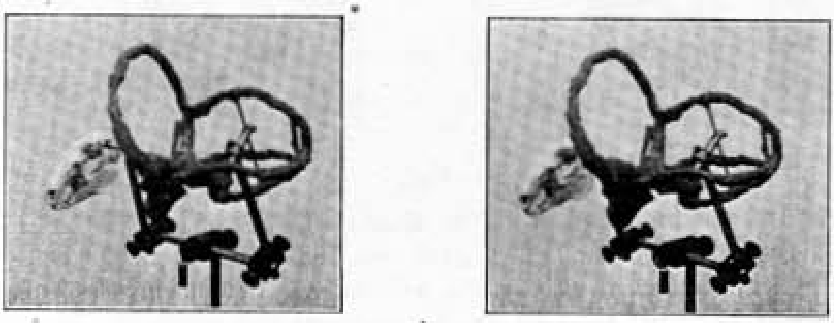

Fig. 6.

determined for the various rotations, i.e. the point at which the horizontal semicircular canal has reached its optimal horizontality and consequently no or hardly any streams can exist in this canal after douching the meatus. This determination was performed with the aid of a model in wax[1]) formerly made of the semicircular canals of a rabbit, which contrivance was arranged, after the indications of DE BURLET and KOSTER[2]), so as to afford an exact imitation of their natural position in the rabbit's skull.

This was to the following effect:

With the animal in ventral position with horizontal mouth-fissure (Fig. 5) the level of the ampulla of the horizontal semicircular canal is higher than the canal itself, so that an ampullo-fugal endolymph-stream will occur on a cold-water douche of the meatus.

With rotation I the horizontal canal is approximately horizontal at 40° (Fig. 6).

With rotation II the horizontal canal is approximately horizontal at 150° (Fig. 7).

With rotation III the horizontal canal is approximately horizontal at 57° (Fig. 8).

In figures 2—4 these points are indicated with crosses. At a glance it may be seen that *a marked change in the nystagmus occurs at the very place where the horizontal canal is approximately horizontal.*

When taking into account the considerable individual variations in the position of the semicircular canals in various animals of the same species, and when also considering the fact that our results are based upon the observation of five different animals, while the correction for the compensatory eye positions as well as the data

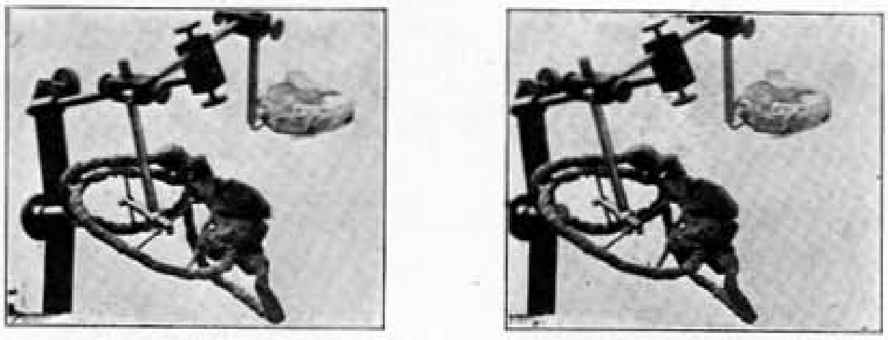

Fig. 7.

[1]) H. M. DE BURLET and A. DE KLEIJN. Ueber den Stand der Otolithenmembranen beim Kaninchen. Pflüg. Arch. Bd. 163. (1916) S. 321.

[2]) H. M. DE BURLET and J. J. J. KOSTER. Zur Bestimmung des Standes der Bogengänge und der acustica im Kaninchenschädel. Arch. f. Anatomie und Physiologie. Anatomische Abteilung. (1916) 59.

from the model in wax, refer to an animal that does not belong to this series, a striking resemblance can be stated between the changes of direction observed and those that could be anticipated with reference to the model.

The fact, however, is that with none of the rotations I—III does the horizontal semicircular canal attain horizontality. DE BURLET and KOSTER's researches showed that the right horizontal semicircular canal is approximately horizontal when the animal turns from the ventral position about 30° round the bi-temporal axis with the head down and at the same time round the fronto-occipital axis about 7° to 8° with the left eye downwards.

We examined different animals in this position, from which it appeared that in most cases the nystagmus had not disappeared altogether and could neither be made to disappear by applying different variations in the rotation round the said axes. We observed, however, that the nystagmus-movements are very small in this position.

Only in two cases could the nystagmus be made to disappear completely, viz. with a rotation about the bi-temporal axis of 37° in the one and 30° in the other rabbit and combined with a rotation about the fronto-occipital axis of 5° in both animals.

This urges us to conclude that *the horizontal semicircular canal plays a principal part in caloric stimulation,* that, however, in most cases also the vertical canals exert some, though a small, influence. This influence, however, was not such as to enable us to make an accurate analysis of it from the curves.

For a positive solution of the problem it would be necessary to determine in one and the same rabbit the nystagmus in various positions of the head in space, as well as the compensatory eye-positions in the said positions and finally through microscopic examination of the labyrinth, to determine accurately the position of the semi-circular canals in that animal, after the method of DE BURLET and KOSTER.

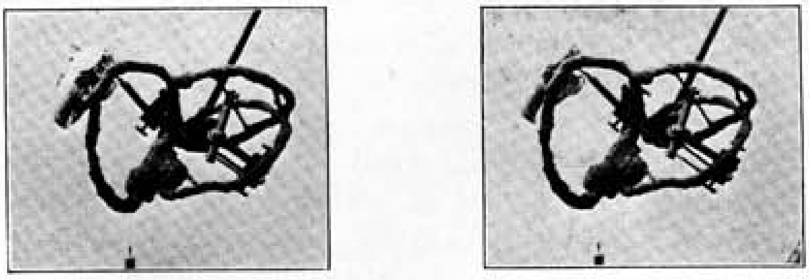

Fig. 8.

## SUMMARY.

1. The above experimental results lend support to the theory of BÁRÁNY of the origin of cold-water nystagmus. The theory of BARTELS, on the other hand, conflicts with these results.

2. In the genesis of cold-water nystagmus the cooling down of the horizontal semi-circular canal plays the principal part; however, in the majority of cases some influence (though little) is also to be assigned to the vertical semicircular canals.

3. Earlier inquiries by MAGNUS and DE KLEYN have demonstrated a distinct cooling of the labyrinth-walls in cats, on douching the meatus with cold water.

4. Compensatory eye-positions should be taken into account when cold-water nystagmus with various positions of the head in space is observed.